UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2020

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM TO**

Commission File Number 001-39273

Lyra Therapeutics, Inc.
(Exact name of Registrant as specified in its Charter)

Delaware	**84-1700838**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
480 Arsenal Way Watertown, MA	**02472**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 393-4600

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, $0.001 par value per share	LYRA	Nasdaq Global Market

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
Emerging growth company	☒		

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of outstanding shares of common stock held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on The Nasdaq Global Market on June 30, 2020, the last business day of the Registrant's most recently completed second fiscal quarter, was $84,280,762. For purposes of this disclosure, shares of common stock held by officers and directors of the Registrant and by persons who hold more than 10% of the Registrant's outstanding common shares have been excluded because such persons may be deemed to be affiliates. This determination of affiliate status is not necessarily conclusive.

The number of shares of Registrant's Common Stock, $0.001 par value per share, outstanding as of March 1, 2021 was 12,947,572.

DOCUMENTS INCORPORATED BY REFERENCE

None.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements. We intend such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. All statements other than statements of historical facts contained in this Annual Report on Form 10-K are forward-looking statements, including but not limited to statements regarding:

- our plans to develop and commercialize our product candidates;
- the timing of our ongoing or planned clinical trials for LYR-210, LYR-220, and any future product candidates;
- the timing of and our ability to obtain and maintain regulatory approvals for LYR-210, LYR-220, and any future product candidates;
- the clinical utility of our product candidates;
- our commercialization, marketing, and manufacturing capabilities and strategy;
- our expectations about the willingness of healthcare professionals to use LYR-210, LYR-220, and any future product candidates;
- our intellectual property position;
- our competitive position and developments and projections relating to our competitors or our industry;
- our ability to identify, recruit, and retain key personnel;
- the impact of laws and regulations;
- risks associated with the COVID-19 pandemic, which may adversely impact our business and clinical trials;
- our expectations regarding the time during which we will be an emerging growth company under the Jumpstart Our Business Startups Act, or the JOBS Act;
- our plans to identify additional product candidates with significant commercial potential that are consistent with our commercial objectives;
- our estimates and statements regarding our future revenue, future results of operations, and financial position;
- our business strategy;
- our research and development costs; and
- the plans and objectives of management for future operations.

These statements involve known and unknown risks, uncertainties, and other important factors that may cause our actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential,” “would,” or “continue” or the negative of these terms or other similar expressions, although not all forward-looking statements contain these words. The forward-looking statements in this Annual Report on Form 10-K are only predictions and are based largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition, and results of operations. These forward-looking statements speak only as of the date of this Annual Report on Form 10-K and are subject to a number of known and unknown risks, uncertainties, and assumptions, including those described under the sections in this Annual Report on Form 10-K entitled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and elsewhere in this Annual Report on Form 10-K. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements.

Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. You should read this Annual Report on Form 10-K and the documents that we reference in this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances, or otherwise.

SUMMARY RISK FACTORS

Our business is subject to numerous risks and uncertainties, including those described in Part I, Item 1A. “Risk Factors” in this Annual Report on Form 10-K. You should carefully consider these risks and uncertainties when investing in our common stock. The principal risks and uncertainties affecting our business include the following:

- We have a limited operating history and a history of escalating operating losses, which may make it difficult to evaluate the prospects for our future viability.
- We have incurred significant losses since inception and expect to incur significant additional losses for the foreseeable future, and we may never achieve profitability.
- We will need significant additional funding in order to complete development of and obtain regulatory approval for our product candidates and commercialize our products, if approved.
- Our business is highly dependent on the success of our most advanced product candidate, LYR-210, which will require significant additional clinical testing before we can seek regulatory approval and potentially launch commercial sales, and if LYR-210 does not receive regulatory approval or is not successfully commercialized, or is significantly delayed in doing so, our business will be harmed.
- clinical trials required for our product candidates are expensive and time-consuming, their outcome is uncertain, and if our clinical trials do not meet safety or efficacy endpoints in these evaluations, or if we experience significant delays in these trials, our ability to commercialize our product candidates and our financial position will be impaired;
- developments by competitors may render our products or technologies obsolete or non-competitive or may reduce the size of our markets;
- the successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish coverage, adequate reimbursement levels and pricing policies, and the failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue;
- even if either LYR-210 or LYR-220 receives marketing approval, it may fail to achieve market acceptance by physicians, patients, third-party payors or others in the medical community necessary for commercial success;
- we will rely on third parties for the manufacture of materials for our research programs, pre-clinical studies and clinical trials and we do not have long-term contracts with any of these parties, which increases the risk that we will not have sufficient quantities of such materials, product candidates, or any therapies that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost, which could delay, prevent, or impair our development or commercialization efforts;
- we rely on third parties to conduct our pre-clinical studies and clinical trials, and any failure by a third party to conduct the clinical trials according to GCPs and in a timely manner may delay or prevent our ability to seek or obtain regulatory approval for or commercialize our product candidates;
- if we are unable to obtain, maintain or adequately protect our intellectual property rights, we may not be able to compete effectively in our markets;
- if we lose key management or scientific personnel, cannot recruit qualified employees, directors, officers or other significant personnel or experience increases in our compensation costs, our business may materially suffer; and
- the pandemic caused by COVID-19 could adversely impact our business and operations, including our clinical trials.

PART I

Unless the context requires otherwise, we use the terms "Lyra," "the Company", "we," "us," "our" and similar designations in this Annual Report on Form 10-K to refer to Lyra Therapeutics, Inc. and its wholly-owned subsidiaries.

Item 1. Business.

Overview

We are a clinical-stage therapeutics company focused on the development and commercialization of novel integrated drug and delivery solutions for the localized treatment of patients with ear, nose, and throat, or ENT, diseases. Our proprietary technology platform, XTreo™, is designed to precisely and consistently deliver medicines directly to the affected tissue for sustained periods with a single administration. Our initial product candidates, LYR-210 and LYR-220, are bioresorbable polymeric matrices designed to be administered in a brief, non-invasive, in-office procedure and intended to deliver up to six months of continuous drug therapy to the sinonasal passages for the treatment of chronic rhinosinusitis, or CRS. The therapeutic embedded within LYR-210 and LYR-220 is mometasone furoate, or MF, which is the active ingredient in various U.S. Food and Drug Administration, or FDA, approved drugs and has a well-established efficacy and safety profile. CRS is an inflammatory disease of the paranasal sinuses which leads to debilitating symptoms and significant morbidities and affects approximately 14 million people in the United States.

We have advanced LYR-210 as a potential preferred alternative to surgery through a Phase 2 randomized, controlled, patient blinded clinical trial, which we refer to as our Phase 2 LANTERN clinical trial, designed to evaluate safety and efficacy in CRS patients both with and without nasal polyps who have failed previous medical management but have not undergone endoscopic sinus surgery, who we refer to as surgically-naïve CRS patients. The trial was designed to enroll 99 evaluable patients with the potential to increase to up to 150 patients and was initiated in May 2019 at sites in Australia, Austria, Czech Republic, New Zealand, and Poland. In December 2019, the FDA authorized our investigational new drug application, or IND, and, prior to the COVID-19 pandemic, we planned to enroll patients in the United States. However, in light of developments relating to the COVID-19 pandemic we discontinued enrollment at 67 patients in our Phase 2 LANTERN clinical trial and did not enroll any patients in the United States.

On December 7, 2020, we reported positive top-line results from our Phase 2 LANTERN clinical trial, including that the 7,500 µg dose of LYR-210 achieved statistically significant improvement in the composite four cardinal symptoms score, or 4CSS, in favor of the treatment arm as measured by the change from baseline at weeks 16, 20, and 24. However, although a strong treatment effect was observed at week 4, LYR-210 did not achieve the primary endpoint of change from baseline in 4CSS at week 4 at either the 7,500 µg dose or 2,500 µg dose relative to the control group. We believe this was due primarily to the discontinuation of enrollment related to the COVID-19 pandemic. As a result of the decrease in the number of patients enrolled from planned (99 evaluable) to actually enrolled (67), a greater magnitude of change from baseline in 4CSS at week 4 and/or a smaller standard deviation associated with the change from baseline was required in order to achieve statistical significance for the primary endpoint at week 4. LYR-210 was observed to be safe and well-tolerated at all doses in the trial, and no treatment-related serious adverse events were reported. For more information on the top-line results from our Phase 2 LANTERN clinical trial, see "—LYR-210 for the Treatment of CRS—Overview of Clinical Development—Phase 2".

In addition, although we collected certain pharmacokinetic data from all patients in our Phase 2 LANTERN clinical trial starting at week 4, our protocol contemplated utilizing a subset of U.S. patients to collect certain additional pharmacokinetic data in order to support the NDA for LYR-210. However, because we were unable to enroll patients in the United States due to the COVID-19 pandemic, we were unable to collect these additional pharmacokinetic data as planned. As a result, in September 2020, we initiated a separate characterization study in the United States to collect these additional data. This study is fully enrolled and all 24 patients have completed the study-required visits. We expect data lock and analysis activities to be completed by the second quarter of 2021.

In our Phase 1 clinical trial, LYR-210 met its primary safety endpoint, and we observed that patients generally experienced significant and rapid, clinically meaningful and durable improvement on a patient symptom severity scale through week 25, which was the end of the trial. Secondary findings from our Phase 1 clinical trial showed that LYR-210 demonstrated significant reduction of sinonasal Type 2 inflammation in surgically-naïve patients with CRS. We believe the reduction of Type 2 inflammation suggests a correlation with rhinologic symptom improvement in CRS and we believe the reduction could be a potential measure of LYR-210's local anti-inflammatory effects at the site of inflammation in the sinonasal passages.

We are also developing LYR-220 for use in CRS patients who have an enlarged nasal cavity due to sinus surgery but continue to require treatment to manage CRS symptoms, and, subject to the impact of COVID-19 on our business, we intend to initiate a Phase 2 clinical trial for LYR-220 by the end of 2021. Beyond CRS, we believe our XTreo platform has potential applications in other disease areas, which we are actively exploring to further broaden its therapeutic potential.

CRS has been described in the literature as an "unrecognized epidemic" due to its high prevalence, its substantial impact on patient quality of life, and the significant limitations of currently available treatment options. We estimate that sinusitis, which includes both CRS and acute rhinosinusitis, impacts approximately 12% of the adult population in the United States, or approximately 30 million people, making it the fifth most common condition in people under the age of 65 and more prevalent than diabetes or heart disease. Of this population, we estimate that approximately 14 million people are affected with CRS. Moreover, we estimate that approximately 8 million people are treated for CRS by physicians annually, of which approximately 4 million fail medical management every year. In the United States, over $60 billion is spent annually in direct treatment costs for sinusitis, including approximately $5 billion on sinus surgeries.

We believe LYR-210 and LYR-220, if successfully developed and approved, will be able to treat the entire spectrum of CRS patients that have failed medical management and present to an ENT physician, including pre- and post-surgical patients and those with and without nasal polyps, with up to six months of treatment in a single administration. Our most advanced product candidate, LYR-210, was evaluated in surgically-naïve CRS patients in our Phase 2 LANTERN clinical trial. On December 7, 2020, we reported positive top-line results from our Phase 2 LANTERN clinical trial, including that the 7,500 µg dose of LYR-210 achieved statistically significant improvement in 4CSS in favor of the treatment arm as measured by the change from baseline at weeks 16, 20, and 24. While a strong treatment effect was observed at week 4, LYR-210 did not achieve the primary endpoint of change from baseline in 4CSS at week 4 at either the 7,500 µg dose or 2,500 µg dose. We believe this was due primarily to the discontinuation of enrollment related to the COVID-19 pandemic. For more information on the top-line results from our Phase 2 LANTERN clinical trial, see "—LYR-210 for the Treatment of CRS—Overview of Clinical Development—Phase 2". In an open-label, multi-center Phase 1 clinical trial, we placed 40 LYR-210 matrices bilaterally in 20 patients at sites in New Zealand and Australia. LYR-210 met its primary safety endpoint in the Phase 1 trial, and we observed significant and rapid, clinically meaningful and durable improvement through week 25 in SinoNasal Outcome Test scores, or SNOT-22 scores, an established patient symptom severity scale. At week 24, improvement versus baseline was observed in 90% of patients in this Phase 1 trial, with similar activity observed across both polyp and non-polyp patients. Additionally, subject to the impact of COVID-19 on our business, we intend to initiate a Phase 2 clinical trial for LYR-220 by the end of 2021, and ultimately plan to pursue a supplemental new drug application, or sNDA, to the FDA for a potentially faster path to approval of LYR-220 if a new drug application, or NDA, for LYR-210 is approved by the FDA.

Our XTreo Platform

XTreo, our innovative and proprietary drug delivery platform, is designed to locally and continuously deliver small molecule drugs to the affected tissue over a sustained period of time from a single administration. The platform is comprised of three interrelated technology components:

- a biocompatible mesh scaffold, which is designed to maximize surface area for drug release while maintaining underlying tissue function;
- an engineered elastomeric matrix, which means a polymeric matrix composed of polymers having elastic characteristics, which has advanced physical properties resulting in implants with "shape memory" that dynamically adapt to nasal anatomy; and
- a versatile polymer-drug complex, which can be customized for the treatment of various chronic diseases treatable with ENT delivery to achieve the desired drug dose and drug elution rate.

Chronic Rhinosinusitis: A Prevalent Disease with High Unmet Medical Needs

CRS is an inflammatory disease of the paranasal sinuses causing the soft, moist layer of mucus-producing tissue, or mucosa, that lines the sinuses to become swollen and inflamed, leading to significant patient morbidities. The inflammation may be caused by infections, allergies, or environmental factors, as well as structural issues such as blockages of an ostium. Patients with CRS on average experience a lower quality of life index than people suffering from congestive heart failure, angina, chronic obstructive pulmonary disease, or back pain.

CRS has two phenotypes: CRS with nasal polyps, which are teardrop-shaped benign masses arising from the mucosa lining, and CRS without nasal polyps. The non-polyp form of CRS represents approximately 70%-to-90% of CRS patients. We estimate that approximately 8 million people are treated for CRS by physicians annually, of which approximately 4 million fail medical management every year.

Current Treatments and Their Limitations

The goals of therapy for CRS are to reduce mucosal swelling resulting from underlying inflammation, promote sinus drainage, and eradicate infections that may be present. The treatment of CRS is progressive in nature and typically begins with medical management, primarily with topical intranasal steroids and oral steroids. If this treatment is unsuccessful, an ENT physician may perform a sinus surgery.

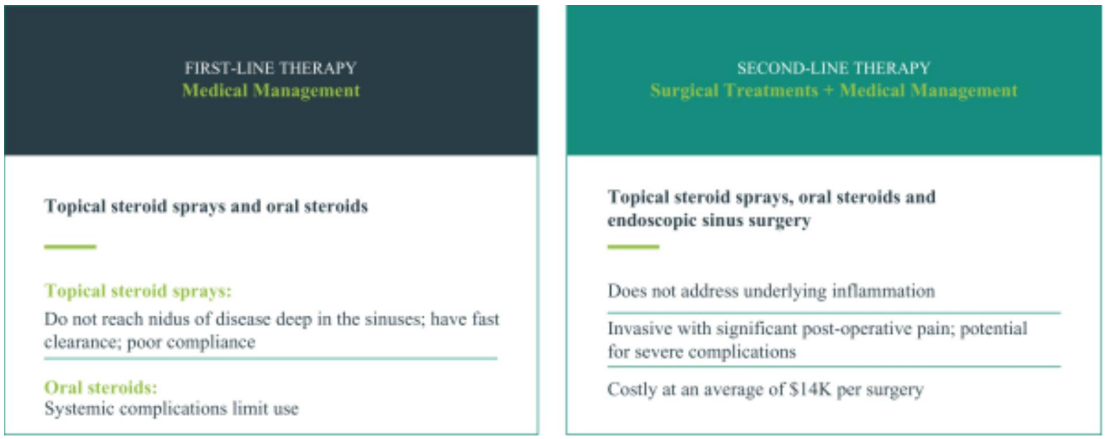


Figure 1. Current Primary Treatment Paradigm for CRS.

Currently, there are no FDA-approved drug therapies for CRS for non-polyp patients, although some drugs approved for nasal polyps are used off-label in this population.

Our Solution for CRS

LYR-210 is an anti-inflammatory implantable drug matrix based on our XTreo platform that is designed to consistently and locally elute MF to the inflamed mucosal tissue for up to six months in surgically-naïve CRS patients who fail medical management. MF, the active ingredient in various FDA-approved drugs, has a well-established efficacy and safety profile, which we believe will support the development process for LYR-210. LYR-210 is designed to enable sustained drug delivery at difficult-to-access nasal inflammation sites without the need for patient compliance, while avoiding the systemic side effects associated with oral steroids. LYR-210 is designed to be administered in a brief, non-invasive, in-office procedure by an ENT physician under endoscopic visualization via a single-use applicator.

We have advanced LYR-210 as a potential preferred alternative to surgery through our Phase 2 LANTERN clinical trial, designed to evaluate the safety and efficacy in surgically-naïve CRS patients both with and without nasal polyps who have failed previous medical management at sites in Australia, Czech Republic, New Zealand, and Poland. On December 7, 2020, we reported positive top-line results from our Phase 2 LANTERN clinical trial, including that the 7,500 µg dose of LYR-210 achieved statistically significant improvement in 4CSS in favor of the treatment arm as measured by the change from baseline at week 16 (-1.47) (p=0.021), week 20 (-1.61) (p=0.012), and week 24 (-1.64) (p=0.016). In addition, the 7,500 µg dose of LYR-210 achieved statistically significant improvement in SNOT-22 score in favor of the treatment arm as measured by the change from baseline at week 8 (-12.2) (p=0.039), week 16 (-15.0) (p=0.008), week 20 (-18.4) (p=0.001), and week 24 (-19.0) (p=0.001). In particular, the improvement in SNOT-22 score of the 7,500 µg dose of LYR-210 at week 24 over the control group (-19.0) was over two times the minimal clinically important difference of -8.9. However, although a strong treatment effect was observed at week 4, LYR-210 did not achieve the primary endpoint of change from baseline in 4CSS at week 4 at either the 7,500 µg dose (-0.36) (p=0.306) or 2,500 µg dose (0.04) (p=0.525) relative to the control group. We believe this was due primarily to the discontinuation of enrollment related to the COVID-19 pandemic. For more information on the top-line results from our Phase 2 LANTERN clinical trial, see “—LYR-210 for the Treatment of CRS—Overview of Clinical Development—Phase 2”. Subject to the impact of COVID-19 on our business, we expect to (i) report six-month post-treatment safety data and to hold an End of Phase 2 meeting with the FDA in mid-2021 and (ii) submit our Phase 3 protocol design for LYR-210 to the FDA in the second half of 2021.

LYR-210 was previously studied in an open-label, Phase 1 clinical trial with 20 patients in New Zealand and Australia, and achieved its primary endpoint of safety at week 4. In the Phase 1 trial, we observed that patients generally experienced significant and rapid, clinically meaningful and durable improvement in SNOT-22 scores. Significant reduction in SNOT-22 scores was observed at week 1, and this reduction persisted through week 25, which was the end of the trial. The changes from baseline, or CFBL, in SNOT-22 score were statistically significant ($P < 0.01$) at all measured intervals. The average change from baseline in SNOT-22 score at week 1 was -13.0 points ($P=0.008$ to pre-treatment), achieving the minimal clinically significant difference of -8.9 points. Further, symptom relief as measured by SNOT-22 score was observed through the entire duration of the trial, achieving an average change from baseline of -20.5 points at week 24, the end of the treatment period ($p < 0.0001$ to pre-treatment), and -20.0 points ($p < 0.0001$) at week 25, one week after the removal of LYR-210.

We are developing our second pipeline product candidate, LYR-220, for use in CRS patients who continue to require treatment to manage CRS symptoms despite having had sinus surgery. LYR-220 is also designed to utilize MF, but will employ an oversized matrix designed for patients whose nasal cavity is enlarged due to sinus surgery. LYR-220 is designed as a potential preferred alternative to revision sinus surgery and post-surgical medical management. Subject to the impact of COVID-19 on our business, we expect to initiate a Phase 2 clinical trial for LYR-220 by the end of 2021.

We believe that the key potential benefits of our current investigational product portfolio, LYR-210 and LYR-220, include:

- **Clinical Activity**: We believe LYR-210 and LYR-220 have the potential to significantly improve symptoms by maintaining a steady, high dose of MF at the site of inflammation for up to six months with a single administration, without any dependence on patient compliance.

- **Patient Compliance**: Because drug delivery for LYR-210 and LYR-220 is designed to be sustained for up to six months with a single administration, the efficacy of LYR-210 and LYR-220 will not depend on patient compliance within the treatment period, unlike other CRS treatment options that require repeated daily administrations, such as topical intranasal steroids and oral steroids.

- **Patient Experience**: LYR-210 and LYR-220 are designed to be administered via a simple, in-office procedure every six months, which is intended to enhance convenience for patients, unlike the repeated daily medical management and/or time-consuming and painful surgery required by certain other CRS treatment options. Moreover, we believe patients may also benefit from the biocompatible, flexible structure of LYR-210 and LYR-220 that is designed to maximize comfort over the therapy period.

- **Physician Experience**: LYR-210 and LYR-220 are designed to enable physicians to perform the placement of LYR-210 and LYR-220 in-office in conjunction with an endoscopy procedure, thereby making the placement aligned with the existing care continuum for CRS patients and eliminating the need for physicians to schedule separate surgical time. Moreover, the elastomeric matrix encapsulates the underlying mesh fibers to facilitate removal.

- **Localized Delivery**: LYR-210 and LYR-220 are designed to benefit from our XTreo platform, which is intended to provide localized delivery to avoid systemic side effects that are common with certain other CRS treatment options, such as oral steroids.

- **Patient Applicability**: LYR-210 and LYR-220 are designed to treat the entire spectrum of CRS patients who have failed medical management, including pre- and post-surgical patients and those with and without polyps.

- **Pharmacoeconomic Impact**: LYR-210 and LYR-220 are designed as an alternative to surgery (initial or revision), and as such have the potential to provide significant savings to the healthcare industry by reducing the number and frequency of expensive surgical treatment options.

We believe LYR-210 and LYR-220, if approved, would be the only products able to deliver up to six months of continuous topical treatment in a single administration to treat the entire spectrum of CRS patients who fail medical management, including pre- and post-surgery patients and those with and without nasal polyps.

Intellectual Property and Barriers to Entry

We own all the material intellectual property rights related to our platform and product candidate portfolio. As of December 31, 2020, our product and product candidate portfolio is protected by issued and pending patents in the U.S. and major foreign countries with claims directed to devices, systems, and method of use, which, exclusive of possible patent term adjustments or extensions or other forms of exclusivity, are projected to expire between 2030 and 2037.

We also rely upon know-how, continuing technological innovation, and technical barriers to entry, including manufacturing and drug delivery complexities, to develop and maintain our competitive intellectual property position.

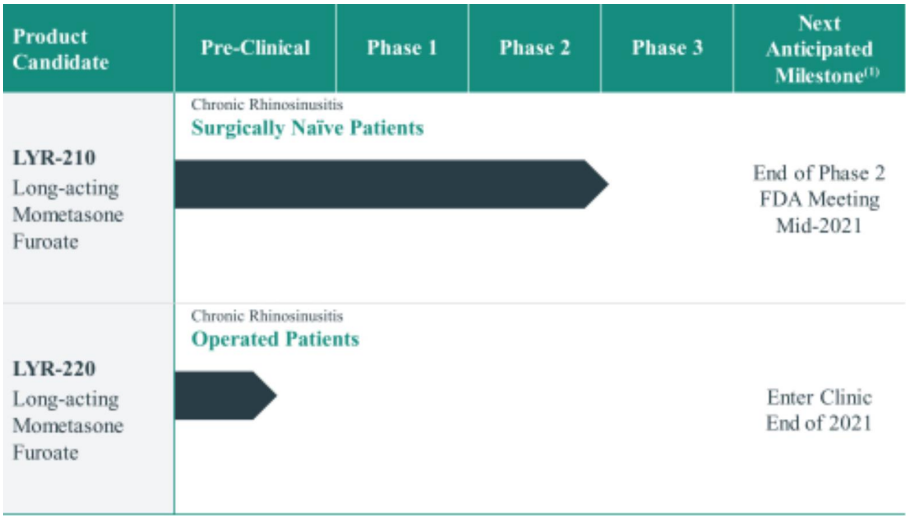
Management Team and Investors

Our management team has extensive drug development, manufacturing, and commercialization experience across a broad spectrum of disease areas, for both drug and drug-device combination products, with a successful track record in large pharmaceutical, medical device, and biotech companies. Additionally, our management team has been involved in the development of successfully approved and commercialized products such as Taxus (drug-eluting stent), AvoneX, Risperdal, Linzess, Vivitrol, XenMatrix, and Photrexa.

Further, we have been supported by a leading group of biotech investors including, among others, ArrowMark Partners, Intersouth Partners, North Bridge Venture Partners, Perceptive Advisors, Polaris Venture Partners, RA Capital, and Soleus Capital.

Our Pipeline

The current status of our product candidates is summarized below.



(1) Anticipated clinical milestones are subject to the impact of COVID-19 on our business.

Our Strategy

Our mission is to transform the ENT treatment paradigm by utilizing our proprietary drug delivery platform, XTreo, to develop safe and effective therapies for the treatment of debilitating diseases treatable with ENT delivery. We intend to achieve this through the following strategies:

- **Complete the development and secure FDA approval of LYR-210 for the treatment of CRS.** We believe LYR-210, if approved, is well positioned in the CRS treatment paradigm to provide a preferred alternative to surgery. LYR-210, which has advanced through our randomized, sham procedure-controlled, patient-blinded Phase 2 LANTERN clinical trial, utilizes MF, the active ingredient in various FDA-approved drugs. Our goal is to advance LYR-210 into one or more pivotal Phase 3 clinical trials, followed by potential marketing approval through a 505(b)(2) NDA submitted to the FDA.

- **Advance our second product candidate, LYR-220, into the clinic to provide a comprehensive solution for CRS patients who have failed medical management and surgery.** We are developing a larger version of LYR-210 designed for use in the enlarged nasal cavity of CRS patients who have had sinus surgery. We believe LYR-220, if successfully developed and approved, is well positioned to provide a preferred alternative to revision surgery and post-surgical medical management. LYR-220 is currently in product feasibility studies. We plan to advance LYR-220 into a Phase 2 clinical trial by the end of 2021, subject to the impact of COVID-19 on our business, and ultimately intend to seek approval through the sNDA pathway if an NDA for LYR-210 is approved by the FDA.

- **Build a commercialization infrastructure in the U.S. market for LYR-210 and LYR-220.** If any of our product candidates are approved, we plan to launch an efficient, go-to-market commercialization model focused on targeted outreach to our key physician, payor, and patient audiences. We plan to build an in-house sales force that will target ENT physicians whose sub-specialty is general otolaryngology or rhinology, which together represent roughly 60% of the 12,000 ENT physicians in the United States. Ensuring physician and patient market access to our products will be critical to our success, and we plan to execute a holistic reimbursement strategy that will integrate payor coverage and physician practice management initiatives. In addition, we also plan to selectively use cost-effective, patient-directed marketing strategies to further increase awareness among the CRS patient community of our products with the goal of increasing ENT physician visits. Finally, we plan to leverage our commercial infrastructure in the subsequent launch of LYR-220 and any future product candidates.

- **Maximize the value of our XTreo platform and expand our product pipeline.** Our XTreo platform provides a versatile drug development engine that enables us to focus on indications where long-term delivery of existing treatments may provide improved local bioavailability and enhanced efficacy or safety. We plan to utilize our platform to identify additional product candidates, with an initial focus on conditions treatable with nasal delivery, potentially including allergic rhinitis, rare disorders where nasal disease contributes to the disease pathology, and central nervous system disorders. In addition, we believe we can adapt our platform to target conditions treatable with delivery to other tissues beyond the nasal cavities, such as the ear.

- **Seek strategic collaborative relationships.** We intend to develop our product candidates on our own in the U.S. and retain all U.S. rights, but seek strategic collaborations ex-U.S. to facilitate the capital-efficient development of our product candidates. We may also enter into collaborative relationships within the U.S. for our future pipeline candidates. We believe these collaborations could potentially provide non-dilutive funding to advance our pipeline candidates while allowing us to benefit from the development expertise of our collaborators.

Our Technology Platform

XTreo, our innovative and proprietary drug delivery platform is designed to locally and continuously deliver small molecule drugs to the affected tissue over a sustained period of time from a single administration. Our technology platform, developed over the past decade, was first patented in 2009 by members of our team who have extensive experience in drug formulation and delivery, materials science, and biotechnology. This expertise has allowed us to significantly improve upon polymer drug delivery technology and add shape-memory properties to bioresorbable polymeric implants, one of our key innovations.

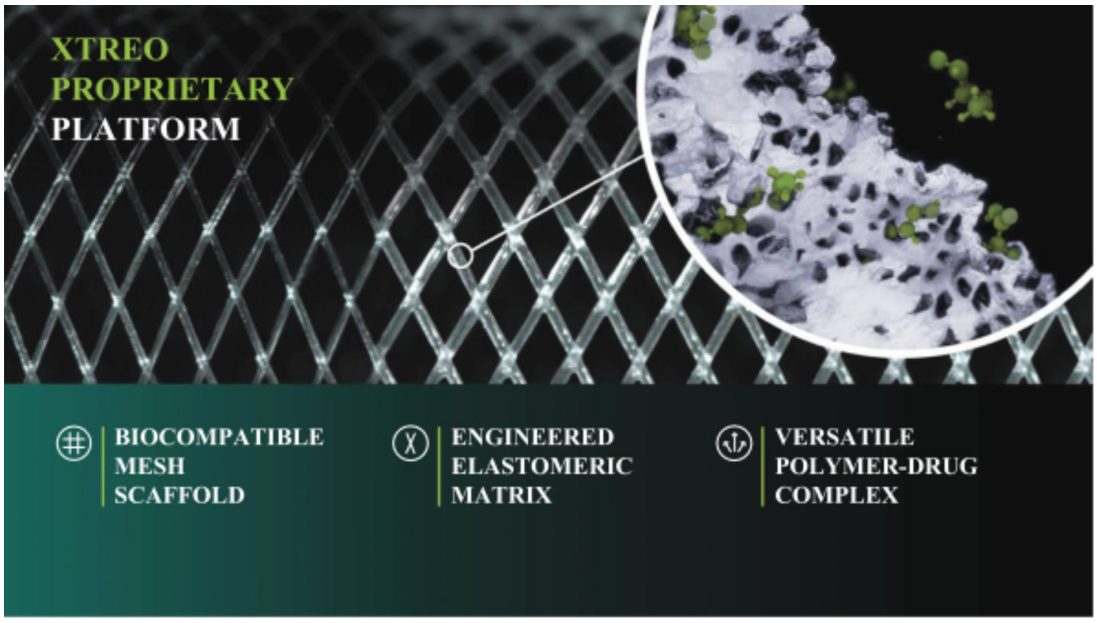


Figure 2. XTreo Proprietary Platform.

XTreo, our drug-eluting bioresorbable technology platform is comprised of three polymeric components, which are designed to work together to enable highly efficient, localized drug delivery (see Figure 2, above). This proprietary technology platform is designed to enable sustained delivery of medications for many months of therapy, targeting tissues deep in the ENT passages and potentially other diseased tissues that are not accessible with conventional therapeutic approaches. The components of our platform include:

- **Biocompatible Mesh Scaffold**—variants of poly(L-lactide-co-glycolide), or PLGA, braided to form an implantable mesh with a high surface area. Our biocompatible mesh scaffold is intended to provide the foundation for efficient drug delivery. We have designed the mesh scaffold to optimize surface area for drug release while maintaining underlying tissue function through an open-cell design. The mesh scaffold is comprised of bioresorbable polymers and is pliable to maximize patient comfort.

- **Engineered Elastomeric Matrix**—overlying elastomer of poly(L-lactide-co-e-caprolactone), or PLCL, coating that constrains the intersection points of the braid. Over the last decade we have developed a highly sophisticated and proprietary engineered elastomeric matrix which has advanced physical properties to dynamically conform to nasal anatomy. Its adaptive elastic tension, which gives it shape-memory to resist deformation, is key to ensuring persistent positioning in the target location. The matrix works in conjunction with the underlying mesh to exert outward retention force, keeping it in place as tissue remodels.

- **Versatile Polymer-Drug Complex**—active therapeutic embedded in a polymer designed to control its release. We have extensive drug-delivery know-how which has enabled us to design a versatile polymer-drug complex that can accommodate most small molecule drugs and achieve tunable elution profiles. We believe our versatile polymer-drug complex is potentially amenable to continuous, prolonged drug release across a wide range of drugs for different therapeutic applications. With proprietary bioresorbable polymer-drug formulations, we believe our platform can be used to customize controlled-release drugs for various chronic diseases treatable with ENT delivery and improve the efficacy of therapeutic properties of existing active pharmaceutical ingredients, or APIs, through more prolonged delivery.

The three integrated components are fundamental to the successful function and versatility of the XTreo technology. For application to a targeted tissue, the implant is compressed into a narrow applicator, which allows non-invasive placement deep within cavities of the ear, nose, and throat. The shape-memory properties ensure the implant self-expands as it is administered through the applicator to comfortably fit within and adapt to the target anatomy. The implant is designed to be oversized for the target anatomy and therefore will push outwards to stay fixed at the target location. Over time, as inflammation recedes due to the local drug therapy, the shape-memory properties are intended to allow the implant to actively adapt to the anatomy and continue to stay in place to elute drug locally for a prolonged period.

In engineering the implant, we use polymers that are biocompatible and bioresorbable which, if left in place, would gradually dissolve over time. The polymers used in our formulations have established safety profiles as they have previously been used in FDA-approved therapeutics. The mesh scaffold and elastomeric matrix are composed of PLGA and PLCL elastomer, both of which are well-established biodegradable polymers commonly used in medical applications. The customizable polymer drug complex consists of the active therapeutic embedded in the inactive ingredients containing PLCL and poly(L-lactide), or PLA, to control the drug elution rate. The polymer composition and drug formulation are tailored to achieve the desired drug dose and dissolution rate. Our expertise allows us to balance polymer resorption with drug elution to achieve a sustained rate of drug release over months in addition to varying the dosing and release rates to provide chronic local treatment.

Chronic Rhinosinusitis and the Treatment Landscape

Sinuses are air-filled pockets within the bones of the face and skull. The four types of sinuses are frontal, ethmoid, sphenoid, and maxillary (see Figure 3, below). One of each type of sinus lies on either side of the face.

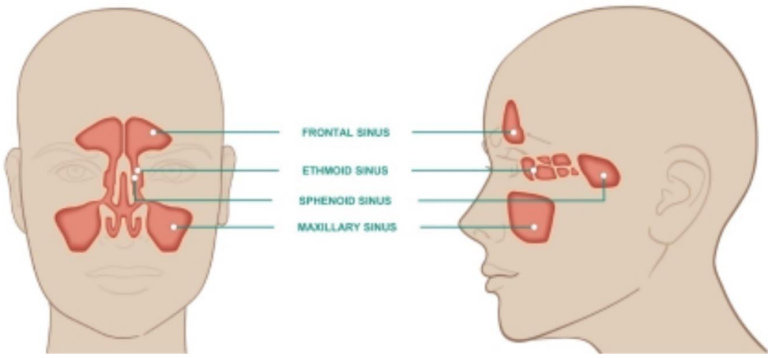


Figure 3. Illustration of Nasal Sinuses.

The sinuses are lined with a soft, moist layer of mucus-producing tissue, or mucosa. Mucus moistens the nasal lining and protects the body from inhaled impurities such as dust, pollutants, and bacteria. Each of the maxillary, sphenoid, and frontal sinuses has a corresponding ostium, or opening, through which mucus drains. The ethmoid sinuses are a series of cells with multiple, often interconnected openings and drainage pathways. The surface tissues of the sinuses are covered with millions of cilia, which are small, hair-like structures that act in coordination to sweep the mucus through the ostium of each sinus cavity to the back of the throat. The drainage of mucus is a normal process that keeps the sinuses healthy.

CRS is an inflammatory disease of the paranasal sinus causing the mucosa lining to become swollen and inflamed, leading to significant patient morbidities. The inflammation may be caused by infections, allergies, or environmental factors, as well as structural issues such as blockages of an ostium. If one or more sinus drainage pathways becomes blocked, normal mucus drainage is prevented and damage to ciliary function may occur. There are two categories of sinusitis: acute and chronic. Acute sinusitis is transient in nature and lasts less than four weeks. Chronic sinusitis is more severe and lasts 12 weeks or longer. The term “chronic sinusitis” is generally used interchangeably with “CRS” in the medical community, and we refer to the condition as CRS in this Annual Report on Form 10-K. The four cardinal symptoms of CRS are nasal obstruction and congestion, facial pain and pressure, nasal discharge, and olfactory loss (loss of sense of smell). Other symptoms include chronic headaches, bodily pain, fatigue, sleep deprivation, depression, and recurrent infections. CRS may be diagnosed when two of the four cardinal symptoms persist for 12 weeks or longer and when inflammation is confirmed via endoscopy or CT scan. Patients with CRS experience a lower quality of life index than people suffering from congestive heart failure, angina, chronic obstructive pulmonary disease, or back pain. In addition, CRS symptoms are estimated to cause patients to miss over 11 million workdays per year in the United States alone, resulting over $1 billion in indirect economic costs.

We estimate that sinusitis impacts approximately 12% of the adult population in the United States, or approximately 30 million people, making it the fifth most common condition in people under the age of 65, and more prevalent than diabetes or heart disease. Beyond the United States, sinusitis has a similarly high prevalence in Europe, with approximately 27 million cases in the EU5 (France, Germany, Italy, Spain, and the United Kingdom), and in Asia, with approximately 104 million cases in China alone. Of the approximately 30 million people impacted by sinusitis in the United States, we estimate approximately 14 million are affected with CRS. Of these, we estimate that approximately 8 million people are treated for CRS by physicians annually, of which approximately 4 million fail medical management every year.

CRS has two phenotypes: CRS with nasal polyps, which are teardrop-shaped benign masses arising from the mucosa, and CRS without nasal polyps, with the non-polyp form representing approximately 70%-to-90% of CRS patients. Patients with polyps develop non-cancerous polyps on the chronically inflamed surfaces, but both subgroups typically share the same symptoms. Currently, the majority of our competitors target CRS patients with polyps, and there are no approved treatments for CRS without polyps, creating a vast untapped market opportunity for a more effective treatment solution. Given no approved treatments for CRS without polyps exist, there is only off-label drug usage for this segment of the patient population.

Current treatments are directed towards managing the symptoms of CRS through a combination of medical management and surgical intervention techniques. The first line of therapy is medical management involving nasal saline irrigation, intranasal corticosteroidal sprays, oral steroids, and antibiotics for patients with an active sinus infection. CRS is the most common reason for adult outpatient antibiotic use in the United States. It has been estimated that antibiotic use to treat infections relating to CRS may cost more than $150 million per year in the aggregate. Patients whose symptoms persist despite medical management are generally recommended to undergo functional endoscopic sinus surgery (or FESS) or balloon sinus dilation (or BSD), or both. FESS is a highly invasive surgery performed in the operating room, under full anesthesia, to open the blocked sinus pathways by removing inflamed tissue and bone using surgical tools. BSD is a less severe form of endoscopic sinus surgery, often used in combination with FESS, in which small balloon catheters are inserted and inflated to drain the large nasal sinuses. Although FESS and BSD can improve symptoms and quality of life, limitations remain. Neither correct the underlying cause of the inflammation and patients who undergo either or both procedures often experience significant pain and require continued post-operative medical therapy to maintain improvements, with a high incidence of repeat surgeries.

Medical Management

The first-line of treatment for CRS is medical therapy, which typically includes nasal saline irrigation, corticosteroids, and antibiotics for patients with an active infection.

Steroids represent the current first-line standard of care for CRS patients, given they are generally pharmacologically effective at treating inflammation. Intranasal steroid sprays and aerosols, commonly indicated for rhinitis, or inflammation of the nasal passage, are routinely prescribed and used over-the-counter for the treatment of CRS symptoms. Physicians may also prescribe oral steroids on an episodic basis to patients who have not received sufficient symptomatic relief. They are generally prescribed for short-term use by patients with severe symptoms or exacerbations of CRS who are already on maintenance therapy, such as nasal irrigation or intranasal corticosteroid sprays. Finally, physicians may prescribe antibiotics for patients with an active infection.

Intranasal steroid sprays, oral steroids, and antibiotics each have significant limitations:

- While intranasal steroid sprays avoid systemic exposure and thus lack such serious side effects, penetration of the spray beyond the nasal cavities into the paranasal sinuses—the site of inflammation—is limited, particularly in pre-operative patients, despite requiring multiple, inconvenient administrations per day. In a published study, a large fraction of the spray is deposited in the anterior nasal cavity without any significant penetration into the paranasal sinuses. Additionally, intranasal spray efficacy is also limited due to fast clearance rates, as it has been demonstrated that mucocilliary action removes approximately 50% of the spray from the nasal cavity within 10 to 15 minutes of dosing. Poor patient compliance further limits the effectiveness of intranasal steroid sprays. While a recently launched intranasal exhalation delivery product has been developed to enhance the delivery of steroid to areas of inflammation within the sinus, the product is still subject to the limitations resulting from fast clearance and poor patient compliance.

- Oral steroid therapy is effective at reaching the sinus lining, but it does so by means of systemic exposure and therefore carries the risk of serious side effects associated with prolonged use, including glaucoma, bone loss, weight gain, psychosis, and difficulty in controlling blood glucose levels in patients with diabetes. Additionally, studies have shown that long-term benefits from their use are limited.

- Although antibiotics are generally prescribed for patients with an active infection, their role for treatment of CRS is unclear, and there is limited evidence that supports their use for the treatment of CRS. In addition, their prolonged use can lead to antibiotic resistance, and CRS is identified as a major target in national efforts to reduce unnecessary antibiotic intervention.

Medical management is used as a first-line of medical therapy for pre-operative patients and as maintenance therapy for post-operative patients. Therefore, patients in both stages of the condition are managed medically and hence are subject to the limitations described above. Based on published medical literature, we estimate that at least 50% of CRS patients who are seen by ENT physicians and receive medical management remain symptomatic.

Sinus Surgery

The primary alternative after medical management is FESS, an invasive surgery during which a physician enlarges the inflamed and obstructed sinus pathways by removing inflamed tissue and bone in order to facilitate normal sinus drainage and aeration as well as provide greater access for delivery of steroids. First introduced in the United States in the 1980s, FESS is considered the standard of care for surgical intervention to treat CRS. However, while approximately 400,000 FESS procedures are performed each year, many surgical candidates opt not to have surgery given that it does not correct the underlying inflammation or obviate the need for medical management. Approximately, 65% of patients have recurrent symptoms post-FESS and up to 20% require a revision surgery.

FESS is a highly invasive procedure, requiring general anesthesia and involving significant post-operative discomfort. During this procedure, a physician inserts an endoscope into the nasal cavity to provide visualization of the patient’s anatomy, the turbinate is identified with help of the endoscope and the uncinated process is removed exposing the ethmoid bulla. Surgical instruments, powered cutting tools, and balloon dilation devices are used to remove or dilate the obstructive tissue and bone. Given the essential role of the ethmoid bulla in sinus function, the ethmoid sinuses are then opened in 75%-to-85% of FESS procedures. The dependent sinuses each drain into the ethmoid sinuses through ostia, which may be enlarged by either surgically removing tissue or via balloon dilation. Following the surgical intervention, physicians often pack the newly opened ethmoid sinuses with gauze or other obstructive sinus packing materials to hold the sinus cavities open. A follow-up office visit is required several days after the procedure to remove the sinus packing materials and depending on the circumstances a patient may have to visit the surgeon two to three times a week for a period of time using nasal irrigation or will be allowed to carry out simple nasal douching several times a day. A typical FESS procedure costs approximately $14,000 on average.

Since the introduction of FESS, several new technologies, such as image-guided surgical navigation systems, powered surgical instruments, and BSD devices have expanded the addressable patient population who can benefit from FESS. For instance, BSD devices were developed to be used in combination with traditional surgical instruments during FESS to treat the dependent sinuses and have now allowed for treatment of some patients in the physician office setting as a standalone procedure. The cost of a BSD procedure can range from $3,000 to $7,000 per treatment.

On an annual basis, approximately 4 million CRS patients fail medical management, but ultimately only approximately 400,000 patients choose to undergo an endoscopic sinus surgery each year. Physicians report that many patients, when presented with sinus surgery as a treatment option, opt to forego the procedure. Some patients regard the often temporary benefits provided by surgery as not worth the expense, recovery time, or use of general anesthesia.

While sinus surgery is the standard of care for treating CRS after the failure of medical management, it has several significant limitations:

- ***Invasive surgery with significant post-operative pain and nasal care.*** FESS is an invasive surgery that results in irreversible changes to the anatomy and significant post-operative pain, discomfort, and recovery time. As with any invasive surgery, a FESS entails the potential for bleeding, infection, and scar tissue.

- ***Requirement for post-operative maintenance.*** As the underlying inflammation of CRS is still unaddressed by sinus surgery, patients are required to post-operatively maintain their treatment with medical management. Additionally, reports have shown nasal polyp regrowth following surgery in many cases and post-nasal discharge often times remains a challenge.

- ***Additional FESS procedures may be needed.*** Approximately 65% of patients have recurring symptoms post-FESS, and approximately 20% of patients will require a revision of sinus surgery within five years, 43% of whom will within the first post-operative year. This is because sinus surgery does not cure the underlying cause of the inflammation of the sinus pathways, which can cause repeat flare ups. We believe the risk of potential revision surgery is a significant deterrent to some patients that would otherwise undergo sinus surgery.

- ***Potential for severe complications.*** As a result of the use of surgical tools in close proximity to the brain, eyes, and other critical anatomy, the potential for significant complications is a concern of physicians and patients alike. The risks of FESS, particularly in the frontal sinuses, cause some ENT physicians to avoid performing surgery in the frontal sinus drainage pathway. Major complications, such as cerebral spinal fluid leaks, swelling of the eye, or blindness, occur in approximately 0.3% of FESS procedures.

Drug Eluting Stents and Monoclonal Antibodies

For patients with nasal polyps who remain symptomatic following surgery, who we refer to as refractory patients, certain non-surgical options are available. A steroid-eluting implant that continuously delivers three months of MF was approved to treat CRS in adults with nasal polyps. In addition, two subcutaneously-administered monoclonal antibodies, or mAbs, were recently approved as add-on maintenance therapy for uncontrolled disease in adults with nasal polyps.

However, each of these treatments has limitations. The drug-eluting stent has only a short elution profile, presenting a more burdensome treatment regimen and requiring patient compliance. Meanwhile, the mAbs are generally reserved for the most refractory patients, given their systemic nature, unknown long-term safety and significant price premium even when compared to surgical options. In addition, both of these treatment modalities are only approved for the treatment of nasal polyps, leaving non-polyp patients (who represent approximately 70%-to-90% of all CRS patients) who are refractory with no approved treatment options.

LYR-210 for the Treatment of CRS

We believe LYR-210, if successfully developed and approved, has the potential to become a preferred alternative to surgery for the treatment of CRS. It is the only product candidate that we are aware of that is designed to provide up to six months of local delivery of anti-inflammatory medication with a single administration. The brief, non-invasive, in-office procedure allows for its implantation without the need for surgery. Further, we believe our studies have shown that LYR-210 has the potential to be an effective treatment for both patients with and without polyps. We believe LYR-210 has the potential to be a safe, effective, and broadly applicable CRS treatment, designed to enhance patient comfort and physician experience and eliminate patient compliance issues associated with other CRS treatments, such as intranasal steroid sprays, while achieving reduced costs compared to other CRS treatments, such as sinus surgery.

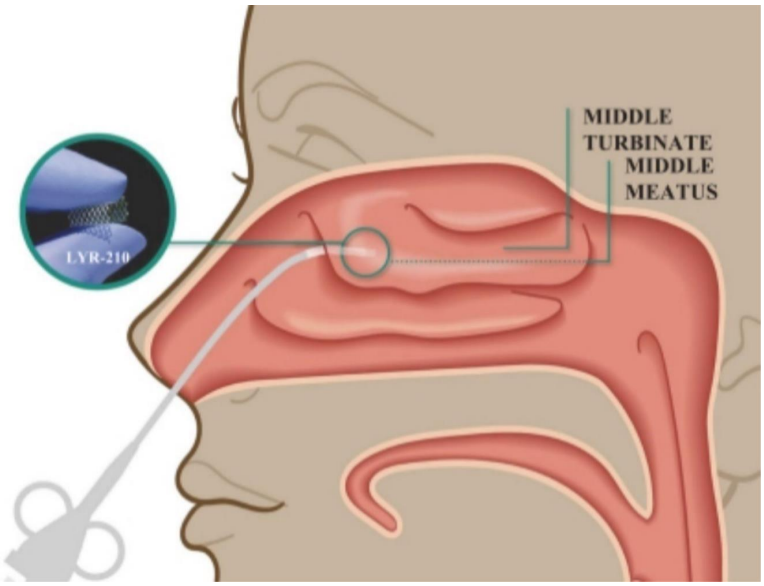


Figure 4. Illustration of Placement of LYR-210 in Middle Meatus.

LYR-210 is an investigational miniaturized local drug delivery system designed to fit within, and conform to, the confined space of a surgically-naïve patient's middle meatus, an air-containing space that plays a fundamental role in drainage of the paranasal sinuses (see Figure 4, above). LYR-210 consists of MF, the active ingredient in various FDA-approved drugs, embedded in biocompatible polymers to aid in the controlled and sustained delivery of MF to the sinonasal mucosal tissue from a single drug administration. LYR-210 has a tubular braid configuration with a uniform diamond pattern throughout and is 13 mm in diameter and 10 mm in length in the unconstrained state. It has elastic properties to promote patient comfort and is designed to be self-retaining against the mucosal tissue to allow effective drug transfer. The matrix is comprised of a base structure and a drug formulation. The base structure is composed of PLGA and PLCL elastomer to provide a 3-dimensional structure and elasticity. The drug formulation matrix consists of the active ingredient, MF, embedded in the inactive ingredients containing PLCL and PLA to control the release rate of MF. The composition and mass of the drug formulation matrix is specified to achieve the drug dose over time.

LYR-210 is intended to be administered bilaterally into the non-operated middle meatus by an ENT physician under endoscopic visualization via a provided, single use applicator. It is designed for office-based administration performed with topical anesthesia. Once administered, LYR-210 is designed to gradually release MF to the inflamed mucosal tissue for up to six months from a single administration. LYR-210 can be removed at six months or earlier at the physician's discretion using standard instruments and, if needed, replaced with a new LYR-210. LYR-210 is made with bioresorbable polymers that, if left in place, would gradually dissolve over time. Moreover, the elastomeric matrix encapsulates the underlying mesh fibers to facilitate removal.

Overview of Our Clinical Development

The table below summarizes our completed and ongoing clinical trials for LYR-210 for CRS in patients who have failed medical management and have not undergone endoscopic sinus surgery. In addition, because we were unable to enroll patients in the United States from whom we intended to collect certain additional pharmacokinetic data due to the COVID-19 pandemic, we initiated a separate characterization study in September 2020, as a follow-on to our Phase 2 LANTERN clinical trial, with certain patients not limited to the foregoing eligibility conditions, in order to collect such data as further described below.

Trial	Status	Trial Design	Trial Objectives	Trial Results
Phase 1	Completed; Results presented in October 2018	•Prospective, multi-center, non-randomized, single-arm, open-label clinical trial •25 week trial, including 24 week treatment period, plus one week post-removal •Bilateral 2,500 µg dose •20 patients •5 study sites	•Study objective: Evaluate the safety and feasibility over 24 weeks of continuous anti-inflammatory treatment with a single administration of LYR-210 •Primary endpoint: Product-related serious adverse events from baseline to 4 weeks post-procedure •Additional data collected: Morning serum cortisol, change in intraocular pressure, plasma pharmacokinetics, quality of life by SNOT-22 (secondary endpoint), endoscopy and MRI	•Primary safety endpoint achieved / 2,500 µg was well tolerated during entire duration of treatment •Significant and rapid, clinically meaningful and durable improvement in SNOT-22 scores was observed from week 1 through week 25 •Average change in baseline SNOT-22 score at week 1 was -13.0 points (P= 0.008 to pre-treatment) •Symptom relief, as measured by SNOT-22 score, was observed through the entire duration of study, achieving an average change from baseline of -20.5 points at week 24 ($p < 0.0001$ to pre-treatment), which was the end of the treatment period, and -20.0 ($p < 0.0001$) at week 25, which was the end of the study
Phase 2 (LANTERN)	Completed December 2020	•Randomized, blinded, sham-controlled, dose-ranging, parallel-group clinical trial •24 week treatment period, plus 24 week safety follow up post-removal •Bilateral 2,500 µg or 7,500 µg dose •99 evaluable patients with the option to increase to up to 150 patients. Enrollment discontinued at 67 patients due to COVID-19 pandemic •Up to 50 study sites globally	•Primary endpoint: Change in composite score of 7-day average of 4 cardinal symptoms from baseline at week 4 •Secondary objectives: Symptom improvement at week 24, sinus imaging to assess reduction in inflammation, SNOT-22, time to treatment failure, reduction in inflammation, frequency of exacerbations, pharmacokinetics/pharmacodynamics	•At the 7,500 µg dose, LYR-210 achieved statistically significant improvement in 4CSS in favor of the treatment arm as measured by the change from baseline at week 16 (-1.47) (p=0.021), week 20 (-1.61) (p=0.012) and week 24 (-1.64) (p=0.016). •At the 7,500 µg dose, LYR-210 achieved statistically significant improvement in SNOT-22 score in favor of the treatment arm as measured by the change from baseline at week 8 (-12.2) (p=0.039), week 16 (-15.0) (p=0.008), week 20 (-18.4) (p=0.001) and week 24 (-19.0) (p=0.001). •Although a strong treatment effect was observed at week 4, LYR-210 did not achieve the primary endpoint of change from baseline in 4CSS at week 4 at either the 7,500 µg dose (-0.36) (p=0.306) or 2,500 µg dose (0.04) (p=0.525). We believe this was due primarily to the discontinuation of enrollment related to the COVID-19 global pandemic.
PK Characterization Study	Initiated September 2020	•Up to 24 patients in the United States with bilateral 2,500 µg or 7,500 µg dose	•Certain additional pharmacokinetic timepoints, safety, SNOT-22	•Enrollment complete and all patients completed all study visits; study data lock and analysis expected in second quarter of 2021

Phase 2

Our Phase 2 LANTERN clinical trial for LYR-210 was initiated in May 2019. The clinical trial was designed as a multi-center, randomized, controlled, patient blinded trial. The study was designed to enroll 99 evaluable patients with the option to expand to up to 150 patients at up to 30 sites in the United States, Australia, Austria, Czech Republic, New Zealand, and Poland. Due to the COVID-19 pandemic, we discontinued enrollment at 67 patients and did not open any sites in the United States.

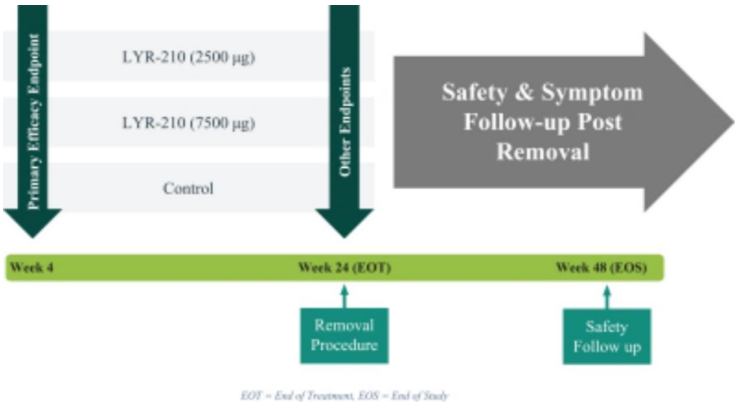


Figure 5. Design of Phase 2 LANTERN Clinical Trial for LYR-210.

The trial consisted of three arms with a 1:1:1 randomization: (1) an experimental arm with bilateral placement of 2,500 µg of LYR-210, with 23 patients; (2) an experimental arm with bilateral placement of 7,500 µg of LYR-210, with 21 patients; and (3) a control arm with a bilateral sham procedure only, with 23 patients (see Figure 5, above). In addition, subjects were supplied with saline for daily nasal irrigation treatment during the course of the treatment period and were permitted to use rescue medication if deemed medically necessary by their physician.

The primary endpoint of the trial was a change from baseline in the 7-day average scores of the 4CSS at week 4. Because the FDA prefers a composite score of the cardinal symptoms of CRS for patients with CRS, we utilized the 4CSS for the trial. The 4CSS is comprised of four domains that are scored 0-3 with a total score of 12. The four domains are: (1) nasal obstruction and congestion; (2) facial pain and pressure; (3) nasal discharge; and (4) olfactory loss (loss of sense of smell).

The key secondary endpoints for the trial were the change from baseline in 7-day average 4CSS at week 24, time to treatment failure, and percentage of subjects with at least 1-point decrease in the bilateral Zinreich score (a measure of inflammation) in at least 1 pair of the anterior ethmoid, maxillary, posterior ethmoid, frontal, or sphenoid sinuses at Week 24.

On December 7, 2020, we reported positive top-line results from our Phase 2 LANTERN clinical trial. In our readout of top-line results, we reported that, at the 7,500 µg dose, LYR-210 achieved statistically significant improvement in 4CSS in favor of the treatment arm as measured by the change from baseline at week 16 (-1.47) (p=0.021), week 20 (-1.61) (p=0.012), and week 24 (-1.64) (p=0.016) (see Figure 6, below). However, although a strong treatment effect was observed at week 4, LYR-210 did not achieve the primary endpoint of change from baseline in 4CSS at week 4 at either the 7,500 µg dose (-0.36) (p=0.306) or 2,500 µg dose (0.04) (p=0.525). We believe this was due primarily to the discontinuation of enrollment related to the COVID-19 pandemic. As a result of the decrease in the number of patients enrolled from planned (99 evaluable) to actually enrolled (67), a greater magnitude of change from baseline in 4CSS at week 4 and/or a smaller standard deviation associated with the change from baseline at week 4 was required in order to achieve statistical significance for the primary endpoint.

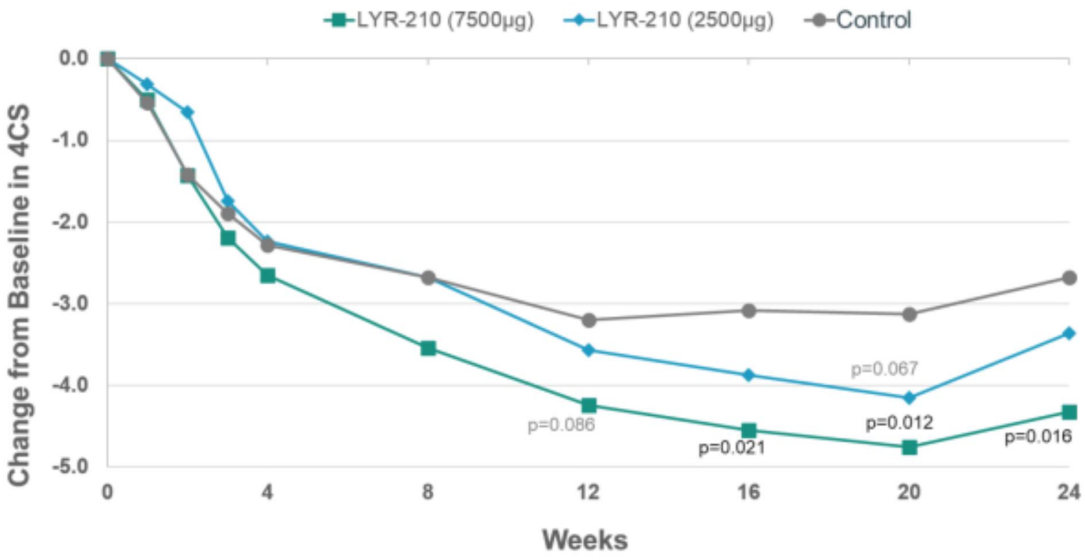


Figure 6. Total Symptom Improvement by 4CSS for Phase 2 LANTERN Clinical Trial.

Furthermore, the 7,500 µg dose of LYR-210 achieved statistically significant improvement in SNOT-22 score in favor of the treatment arm as measured by the change from baseline at week 8 (-12.2) (p=0.039), week 16 (-15.0) (p=0.008), week 20 (-18.4) (p=0.001), and week 24 (-19.0) (p=0.001) (see Figure 7, below). In particular, the improvement of the 7,500 µg dose of LYR-210 at week 24 over the control group (-19.0) was over two times the minimal clinically important difference of -8.9.

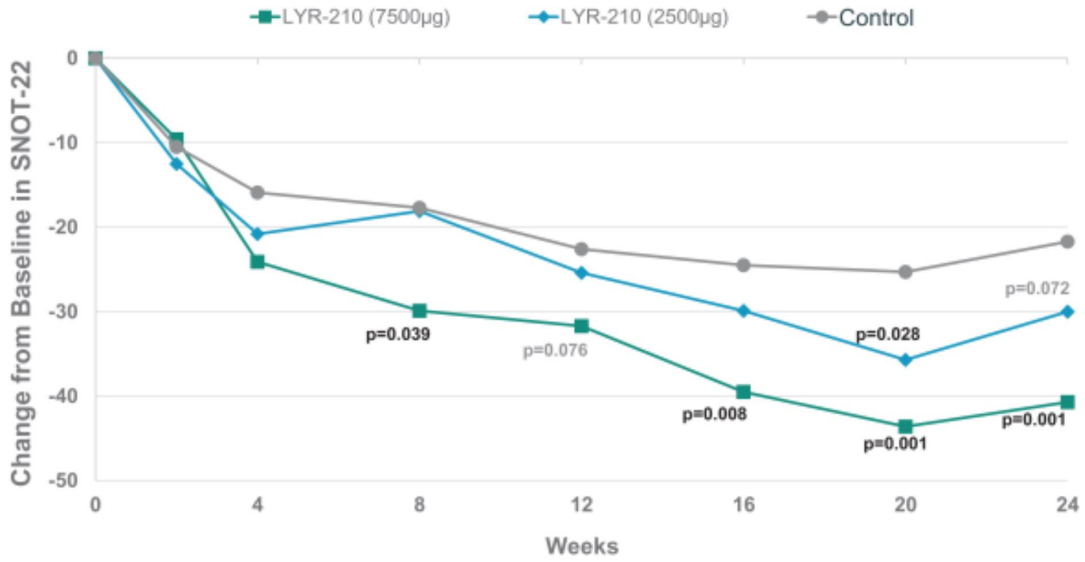


Figure 7. Total Symptom Improvement by SNOT-22 for Phase 2 LANTERN Clinical Trial.

LYR-210 was observed to be safe and well-tolerated at all doses in the trial. There was one serious adverse event, which was deemed to be unrelated to LYR-210. No treatment-related serious adverse events were reported. Treatment-related adverse events included epistaxis, rhinitis, rhinorrhea, and headache. All treatment-related adverse events were generally mild to moderate in nature, other than one incident of increased viscosity of upper respiratory secretion in the 2,500 µg dose treatment arm, and in line with the known safety profile of MF.

We intend to submit full results from our Phase 2 LANTERN study for future presentation at a scientific meeting. Given the comparable safety profile of LYR-210 at both 2,500 µg and 7,500 µg doses, we anticipate progressing the LYR-210 program at the 7,500 µg dose level, and plan to initiate a pivotal Phase 3 study for LYR-210 in CRS for both non-polyp and polyp patients following an end of Phase 2 meeting with the FDA which we anticipate will take place in mid-2021.

In addition, because of developments relating to the COVID-19 pandemic, we discontinued enrollment at 67 patients in our Phase 2 LANTERN clinical trial and did not enroll any patients in the United States as planned. Although we collected certain pharmacokinetic data from all patients starting at week 4, we had planned (consistent with the existing protocol for the Phase 2 LANTERN clinical trial) to utilize a subset of these U.S. patients to collect certain additional pharmacokinetic data in order to support the NDA for LYR-210. Our protocol contemplated obtaining these additional data in only a subset of the total patients both because of the additional burden required from patients in doing so, including requiring patients to make additional site visits for blood draws, and because only a subset of patients is required in order to measure these additional pharmacokinetic endpoints.

Because we were unable to enroll patients in the United States and collect these additional pharmacokinetic data in the Phase 2 LANTERN clinical trial, in September 2020, we initiated a separate characterization study in the United States to collect these additional data. The characterization study is designed as an open-label study with enrollment of up to 24 patients at multiple sites in the United States. The purpose of the study is to collect pharmacokinetic data for LYR-210 over a 56-day treatment period at several timepoints after dosing, including at one hour, day 2 or 3, day 7, day 14, day 21, day 28, day 42, and day 56. We will also monitor safety and collect SNOT-22 scores as secondary endpoints. Unlike our Phase 2 LANTERN clinical trial, patient eligibility is not limited to adult surgically-naïve CRS patients who have failed medical management and have moderate-to-severe CRS symptoms, and there is no overlap in patients between our Phase 2 LANTERN clinical trial and this characterization study. The study will consist of two arms: one arm with bilateral placement of 2,500 µg of LYR-210 and one arm with bilateral placement of 7,500 µg of LYR-210, which are the same dosages evaluated in the Phase 2 LANTERN clinical trial. This study is fully enrolled and all 24 patients have completed the study-required visits. We expect data lock and analysis activities to be completed by the second quarter of 2021.

Phase 1

Our Phase 1 clinical trial for LYR-210 was a prospective, multi-center, non-randomized, single-arm, open-label clinical trial with adult surgically-naïve CRS patients who have failed medical management. The objective of the trial was to evaluate safety and feasibility over 24 weeks of continuous anti-inflammatory treatment with a single administration of LYR-210 with an additional measurement taken one week post-removal. The trial was conducted across five sites in New Zealand and Australia. Forty LYR-210 matrices were placed bilaterally in 20 patients with and without nasal polyps. Each matrix contained 2,500 µg of MF. LYR-210 met its primary safety endpoint, and significant and rapid, clinically meaningful and durable improvement on a patient symptom severity scale was observed through 25 weeks.

Study Design	Prospective, multi-center, non-randomized, single-arm, open-label clinical trial	
Study Objectives	Safety and feasibility over 24 weeks of continuous anti-inflammatory treatment with a single administration of LYR-210 with an additional measurement taken one week post-removal	
Patient Population	Adult CRS patients who have failed medical management and have not had surgery	
Number of Subjects	20 patients with CRS (40 LYR-210 matrices placed)	
Number of Sites	5 study sites (New Zealand and Australia)	
Dose	2,500 mcg bilaterally	
Primary Endpoint	Product-related serious adverse events from baseline to week 4	
Additional Data Collected	•Morning serum cortisol •Intraocular pressure •Plasma pharmacokinetics	•Quality of life by SNOT-22 •Endoscopy and MRI

Figure 8. Description of Phase 1 Clinical Trial for LYR-210.

Twenty patients were enrolled, 12 of whom exhibited no bilateral nasal polyps and eight of whom exhibited bilateral nasal polyps. All 20 patients received bilateral administration of LYR-210 at 2,500 µg in an office setting. The study population was predominantly male with a mean age of 39.9 (range: 24-67) years old. All patients reported moderate-to-severe CRS symptoms with a mean SNOT-22 score of 50.9, of which nine patients reported severe symptoms (SNOT-22 score > 50). All patients complained of nasal obstruction.

The Phase 1 trial achieved its primary safety endpoint at week 4. LYR-210 at 2,500 µg was well tolerated by patients during the entire duration of treatment and also gave insight into the successful office-based placement of the matrix and clinical outcomes in non-polyp and polyp patients. There were no reports of unexpected adverse events, or AEs, or local nasal AEs, including epistaxis, nasal burning, nasal dryness, nasal irritation, and nasal septal perforation during the 24-week MF local dosing treatment duration. Additionally, no change in morning serum cortisol levels or intraocular pressures were noted.

Event[1] Systemic Organ Class	Number of Patients with Event over full 25-week period[2]
All Adverse Events	**16**
Common AE (> 1 Patient)	
General disorders and administration site conditions	
Facial pain	2
Infections and infestations	
Nasopharyngitis	7
Sinusitis	4
Upper respiratory tract infection	5
Injury, poisoning and procedural complications	
Procedural headache	2
Respiratory, thoracic and mediastinal disorders	
Nasal discomfort	2
Nasal odor	4
All Serious Adverse Events	
Cardiac disorders	
Acute Myocardial Infarction	1

(1) AEs coded using the MedDRA dictionary, version 21.0.

(2) N=20 total patients. Patients experiencing the same AEs are counted only once. An additional 5 AEs occurred during the screening period, prior to treatment and are not included in this table. 25-week period includes one week post-removal.

Figure 9. Adverse Event Profile for Phase 1 Clinical Trial for LYR-210.

The most common reported AEs were nasopharyngitis, upper respiratory tract infection, sinusitis, nasal odor, procedural headache, nasal discomfort, and facial pain. There was one serious adverse event, an acute myocardial infarction, which was deemed to be unrelated to LYR-210. LYR-210 was removed due to AEs before the end of the 24-week treatment period from two patients who dropped out of the trial prior to completion. One patient requested removal after 20 weeks of treatment due to complaints of memory loss, which was deemed to be unrelated to LYR-210. The other patient requested removal after 17 weeks of treatment due to a recurrence of a sinus infection that was non-serious and moderate in severity and the patient reported relief of AE symptoms within four days following removal and medical treatment.

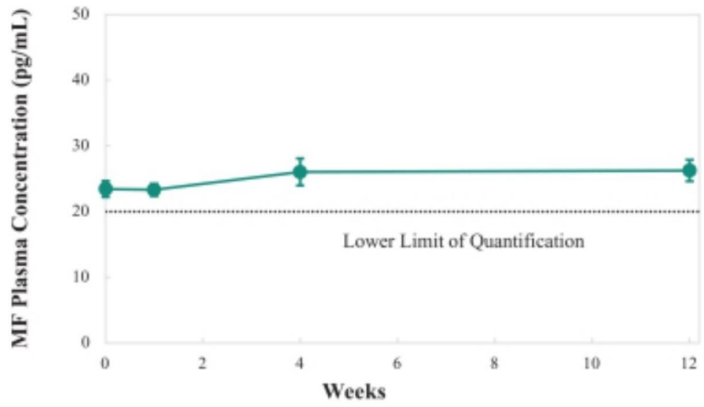
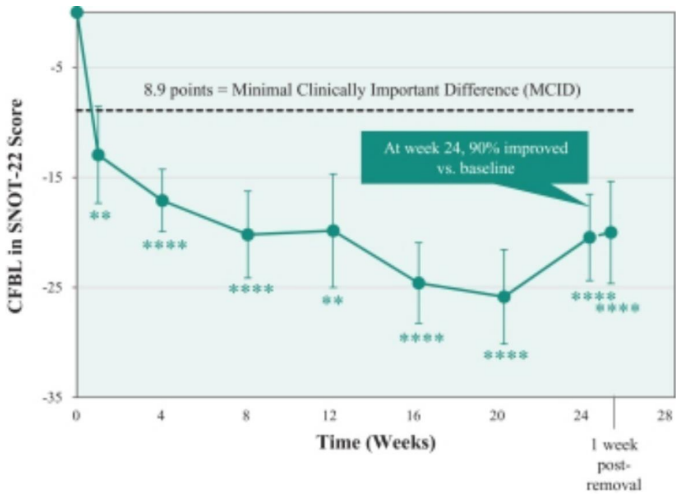


Figure 10. Plasma Drug Concentration for the 50% of Patients with Levels Above LLQ. Note: at day 1, week 1, week 4, and week 12, there were 11, 10, 16, and 10 patients, respectively, whose plasma drug concentration was below the lower limit of quantification, or LLQ.

The trial results indicated low levels of systemically circulated steroid from LYR-210. MF plasma concentrations were unquantifiable in about 50% of patients and near the lower limit of quantification of 20 pg/ML in the other 50% of patients (see Figure 10, above). There were no AEs associated with systemic levels of MF.

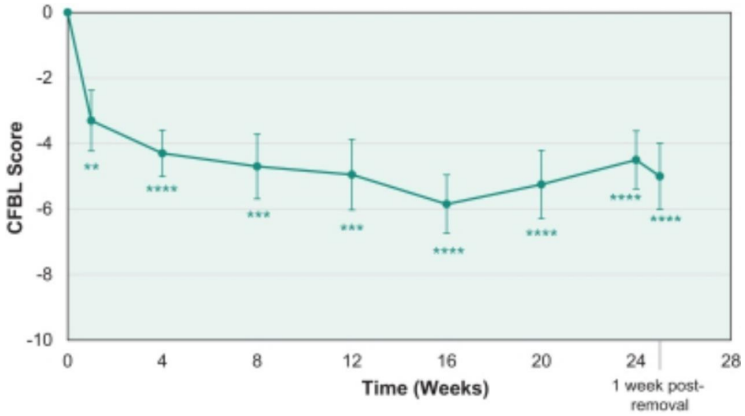
All of the matrices were successfully bilaterally placed in the sinonasal passages, in both non-polyp and polyp patients. In 7 out of the 40 matrices placed, the investigator felt that the initial placement was not ideal, and therefore the matrix was removed and a new matrix was placed. Patients did not report feeling the matrices post-administration. Further, LYR-210 had high levels of intranasal retention out to 24 weeks, with a retention rate of more than 80%. There were no AEs associated with the matrices that were dislodged.

The Sino-Nasal Outcome Test, or SNOT-22, is a disease-specific questionnaire for sinus disease. A validated patient-reported outcome measure, the SNOT-22 is used widely by ENTs to assess disease status and treatment outcomes in CRS patients with and without polyps. It is comprised of 20 questions which address CRS-related symptoms and quality of life that can be grouped into 5 domains including rhinologic, extranasal rhinologic, ear/facial, psychological, and sleep. Each question is scored on a scale from 0 to 5 for a total score ranging from 0 to 110 points. Mild disease is defined on the SNOT-22 as a score of 8 to 20, moderate as a score of 21 to 50, and severe as greater than 50. If a patient has a SNOT-22 score of 7 or lower they are considered “normal” or absent of sino-nasal disease. The SNOT-22 minimal clinically important difference, or MCID, which is the smallest change in SNOT-22 score that can be detected by a patient, has been established as a change of 8.9 points.



** P<0.05, **P<0.01, *** P<0.001, **** P<0.0001 to baseline by paired two tailed t-test*

Figure 11. Total Symptom Improvement by SNOT-22 Score in Phase 1 Clinical Trial for LYR-210.



** P<0.01, ***P<0.001, **** P<0.0001 to baseline by paired two tailed t-test

Figure 12. Symptom Improvement by Retrospective Analysis of the Scores Corresponding to the Composite 4CSS Extracted from the Corresponding Individual SNOT-22 Scores. This composite score produced as a result of the retrospective analysis was not an endpoint of our Phase 1 clinical trial or addressed in our statistical analysis plan and was done for illustrative purposes only.

Patients generally experienced significant and rapid, clinically meaningful and durable improvements in CRS symptoms in the Phase 1 trial, as measured by SNOT-22 score (see Figure 11, above). Significant reduction in SNOT-22 scores was observed at week 1 and this reduction persisted through week 25, the end of the trial (see Figure 11, above). Changes from baseline, or CFBL, in SNOT-22 score were statistically significant ($P < 0.01$) at all measured intervals. The average change from baseline in SNOT-22 score at week 1 was -13.0 points ($P= 0.008$ to pre-treatment), achieving the MCID of -8.9 points. Further, symptom relief was observed through the entire duration of study, and achieved -20.5 points at week

24 ($p < 0.0001$ to pre-treatment), the time LYR-210 was removed. Significant symptom improvement was achieved in all of the SNOT-22 subdomains at week 24. We also conducted a retrospective analysis of symptom improvement, as measured by CFBL, in the individual domain scores extracted from individual SNOT-22 scores that correspond to the cardinal symptoms comprising the 4CSS in order to retrospectively assess the improvement of these cardinal symptoms in these patients (see Figure 12, above). This retrospective analysis showed that the CFBL in the individual domain scores were generally consistent with the CFBL in the SNOT-22 scores. This composite score produced as a result of the retrospective analysis was not an endpoint of our Phase 1 clinical trial or addressed in our statistical analysis plan and was done for illustrative purposes only. Our Phase 2 LANTERN clinical trial used a composite score of 4CSS as its primary endpoint at week 4. However, there are differences related to how the endpoint was calculated compared to the retrospective analysis of the Phase 1 clinical trial data. For example, the wording of the questions in the SNOT-22 questionnaire relating to the four cardinal symptom domains was similar, but not identical, to the wording in the 4CSS questionnaire used in our Phase 2 LANTERN clinical trial. In addition, the SNOT-22 questions use a scale of 0 to 5 while the 4CSS questions in our Phase 2 LANTERN clinical trial used a scale of 0 to 3. Finally, the individual SNOT-22 domain scores used in the retrospective analysis were measured every two weeks and were not averaged, while the primary endpoint in our Phase 2 LANTERN clinical trial was the CFBL of the 7-day average scores of 4CSS at week 4.

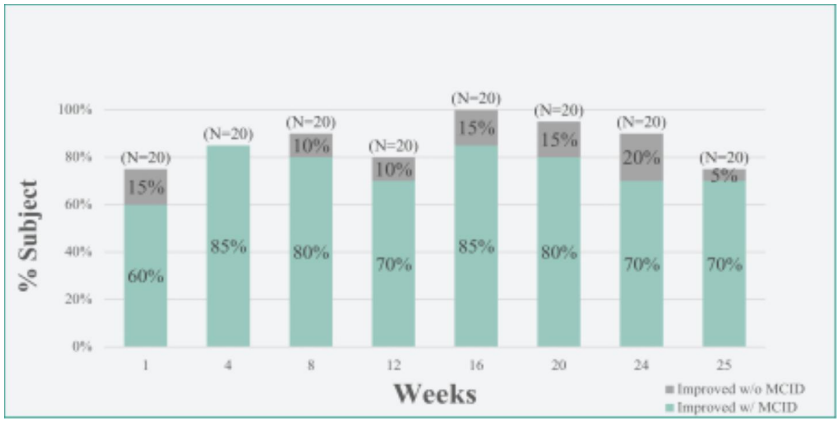
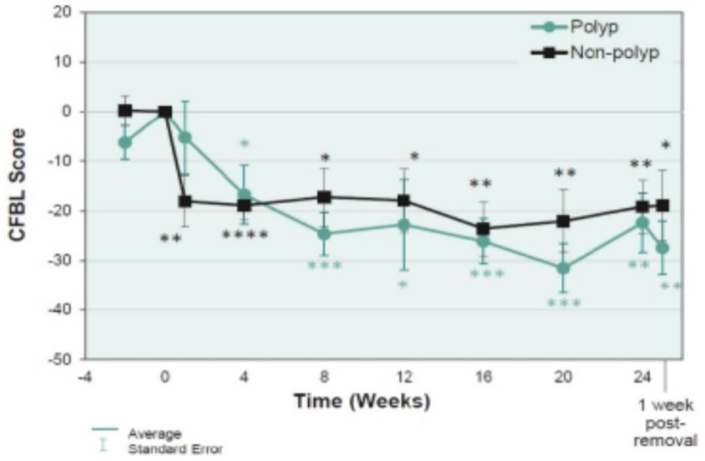


Figure 13. Percent of Patients with Symptom Improvement by SNOT-22 Score, Showing Improvement with MCID and without MCID, in Phase 1 Clinical Trial for LYR-210.

At week 24, 90% of patients improved versus the baseline score, with clinically meaningful improvement observed in 70% of patients (see Figure 13, above).



** P<0.05, **P<0.01, ***P<0.001, **** P<0.0001 to baseline by paired two tailed t-test*

Figure 14. Symptom Improvement in Polyp and Non-Polyp Patients by Change from Baseline in SNOT-22 Score in Phase 1 Clinical Trial for LYR-210.

Similar efficacy was observed in both polyp and non-polyp patients (see Figure 14, above). Further, even though each of the clinical trial patients were surgery candidates at the trial entry and no topical intranasal spray was utilized in conjunction with LYR-210 during the 25-week trial, none of the patients underwent sinus surgery during the treatment period.

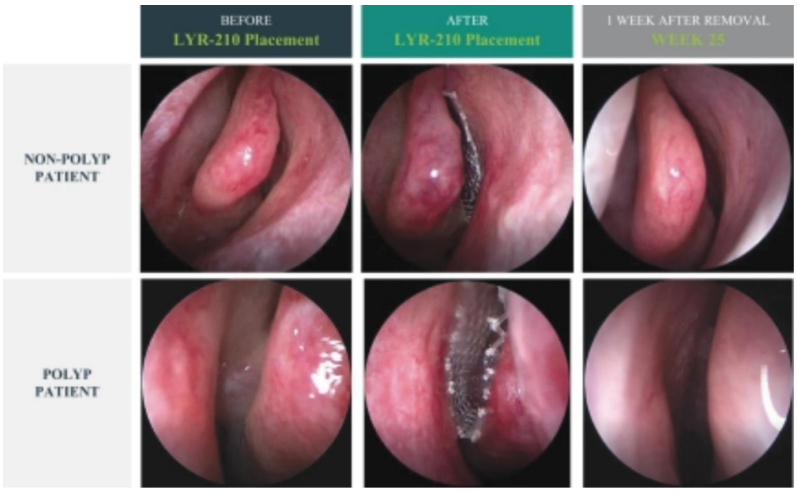


Figure 15. Endoscopy Images Before and After Treatment with LYR-210 in Phase 1 Clinical Trial. For illustrative purposes only.

Figure 15, above, shows via nasal endoscopy images from our Phase 1 clinical trial the impact of LYR-210 observed in a patient without nasal polyps and a patient with nasal polyps at three time points: before LYR-210 placement, after LYR-210 placement, and at week 25, one week after LYR-210 was removed. The middle image for each patient shows the deployment of LYR-210 in the middle meatus of a non-polyp and a polyp patient, and how LYR-210 conformed to the walls of the obstructed nasal anatomy to maximize tissue contact. In the third image for each patient, the erythema and inflammation present before treatment was observed to be resolved and less evident after 24 weeks of treatment and one week post-removal.

LYR-220 for the Treatment of CRS

LYR-220 is a new investigative therapy for CRS patients with and without nasal polyps that have failed medical management and have had a prior endoscopic sinus surgery. In the treatment paradigm, LYR-220, if approved, is positioned for use for patients post-surgical intervention who continue to have recurrent CRS symptoms or relapse, as a potential preferred alternative to revision surgery. LYR-220 utilizes the same API as LYR-210, but with a larger matrix to treat larger nasal cavities consistent with those in post-surgical CRS patients. We estimate that 40% of patients that present to an ENT physician with CRS have had a prior surgery. These patients represent the addressable market for LYR-220.

No product is currently approved by the FDA to treat post-surgery CRS patients that do not have polyps, representing the vast majority of such CRS patients, and only a three-month steroid-eluting sinus implant was approved by the FDA to treat CRS in adults with nasal polyps and two subcutaneously-administered mAbs were recently approved as add-on maintenance therapy for uncontrolled disease in adults with nasal polyps. We believe LYR-220 is meaningfully differentiated from currently approved products because, if successfully developed and approved, it would be the only product able to deliver up to six months of topical treatment in a single administration to treat both polyp and non-polyp post-surgery CRS patients who fail medical management. Further, with respect to the mAb, LYR-220 is differentiated because it would provide localized delivery so as to avoid systemic side effects with the added benefit of being a significantly more economical treatment alternative.

Subject to the impact of COVID-19 on our business, we expect to initiate a Phase 2 clinical trial for LYR-220 by the end of 2021 and, if LYR-210 is approved by the FDA, to submit an sNDA for a potentially faster path to approval for LYR-220. We believe the clinical development of LYR-220 may require only a single Phase 3 study for registration.

Early Stage and Future Product Candidates

Our XTreo platform provides a versatile drug development engine that enables us to focus on indications where long-term delivery of existing treatments may provide improved local bioavailability and enhanced efficacy or safety. In addition to CRS, LYR-210 may have the potential to address the significant unmet need that exists for allergic rhinitis patients who have failed medical management. We believe an allergic rhinitis indication could provide meaningful differentiation in those CRS patients that have allergic rhinitis and additionally could expand the addressable pool of patients for LYR-210 to include allergic rhinitis patients that do not have co-morbid CRS. We are currently evaluating the development path for this additional indication. We may also pursue other nasal delivery applications of our platform, such as rare disorders where nasal disease contributes to the disease pathology and central nervous system disorders. Additionally, we believe our platform can be adapted to locally address conditions of the ear.

Post-Approval Commercialization Strategy

If LYR-210 and LYR-220 are successfully developed and approved, we intend to engage in targeted outreach to our key physician, payor, and patient audiences. ENT physicians are the primary treaters of CRS patients who have failed medical management and thus represent our target physician base. Given the requirement for endoscopic placement of our products, we plan to build an in-house sales force, consisting of approximately 75-100 employees, that will target ENT physicians whose sub-specialty is general otolaryngology or rhinology, which together represent approximately 60% of the approximately 12,000 ENT physicians in the United States. Given that LYR-210 and LYR-220 can be administered in a brief, simple procedure requiring no additional equipment, we anticipate that our sales representatives' time will primarily be directed at educating the ENT physicians around product attributes and patient selection. We plan to supplement our direct physician outreach with appropriate medical education and marketing efforts to further penetrate our physician base and drive adoption of our products.

Ensuring physician and patient market access to our products will be critical to our success, and we plan to execute a holistic reimbursement strategy, consisting of a reimbursement support hub and approximately 15-20 field-based reimbursement experts, that will integrate payor coverage and physician practice management initiatives. We believe that the primary decision makers from a payor perspective are private payors, which represent approximately 80% of the payor mix for our products. We intend to deploy a market access team to educate payors on the clinical and pharmacoeconomic attributes of our products and to seek to secure favorable coverage policies and to maximize the covered lives that have reimbursement for our products. The team will also secure the necessary codes to facilitate physician and patient payment including a J-code, which is required for physician-administered products. In addition, we expect to be able to use existing current procedural terminology codes for procedures involving the placement and removal of our product candidates, if approved. To maximize access to LYR-210 and LYR-220, we plan to develop a reimbursement support model which aims to reduce physician financial risk associated with physician-administered products.

Subsequent to our initial ENT physician and payor efforts, we also plan to selectively use cost-effective, patient-directed marketing strategies to further increase awareness among the CRS patient community of our products with the goal of increasing ENT physician visits.

In addition, we may also consider entering into collaborative relationships with established entities outside the U.S. for a potentially faster path to bringing our products to market. We may also enter into collaborative relationships within the U.S. for future pipeline product candidates.

Competition

Our industry is highly competitive and subject to rapid and significant technological change as research provides a deeper understanding of the pathology of diseases and new technologies and treatments are developed. We believe our scientific knowledge, technology, and development capabilities provide us with substantial competitive advantages, but we face potential competition from multiple sources, including large pharmaceutical, biotechnology, specialty pharmaceutical, and, to a lesser degree, medical device companies.

Our competitors may have significantly greater financial resources, robust drug pipelines, established presence in the market, and expertise in research and development, manufacturing, pre-clinical and clinical testing, obtaining regulatory approvals and reimbursement, and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified clinical, regulatory, scientific, sales, marketing, and management personnel, in establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

LYR-210 and LYR-220 are positioned following the failure of medical management and therefore are not anticipated to compete directly with branded, generic, or over-the-counter inhaled corticosteroids. LYR-210 is positioned for use in surgically-naïve CRS patients where the primary competitive treatment is surgical procedures, including FESS with and without BSD and BSD as a standalone procedure. In this space, LYR-210 would be the only product we are aware of that may deliver six months of local treatment with a single administration for both patients with and without polyps as a preferred alternative to surgical interventions. LYR-220 is positioned for use in patients that have had a prior FESS. Currently there are no competitive treatments for post-surgical patients without polyps. For patients with polyps, LYR-220 would compete against steroid-releasing sinus implants and mAbs. We believe LYR-220 has competitive advantages over these interventions, including a longer elution profile than the existing sinus implant and no systemic exposure relative to the mAb. Key competitive factors affecting the commercial success of both LYR-210 and LYR-220 and any other product candidates we may develop are likely to be efficacy, safety, and tolerability profile, reliability, convenience of administration, price, and reimbursement.

Several companies are also currently developing treatments for CRS patients with nasal polyps, including Hoffmann-La Roche, GlaxoSmithKline, AnaptysBio, Regeneron, OptiNose, and Intersect ENT. If these treatments are approved by the FDA, they could represent competition across the spectrum of CRS patients.

Manufacturing and Supply

We currently manufacture our drug delivery products at our facility in Watertown, Massachusetts with components supplied by external suppliers. We perform inspections of these components before use in our manufacturing operations. Using these components, we manufacture, assemble, inspect, and package our implants, and send them to a third-party sterilization vendor. After sterilization, we inspect the product and test via third-party laboratories to determine compliance with our specifications. Upon release of the lot to inventory, the product is labeled and distributed via a third-party vendor to clinical sites.

The API and a number of the components used in our implants are currently supplied to us from single source suppliers. We source our supplies from manufacturers with a track record of compliance with current good manufacturing practices, or cGMP. We rely on single source suppliers for some of our polymer materials, some extrusions, and molded components, and for finished goods testing, labeling, and distribution. Our ability to supply our products and to develop our product candidates depends, in part, on our ability to obtain successfully the API and polymer materials used in these products in accordance with regulatory requirements and in sufficient quantities. We plan to enter into manufacturing, supply, and quality agreements with our single source suppliers. We generally acquire our single source components pursuant to purchase orders placed in the ordinary course of business. We currently maintain sufficient supplies of the API and components from our single source suppliers to support our ongoing development activities. In the future, we intend to maintain sufficient supplies such that our ability to supply the clinic or commercial market will not be compromised and so as to allow for sufficient time necessary to obtain another source of API or components.

We are currently improving our manufacturing capabilities and increasing capacity to better support further clinical studies and commercialization. We plan to use an outsourcing model and choose a contract manufacturer with the appropriate infrastructure, technical experience, and quality systems and a track record of FDA compliance. We plan to continue to use an outsourcing model for our operations until we reach a sufficient scale to justify investment in internal manufacturing capacity.

Intellectual Property

We actively seek to protect the intellectual property and proprietary technology platform that we believe is important to our business, which includes seeking and maintaining patents covering our technology platform and products, and any other inventions that are commercially or strategically important to the development of our business. We also rely upon trademarks to build and maintain the integrity of our brand, and we seek to protect the confidentiality of trade secrets that may be important to the development of our business. For more information, please see “Risk Factors—Risks Related to Our Intellectual Property”.

Patents and Patent Applications

As of December 31, 2020, we own 23 issued U.S. patents, nine foreign issued patents, eight U.S. pending applications, and 22 foreign pending applications, out of which 16 issued U.S. patents, nine foreign issued patents, eight U.S. pending applications, and 22 foreign pending applications are directed to our XTreo platform, LYR-210, and LYR-220.

All technology material to our business has been developed in-house and is protected with patents and patent applications in two major lineages, along with the beginning of a third, more recent lineage of patent applications. The first lineage dates from 2009 and provides protection potentially until 2030, exclusive of possible patent term adjustments or extensions or other forms of exclusivity. This first lineage includes issued patents in the U.S., Europe, Japan, Canada, and Great Britain that are not limited to any particular drug, site of delivery, or patient condition, but specify features of the implant, system, method, and polymers. The second lineage dates from 2015 and provides protection potentially until 2036, exclusive of possible patent term adjustments or extensions or other forms of exclusivity. This second lineage includes issued U.S. patents with ENT-specific method claims directed to the specific drug, site of delivery (i.e. middle meatus), and patient condition, along with numerous pending applications in the U.S., Europe, Japan, Canada, China, and the Great Britain. The third, more recent lineage dates from 2017 with the prospect of patent protection potentially until 2037, exclusive of possible patent term adjustments or extensions or other forms of exclusivity. This third lineage attempts to capture the drug release features and patient results from the recent clinical trial. It includes pending applications in the U.S. and Great Britain, along with a patent application filed under the Patent Cooperation Treaty that entered the National Phase in October of 2019 in the following countries: the U.S., Canada, Australia, Europe, Korea, Singapore, China, and Japan.

Trademarks and Trade Secrets

As of December 31, 2020, our trademark portfolio contained eight foreign trademark registrations and one pending U.S. trademark application.

We also rely upon trade secrets, know-how, and continuing technologies innovation, and may pursue licensing opportunities in the future, to develop and maintain our competitive position. We seek to protect our proprietary rights through a variety of methods, including confidentiality agreements, invention assignment agreements, and non-solicitation and non-compete agreements with suppliers, employees, consultants, and others who may have access to proprietary information.

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state, and local levels, and in other countries extensively regulate, among other things, the research, development, testing, manufacturing, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, import, and export of pharmaceutical products such as those we are developing. We will be required to navigate the various preclinical, clinical, and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval of our product candidates. The processes for obtaining regulatory approvals in the United States and other countries, as appropriate, along with subsequent compliance with appropriate federal, state, local, and foreign statutes and regulations, require the expenditure of substantial time and resources.

U.S. Government Regulation

In the United States, we are subject to extensive regulation by the FDA, which regulates drugs under the Federal Food, Drug, and Cosmetic Act, or the FDCA, and its implementing regulations, and other federal, state, and local regulatory authorities. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local, and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process, or after approval may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending NDAs, withdrawal of an approval, imposition of a clinical hold, issuance of warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies, and formulation studies in compliance with the FDA's Good Laboratory Practice regulations;

- submission to the FDA of an IND which must become effective before human clinical trials may begin;

- approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practice, or GCP, requirements to establish the safety and efficacy of the proposed drug product for each indication;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with cGMP requirements and to assure that the facilities, methods, and controls are adequate to preserve the drug's identity, strength, quality, and purity;
- satisfactory completion of an FDA inspection of selected clinical sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of user fees; and
- FDA review and approval of the NDA.

We are developing our product candidates using an innovative drug delivery platform comprised of a mesh scaffold, an elastomeric matrix, and a polymer-drug complex delivered through a narrow applicator. In the United States, products composed of components that would normally be regulated by different centers at the FDA are known as combination products. Typically, the FDA's Office of Combination Products assigns a combination product to a specific Agency Center as the lead reviewer. The FDA determines which Center will lead a product's review based upon the product's primary mode of action. Depending on the type of combination product, its approval, clearance, or licensure may usually be obtained through the submission of a single marketing application. We anticipate that LYR-210 and LYR-220 will be regulated as drugs, and for each product candidate, the FDA will permit a single regulatory submission seeking approval. However, the FDA sometimes will require separate marketing applications for individual constituent parts of the combination product which may require additional time, effort, and information. Even when a single marketing application is required for a combination product, such as an NDA for a combination pharmaceutical and device product, both the FDA's Center for Drug Evaluation and Research and the FDA's Center for Devices and Radiological Health may participate in the review. An applicant will also need to discuss with the Agency how to apply certain premarket requirements and post-marketing regulatory requirements, including conduct of clinical trials, adverse event reporting, and cGMPs, to their combination product.

Preclinical Studies

Preclinical studies include laboratory evaluation of product chemistry, toxicity, and formulation, as well as animal studies to assess potential safety and efficacy. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, and any available clinical data or literature, among other things, to the FDA as part of an IND. Some preclinical testing may continue even after the IND is submitted. An IND automatically becomes effective and a clinical trial proposed in the IND may begin 30 days after the FDA receives the IND, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. An IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must continue to oversee the clinical trial while it is being conducted. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on their www.clinicaltrials.gov website.

Human clinical trials are typically conducted in three or four sequential phases, which may overlap or be combined:

- Phase 1: The drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion, and, if possible, to gain an early indication of its effectiveness.

- Phase 2: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases, and to determine dosage tolerance and optimal dosage.

- Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

- Phase 4: In some cases, the FDA may conditionally approve an NDA for a product candidate on the sponsor's agreement to conduct additional clinical trials after NDA approval. In other cases, a sponsor may voluntarily conduct additional clinical trials post approval to gain more information about the drug. Such post-approval trials are typically referred to as Phase 4 clinical trials.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA, and more frequently if serious adverse events occur. Phase 1, Phase 2, and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality, and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

Marketing Approval

Assuming successful completion of the required clinical testing, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls, and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee. Under the Prescription Drug User Fee Act, or PDUFA, guidelines that are currently in effect, the FDA has a goal of 10 months to review and act on a standard NDA and 6 months to review and act on a priority NDA, measured from the "filing" date for an NDA for a new molecular entity, or NME, or from the receipt date for an NDA for a non-NME product. Measuring from the "filing" date typically adds approximately two months to the timeline for review and decision because the FDA has sixty days from receipt to make a "filing" decision, as described below.

In addition, under the Pediatric Research Equity Act of 2003 as amended and reauthorized, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements.

The FDA also may require submission of a risk evaluation and mitigation strategy, or REMS, plan to ensure that the benefits of the drug outweigh its risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged, or held meets standards designed to assure the product's continued safety, quality, and purity.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates, and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP requirements.

The FDA generally accepts data from foreign clinical trials in support of an NDA if the trials were conducted under an IND. If a foreign clinical trial is not conducted under an IND, the FDA nevertheless may accept the data in support of an NDA if the study was conducted in accordance with GCP requirements and the FDA is able to validate the data through an on-site inspection, if deemed necessary. Although the FDA generally requests that marketing applications be supported by some data from domestic clinical studies, the FDA may accept foreign data as the sole basis for marketing approval if (1) the foreign data are applicable to the U.S. population and U.S. medical practice, (2) the studies were performed by clinical investigators with recognized competence, and (3) the data may be considered valid without the need for an on-site inspection or, if the FDA considers the inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means.

The testing and approval process for an NDA requires substantial time, effort, and financial resources, and each may take several years to complete. Data obtained from preclinical and clinical testing are not always conclusive and may be susceptible to varying interpretations, which could delay, limit, or prevent regulatory approval. The FDA may not grant approval on a timely basis, or at all.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met to secure final approval of the NDA and may require additional clinical testing, preclinical testing, manufacturing, or formulation modifications or other changes in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings, or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

The Hatch-Waxman Amendments

Our current regulatory strategy is to pursue development of LYR-210 as a Section 505(b)(2) NDA. As an alternative path to FDA approval for modifications to formulations or uses of drugs previously approved by the FDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA. Section 505(b)(2) was enacted as part of the Hatch-Waxman Amendments. A Section 505(b)(2) NDA is an application that contains full reports of investigations of safety and effectiveness, but where at least some of the information required for approval comes from studies not conducted by, or for, the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. This type of application permits reliance for such approvals on literature or on an FDA finding of safety, effectiveness, or both for an approved drug product. As such, under Section 505(b)(2), the FDA may rely, for approval of an NDA, on data not developed by the applicant. Therefore, if we can satisfy the conditions required for a Section 505(b)(2) NDA submission, it may eliminate the need for us to conduct some of the preclinical studies or clinical trials for the new product candidate that might otherwise have been required, although the review time is not shortened. The FDA may then approve the new product candidate for the new indication sought by the 505(b)(2) applicant.

Orange Book Listing

In seeking approval for a drug through an NDA, applicants are required to list with the FDA certain patents whose claims cover the applicant's product. Upon approval of an NDA, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, known as the Orange Book. Any applicant who files an Abbreviated New Drug Application (ANDA) seeking approval of a generic equivalent version of a drug listed in the Orange Book or a 505(b)(2) NDA referencing a drug listed in the Orange Book must certify, for each patent listed in the Orange Book for the referenced drug, to the FDA that (1) no patent information on the drug product that is the subject of the application has been submitted to the FDA, (2) such patent has expired, (3) the date on which such patent expires, or (4) such patent is invalid or will not be infringed upon by the manufacture, use, or sale of the drug product for which the application is submitted. The fourth certification described above is known as a paragraph IV certification. A notice of the paragraph IV certification must be provided to each owner of the patent that is the subject of the certification and to the holder of the approved NDA to which the ANDA refers. The applicant may also elect to submit a "section viii" statement certifying that its proposed label does not contain (or carves out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent. This section viii statement does not require notice to the patent holder or NDA owner. There might also be no relevant patent certification.

If the reference NDA holder and patent owners assert a patent challenge directed to one of the Orange Book listed patents within 45 days of the receipt of the paragraph IV certification notice, the FDA is prohibited from approving the application until the earlier of 30 months from the receipt of the paragraph IV certification expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the applicant. Even if the 45 days expire, a patent infringement lawsuit can be brought and could delay market entry, but it would not extend the FDA-related 30-month stay of approval.

The ANDA or 505(b)(2) application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the branded reference drug has expired. Specifically, the holder of the NDA for the listed drug may be entitled to a period of non-patent exclusivity, during which the FDA cannot approve an ANDA or 505(b)(2) application that relies on the listed drug. For example, a pharmaceutical manufacturer may obtain five years of non-patent exclusivity upon NDA approval of an NCE, which is a drug that contains an active moiety that has not been approved by FDA in any other NDA. An "active moiety" is defined as the molecule or ion responsible for the drug substance's physiological or pharmacologic action. During the five-year exclusivity period, the FDA cannot accept for filing any ANDA seeking approval of a generic version of that drug or any 505(b)(2) NDA for the same active moiety and that relies on the FDA's findings regarding that drug, except that FDA may accept an application for filing after four years if the follow-on applicant makes a paragraph IV certification. This exclusivity period may be extended by an additional six months if certain requirements are met to qualify the product for pediatric exclusivity, including the receipt of a written request from the FDA that the NDA holder conduct certain pediatric studies, the submission of study reports from such studies to the FDA after receipt of the written request, and satisfaction of the conditions specified in the written request.

Expedited Review and Approval Programs

The FDA has various programs, including Fast Track Designation, accelerated approval, priority review, and breakthrough therapy designation, which are intended to expedite or simplify the process for the development and FDA review of drugs that are intended for the treatment of serious or life threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

To be eligible for a Fast Track Designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. The FDA may review sections of the NDA for a fast track product on a rolling basis before the complete application is submitted if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

The FDA may give a priority review designation to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under current PDUFA guidelines. Under the new PDUFA agreement, these six and ten month review periods are measured from the “filing” date rather than the receipt date for NDAs for new molecular entities, which typically adds approximately two months to the timeline for review and decision from the date of submission. Most products that are eligible for Fast Track Designation are also likely to be considered appropriate to receive a priority review.

In addition, products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may be eligible for accelerated approval and may be approved on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require a sponsor of a drug receiving accelerated approval to perform post-marketing studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the drug may be subject to accelerated withdrawal procedures.

Moreover, under the provisions of the Food and Drug Administration Safety and Innovation Act, a sponsor can request designation of a product candidate as a “breakthrough therapy.” A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are also eligible for accelerated approval. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. We may explore some of these opportunities for our product candidates as appropriate.

Post Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA and other government authorities, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion, and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications, manufacturing changes, or other labeling claims, are subject to prior FDA review and approval. There also are continuing annual program fee requirements for any marketed products.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product’s safety and effectiveness after commercialization.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state authorities, and are subject to periodic unannounced inspections by the FDA and these state authorities for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program.

Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market, or product recalls;
- fines, warning letters, or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label, although physicians, in the practice of medicine, may prescribe approved drugs for unapproved indications. The FDA and other authorities actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Other Healthcare and Data Privacy and Security Laws

Pharmaceutical and medical device manufacturers are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business. Such laws include, without limitation, U.S. federal anti-kickback, fraud and abuse, false claims, consumer fraud, pricing reporting, data privacy and security, and transparency laws and regulations, as well as similar foreign laws in the jurisdictions outside the U.S. Similar state and local laws and regulations may also restrict business practices in the pharmaceutical industry, such as state anti-kickback and false claims laws, which may apply to business practices, including but not limited to, research, distribution, sales, and marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, or by patients themselves; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information or which require tracking gifts and other remuneration and items of value provided to physicians, other healthcare providers, and entities; state and local laws that require the registration of pharmaceutical sales representatives; and state and local laws governing the privacy and security of health-related and other personal information in some circumstances, many of which differ from each other in significant ways and often are not preempted by the Health Insurance Portability and Accountability Act, or HIPAA, thus complicating compliance efforts. Violation of any of such laws or any other governmental regulations that apply may result in penalties, including, without limitation, civil and criminal penalties, damages, fines, additional reporting obligation, the curtailment or restructuring of operations, exclusion from participation in governmental healthcare programs, and individual imprisonment.

Coverage and Reimbursement

Sales of any pharmaceutical product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state, and foreign government healthcare programs, commercial insurance, and managed healthcare organizations, and the level of reimbursement for such product by third-party payors. Significant uncertainty exists as to the coverage and reimbursement status of any newly approved product. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. One third-party payor's decision to cover a particular product does not ensure that other payors will also provide coverage for the product. As a result, the coverage determination process can require manufactures to provide scientific and clinical support for the use of a product to each payor separately and can be a time-consuming process, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization.

In addition, third-party payors are increasingly reducing reimbursements for pharmaceutical products and services. The U.S. government and state legislatures have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement, and requirements for substitution of generic products. Third-party payors are increasingly challenging the prices charged and examining the medical necessity and reviewing the cost effectiveness of pharmaceutical products, in addition to questioning their safety and efficacy. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product.

In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Pharmaceutical products may face competition from lower-priced products in foreign countries that have placed price controls on pharmaceutical products and may also compete with imported foreign products. Furthermore, there is no assurance that a product will be considered medically reasonable and necessary for a specific indication, will be considered cost-effective by third-party payors, that an adequate level of reimbursement will be established even if coverage is available, or that the third-party payors' reimbursement policies will not adversely affect the ability for manufacturers to sell products profitably.

Healthcare Reform

In the United States and certain foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system. In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, was signed into law, which substantially changed the way healthcare is financed by both governmental and private insurers in the United States. By way of example, the ACA increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs from 15.1% to 23.1%; required collection of rebates for drugs paid by Medicaid managed care organizations; imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell certain "branded prescription drugs" to specified federal government programs; implemented a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected; expanded eligibility criteria for Medicaid programs; created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and established a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. For example, in 2017, Congress enacted the Tax Cuts and Jobs Act, which eliminated the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, or the Texas District Court Judge, ruled that the individual mandate is a critical and inseverable feature of the ACA, and therefore, because it was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. On March 2, 2020, the U.S. Supreme Court granted the petitions for writs of certiorari to review this case, although it is unclear when or how the Supreme Court will rule. It is also unclear how other efforts to challenge, repeal, or replace the ACA will impact the ACA.

Other legislative changes have been proposed and adopted since the ACA was enacted, including aggregate reductions of Medicare payments to providers of 2% per fiscal year and reduced payments to several types of Medicare providers, which will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through December 31, 2020, absent additional congressional action. Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted legislation designed, among other things, to bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical products. Individual states in the United States have also become increasingly active in implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, and marketing cost disclosure and transparency measures and, in some cases, mechanisms to encourage importation from other countries and bulk purchasing. Furthermore, there has been increased interest by third party payors and governmental authorities in reference pricing systems and publication of discounts and list prices.

Employees

As of December 31, 2020, we had 38 full-time employees. None of our employees is represented by a labor union or covered by a collective bargaining agreement. Employee turnover has not had a material impact on our operations. We consider our relationship with our employees to be good.

Corporate Information

We were incorporated under the laws of the state of Delaware in November 2005 under the name WMR Biomedical, Inc. In July 2018, we changed our name to Lyra Therapeutics, Inc. Our principal executive offices are located at 480 Arsenal Way, Watertown, MA 02472 and our telephone number is (617) 393-4600. Our website address is *www.lyratherapeutics.com*. The information contained in, or accessible through, our website does not constitute a part of this Annual Report on Form 10-K. We have included our website address in this Annual Report on Form 10-K solely as an inactive textual reference.

Available Information

Our Internet address is *www.lyratherapeutics.com*. Our Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, including exhibits, proxy and information statements and amendments to those reports filed or furnished pursuant to Sections 13(a), 14, and 15(d) of the Securities Exchange Act of 1934, as amended, are filed with the SEC and are available through the “Investors” portion of our website free of charge as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Information on our website is not part of this Annual Report on Form 10-K or any of our other securities filings unless specifically incorporated herein by reference. Our filings with the SEC may be accessed through the SEC’s website at http://www.sec.gov, which contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. All statements made in any of our securities filings, including all forward-looking statements or information, are made as of the date of the document in which the statement is included, and we do not assume or undertake any obligation to update any of those statements or documents unless we are required to do so by law.

Item 1A. Risk Factors.

You should carefully consider the risks and uncertainties described below and the other information in this Annual Report on Form 10-K before making an investment in our common stock. Our business, financial condition, results of operations, or prospects could be materially and adversely affected if any of these risks occurs, and as a result, the market price of our common stock could decline and you could lose all or part of your investment. This Annual Report on Form 10-K also contains forward-looking statements that involve risks and uncertainties. See "Special Note Regarding Forward-Looking Statements." Our actual results could differ materially and adversely from those anticipated in these forward-looking statements as a result of certain factors, including those set forth below.

Risks Related to Our Financial Position and Need for Additional Capital

We have a limited operating history and a history of escalating operating losses, which may make it difficult to evaluate the prospects for our future viability.

We are a clinical-stage therapeutics company established in November 2005. Our operations to date have been limited to financing and staffing our company, developing our technology, and identifying and developing our product candidates. Our prospects must be considered in light of the uncertainties, risks, expenses, and difficulties frequently encountered by companies in their early stages of operations. We have not yet demonstrated an ability to obtain marketing approval, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing, obtaining marketing approval for, and commercializing CRS treatments.

In addition, we may encounter unforeseen expenses, difficulties, complications, delays, and other known and unknown obstacles. We will eventually need to transition from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

As we continue to build our business, we expect our financial condition and operating results may fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any particular quarterly or annual period as indications of future operating performance.

We have incurred significant losses since inception and expect to incur significant additional losses for the foreseeable future. We may never achieve or maintain profitability.

We have incurred significant operating losses in each year since our inception, including operating losses of approximately $22.1 million and $16.3 million for the fiscal years ended December 31, 2020 and December 31, 2019, respectively. In addition, we have not commercialized any products and have never generated any revenue from product sales. We have devoted almost all of our financial resources to research and development, including our pre-clinical development activities.

In addition, we expect to continue to incur significant additional operating losses for the foreseeable future as we seek to advance product candidates through pre-clinical and clinical development, expand our research and development activities, develop new product candidates, complete pre-clinical studies and clinical trials, seek regulatory approval, and, if we receive FDA approval, commercialize our products. In order to obtain FDA approval of any product candidate, we must submit to the FDA an NDA demonstrating that the product candidate is safe for humans and effective for its intended use. This demonstration requires significant research and animal tests, which are referred to as non-clinical or pre-clinical studies, as well as human tests, which are referred to as clinical trials. Furthermore, the costs of advancing product candidates into each succeeding clinical phase tend to increase substantially over time. The total costs to advance any of our product candidates to marketing approval in even a single jurisdiction would be substantial. Because of the numerous risks and uncertainties associated with ENT disease treatment product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to begin generating revenue from the commercialization of products or achieve or maintain profitability. Our expenses will also increase substantially if and as we:

- continue additional clinical trials of our most advanced product candidate, LYR-210, including the characterization study for LYR-210 initiated in September 2020 to collect pharmacokinetic data and one or more planned pivotal Phase 3 clinical trials of LYR-210;

- advance the development of LYR-220;
- continue to discover and develop additional product candidates;
- establish manufacturing and supply chain capacity sufficient to provide commercial quantities of any product candidates for which we may obtain marketing approval;
- seek regulatory and marketing approvals for product candidates that successfully complete clinical trials, if any;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain regulatory approval in geographies in which we plan to commercialize our products ourselves;
- maintain, expand, and protect our intellectual property portfolio;
- hire additional staff, including clinical, scientific, technical, regulatory, operational, financial, commercial, and support personnel, to execute our business plan;
- add clinical, scientific operational, financial, and management information systems and personnel to support our product development and potential future commercialization efforts, and as to enable us to operate as a public reporting company;
- utilize external vendors for support with respect to research, development, commercialization, regulatory, pharmacovigilance, and other functions;
- acquire or in-license other commercial products, product candidates, and technologies;
- expand internationally;
- make royalty, milestone, or other payments under any future in-license agreements;
- implement additional internal systems and infrastructure; and
- operate as a public company.

Furthermore, our ability to successfully develop, commercialize, and license our products and generate product revenue is subject to substantial additional risks and uncertainties. Each of our product candidates will require additional pre-clinical and/or clinical development, potential regulatory approval in multiple jurisdictions, the securing of manufacturing supply, capacity, and expertise, the use of external vendors, the building of a commercial organization, substantial investment, and significant marketing efforts before we generate any revenue from product sales. As a result, we expect to continue to incur net losses and negative cash flows for the foreseeable future. These net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital.

The amount of future losses and when, if ever, we will achieve profitability are uncertain. We have no products that have generated any commercial revenue, do not expect to generate revenues from the commercial sale of products in the foreseeable future, and might never generate revenues from the sale of products. Our ability to generate revenue and achieve profitability will depend on, among other things, successful completion of the clinical development of our product candidates; obtaining necessary regulatory approvals from the FDA and international regulatory agencies; establishing manufacturing, sales, and market acceptance of our products and marketing infrastructure to commercialize our product candidates for which we obtain approval; and raising sufficient funds to finance our activities. We might not succeed at any of these undertakings. If we are unsuccessful at some or all of these undertakings, our business, prospects, and results of operations may be materially adversely affected.

We will need significant additional funding in order to complete development of and obtain regulatory approval for our product candidates and commercialize our products, if approved. If we are unable to raise capital when needed, we could be forced to delay, reduce, or eliminate our product development programs or commercialization efforts.

We will continue to need additional capital, which we may raise through equity offerings, debt financings, marketing, and distribution arrangements and other collaborations, strategic alliances, and licensing arrangements or other sources. Additional sources of financing might not be available on favorable terms, if at all. If we do not succeed in raising additional funds on acceptable terms, we might be unable to complete planned clinical trials or obtain approval of any of our product candidates from the FDA, or any foreign regulatory authorities, and could be forced to discontinue product development. In addition, attempting to secure additional financing may divert the time and attention of our management from day-to-day activities and harm our product candidate development efforts.

We will require substantial funds to further develop, obtain approval for, and commercialize our product candidates, including LYR-210, for which we plan to commence one or more pivotal Phase 3 clinical trials. We will also require substantial funds to further develop, obtain approval for, and commercialize our other product candidate, LYR-220, which is in pre-clinical development.

Based on our current operating plan, we believe that our current cash and cash equivalents will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into 2023. This estimate is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances could cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more than currently expected because of circumstances beyond our control. Because the length of time and activities associated with successful development of LYR-210 and LYR-220 is highly uncertain, we are unable to estimate the actual funds we will require for development, approval, and any approved marketing and commercialization activities. Our future funding requirements, both near and long-term, will depend on many factors, including, but not limited to:

- the scope and results of our pre-clinical studies and clinical trials, including any unforeseen costs we may incur as a result of pre-clinical study or clinical trial delays due to the COVID-19 pandemic or other causes;
- the timing of, and the costs involved in, obtaining regulatory approvals for LYR-210 and LYR-220;
- the costs and timing of changes in the regulatory environment and enforcement rules;
- the costs and timing in changes in pharmaceutical pricing and reimbursement infrastructure;
- the costs involved in preparing, filing, prosecuting, maintaining, and enforcing patent claims and other patent-related costs, including any litigation costs and the results of such litigation;
- the effect of competing technological and market developments;
- the extent to which we in-license or acquire other products and technologies;
- the cost of establishing sales, marketing, and distribution capabilities for our product candidates in regions where we choose to commercialize our products; and
- the initiation, progress, timing, and results of our commercialization of LYR-210 and LYR-220, if approved for commercial sale.

Depending on our business performance, the economic climate, and market conditions, we may be unable to raise additional funds through any sources. Market volatility resulting from the COVID-19 pandemic or other causes could also adversely impact our ability to access capital as and when needed. If we are unable to obtain adequate funding on a timely basis, we may be required to curtail or discontinue one or more of our development programs for LYR-210 or LYR-220, or to reduce our operations. If we raise additional funds by issuing equity securities, our then-existing stockholders will experience dilution and the terms of any new equity securities may have preference over those of our existing common stock.

Raising additional capital may cause dilution to our stockholders, restrict our operations, or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial revenue, we may finance our cash needs through a combination of equity offerings, debt financings, marketing, and distribution arrangements and other collaborations, strategic alliances, and licensing arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our shareholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our operations and our ability to take specific actions, such as incurring additional debt, making capital expenditures, declaring dividends, redeeming our stock, making certain investments, and engaging in certain merger, consolidation, or asset sale transactions, among other restrictions. If we raise additional funds through collaborations, strategic alliances, or marketing, distribution, or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, future revenue streams, or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce, or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

We have no approved products.

To date, we have no approved product on the market and have generated no product revenues. Unless we receive approval from the FDA or other regulatory authorities for our product candidates, we will not have product revenues. Therefore, for the foreseeable future, we will have to fund all of our operations and capital expenditures from cash on hand and licensing fees and grants, if any.

Our product candidates are in various stages of development.

We are a therapeutics company focused on the development and commercialization of novel integrated drug and drug delivery solutions for the localized treatment of patients with ENT diseases. Our product candidates are at stages of pre-clinical or clinical development, and favorable results in pre-clinical or early-stage clinical trials may not be predictive of success in later clinical trials and may not lead to commercially viable products for any of several reasons. For example, our product candidates may fail to be safe and effective in current or future clinical trials or pre-clinical studies, or we may have inadequate financial or other resources to pursue discovery and development efforts for new product candidates. Our product candidates will require significant additional development, clinical trials, regulatory authorizations, and additional investment by us before they can be commercialized.

Our business is highly dependent on the success of our most advanced product candidate, LYR-210, which will require significant additional clinical testing before we can seek regulatory approval and potentially launch commercial sales. If LYR-210 does not receive regulatory approval or is not successfully commercialized, or is significantly delayed in doing so, our business will be harmed.

A substantial portion of our business and future success depends on our ability to develop, obtain regulatory approval for, and successfully commercialize our most advanced product candidate, LYR-210. We currently have no products that are approved for commercial sale and have not completed the development of any product candidates, and may never be able to develop marketable products. We expect that a substantial portion of our efforts and expenditures over the next few years will be devoted to LYR-210, which will require additional clinical development and potential additional pre-clinical development, management of clinical and medical affairs and manufacturing activities, regulatory approval in multiple jurisdictions, the securing of manufacturing supply, the building of a commercial organization, substantial investment, and significant marketing efforts before we can generate any revenues from any commercial sales. We cannot be certain that LYR-210 will be successful in ongoing or future clinical trials, receive regulatory approval, or be successfully commercialized even if we receive regulatory approval. Even if we receive approval to market LYR-210 from the FDA or other regulatory bodies, we cannot be certain that our product candidates will be successfully commercialized, widely accepted in the marketplace, or more effective than other commercially available alternatives. Nor can we be certain that, if and when approved, the safety and efficacy profile of LYR-210 or our other product candidates will be consistent with the profiles observed in clinical trials.

We advanced LYR-210 through our Phase 2 randomized, controlled, patient blinded LANTERN clinical trial, evaluating the safety and efficacy in surgically-naïve CRS patients who have failed previous medical management. The trial was designed to enroll 99 evaluable patients with the potential to increase to up to 150 patients and was initiated in May 2019 at sites in Australia, Austria, Czech Republic, New Zealand, and Poland. In December 2019, the FDA authorized our investigational new drug application, and, prior to the COVID-19 pandemic, we planned to enroll patients in the United States. However, in light of developments relating to the COVID-19 global pandemic, as described below, we discontinued enrollment at 67 patients in our Phase 2 LANTERN clinical trial and did not enroll any patients in the United States.

On December 7, 2020, we reported top-line results from our Phase 2 LANTERN clinical trial, including that LYR-210 failed to meet the primary endpoint of the trial. We believe this was primarily due to the discontinuation of enrollment related to the COVID-19 pandemic. As a result of the decrease in the number of patients enrolled from planned (99 evaluable) to actually enrolled (67) patients in our Phase 2 LANTERN clinical trial, a greater magnitude of change in composite score of the seven-day average of four cardinal symptoms from baseline at week 4 and/or a smaller standard deviation associated with the change from baseline at week 4 was required in order for the trial to achieve statistical significance for the primary endpoint. There can be no assurance that we will be able to design a Phase 3 clinical trial for LYR-210 with a primary endpoint we desire, and in any event there can be no assurance that we will achieve the primary endpoint or any other endpoints in any Phase 3 clinical trial we commence for LYR-210.

Moreover, while we leveraged remote electronic data collection to enable us to complete the clinical assessments and generate sufficient information in our Phase 2 LANTERN clinical trial to commence designing our Phase 3 clinical trial, there can be no assurance that the COVID-19 pandemic or other delays or disruptions will not hinder our electronic data collection or our ability to collect data or measurements requiring sinus imaging to assess reduction in inflammation and phlebotomy to assess pharmacokinetics/pharmacodynamics. For example, we were unable to enroll patients in our Phase 2 LANTERN clinical trial in the United States from whom we intended to collect certain additional pharmacokinetic data due to the COVID-19 pandemic, and as a result, we initiated a separate characterization study in September 2020, as a follow-on to our Phase 2 LANTERN clinical trial, in order to collect such data. There can be no assurance that this separate study or any future trial we may conduct will not be affected or further affected by the COVID-19 pandemic or other delays and disruptions.

If the required regulatory approvals for LYR-210 are not obtained or are significantly delayed, including as a result of the COVID-19 pandemic, or any approved products are not commercially successful, our business, financial condition, and results of operations may be materially harmed.

LYR-210 is our most advanced product candidate, and if we experience regulatory or developmental issues with respect to LYR-210, our development plans and business could be significantly harmed. Moreover, if we experience similar regulatory or developmental issues with our other pipeline product candidates, our development plans and business could be significantly harmed. Further, our competitors may be developing products with similar mechanisms of action and may experience problems with their products that could identify problems that would potentially harm our business.

We may not be successful in our efforts to identify and successfully commercialize additional product candidates.

Part of our strategy involves identifying novel product candidates. The process by which we identify product candidates may fail to yield product candidates for clinical development for a number of reasons, including those discussed in these risk factors and also:

- we may not be able to assemble sufficient resources to acquire or discover additional product candidates;
- competitors may develop alternatives that render our potential product candidates obsolete or less attractive;
- potential product candidates we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- potential product candidates may, on further study, be shown to have harmful side effects, toxicities, or other characteristics that indicate that they are unlikely to be products that will receive marketing approval or achieve market acceptance;
- potential product candidates may not be effective in treating their targeted diseases or symptoms;

- the market for a potential product candidate may change so that the continued development of that product candidate is no longer reasonable;

- a potential product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; or

- the regulatory pathway for a potential product candidate is highly complex and difficult to navigate successfully or economically.

In addition, we may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful, or to license or purchase a marketed product that does not meet our financial expectations. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases that may later prove to have greater commercial potential, or relinquish valuable rights to such product candidates through collaboration, licensing, or other royalty arrangements in cases in which it would have been advantageous for us to retain sole development and commercialization rights. If we are unable to identify and successfully commercialize additional suitable product candidates, this would adversely impact our business strategy and our financial position.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to timely capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing, or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

Risks Related to Discovery, Development, Clinical Testing, Manufacturing, and Regulatory Approval

Clinical trials required for our product candidates are expensive and time-consuming, their outcome is uncertain, and if our clinical trials do not meet safety or efficacy endpoints in these evaluations, or if we experience significant delays in these trials, our ability to commercialize our product candidates and our financial position will be impaired.

We plan to commence one or more pivotal Phase 3 clinical trials for our most advanced product candidate, LYR-210. Our other product candidate, LYR-220, is in pre-clinical development. It is impossible to predict when or if either of our product candidates will prove effective and safe in humans or if we will receive regulatory approval for any of our product candidates, and the risk of failure through the development process is high. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete pre-clinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans.

Clinical development is a long, expensive, and uncertain process that is subject to significant delays. Due to known or unknown circumstances beyond our control, it may take us several years to complete our testing, and failure can occur at any stage of testing. The outcome of pre-clinical testing and early clinical trials may not be predictive of the results of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. We cannot assure you that any clinical trial that we are conducting, or may conduct in the future, will demonstrate consistent or adequate efficacy and safety to obtain regulatory approval to market our product candidates. Moreover, pre-clinical and clinical data are often susceptible to varying interpretations and analysis, and many companies that have believed their product candidates performed satisfactorily in pre-clinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

Delays associated with products for which we are directly conducting pre-clinical studies or clinical trials may cause us to incur additional operating expenses. The commencement and rate of completion of pre-clinical studies or clinical trials may be delayed by, or terminated because of, many factors, including:

- the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our pre-clinical studies or clinical trials;
- failure to obtain regulatory approval to commence a trial;
- failure to reach, or delays in reaching, an agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- slower than expected rates of recruitment of patients or failure to recruit a sufficient number of patients;
- modification of pre-clinical studies or clinical trial protocols;
- changes in regulatory requirements for pre-clinical studies or clinical trials;
- the impact of unusual placebo effects;
- the lack of effectiveness during pre-clinical studies or clinical trials;
- the emergence of unforeseen safety issues or undesirable side effects;
- failure to obtain institutional review board, or the IRB, approval at each site;
- delays, suspension, or termination of clinical trials by the IRB responsible for overseeing the trial at a particular trial site;
- failure of patients in completing a trial or returning for post-treatment follow-up;
- clinical sites deviating from trial protocol, dropping out of a trial, or failing to comply with regulatory requirements;
- failure to address patient safety concerns that arise during the course of a trial;
- failure to manufacture sufficient quantities of product candidate for use in clinical trials;
- government, IRB, or other regulatory delays or “clinical holds” requiring suspension or termination of the trials; and
- business interruptions resulting from the COVID-19 pandemic.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates or significantly increase the cost of such trials, including:

- we may receive feedback from regulatory authorities that requires us to modify the design of our clinical trials;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon development programs;

- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, or participants may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;

- we may be unable to enroll a sufficient number of patients in our clinical trials to ensure adequate statistical power to detect any statistically significant treatment effects;

- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;

- regulators, IRBs, or independent ethics committees, or IECs, may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site or may require that we or our investigators suspend or terminate clinical trials of our product candidates for various reasons, including non-compliance with regulatory requirements, a finding that our product candidates have undesirable side effects or other unexpected characteristics, or a finding that the participants are being exposed to unacceptable health risks;

- we may experience delays in reaching or fail to reach agreement on acceptable pre-clinical study or clinical trial contracts or pre-clinical study or clinical trial protocols with prospective trial sites;

- the cost of pre-clinical studies or clinical trials of our product candidates may be greater than we anticipate and we may not have funds to cover the costs;

- the supply or quality of our product candidates or other materials necessary to conduct pre-clinical studies or clinical trials of our product candidates may be insufficient or inadequate;

- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate; and

- any current or future collaborators that conduct pre-clinical studies or clinical trials may face any of the above issues, and may conduct pre-clinical studies or clinical trials in ways they view as advantageous to them but that are suboptimal for us.

If we are required to extend the duration of current pre-clinical studies or clinical trials or to conduct additional pre-clinical studies or clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete pre-clinical studies or clinical trials of our product candidates or other testing, if the results of these trials, studies, or tests are not positive or are only modestly positive, if there are safety concerns, or if we determine that the observed safety or efficacy profile would not be competitive in the marketplace, we may:

- incur unplanned costs;

- be delayed in obtaining marketing approval for our product candidates or not obtain marketing approval at all;

- obtain marketing approval in some countries and not in others;

- obtain marketing approval for indications or patient populations that are not as broad as intended or desired;

- obtain marketing approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;

- be subject to additional post-marketing testing requirements; or

- have the product removed from the market after obtaining marketing approval.

We could encounter delays if a clinical trial is materially modified, suspended, or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board, or DSMB, for such trial, or by the FDA or other regulatory authorities. Such authorities may impose a material modification, suspension, or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects for our product candidates, or other products or product candidates in the same drug class, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions, or lack of adequate funding to continue the clinical trial. Furthermore, we may rely on CROs and clinical trial sites to ensure the proper and timely conduct of clinical trials and while we would have agreements governing their committed activities, we would have limited influence over their actual performance, as described in "—Risks Related to Our Dependence on Third Parties."

Our most advanced product candidate, LYR-210, is in clinical development and will require the completion of clinical testing before we are prepared to submit an NDA for regulatory approval. Further, there can be no assurance that the separate clinical trial initiated in September 2020 to collect pharmacokinetic data will not experience delays that impact this timeline. We cannot predict if or when we might complete the development of LYR-210 and submit an NDA or whether any such NDA will be approved by the FDA. We may also seek feedback from the FDA or other regulatory authorities on our clinical development programs, and the FDA or such regulatory authorities may not provide such feedback on a timely basis, or such feedback may not be favorable, which could further delay our development programs. If the results of ongoing and future clinical trials for LYR-210 are positive, we plan to submit an NDA in the United States. However, no assurance can be given that we will be successful in the near term, obtain regulatory approval, or have any commercial sales of LYR-210.

Any clinical test may fail to produce results satisfactory to the FDA or foreign regulatory authorities. For example, our Phase 2 LANTERN clinical study for LYR-210 did not meet its primary endpoint and the FDA may not find such result to be sufficient to advance to a Phase 3 pivotal study. Pre-clinical and clinical data can be interpreted in different ways by different reviewers and regulators, which could delay, limit, or prevent regulatory approval. Drug-related adverse events during a pre-clinical study or clinical trial could cause us to repeat a trial or study, perform an additional trial or study, expand the size and/or duration of a trial or study, terminate a trial or study, or even cancel a pre-clinical or clinical program. The failure of pre-clinical studies or clinical trials to demonstrate safety and effectiveness for the desired indications could harm the development of that product candidate and other product candidates. This failure could cause us to abandon a product candidate and could delay development of other product candidates. Any delay in, or termination of, our clinical trials would delay the filing of our NDAs with the FDA and, ultimately, our ability to commercialize our product candidates and generate product revenues. A number of companies in the biotechnology and pharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Even if our future and ongoing pre-clinical studies and clinical trials are completed as planned, we cannot be certain that their results will support the safety and effectiveness of LYR-210, LYR-220, and/or any future product candidate.

If we experience delays in the commencement or completion of, or have to extend or expand, our pre-clinical studies or clinical trials, or if we terminate a pre-clinical study or clinical trial prior to completion, the commercial prospects of LYR-210, LYR-220, or any future product candidate could be harmed, and our ability to generate revenues from LYR-210, LYR-220, or any future product candidate may be delayed. In addition, any delays in our pre-clinical studies or clinical trials could increase our costs, slow down the development and approval process, and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may harm our business, financial condition, and results of operations. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of pre-clinical studies or clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

Our pre-clinical studies and clinical trials may fail to demonstrate adequately the safety and efficacy of any of our product candidates and the development of our product candidates may be delayed or unsuccessful, which could prevent or delay regulatory approval and commercialization.

Both of our current product candidates are in clinical or pre-clinical development stages. Notwithstanding the data obtained to date with respect to LYR-210 and LYR-220 in CRS, LYR-210 and LYR-220 will require additional clinical and non-clinical development, regulatory review and approval in multiple jurisdictions, substantial investment, access to sufficient commercial manufacturing capacity, and significant marketing efforts before we can generate any revenue from our product sales. In addition, if we encounter safety or efficacy problems, developmental delays or regulatory issues, delays caused by the COVID-19 pandemic, or other problems, our developmental plans and business could be significantly harmed. For example, our Phase 2 LANTERN clinical trial for LYR-210 failed to meet its primary endpoint which may delay our overall commercialization efforts.

If the development of LYR-210, LYR-220, or any other future product candidate is unsuccessful, our ability to generate revenues will be adversely affected. Our development of current and future product candidates is subject to the risks of failure and delay inherent in the development of new products and product candidates, including:

- delays in product development, pre-clinical, or clinical testing or manufacturing;
- unplanned expenditures in product development, pre-clinical, or clinical testing or manufacturing;
- failure to receive regulatory approvals;
- failure to secure rights from third parties for new technology;
- failure to achieve market acceptance; and
- emergence of superior or equivalent products.

In addition, product candidates in later stages of clinical trials may fail to show the desired safety profiles and efficacy results despite having progressed through pre-clinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Based upon negative or inconclusive results, we may decide, or regulators may require us, to conduct additional clinical trials or pre-clinical studies. In addition, data obtained from trials and studies are susceptible to varying interpretations, and regulators may not interpret our data as favorably as we do, which may delay, limit, or prevent regulatory approval.

Additionally, we have not conducted, nor do we believe we are required to conduct, any head-to-head trials comparing LYR-210 to other approved or experimental treatments for CRS. Any such head-to-head trial, if conducted, may show that LYR-210 is not more effective than any of such other drugs. Material adverse differences in the relative efficacy of LYR-210 could significantly harm the adoption of LYR-210 and our business prospects.

Because of these risks, our research and development efforts may not result in any commercially viable products. If a significant portion of these development efforts are not successfully completed, required regulatory approvals are not obtained, or any approved products are not commercially successful, our business, financial condition, and results of operations may be materially harmed.

Success in pre-clinical or earlier clinical trials may not be indicative of results in future clinical trials.

Success in pre-clinical studies and early clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidate. Pre-clinical studies and Phase 1 and Phase 2 clinical trials are primarily designed to test safety, study pharmacokinetics and pharmacodynamics, and understand the side effects of product candidates at various doses and schedules. Success in pre-clinical studies and early clinical trials does not ensure that later, large-scale efficacy trials will be successful nor does it predict final results. Our product candidates may fail to show the desired safety and efficacy in clinical development despite positive results in pre-clinical studies or having successfully advanced through initial clinical trials. For example, our Phase 2 LANTERN clinical trial for LYR-210 failed to meet its primary endpoint and we may be required to conduct additional trials to evaluate the efficacy of this product candidate beyond those trials we currently anticipate.

In addition, the design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. As an organization, we have limited experience designing clinical trials and may be unable to design and execute a clinical trial to support regulatory approval. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in pre-clinical studies and earlier-stage clinical trials. Data obtained from pre-clinical and clinical activities are subject to varying interpretations, which may delay, limit, or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including changes in regulatory policy during the period of our product candidate development. Any such delays could negatively impact our business, financial condition, results of operations, and prospects.

If the FDA does not conclude that certain of our product candidates satisfy the requirements for the Section 505(b)(2) regulatory approval pathway, or if the requirements for such product candidates under Section 505(b)(2) are not as we expect, the approval pathway for those product candidates may likely take significantly longer, cost significantly more, and entail significantly greater complications and risks than anticipated, and in either case may not be successful.

We intend to seek FDA approval for our current product candidates, LYR-210 and LYR-220, and we may seek FDA approval for future product candidates, through the Section 505(b)(2) regulatory pathway. The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Amendments, added Section 505(b)(2) to the Federal Food, Drug and Cosmetic Act, or FDCA. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from trials that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference. Section 505(b)(2), if applicable to us under the FDCA, would allow an NDA we submit to the FDA to rely in part on data in the public domain or the FDA's prior conclusions regarding the safety and effectiveness of approved drugs, which could expedite the development program for our product candidates by potentially decreasing the amount of clinical data that we would need to generate in order to obtain FDA approval. If the FDA does not allow us to pursue the Section 505(b)(2) regulatory pathway as we anticipate, we may need to conduct additional clinical trials, provide additional data and information, and meet additional standards for regulatory approval. If this were to occur, the time and financial resources required to obtain FDA approval for our product candidates, and complications and risks associated with the development of our product candidates, would likely substantially increase. Moreover, inability to pursue the Section 505(b)(2) regulatory pathway could result in competitive products reaching the market before our product candidates, which could impact our competitive position and prospects. Even if we are allowed to pursue the Section 505(b)(2) regulatory pathway, we cannot assure you that our product candidates will receive the requisite approvals for commercialization, or that a competitor would not obtain approval first along with subsequent market exclusivity from the FDA, thereby delaying potential approval of our product.

In addition, the pharmaceutical industry is highly competitive, and Section 505(b)(2) NDAs are subject to special requirements designed to protect the patent rights of sponsors of previously approved drugs that are referenced in a Section 505(b)(2) NDA. These requirements may give rise to patent litigation and mandatory delays in approval of our NDAs for up to 30 months or longer depending on the outcome of any litigation. It is not uncommon for a manufacturer of an approved product to file a citizen petition with the FDA seeking to delay approval of, or impose additional approval requirements for, pending competing products. If successful, such petitions can significantly delay, or even prevent, the approval of the new product. However, even if the FDA ultimately denies such a petition, the FDA may substantially delay approval while it considers and responds to the petition. In addition, even if we are able to utilize the Section 505(b)(2) regulatory pathway, there is no guarantee this would ultimately lead to accelerated product development or earlier approval.

Moreover, even if our product candidates are approved under Section 505(b)(2), the approval may be subject to limitations on the indicated uses for which the products may be marketed or to other conditions of approval, or may contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the products.

We have conducted, are conducting, and, in the future, may conduct clinical trials for our product candidates in sites outside the United States, and the FDA may not accept data from trials conducted in foreign locations.

We have conducted and are conducting clinical trials for LYR-210 outside the United States, specifically in Australia, Austria, Czech Republic, New Zealand, and Poland, and we may in the future choose to conduct other clinical trials outside the United States for LYR-210, LYR-220, or any of our other future product candidates. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of this data is subject to certain conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with good clinical practice, or GCP, including review and approval by an IEC and receipt of informed consent from subjects. In general, the patient population for any clinical trials conducted outside of the United States must be representative of the population for which we intend to seek approval for the product in the United States. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will be dependent upon its determination that the trials also complied with all applicable U.S. laws and regulations. There can be no assurance the FDA will accept data from trials conducted outside of the United States. If the FDA does not accept the data from our clinical trials of our product candidates, it would likely result in the need for additional trials, which would be costly and time-consuming and delay or permanently halt our development of our product candidates.

In addition, there are risks inherent in conducting clinical trials in multiple jurisdictions, inside and outside of the United States, such as:

- regulatory and administrative requirements of the jurisdiction where the trial is conducted that could burden or limit our ability to conduct our clinical trials;
- foreign exchange fluctuations;
- manufacturing, customs, shipment, and storage requirements;
- cultural differences in medical practice and clinical research; and
- the risk that the patient populations in such trials are not considered representative as compared to the patient population in the target markets where approval is being sought.

Interim and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim or preliminary data from our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Interim or preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Differences between interim or preliminary data and final data could significantly harm our business prospects.

LYR-210 and LYR-220 are drug-device combinations, which may result in additional regulatory and other risks.

LYR-210 and LYR-220 are drug-device combination products. We may experience delays in obtaining regulatory approval of these product candidates given the increased complexity of the review process when approval of a drug and a delivery device is sought under a single marketing application. Both LYR-210 and LYR-220 will be regulated as drug-device combination products, which require coordination within the FDA and similar foreign regulatory agencies for review of the product candidates' device and drug components. The determination whether a combination product requires a single marketing application or two separate marketing applications for each component is made by the FDA on a case-by-case basis. Although we believe a single marketing application for the approval of a combination product would be successful, there can be no assurance that the FDA will not determine that separate marketing applications are necessary. This determination could significantly increase the resources and time required to bring a particular combination product to market. Although the FDA and similar foreign regulatory agencies have systems in place for the review and approval of combination products such as ours, we may experience delays in the development and commercialization of our product candidates due to regulatory timing constraints and uncertainties in the product development and approval process, as well as coordination between two different centers within FDA responsible for review of the different components of the combination product.

Failure to successfully develop or supply the device component, delays in or failure of the studies conducted by us, our collaborators, or third-party providers, or failure of our Company, our collaborators, or third-party providers to obtain or maintain regulatory approval or clearance of the device component of LYR-210 or LYR-220, as appropriate, could result in increased development costs, delays in or failure to obtain regulatory approval, and associated delays in these product candidates reaching the market. Further, failure to successfully develop or supply the device, or to gain or maintain its approval, could adversely affect sales of LYR-210 and LYR-220.

If we fail to obtain the necessary U.S. regulatory approvals to commercialize any product candidate, we will not be able to generate revenue in the U.S. market.

We cannot assure you that we will receive the approvals necessary to commercialize our product candidates, or any product candidate we acquire or develop in the future. We will need FDA approval to commercialize our product candidates in the United States and approvals from equivalent regulatory authorities in foreign jurisdictions to commercialize our product candidates in those jurisdictions. Satisfaction of the FDA's regulatory requirements typically takes many years, depends upon the type, complexity, and novelty of the product candidate, and requires substantial resources for research, development, and testing. We cannot predict whether our research and clinical efforts will result in drugs that the FDA will determine are safe for humans and effective for their intended uses. The FDA has substantial discretion in the drug approval process and may require us to conduct additional pre-clinical and clinical testing, perform post-marketing studies, address manufacturing concerns, or otherwise limit or impose conditions on any approval we obtain. The approval process may also be delayed by changes in government regulation, the impact of the COVID-19 pandemic, future legislation or administrative action, or changes in FDA policy that occur prior to or during our regulatory review. Delays in obtaining regulatory approvals may:

- delay commercialization of, and our ability to derive product revenues from, our product candidates;
- impose costly procedures on us; and
- diminish any competitive advantages that we may otherwise enjoy.

Even if we receive approval of an NDA or comparable foreign regulatory filing for our product candidates, the FDA or the applicable foreign regulatory body may approve our product candidates for a more limited indication than we originally requested, and the FDA may not approve the labeling that we believe is necessary or desirable for the successful commercialization of our product candidates.

Even if we comply with all FDA requests, the FDA may ultimately reject one or more of our NDAs. We cannot be sure that we will ever obtain regulatory clearance for our product candidates. Failure to obtain FDA approval of our product candidates will severely undermine our business by leaving us without a commercially available product, and therefore without any source of revenues, until another product candidate can be developed or obtained and ultimately approved. There is no guarantee that we will ever be able to develop or acquire another product candidate or that we will be able to obtain FDA approval to commercialize such product candidate.

Even if we obtain FDA approval for our product candidates in the United States, we may never obtain approval for or commercialize them in any other jurisdiction, which would limit our ability to realize their full market potential.

We intend, either on our own or through collaborations or partnerships, to market our products in international markets. In order to market any products in the European Union and many other foreign jurisdictions, we must establish and comply with numerous and varying regulatory requirements on a country-by-country basis regarding safety and efficacy. Approval by the FDA in the United States does not ensure approval by regulatory authorities in other countries or jurisdictions. However, the failure to obtain approval in one jurisdiction may negatively impact our ability to obtain approval elsewhere. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country.

Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and increased costs for us and require additional pre-clinical studies or clinical trials which could be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. We do not have any product candidates approved for sale in any jurisdiction, including in international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of any product we develop will be unrealized.

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, costly, time-consuming, and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed. We cannot predict when or if, and in which territories, we, or any of our potential future collaborators, will obtain marketing approval to commercialize a product candidate.

The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including substantial discretion of regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate and it is possible that neither LYR-210, LYR-220, nor any future product candidates we may seek to develop in the future will ever obtain regulatory approval. Neither we nor any future collaborator is permitted to market any of our product candidates in the United States until we receive regulatory approval of an NDA from the FDA. It is possible that the FDA may refuse to accept for substantive review any NDAs that we submit for our product candidates or may conclude after review of our data that our application is insufficient to obtain marketing approval of our product candidates.

Prior to obtaining approval to commercialize a product candidate in the United States or abroad, we or our collaborators must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA or foreign regulatory agencies, that such product candidates are safe and effective for their intended uses in patients. Results from non-clinical studies and clinical trials can be interpreted in different ways. Even if we believe the non-clinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. The FDA may also require us to conduct additional pre-clinical studies or clinical trials for our product candidates either prior to or post-approval, or it may object to elements of our clinical development program. Depending on the extent of these or any other FDA-required studies, approval of any NDA or other application that we submit may be delayed by several years, or may require us to expend significantly more resources than we have available.

Of the large number of potential products in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. The lengthy and costly approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, results of operations, and prospects.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authorities may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authorities may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authorities, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

Separately, in response to the COVID-19 pandemic, on March 10, 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities and products through April 2020, and on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, on July 10, 2020, the FDA announced its intention to resume certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA intends to use this risk-based assessment system to identify the categories of regulatory activity that can occur within a given geographic area, ranging from mission critical inspections to resumption of all regulatory activities. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic, including providing guidance regarding the conduct of clinical trials. If global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

If we encounter delays or difficulties enrolling patients in our clinical trials, our clinical development activities and receipt of regulatory approvals could be delayed or otherwise adversely affected.

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. For example, we were unable to enroll patients in our Phase 2 LANTERN clinical trial in the United States from whom we intended to collect certain additional pharmacokinetic data due to the COVID-19 pandemic, and, as a result, we initiated a separate characterization study in September 2020 as a follow-on to our Phase 2 LANTERN clinical trial in order to collect such data. Trials may be subject to delays as a result of patient enrollment taking longer than anticipated or patient withdrawal. We may encounter delays in enrolling, or be unable to enroll, a sufficient number of patients to complete any of our clinical trials, and even once enrolled we may be unable to retain a sufficient number of patients to complete any of our trials. We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. We cannot predict how successful we will be at enrolling subjects in future clinical trials. The enrollment of patients depends on many factors, including:

- the patient eligibility criteria defined in the protocol;
- the size of the patient population required for analysis of the trial's primary endpoints;
- the proximity of patients to trial sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new products that may be approved for the indications we are investigating;
- the perceived risks and benefits of the product candidate in the trial;
- the availability of alternative therapies;
- our ability to obtain and maintain patient consents;
- the risk that patients enrolled in clinical trials will drop out of the trials before completion; and
- the impact of the ongoing COVID-19 pandemic.

In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials in such clinical trial site.

Delays or failures in planned patient enrollment or retention may result in increased costs, program delays, or both, which could have a harmful effect on our ability to develop LYR-210, LYR-220, and/or any other future product candidates, or could render further development impossible.

Our product candidates may cause serious adverse events or undesirable side effects including injury and death or have other properties which may delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval. If any of our product candidates receives marketing approval and we, or others, later discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, our ability, or that of any potential future collaborators, to market the drug could be compromised.

Before obtaining regulatory approvals for the commercial sale of our product candidates, we must demonstrate through lengthy, complex, and expensive pre-clinical testing and clinical trials that our product candidates are both safe and effective for use in each target indication, and failures can occur at any stage of testing. Clinical trials often fail to demonstrate safety and efficacy of the product candidate studied for the target indication. Serious adverse events, or SAEs, or undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay, or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. Results of our clinical trials or pre-clinical studies could reveal a high and unacceptable severity and prevalence of side effects, toxicities, or unexpected characteristics, including death. For example, in our Phase 1 clinical trial for our most advanced product candidate, LYR-210, there was one SAE in the active group (acute myocardial infarction), which was considered not related to LYR-210. For more information, see "Business—LYR-210 for the Treatment of CRS—Overview of Our Clinical Development."

In addition, subjects treated with LYR-210 have experienced adverse events, including epistaxis, rhinitis, rhinorrhea, facial pain, nasopharyngitis, sinusitis, upper respiratory tract infection, procedural headache, nasal discomfort, and nasal odor, among others. In our Phase 2 LANTERN clinical trial, treatment-related adverse events were reported in 16 patients, and all treatment-related adverse events except one (increased viscosity of upper respiratory secretion) were mild or moderate in nature. In addition, there was one patient who had a serious adverse event of Acarodermatitis in our Phase 2 LANTERN clinical trial, which was deemed to be not related to treatment.

If unacceptable side effects arise in the development of our product candidates, we, the FDA, the IRBs at the institutions in which our studies are conducted, or DSMB, could materially modify, suspend, or terminate our clinical trials or the FDA or comparable foreign regulatory authorities could order us to cease pre-clinical studies or clinical trials, require us to conduct additional animal or human studies regarding the safety and efficacy of our product candidates which we have not planned or anticipated, or deny approval of our product candidates for any or all targeted indications. Many product candidates that initially showed promise in early-stage testing have later been found to cause side effects that prevented further development of the product candidate. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We currently train and expect to have to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury or death. Any of these occurrences may harm our business, financial condition, and prospects significantly.

If any of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by any such product, including during any long-term follow-up observation period recommended or required for patients who receive treatment using our products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;
- we may be required to recall a product or change the way such product is administered to patients;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product;
- regulatory authorities may require additional warnings on the label, such as a "black box" warning or contraindication;
- regulatory authorities may require long-term patient registries for the product;

- we may be required to implement a Risk Evaluation and Mitigation Strategy, or REMS, or create a medication guide outlining the risks of such side effects for distribution to patients;
- the product could become less competitive;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

There can be no assurance that we will resolve any issues related to any product-related adverse events to the satisfaction of the FDA or any regulatory agency in a timely manner or at all. Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations, and prospects.

Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay.

As product candidates proceed through pre-clinical studies to late-stage clinical trials towards potential approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. Such changes may also require additional testing, FDA notification or FDA approval. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commence sales and generate revenue.

Our insurance policies are expensive and protect us only from some business risks, which leaves us exposed to significant uninsured liabilities.

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, employment practices liability, and property, auto, workers' compensation, umbrella, and directors' and officers' insurance.

Any additional product liability insurance coverage we acquire in the future may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and in the future we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If we obtain marketing approval for LYR-210 and/or LYR-220, we intend to acquire insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. A successful product liability claim or series of claims brought against us could cause our share price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business, including preventing or limiting the development and commercialization of any product candidates we develop. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty, and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

Operating as a public company has made it more difficult and more expensive for us to obtain director and officer liability insurance, and in the future we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified people to serve on our board of directors, our board committees, or as executive officers. We do not know, however, if we will be able to maintain existing insurance with adequate levels of coverage. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our cash position and results of operations.

Our employees and independent contractors, including principal investigators, CROs, consultants, vendors, and any third parties we may engage in connection with research, development, regulatory, manufacturing, quality assurance, and other pharmaceutical functions and commercialization may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

Misconduct by our employees and independent contractors, including principal investigators, CROs, consultants, vendors, and any third parties we may engage in connection with research, development, regulatory, manufacturing, quality assurance, and other pharmaceutical functions and commercialization, could include intentional, reckless, or negligent conduct or unauthorized activities that violate: (i) the laws and regulations of the FDA, the European Medicines Agency, or the EMA, and other similar regulatory authorities, including those laws that require the reporting of true, complete, and accurate information to such authorities; (ii) manufacturing standards; (iii) data privacy, security, fraud and abuse, and other healthcare laws and regulations; or (iv) laws that require the reporting of true, complete, and accurate financial information and data. Specifically, sales, marketing, and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing, and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements. Activities subject to these laws could also involve the improper use or misrepresentation of information obtained in the course of pre-clinical studies or clinical trials, creation of fraudulent data in pre-clinical studies or clinical trials, or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with such laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant civil, criminal, and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid, other U.S. federal healthcare programs or healthcare programs in other jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

Our business and operations would suffer in the event of system failures.

Our computer systems, as well as those of our CROs and other contractors, vendors, suppliers, and consultants, are vulnerable to damage from computer viruses, unauthorized access, natural disasters (including hurricanes), terrorism, war, and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our product candidate development programs and our business. For example, the loss of pre-clinical studies or clinical trial data from completed, ongoing, or planned trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of personal, confidential, or proprietary information, we could incur liability and the further development of LYR-210, LYR-220, or any other product candidate could be delayed.

In the ordinary course of our business, we directly or indirectly collect and store sensitive data, including intellectual property, confidential information, pre-clinical and clinical trial data, proprietary business information, personal data, and personally identifiable health information of our clinical trial subjects and employees, in our data centers and on our networks, or on those of third parties. The secure processing, maintenance, and transmission of this information is critical to our operations. Despite our security measures, our information technology and infrastructure has been and, from time to time, may be vulnerable to attacks by hackers or internal bad actors, or breached due to employee error, a technical vulnerability, malfeasance, or other disruptions. For example, companies have experienced an increase in phishing and social engineering attacks from third parties in connection with the COVID-19 pandemic. Although, to our knowledge, we have not experienced any material security breach to date, any such breach could compromise our networks and the information stored there could be accessed, publicly disclosed, lost, or stolen. Any such access, disclosure, or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, or significant regulatory penalties, and such an event could disrupt our operations, damage our reputation, and cause a loss of confidence in us and our ability to conduct clinical trials, which could adversely affect our business reputation and delay our clinical development of our product candidates.

Risks Related to Healthcare Laws and Other Legal Compliance Matters

We will be subject to extensive and costly government regulation.

Product candidates employing our technology will be subject to extensive and rigorous domestic government regulation including regulation by the FDA, the Centers for Medicare and Medicaid Services, or CMS, other divisions of the United States Department of Health and Human Services, the United States Department of Justice, state and local governments, and their respective equivalents outside of the United States. The FDA regulates the research, development, pre-clinical and clinical testing, manufacture, safety, effectiveness, record-keeping, reporting, labeling, packaging, storage, approval, advertising, promotion, sale, distribution, import, and export of pharmaceutical products. If products employing our technologies are marketed abroad, they will also be subject to extensive regulation by foreign governments, whether or not they have obtained FDA approval for a given product and its uses. Such foreign regulation may be equally or more demanding than corresponding United States regulation.

Government regulation substantially increases the cost and risk of researching, developing, manufacturing, and selling our products. The regulatory review and approval process, which includes pre-clinical testing and clinical trials of each product candidate, is lengthy, expensive, and uncertain. We or our collaborators must obtain and maintain regulatory authorization to conduct pre-clinical studies and clinical trials. We or our collaborators must obtain regulatory approval for each product we intend to market, and the manufacturing facilities used for the products must be inspected and meet legal requirements. Securing regulatory approval requires the submission of extensive pre-clinical and clinical data and other supporting information for each proposed therapeutic indication in order to establish the product's safety and efficacy, potency, and purity, for each intended use. The development and approval process takes many years, requires substantial resources, and may never lead to the approval of a product.

Even if we are able to obtain regulatory approval for a particular product, the approval may limit the indicated medical uses for the product, may otherwise limit our ability to promote, sell, and distribute the product, may require that we conduct costly post-marketing surveillance, and/or may require that we conduct ongoing post-marketing studies. Material changes to an approved product, such as, for example, manufacturing changes or revised labeling, may require further regulatory review and approval. Once obtained, any approvals may be withdrawn, including, for example, if there is a later discovery of previously unknown problems with the product, such as a previously unknown safety issue.

If we, our collaborators, consultants, contract manufacturers, CROs, or other vendors fail to comply with applicable regulatory requirements at any stage during the regulatory process, such noncompliance could result in, among other things, delays in the approval of applications or supplements to approved applications; refusal of a regulatory authority, including the FDA, to review pending market approval applications or supplements to approved applications; warning letters; fines; import and/or export restrictions; product recalls or seizures; injunctions; total or partial suspension of production; civil penalties; withdrawals of previously approved marketing applications or licenses; recommendations by the FDA or other regulatory authorities against governmental contracts; and/or criminal prosecutions.

Enacted and future healthcare legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and could adversely affect our business.

In the United States, the EU, and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could prevent or delay marketing approval of our products in development, restrict or regulate post-approval activities involving any product candidates for which we obtain marketing approval, impact pricing and reimbursement, and impact our ability to sell any such products profitably. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. In addition, new regulations and interpretations of existing healthcare statutes and regulations are frequently adopted.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA, those of greatest importance to the pharmaceutical and biotechnology industries include the following:

- an annual, non-deductible fee payable by any entity that manufactures or imports certain branded prescription drugs and biologic agents (other than those designated as orphan drugs), which is apportioned among these entities according to their market share in certain government healthcare programs;

- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;

- new requirements to report certain financial arrangements with physicians and teaching hospitals, including reporting "transfers of value" made or distributed to prescribers and other healthcare providers and reporting investment interests held by physicians and their immediate family members;

- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;

- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected;

- extension of a manufacturer's Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;

- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and

- establishment of a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. On March 2, 2020, the U.S. Supreme Court granted the petitions for writs of certiorari to review the constitutionality of the ACA, although it is unclear when or how the Supreme Court will rule. It is also unclear how other efforts to challenge, repeal, or replace the ACA will impact the law and may impact our business or financial condition.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011 resulted in aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030, with the temporary suspension from May 1, 2020 through December 31, 2020, unless additional action is taken by Congress. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers, and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws or any other similar laws introduced in the future may result in additional reductions in Medicare and other healthcare funding, which could negatively affect our customers and accordingly, our financial operations.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, and review the relationship between pricing and manufacturer patient programs. While any proposed measures will require authorization through additional legislation to become effective, Congress has indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally-mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition, and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates or put pressure on our product pricing.

In the EU, similar political, economic, and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of healthcare and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities, and affect our ability to commercialize our product candidates, if approved.

In markets outside of the United States and the EU, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

In addition, legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA's regulations, guidance, or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

We cannot predict the likelihood, nature, or extent of government regulation that may arise from future legislation or administrative action in the United States, the EU, or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

Even if we receive regulatory approval of our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, packaging, distribution, adverse event reporting, storage, recordkeeping, export, import, and advertising and promotional activities for such product, among other things, will be subject to extensive and ongoing requirements of and review by the FDA, the EMA, and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, establishment registration and drug listing requirements, continued compliance with current good manufacturing practice, or cGMP, requirements relating to manufacturing, quality control, quality assurance, and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians, and recordkeeping and GCP requirements for any clinical trials that we conduct post-approval. In addition, the sponsor of an approved NDA is subject to periodic inspections and other FDA monitoring and reporting obligations, including obligations to monitor and report adverse events and other information such as the failure of a product to meet the specifications in the NDA. NDA sponsors must submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling, or manufacturing process. Application holders must also submit advertising and other promotional material to the FDA and report on ongoing clinical trials. The FDA may require changes in the labeling of already approved drug products and require that sponsors conduct post-marketing studies. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control.

Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a REMS, which could include requirements for a medication guide, physician communication plans, or additional elements to ensure safe use, such as restricted distribution methods, patient registries, and other risk mitigation tools. If any of our product candidates receives marketing approval, the accompanying label may limit the approved use of our product, which could limit sales of the product.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of our approved products. In addition, advertising and promotional materials must comply with FDA rules in addition to other potentially applicable federal and state laws. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use, and if we market our products outside of their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the FDA's restrictions relating to the promotion of prescription products may also lead to investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

The distribution of product samples to physicians must comply with the requirements of the FDCA. NDA sponsors must obtain FDA approval for product, manufacturing, and labeling changes, depending on the nature of the change. Depending on the circumstances, failure to meet these post-approval requirements can result in criminal prosecution, fines, injunctions, consent decrees of permanent injunction, recall or seizure of products, total or partial suspension of production, denial or withdrawal of pre-marketing product approvals, or refusal to allow us to enter into supply contracts, including government contracts.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers, or manufacturing processes, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on manufacturing such products;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or holds on clinical trials;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution, or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure or detention; or
- injunctions or the imposition of civil or criminal penalties.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenues. If regulatory sanctions are applied or if regulatory approval is withheld or withdrawn, the value of our company and our operating results will be adversely affected.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit, or delay regulatory approval of LYR-210, LYR-220, and/or any other future product candidate. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained which would adversely affect our business, prospects, and ability to achieve or sustain profitability.

Changes in funding for the FDA and other government agencies could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new products and services from being developed or commercialized in a timely manner, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, on March 10, 2020 the FDA announced its intention to postpone most inspections of foreign manufacturing facilities and products through April 2020, and on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, on July 10, 2020, the FDA announced its intention to resume certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA intends to use this risk-based assessment system to identify the categories of regulatory activity that can occur within a given geographic area, ranging from mission critical inspections to resumption of all regulatory activities. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic, including providing guidance regarding the conduct of clinical trials. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns or delays could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations, and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations, and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell, and distribute our product candidates, if approved. Such laws include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving, or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order, or recommendation of, any good, facility, item, or service, for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- the U.S. federal civil and criminal false claims laws, including the civil False Claims Act, which, among other things, impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using, or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease, or conceal an obligation to pay money to the U.S. federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;

- the federal civil monetary penalties laws, which impose civil fines for, among other things, the offering or transfer of remuneration to a Medicare or state healthcare program beneficiary if the person knows or should know it is likely to influence the beneficiary's selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state healthcare program, unless an exception applies;

- the U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items, or services; similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- the FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics, and medical devices;

- the U.S. Physician Payments Sunshine Act and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics, and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to the government information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors) and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members. Beginning in 2022, such obligations will include payments and other transfers of value provided in the previous year to certain other healthcare professionals, including physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse midwives;

- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;

- analogous U.S. state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales, and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; and state and local laws that require the registration of pharmaceutical sales representatives; and

- similar healthcare laws and regulations in the EU and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices, including our relationships with physicians and other healthcare providers, some of whom are compensated in the form of stock options for consulting services provided, may not comply with current or future statutes, regulations, agency guidance, or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal, and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil, or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment, which could affect our ability to operate our business. Further, defending against any such actions can be costly, time-consuming, and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

We are subject to governmental regulation and other legal obligations, particularly related to privacy, data protection, and information security, and we are subject to consumer protection laws that regulate our marketing practices and prohibit unfair or deceptive acts or practices. Our actual or perceived failure to comply with such obligations could harm our business.

We and our partners may be subject to diverse laws and regulations relating to data privacy and security, including, in the United States, HIPAA and, in the EU and the European Economic Area, or EEA, the General Data Protection Regulation, or the GDPR. New privacy rules are being enacted in the United States and globally, and existing ones are being updated and strengthened. For example, on June 28, 2018, California enacted the California Consumer Privacy Act, or CCPA, which took effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Complying with these numerous, complex, and often changing regulations is expensive and difficult, and failure to comply with any privacy laws or data security laws or any security incident or breach involving the misappropriation, loss, or other unauthorized use or disclosure of sensitive or confidential patient or consumer information, whether by us or another third-party, could adversely affect our business, financial condition, and results of operations, including but not limited to: investigation costs, material fines and penalties; compensatory, special, punitive, and statutory damages; litigation; consent orders regarding our privacy and security practices; requirements that we provide notices, credit monitoring services, and/or credit restoration services or other relevant services to impacted individuals; adverse actions against our licenses to do business; and injunctive relief.

In Europe, the GDPR went into effect on May 25, 2018. The GDPR requires us, among other things, to make detailed disclosures to data subjects, to disclose the legal basis on which we can process personal data, to obtain valid consent for processing, to appoint data protection officers when sensitive personal data, such as health data, is processed on a large scale, and provides robust rights for data subjects, introduces mandatory data breach notification, imposes additional obligations on us when contracting with service providers, and requires us to adopt appropriate privacy governance including policies, procedures, training, and data audit. In addition, the GDPR increases the scrutiny of transfers of personal data from clinical trial sites located in the EEA to the United States and other jurisdictions that the European Commission does not recognize as having "adequate" data protection laws; in July 2020, the Court of Justice of the European Union limited how organizations could lawfully transfer personal data from the EEA to the United States by invalidating the EU-US Privacy Shield and imposing further restrictions on use of the standard contractual clauses, which could increase our costs and our ability to efficiently process personal data from the EEA. If we do not comply with our obligations under the GDPR, we could be exposed to fines of up to the greater of €20 million or up to 4% of our total global annual revenue in the event of a significant breach. In addition, we may be the subject of litigation and/or adverse publicity, which could adversely affect our business, results of operations, and financial condition. Additionally, following the United Kingdom's withdrawal from the EEA and the EU, and the expiry of the transition period, companies will have to comply with the GDPR and the GDPR as incorporated into United Kingdom national law, the latter regime having the ability to separately fine up to the greater of £17.5 million or 4% of global turnover. The relationship between the United Kingdom and the EU in relation to certain aspects of data protection law remains unclear, for example around how data can lawfully be transferred between each jurisdiction, which exposes us to further compliance risk.

We cannot assure you that our third-party service providers with access to our or our customers', suppliers', trial patients', and employees' personally identifiable and other sensitive or confidential information in relation to which we are responsible will not breach contractual obligations imposed by us, or that they will not experience data security breaches or attempts thereof, which could have a corresponding effect on our business, including putting us in breach of our obligations under privacy laws and regulations and/or which could in turn adversely affect our business, results of operations, and financial condition. We cannot assure you that our contractual measures and our own privacy and security-related safeguards will protect us from the risks associated with the third-party processing, storage, and transmission of such information.

We face potential liability related to the privacy of health information we obtain from clinical trials sponsored by us.

Most healthcare providers, including research institutions from which we obtain patient health information, are subject to privacy and security regulations promulgated under HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or the HITECH Act. We are not currently classified as a covered entity or business associate under HIPAA and thus are not subject to its requirements or penalties. However, any person may be prosecuted under HIPAA's criminal provisions either directly or under aiding-and-abetting or conspiracy principles. Consequently, depending on the facts and circumstances, we could face substantial criminal penalties if we knowingly receive individually identifiable health information from a HIPAA-covered healthcare provider or research institution that has not satisfied

HIPAA's requirements for disclosure of individually identifiable health information. In addition, we may maintain sensitive personally identifiable information, including health information, that we receive throughout the clinical trial process, in the course of our research collaborations, and directly from individuals (or their healthcare providers) who enroll in our patient assistance programs. As such, we may be subject to state laws requiring notification of affected individuals and state regulators in the event of a breach of personal information, which is a broader class of information than the health information protected by HIPAA. Our clinical trial programs outside the United States may implicate international data protection laws, including the GDPR and legislation of the EU and EEA member states implementing it.

Our activities outside the United States impose additional compliance requirements and generate additional risks of enforcement for noncompliance. Failure by our CROs and other third-party contractors to comply with the strict rules on the transfer of personal data outside of the European Union into the United States may result in the imposition of criminal and administrative sanctions on such collaborators, which could adversely affect our business. Furthermore, certain health privacy laws, data breach notification laws, consumer protection laws, and genetic testing laws may apply directly to our operations and/or those of our collaborators and may impose restrictions on our collection, use, and dissemination of individuals' health information. The GDPR provides that EU and EEA member states may establish their own laws and regulations limiting the processing of personal data, including genetic, biometric, or health data, which could limit our ability to use and share personal data or could cause our costs to increase. Moreover, patients about whom we or our collaborators obtain health information, as well as the providers who share this information with us, may have statutory or contractual rights that limit our ability to use and disclose the information. We may be required to expend significant capital and other resources to ensure ongoing compliance with applicable privacy and data security laws. Claims that we have violated individuals' privacy rights or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

If we or third-party CMOs, CROs, or other contractors or consultants fail to comply with applicable federal, state, or local regulatory requirements, we could be subject to a range of regulatory actions that could affect our or our contractors' ability to develop and commercialize our product candidates and could harm or prevent sales of any affected products that we are able to commercialize, or could substantially increase the costs and expenses of developing, commercializing, and marketing our products. Any threatened or actual government enforcement action could also generate adverse publicity and require that we devote substantial resources that could otherwise be used in other aspects of our business. Increasing use of social media could give rise to liability, breaches of data security, or reputational damage.

We are subject to environmental, health, and safety laws and regulations, and we may become exposed to liability and substantial expenses in connection with environmental compliance or remediation activities.

Our operations, including our development, testing, and manufacturing activities, are subject to numerous environmental, health, and safety laws and regulations. These laws and regulations govern, among other things, the controlled use, handling, release, and disposal of and the maintenance of a registry for, hazardous materials and biological materials, such as chemical solvents, human cells, carcinogenic compounds, mutagenic compounds, and compounds that have a toxic effect on reproduction, laboratory procedures, and exposure to blood-borne pathogens. If we fail to comply with such laws and regulations, we could be subject to fines or other sanctions.

As with other companies engaged in activities similar to ours, we face a risk of environmental liability inherent in our current and historical activities, including liability relating to releases of or exposure to hazardous or biological materials. Environmental, health, and safety laws and regulations are becoming more stringent. We may be required to incur substantial expenses in connection with future environmental compliance or remediation activities, in which case, the production efforts of our third-party manufacturers or our development efforts may be interrupted or delayed.

We and our employees are increasingly utilizing social media tools as a means of communication both internally and externally.

Despite our efforts to monitor evolving social media communication guidelines and comply with applicable rules, there is risk that the use of social media by us or our employees to communicate about our product candidates or business may cause us to be found in violation of applicable requirements. In addition, our employees may knowingly or inadvertently make use of social media in ways that may not comply with our policies and other legal or contractual requirements, which may give rise to liability, lead to the loss of trade secrets or other intellectual property, or result in public exposure of personal information of our employees, clinical trial patients, customers, and others. Furthermore, negative posts or comments about us or our product candidates in social media could seriously damage our reputation, brand image, and goodwill. Any of these events could have a material adverse effect on our business, prospects, operating results, and financial condition and could adversely affect the price of our common stock.

Risks Related to Commercialization

Developments by competitors may render our products or technologies obsolete or non-competitive or may reduce the size of our markets.

Our industry has been characterized by extensive research and development efforts, rapid developments in technologies, intense competition, and a strong emphasis on proprietary products. We face potential competition from many different sources, including pharmaceutical, biotechnology, and specialty pharmaceutical companies either marketing or developing therapeutics to treat CRS. Academic research institutions, governmental agencies, as well as public and private institutions are also potential sources of competitive products and technologies. Our competitors may have or may develop superior technologies or approaches, which may provide them with competitive advantages. Our potential products may not compete successfully. If these competitors access the marketplace before we do with better or less expensive therapeutics, our product candidates, if approved for commercialization, may not be profitable to sell or worthwhile to continue to develop. Technology in the pharmaceutical industry has undergone rapid and significant change, and we expect that it will continue to do so. Any compounds, products, or processes that we develop may become obsolete or uneconomical before we recover any expenses incurred in connection with their development. The success of our product candidates will depend upon factors such as product efficacy, safety, reliability, availability, timing, scope of regulatory approval, acceptance, and price, among other things. Other important factors to our success include speed in developing product candidates, completing clinical development and laboratory testing, obtaining regulatory approvals, and manufacturing and selling commercial quantities of potential products.

Our product candidates are intended to compete directly or indirectly with existing products and treatments. Even if approved and commercialized, our product candidates may fail to achieve market acceptance with hospitals, physicians, or patients. Hospitals, physicians, or patients may conclude that our potential products are less safe or effective or otherwise less attractive than these existing drugs. If our product candidates do not receive market acceptance for any reason, our revenue potential would be diminished, which would materially adversely affect our ability to become profitable.

Significant competition exists in the treatment of CRS. We will need to compete with all currently available or future therapies within the indications where our development is focused. LYR-210, if approved and commercialized, will face significant competition. The main classes of marketed products that are available for the treatment of CRS include nasal saline irrigation, intranasal corticosteroidal sprays and antibiotics, as well as surgical intervention. In addition, one company is currently marketing, and several companies are also currently developing, biologic monoclonal antibodies, or mAbs, for the treatment of nasal polyps. If these biologic mAbs are successfully developed and approved for marketing, they could represent competition for LYR-220 for the segment of patients that have polyps.

There are a number of companies developing or marketing therapies for the treatment and management of CRS that may compete with our current product candidates, including many major pharmaceutical and biotechnology companies. These companies include, among others: Hoffman-La Roche, GlaxoSmithKline, AnaptysBio, Regeneron, OptiNose, and Intersect ENT.

Most of our competitors, including many of those listed above, have substantially greater capital resources, robust product candidate pipelines, established presence in the market, and expertise in research and development, manufacturing, pre-clinical and clinical testing, obtaining regulatory approvals and reimbursement, and marketing approved products than we do. As a result, our competitors may achieve product commercialization or patent protection earlier than we can. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified clinical, regulatory, scientific, sales, marketing, and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop or that would render any products that we may develop obsolete or noncompetitive.

The successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish coverage, adequate reimbursement levels, and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

The availability of coverage and adequacy of reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers, and other third-party payors are essential for most patients to be able to afford medical services and pharmaceutical products such as our product candidates, assuming FDA approval. Our ability to achieve acceptable levels of coverage and reimbursement for our products or procedures using our products by governmental authorities, private health insurers, and other organizations will have an effect on our ability to successfully commercialize our product candidates. Obtaining coverage and adequate reimbursement for our products may be particularly difficult because of the higher prices often associated with drugs administered under the supervision of a physician. Separate reimbursement for the product itself or the treatment or procedure in which our product is used may not be available. A decision by a third-party payor not to cover or separately reimburse for our products or procedures using our products could reduce physician utilization of our products once approved. Assuming there is coverage for our product candidates or procedures using our product candidates by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Patients are unlikely to use our product candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our product candidates. Similarly, our product candidates are physician-administered treatments and as such, separate reimbursement for the product itself may or may not be available. Instead, the hospital or administering physician may be reimbursed only for providing the treatment or procedure in which our product is used. To the extent separate coverage and reimbursement should become available for LYR-210, we anticipate that it will be sold to physicians on a “buy and bill” basis. Buy and bill products must be purchased by healthcare providers before they can be administered to patients. Healthcare providers subsequently must seek reimbursement for the product from the applicable third-party payor, such as Medicare or a health insurance company. Healthcare providers may be reluctant to administer our product candidates, if approved, because they would have to fund the purchase of the product and then seek reimbursement, which may be lower than their purchase price, or because they do not want the additional administrative burden required to obtain reimbursement for the product.

Further, the status of reimbursement codes for any of our product candidates, if approved, could also affect reimbursement. J-Codes and Q-Codes are reimbursement codes maintained by the Centers for Medicare and Medicaid Services, or CMS, that are a component of the Healthcare Common Procedure Coding System and are typically used to report injectable drugs that ordinarily cannot be self-administered. We currently do not have a specific J-Code or Q-Code for any of our product candidates. If our product candidates are approved, we may apply for one but cannot guarantee that a J-Code or Q-Code will be granted. To the extent separate coverage or reimbursement is available for any product candidate, if approved, and a specific J-Code or Q-Code is not available, physicians would need to use a non-specific miscellaneous J-Code to bill third-party payors for these physician-administered drugs. Because miscellaneous J-Codes may be used for a wide variety of products, health plans may have more difficulty determining the actual product used and billed for the patient. These claims must often be submitted with additional information and manually processed, which can delay claims processing times as well as increase the likelihood for claim denials and claim errors. We cannot be sure that coverage and reimbursement in the United States, the EU, or elsewhere will be available for our product candidates or any product that we may develop, and any reimbursement that may become available may not be adequate or may be decreased or eliminated in the future.

Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs and biologics when an equivalent generic drug, biosimilar, or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidates as substitutable and only offer to reimburse patients for the less expensive product. Even if we show improved efficacy or improved convenience of administration with our product candidates, pricing of existing third-party therapeutics may limit the amount we will be able to charge for our product candidates. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in our product candidates. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates, and may not be able to obtain a satisfactory financial return on our product candidates.

There is significant uncertainty related to the insurance coverage and reimbursement of newly-approved products. In the United States, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered. The Medicare and Medicaid programs increasingly are used as models in the United States for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs and biologics. Some third-party payors may require pre-approval of coverage for new or innovative drug therapies before they will reimburse healthcare providers who use such therapies. We cannot predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in the EU and other jurisdictions have and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our product candidates may be reduced compared with the United States and may be insufficient to generate commercially-reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and biologics and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products.

Our clinical studies were designed to demonstrate the safety and efficacy of LYR-210 based on FDA requirements and may not be seen as compelling to physicians or patients.

Our success depends on the medical community's acceptance of LYR-210, if approved, as a treatment for CRS patients. LYR-210 was previously studied in an open-label, Phase 1 clinical trial with 20 patients in New Zealand and Australia, which achieved its primary endpoint of safety at week 4. In the Phase 1 trial, we also observed that patients generally experienced significant and rapid, clinically meaningful and durable improvement in SNOT-22 scores. Significant reduction in SNOT-22 scores was observed at week 1, and this reduction persisted through week 25, which was the end of the trial. In our Phase 2 LANTERN clinical trial, we reported positive top-line results but failed to achieve the primary endpoint. Although not statistically significant at week 4 (the primary endpoint), at the 7,500 µg dose, LYR-210 achieved statistically significant improvement in 4CSS in favor of the treatment arm as measured by the change from baseline at weeks 16, 20, and 24. Furthermore, at the 7,500 µg dose, LYR-210 achieved statistically significant improvement in SNOT-22 score in favor of the treatment arm at weeks 8, 16, 20, and 24. Even if the results of these clinical trials suggest a favorable safety and efficacy profile, the study designs and results, and the designs and results of future clinical trials we conduct, may not be viewed as compelling to our physician customers or patients. If physicians do not find our data compelling, even if LYR-210 receives marketing approval they may choose not to use our products or limit their use. We cannot assure you that any data that we or others generate, including from any pivotal Phase 3 clinical study we may pursue for LYR-210, will be consistent with that observed in the Phase 1 clinical trial of LYR-210 and Phase 2 LANTERN clinical trial, nor that results will be maintained beyond the time points studied. We also cannot assure you that any data that may be collected will be compelling to the medical community because the data may not be clinically meaningful and may not demonstrate that LYR-210 is an attractive procedure when compared against data from alternative treatments.

Even if either LYR-210 or LYR-220 receives marketing approval, it may fail to achieve market acceptance by physicians, patients, third-party payors, or others in the medical community necessary for commercial success.

If either LYR-210 or LYR-220 receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors, and others in the medical community. If it does not achieve an adequate level of acceptance, we may not generate significant product revenues or become profitable. The degree of market acceptance of LYR-210 or LYR-220, if approved for commercial sale, will depend on a number of factors, including but not limited to:

- perceptions by members of the healthcare community, including physicians, about the safety and effectiveness of our platform;
- the perception by members of the healthcare community, including physicians, or patients that the process of administering LYR-210 or LYR-220 is not unduly cumbersome;
- the efficacy and potential advantages compared to alternative treatments;
- effectiveness of sales and marketing efforts;
- the cost of treatment in relation to alternative treatments;
- our ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products;
- the availability of third-party coverage and adequate reimbursement;
- product labeling or product insert requirements of the FDA, the EMA, or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our product together with other medications.

If our product candidates are approved, but do not achieve an adequate level of acceptance by physicians, healthcare payors, and patients, we may not generate sufficient revenue from these products, and we may not be able to achieve or sustain profitability. Our efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may never be successful. In addition, our ability to successfully commercialize our product candidates will depend on our ability to manufacture our products through third-party manufacturers, differentiate our products from competing products, and defend the intellectual property of our products.

Because we expect sales of LYR-210, if approved, to generate substantially all of our product revenues for a substantial period, the failure of this product to find market acceptance would harm our business and could require us to seek additional financing.

If physicians or patients are not willing to change current practices and adopt our office-based administration procedure for LYR-210 and LYR-220, our products may fail to gain market acceptance, and our business will be harmed.

Our initial product candidates, LYR-210 and LYR-220, are bioresorbable polymeric matrices designed to be administered in a brief, non-invasive, in-office procedure by an ENT physician under endoscopic visualization via a single-use applicator. While we believe ENT physicians will be able to administer our product candidates, if successfully developed and approved, in conjunction with an endoscopy procedure, thereby making the placement aligned with the existing care continuum for CRS patients and eliminating the need for ENT physicians to schedule separate surgical time, ENT physicians may not adopt our in-office procedure for a number of reasons, including:

- lack of significant experience with the placement procedure via a single-use applicator;
- lack of availability of adequate insurance coverage or reimbursement for the placement procedure;
- perceived inadequacy of evidence supporting clinical benefits or cost-effectiveness of the placement procedure and/or our products in general over existing alternatives;
- a perception that patients may be unable to tolerate the placement procedure in the physician office setting; and
- liability risks generally associated with the use of new products and procedures.

If ENT physicians do not adopt the placement procedure for any reason, including those listed above, our ability to grow our business would be impaired, even if LYR-210 and LYR-220 receive marketing approval.

We believe recommendations and support of our products by notable ENT physicians could influence market acceptance and adoption. If we do not receive support from influential ENT physicians, our ability to achieve broad market acceptance for our products may be impaired.

In addition, if patient receptivity toward treatment in an ENT physician office setting becomes less favorable in the future, this shift could negatively impact market acceptance of our products. Any negative change due to patient receptivity could also be compounded by patients reporting to physicians or other patients through word-of-mouth or social media.

Additionally, while it is currently more cost-effective to the healthcare system for providers to perform the placement procedure in an ENT physician's office than a FESS procedure in an operating room, healthcare economics are subject to change. If the use of our products were to cease being more cost-effective than FESS due to changes in reimbursement economics, our products may fail to gain market acceptance, our future growth would be limited, and our business may be adversely affected.

If we are unable to establish sales, marketing, and distribution capabilities either on our own or in collaboration with third parties, we may not be successful in commercializing LYR-210 or LYR-220, if approved, and we may not be able to generate any revenue.

We do not have any infrastructure for the sales, marketing, or distribution of our products, and the cost of establishing and maintaining such an organization may exceed the cost-effectiveness of doing so.

We expect to build our own focused sales, distribution, and marketing infrastructure to market LYR-210 and LYR-220 in the United States, if approved. There are significant expenses and risks involved with establishing our own sales, marketing, and distribution capabilities, including our ability to hire, retain, and appropriately incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing, and distribution capabilities could delay any product launch, which would adversely impact the commercialization of LYR-210. Additionally, if the commercial launch of LYR-210 or LYR-220 for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our product candidates on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products;
- our inability to equip medical and sales personnel with effective materials, including medical and sales literature to help them educate physicians and other healthcare providers regarding applicable diseases and our future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;
- our inability to develop or obtain sufficient operational functions to support our commercial activities; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

We do not anticipate having the resources in the foreseeable future to allocate to the sales and marketing of LYR-210, LYR-220, or any future product candidates in markets outside of the United States. Therefore, our future sales in these markets will largely depend on our ability to enter into and maintain collaborative relationships for such capabilities, the collaborator's strategic interest in the product, and such collaborator's ability to successfully market and sell the product. We intend to selectively pursue collaborative arrangements regarding the sale and marketing of LYR-210, if approved, for certain markets outside of the United States; however, we cannot assure that we will be able to establish or maintain such collaborative arrangements, or if able to do so, that they will have effective sales forces.

If we are unable to build our own sales force or negotiate a collaborative relationship for the commercialization of LYR-210 or LYR-220, we may be forced to delay the potential commercialization of LYR-210 or LYR-220 or reduce the scope of our sales or marketing activities for LYR-210 or LYR-220. If we elect to increase our expenditures to fund commercialization activities ourselves, we will need to obtain additional capital, which may not be available to us on acceptable terms, or at all. We could enter into arrangements with collaborative partners at an earlier stage than otherwise would be ideal and we may be required to relinquish rights to LYR-210 or LYR-220 or otherwise agree to terms unfavorable to us, any of which may have an adverse effect on our business, operating results and prospects.

If we are unable to establish adequate sales, marketing, and distribution capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing LYR-210 or LYR-220 and may not become profitable and may incur significant additional losses. We will be competing with many companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

Our future growth may depend, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Our future profitability may depend, in part, on our ability to commercialize our product candidates in foreign markets for which we may rely on collaboration with third parties. We are evaluating the opportunities for the development and commercialization of our product candidates in foreign markets. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the applicable regulatory authority in that foreign market, and we may never receive such regulatory approval for any of our product candidates. To obtain separate regulatory approvals in other countries we may be required to comply with numerous and varying regulatory requirements of such countries regarding the safety and efficacy of our product candidates and governing, among other things, clinical trials and commercial sales, pricing, and distribution of our product candidates, and we cannot predict success in these jurisdictions. If we obtain approval of our product candidates and ultimately commercialize our product candidates in foreign markets, we would be subject to additional risks and uncertainties, including:

- our customers' ability to obtain reimbursement for our product candidates in foreign markets;
- our inability to directly control commercial activities if we are relying on third parties;

- the burden of complying with complex and changing foreign regulatory, tax, accounting, and legal requirements;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer accounts receivable collection times;
- longer lead times for shipping;
- language barriers for technical training and the need for language translations;
- reduced protection of intellectual property rights in some foreign countries;
- the existence of additional potentially relevant third-party intellectual property rights;
- foreign currency exchange rate fluctuations; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Foreign sales of our product candidates could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions, and changes in tariffs.

In some countries, particularly the countries in Europe, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

The sizes of the patient populations that our product candidates are intended to treat have not been established with precision. If the market opportunities for our product candidates are smaller than we estimate, or if any approval that we obtain is based on a narrower definition of the patient population than we anticipate, our revenue and ability to achieve profitability may be materially adversely affected.

The precise incidence and prevalence of the conditions we aim to address with our programs is unknown and cannot be precisely determined. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations, or market research, and may prove to be incorrect. Further, new information may change the estimated incidence or prevalence of these diseases, and the incidence or prevalence of these diseases is subject to change.

The total addressable market across all of our product candidates will ultimately depend upon, among other things, the indications and conditions of use for which the product candidates are approved and may be marketed, acceptance by the medical community, and patient access, drug pricing, and reimbursement. The sizes of the patient populations that our product candidates are intended to treat in the United States and other major markets and elsewhere may turn out to be smaller than expected, patients may not be otherwise amenable to treatment with our product candidates, or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our product candidates, we may never achieve profitability despite obtaining such significant market share.

If we cannot compete for market share against other drug companies, we may not achieve sufficient product revenues and our business will suffer.

If our product candidates receive FDA approval, they will compete with a number of existing and future drugs and therapies developed, manufactured, and marketed by other companies. Existing or future competing products may provide greater therapeutic convenience or clinical or other benefits for a specific indication than our products, or may offer comparable performance at a lower cost. If our products fail to capture and maintain market share, we may not achieve sufficient product revenues and our business will suffer.

We will compete against fully integrated pharmaceutical companies and smaller companies that are collaborating with larger pharmaceutical companies, academic institutions, government agencies, and other public and private research organizations. Many of these competitors may have compounds already approved or in development in the therapeutic categories that we are targeting with our current and future product candidates. In addition, many of these competitors, either alone or together with their collaborative partners, may operate larger research and development programs or have substantially greater financial resources than we do, as well as greater experience in:

- developing product candidates;
- undertaking pre-clinical testing and clinical trials;
- obtaining NDA approval by the FDA and comparable foreign regulatory approvals of product candidates;
- formulating and manufacturing products; and
- launching, marketing, and selling products.

If we obtain approval to commercialize any products outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

If either LYR-210 or LYR-220 is approved for commercialization, we intend to selectively partner with third parties to market it in certain jurisdictions outside the United States. We expect that we will be subject to additional risks related to international pharmaceutical operations, including:

- different regulatory requirements for drug approvals and rules governing drug commercialization in foreign countries;
- reduced protection for intellectual property rights;
- foreign reimbursement, pricing, and insurance regimes;
- potential noncompliance with the U.S. Foreign Corrupt Practices Act, the U.K. Bribery Act 2010, and similar anti-bribery and anticorruption laws in other jurisdictions; and
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad.

We have no prior experience in these areas. In addition, there are complex regulatory, tax, labor, and other legal requirements imposed by both the European Union and many of the individual countries in Europe with which we will need to comply. Many U.S.-based biotechnology companies have found the process of marketing their own products in Europe to be very challenging.

Certain legal and political risks are also inherent in foreign operations. For example, it may be more difficult for us to enforce our agreements or collect receivables through foreign legal systems. There is a risk that foreign governments may nationalize private enterprises in certain countries where we may operate. In certain countries or regions, terrorist activities and the response to such activities may threaten our operations more than in the United States. Social and cultural norms in certain countries may not support compliance with our corporate policies including those that require compliance with substantive laws and regulations. Also, changes in general economic and political conditions in countries where we may

operate are a risk to our financial performance and future growth. Additionally, the need to identify financially and commercially strong partners for commercialization outside the United States who will comply with the high manufacturing and legal and regulatory compliance standards we require is a risk to our financial performance. As we operate our business globally, our success will depend, in part, on our ability to anticipate and effectively manage these and other related risks. There can be no assurance that the consequences of these and other factors relating to our international operations will not have an adverse effect on our business, financial condition or results of operations.

Potential product liability lawsuits against us could cause us to incur substantial liabilities and limit commercialization of any products that we may develop.

The use of our product candidates, including LYR-210 and LYR-220, in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. For example, complications arising from the placement procedure for LYR-210 or LYR-220, or from the degradation or dislodgment of the LYR-210 or LYR-220 polymeric matrix within the sinuses after placement, or from foreign growth occurring in the sinus after placement, could give rise to product liability claims against us. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies, or others selling or otherwise coming into contact with our products. On occasion, large judgments have been awarded in class action lawsuits based on products that had unanticipated adverse effects. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs, which may not be covered by insurance. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation and significant negative media attention;
- withdrawal of participants from our clinical trials;
- significant costs to defend the related litigation and related litigation;
- distraction of management’s attention from our primary business;
- substantial monetary awards to patients or other claimants;
- inability to commercialize LYR-210 or LYR-220 or any other product candidate;
- product recalls, withdrawals or labeling, marketing, or promotional restrictions;
- decreased demand for LYR-210 or LYR-220 or any other product candidate, if approved for commercial sale; and
- loss of revenue.

Risks Related to Our Dependence on Third Parties

We will rely on third parties for the manufacture of materials for our research programs, pre-clinical studies, and clinical trials and we do not have long-term contracts with any of these parties. This reliance on third parties increases the risk that we will not have sufficient quantities of such materials, product candidates, or any therapies that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost, which could delay, prevent, or impair our development or commercialization efforts.

Although we currently conduct certain manufacturing operations internally, we currently have no plans to build our own clinical or commercial scale manufacturing capabilities. Instead, we expect to rely on third parties for the manufacture of our product candidates and related raw materials for future pre-clinical and clinical development, as well as for commercial manufacture if any of our product candidates receive marketing approval. We do not have a long-term agreement with any of the third-party manufacturers we currently use to provide pre-clinical and clinical drug supply, and purchase any required materials on a purchase order basis. Certain of these manufacturers are critical to our production and the loss of these manufacturers to one of our competitors or otherwise, or an inability to obtain quantities at an acceptable cost or quality, could delay, prevent, or impair our ability to timely conduct pre-clinical studies or clinical trials, and would materially and adversely affect our development and commercialization efforts. The facilities used by third-party

manufacturers to manufacture our product candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit an NDA to the FDA. We do not control the manufacturing process of, and are completely dependent on, third-party manufacturers for compliance with cGMP requirements for manufacture of drug products and other laws and regulations. If these third-party manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. Some of our contract manufacturers may not have produced a commercially-approved product and therefore may not have obtained the requisite FDA approvals to do so. In addition, we have no control over the ability of third-party manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for, or market our product candidates, if approved.

Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, seizures or recalls of product candidates or products, operating restrictions, and criminal prosecutions, any of which could significantly and adversely affect supplies of our products. In addition, we may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms.

Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- failure of third-party manufacturers to comply with regulatory requirements and maintain quality assurance;
- breach of the manufacturing agreement by the third party;
- failure to manufacture our product according to our specifications;
- failure to manufacture our product according to our schedule or at all;
- misappropriation of our proprietary information, including our trade secrets and know-how; and
- termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval, and any related remedial measures may be costly or time-consuming to implement. We do not currently have arrangements in place for redundant supply or a second source for all required raw materials used in the manufacture of our product candidates. The extent to which the COVID-19 pandemic impacts our ability to procure sufficient supplies for the development of our products and product candidates will depend on the severity and duration of the spread of the virus, and the actions undertaken to contain COVID-19 or treat its effects and may cause delays. If our current third-party manufacturers cannot perform as agreed, we may be required to replace such manufacturers and we may be unable to replace them on a timely basis or at all. Our current and anticipated future dependence upon others for the manufacture of our product candidates or products may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

We rely on third parties to conduct our pre-clinical studies and clinical trials. Any failure by a third party to conduct the clinical trials according to GCPs and in a timely manner may delay or prevent our ability to seek or obtain regulatory approval for or commercialize our product candidates.

We are dependent on third parties to conduct our pre-clinical studies and clinical trials, including our planned and ongoing clinical trials for LYR-210, and we expect to rely on third parties to conduct any future clinical trials and pre-clinical studies for our product candidates, including LYR-220. Specifically, we have used and relied on, and intend to continue to use and rely on, medical institutions, clinical investigators, CROs, and consultants to conduct our clinical trials in accordance with our clinical protocols and regulatory requirements. These CROs, investigators, and other third parties play a significant role in the conduct and timing of these trials and subsequent collection and analysis of data. While we have agreements governing the activities of our third-party contractors, we have limited influence over their actual performance. Nevertheless,

we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol and legal, regulatory, and scientific standards, and our reliance on the CROs and other third parties does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for all of our product candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators, and trial sites. If we or any of our CROs or trial sites fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

There is no guarantee that any such CROs, investigators, or other third parties will devote adequate time and resources to such trials or perform as contractually required. If any of these third parties fail to meet expected deadlines, adhere to our clinical protocols, or meet regulatory requirements, or otherwise performs in a substandard manner, our clinical trials may be extended, delayed, or terminated. In addition, many of the third parties with whom we contract may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA concludes that the financial relationship may have affected the interpretation of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned, and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of any NDA we submit to the FDA. Any such delay or rejection could prevent us from commercializing our product candidates.

If any of our relationships with these third-parties terminate, we may not be able to enter into arrangements with alternative third parties or do so on commercially reasonable terms. Switching or adding additional CROs, investigators, and other third parties involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. The COVID-19 pandemic and government measures taken in response have also had a significant impact on our CROs, and we expect that they will face further disruption which may affect our ability to initiate and complete our pre-clinical studies and clinical trials. Though we carefully manage our relationships with our CROs, investigators, and other third parties, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition, and prospects.

We may collaborate with third parties for the development and commercialization of LYR-210, LYR-220, and any of our future product candidates. We may not succeed in establishing and maintaining collaborative relationships, which may significantly limit our ability to develop and commercialize LYR-210, LYR-220, or our future product candidates successfully, if at all.

We may seek collaborative relationships for the development and commercialization of LYR-210, LYR-220, or any future product candidates. Failure to obtain a collaborative relationship for LYR-210, LYR-220, or any future product candidates may significantly impair the potential for these product candidates. We also may need to enter into collaborative relationships to provide funding to support our other research and development programs. The process of establishing and maintaining collaborative relationships is difficult, time-consuming, and involves significant uncertainty, such as:

- a collaboration partner may shift its priorities and resources away from our product candidates due to a change in business strategies, or a merger, acquisition, sale, or downsizing;
- a collaboration partner may seek to renegotiate or terminate their relationships with us due to unsatisfactory clinical results, manufacturing issues, a change in business strategy, a change of control, or other reasons;
- a collaboration partner may cease development in therapeutic areas which are the subject of our strategic collaboration;
- a collaboration partner may not devote sufficient capital or resources towards our product candidates;

- a collaboration partner may change the success criteria for a product candidate, thereby delaying or ceasing development of such candidate;

- a significant delay in initiation of certain development activities by a collaboration partner will also delay payment of milestones tied to such activities, thereby impacting our ability to fund our own activities;

- a collaboration partner could develop a product that competes, either directly or indirectly, with our product candidate;

- a collaboration partner with commercialization obligations may not commit sufficient financial or human resources to the marketing, distribution, or sale of a product;

- a collaboration partner with manufacturing responsibilities may encounter regulatory, resource, or quality issues and be unable to meet demand requirements;

- a collaboration partner may terminate a strategic alliance;

- a dispute may arise between us and a partner concerning the research, development, or commercialization of a product candidate resulting in a delay in milestones, royalty payments, or termination of an alliance and possibly resulting in costly litigation or arbitration which may divert management attention and resources; and

- a partner may use our products or technology in such a way as to invite litigation from a third party.

If any collaborator fails to fulfill its responsibilities in a timely manner, or at all, our research, clinical development, manufacturing, or commercialization efforts related to that collaboration could be delayed or terminated, or it may be necessary for us to assume responsibility for expenses or activities that would otherwise have been the responsibility of our collaborator. If we are unable to establish and maintain collaborative relationships on acceptable terms or to successfully transition terminated collaborative agreements, we may have to delay or discontinue further development of one or more of our product candidates, undertake development and commercialization activities at our own expense, or find alternative sources of capital. Moreover, any collaborative partners we enter into agreements with in the future may shift their priorities and resources away from our product candidates or seek to renegotiate or terminate their relationships with us.

If we seek, but are not able to establish, collaborations, we may have to alter our development and commercialization plans.

Our product development programs and the potential commercialization of our product candidates will require substantial additional capital. We may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of our product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or comparable regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of such product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate revenue.

Data provided by collaborators and others upon which we rely that has not been independently verified could turn out to be false, misleading, or incomplete.

We rely on third-party vendors, such as CROs, scientists, and collaborators to provide us with significant data and other information related to our projects, pre-clinical studies, or clinical trials and our business. If such third parties provide inaccurate, misleading, or incomplete data, our business, prospects, and results of operations could be materially adversely affected.

We do not have multiple sources of supply for some of the components used in LYR-210 or LYR-220, nor long-term supply contracts, and certain of our suppliers are critical to our production. If we were to lose a supplier, it could have a material adverse effect on our ability to complete the development of LYR-210 or LYR-220. If we obtain regulatory approval for LYR-210 or LYR-220, we would need to expand the supply of their components in order to commercialize them.

We do not have multiple sources of supply for the components used in the manufacturing of LYR-210 or LYR-220. We also do not have long-term supply agreements with any of our component suppliers. We may not be able to establish additional sources of supply for our product candidates, or may be unable to do so on acceptable terms. Manufacturing suppliers are subject to cGMP quality and regulatory requirements covering manufacturing, testing, quality control, and record keeping relating to our product candidates and are subject to ongoing inspections by the regulatory agencies. Failure by any of our suppliers to comply with applicable regulations may result in long delays and interruptions in supply. Manufacturing suppliers are also subject to local, state, and federal regulations and licensing requirements. Failure by any of our suppliers to comply with all applicable regulations and requirements may result in long delays and interruptions in supply.

The number of suppliers of the raw material components of our product candidates is limited. In the event it is necessary or desirable to acquire supplies from alternative suppliers, we might not be able to obtain them on commercially reasonable terms, if at all. It could also require significant time and expense to redesign our manufacturing processes to work with another company. Additionally, certain of our suppliers are critical to our production and the loss of these suppliers to one of our competitors or otherwise would materially and adversely affect our development and commercialization efforts.

As part of any marketing approval, regulatory authorities conduct inspections that must be successful prior to the approval of the product. Failure of manufacturing suppliers to successfully complete these regulatory inspections will result in delays. If supply from the approved supplier is interrupted, there could be a significant disruption in commercial supply. An alternative vendor would need to be qualified through an NDA amendment or supplement which could result in further delay. The FDA or other regulatory agencies outside of the United States may also require additional studies if a new supplier is relied upon for commercial production. Switching vendors may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

If we are unable to obtain the supplies we need at a reasonable price or on a timely basis, it could have a material adverse effect on our ability to complete the development of LYR-210 or LYR-220 or, if we obtain regulatory approval for LYR-210 or LYR-220, to commercialize them.

We may enter into collaborations, in-licensing arrangements, joint ventures, strategic alliances, or partnerships with third-parties that may not result in the development of commercially viable products or the generation of significant future revenues.

In the ordinary course of our business, we may enter into collaborations, in-licensing arrangements, joint ventures, strategic alliances, partnerships, or other arrangements to develop new products and to pursue new markets. Proposing, negotiating, and implementing collaborations, in-licensing arrangements, joint ventures, strategic alliances, or partnerships may be a lengthy and complex process. Other companies, including those with substantially greater financial, marketing, sales, technology, or other business resources, may compete with us for these opportunities or arrangements. We may not identify, secure, or complete any such transactions or arrangements in a timely manner, on a cost-effective basis, on acceptable terms, or at all. We have limited institutional knowledge and experience with respect to these business development activities, and we may also not realize the anticipated benefits of any such transaction or arrangement. In particular, these collaborations may not result in the development of products that achieve commercial success or result in significant revenues and could be terminated prior to developing any products.

Additionally, we may not be in a position to exercise sole decision making authority regarding the transaction or arrangement, which could create the potential risk of creating impasses on decisions, and our future collaborators may have economic or business interests or goals that are, or that may become, inconsistent with our business interests or goals. It is possible that conflicts may arise with our collaborators, such as conflicts concerning the achievement of performance milestones, or the interpretation of significant terms under any agreement, such as those related to financial obligations or the ownership or control of intellectual property developed during the collaboration. If any conflicts arise with any current or future collaborators, they may act in their self-interest, which may be adverse to our best interest, and they may breach their obligations to us. In addition, we may have limited control over the amount and timing of resources that any current or future collaborators devote to our or their future products. Disputes between us and our collaborators may result in litigation or arbitration which would increase our expenses and divert the attention of our management. Further, these transactions and arrangements will be contractual in nature and will generally be terminable under the terms of the applicable agreements and, in such event, we may not continue to have rights to the products relating to such transaction or arrangement or may need to purchase such rights at a premium.

If we enter into in-bound intellectual property license agreements, we may not be able to fully protect the licensed intellectual property rights or maintain those licenses. Future licensors could retain the right to prosecute and defend the intellectual property rights licensed to us, in which case we would depend on the ability of our licensors to obtain, maintain, and enforce such licensed intellectual property. These licensors may determine not to pursue litigation against other companies or may pursue such litigation less aggressively than we would. If our licensors do not adequately protect such licensed intellectual property, competitors may be able to use such intellectual property and erode or negate any competitive advantage we may have, which could materially harm our business, negatively affect our position in the marketplace, limit our ability to commercialize our products and product candidates, and delay or render impossible our achievement of profitability. Further, entering into such license agreements could impose various diligence, commercialization, royalty, or other obligations on us. Future licensors may allege that we have breached our license agreement with them, and accordingly seek to terminate our license, which could adversely affect our competitive business position and harm our business prospects.

Risks Related to Our Intellectual Property

If we are unable to obtain, maintain, or adequately protect our intellectual property rights, we may not be able to compete effectively in our markets.

We rely upon a combination of patents, trade secret protection, and confidentiality agreements to protect our intellectual property and prevent others from duplicating LYR-210, LYR-220, and any future product candidates.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal, factual, and scientific questions and can be uncertain. It is possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. The patent applications that we own may fail to result in issued patents with claims that cover our product candidates in the United States or in other foreign countries. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue and even if such patents cover our product candidates, third parties may challenge the inventorship, ownership, validity, enforceability, or scope of such patents, which may result in such patents being narrowed or invalidated, or being held unenforceable. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property, provide exclusivity for our product candidates, or prevent others from designing around our claims. In addition, no assurances can be given that third parties will not create new products or methods that achieve similar results without infringing upon our patents. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

If the patent applications we hold with respect to our programs or product candidates fail to issue, if their breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for our product candidates, it could dissuade companies from collaborating with us to develop product candidates, and threaten our ability to commercialize future products. Several patent applications covering our product candidates have been filed recently. We cannot offer any assurances about which, if any, patents will issue, the breadth of any such patents, or whether any issued patents will be found invalid or unenforceable or will be threatened by third parties. Any successful opposition to these patents or any other patents owned by us could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop.

Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we were the first to file any patent application related to a product candidate. Furthermore, if third parties have filed such patent applications before enactment of the Leahy-Smith Act on March 16, 2013, an interference proceeding in the United States can be initiated by a third party to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. In addition, patents have a limited lifespan. In the United States, the expiration of a patent is generally 20 years after it is filed. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for the patent covering a product, we may be open to competition from generic competing products.

The issuance of a patent is not conclusive as to its inventorship, ownership, scope, validity, or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. In addition, the issuance of a patent does not give us the right to practice the patented invention. Third parties may have blocking patents that could prevent us from marketing our product candidate, if approved, or practicing our own patented technology. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is either not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information, or technology that is not covered by patents. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors, and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations, and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. Once disclosed, we are likely to lose trade secret protection.

Although we require all of our employees and consultants to assign their inventions to us, to the extent that employees or consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions. Further, although we require that all of our employees, consultants, collaborators, advisors, and any third parties who have access to our proprietary know-how, information, or technology enter into confidentiality agreements, we cannot provide any assurances that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently discover our trade secrets or develop substantially equivalent information and techniques. Any of these parties may breach these agreements and we may not have adequate remedies for any specific breach. Misappropriation or unauthorized disclosure of our trade secrets or other confidential proprietary information could impair our competitive position and may have a material adverse effect on our business. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time-consuming, and the outcome is unpredictable. Additionally, if the steps taken to maintain our trade secrets or other confidential proprietary information are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret or other confidential proprietary information.

If we are unable to prevent material disclosure of the non-patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

Third-party claims of intellectual property infringement may prevent or delay our development and commercialization efforts.

Our commercial success depends in part on our avoiding infringement, or allegations of infringement, of the patents and other proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, reexamination, and inter partes review proceedings before the United States Patent and Trademark Office, or USPTO, and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are pursuing development candidates. Many companies in intellectual property-dependent industries, including the biotechnology and pharmaceutical industries, have employed intellectual property litigation as a means to gain an advantage over their competitors. As the biotechnology and pharmaceutical industries expand and more patents are issued, and as we gain greater visibility and market exposure as a public company, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. Some claimants may have substantially greater resources than we do and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to composition of matter, drug delivery, methods of manufacture, or methods for treatment related to the use or manufacture of our product candidates. We cannot guarantee that our technologies, products, compositions, and their uses do not or will not infringe third party patent or other intellectual property rights. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates or the use of our product candidates. After issuance, the scope of patent claims remains subject to construction as determined by an interpretation of the law, the written disclosure in a patent, and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our product candidates. If any third-party patents were held by a court of competent jurisdiction to cover the composition of matter of any of our product candidates, the manufacturing process of any of our product candidates, or the method of use for any of our product candidates, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, which may not be available or may not be available on commercially reasonable terms, or until such patents expire.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates and/or harm our reputation and financial results. Defense of these claims, regardless of their merit, could involve substantial litigation expense and could be a substantial diversion of management and employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products, in the case of claims concerning registered trademarks, rename our product candidates, or obtain one or more licenses from third parties, which may require substantial time and monetary expenditure, and which might be impossible or technically infeasible. Furthermore, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us; alternatively or additionally it could include terms that impede or destroy our ability to compete successfully in the commercial marketplace.

We may be involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe our patents, trademarks, copyrights, or other intellectual property. It may be difficult to detect infringers who do not advertise the components that are used in their products. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's product. To counter infringement or unauthorized use, we may be required to file infringement claims on a country-by-country basis, which can be expensive and time-consuming and divert the time and attention of our management and scientific personnel. There can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Any claims we assert against perceived infringers could also provoke these parties to assert counterclaims against us alleging that we infringe their patents, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both.

In addition, in an infringement proceeding, a court may decide that a patent of ours is not valid, is unenforceable and/or is not infringed, or may construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, interpreted narrowly, or held unenforceable, could put our patent applications at risk of not issuing, and could limit our ability to assert those patents against those parties or other competitors and curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks, which could materially harm our business and negatively affect our position in the marketplace.

Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

Recent patent reform legislation has increased the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, and may diminish the value of patents in general.

As is the case with other biopharmaceutical companies, our commercial success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is therefore costly, time consuming, and inherently uncertain. Recent wide-ranging patent reform legislation in the United States, including the Leahy-Smith America Invents Act, or the Leahy-Smith Act, could increase those uncertainties and costs.

The Leahy-Smith Act includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications are prosecuted and may also affect patent litigation. Under The Leahy-Smith Act, the United States transitioned from a "first-to-invent" to a "first-to-file" system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. This will require us to be cognizant going forward of the time from invention to filing of a patent application and be diligent in filing patent applications, but circumstances could prevent us from promptly filing patent applications on our inventions. The Leahy-Smith Act also enlarged the scope of disclosures that qualify as prior art, and it expanded the scope of procedures that a third party may use to challenge a U.S. patent, including post grant review and inter partes review procedures. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. The Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

In addition, recent court rulings in cases such as *Association for Molecular Pathology v. Myriad Genetics, Inc.*, *BRCA1- & BRCA2-Based Hereditary Cancer Test Patent Litigation*, and *Promega Corp. v. Life Technologies Corp.* have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO, and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

We may be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

We may employ individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants, and independent contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants, or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any of our employee's former employers or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, or our ability to hire personnel, which, in any case of the foregoing, could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO, European, and other patent agencies require compliance with a number of procedural, documentary, fee payment, and other similar provisions during the patent application process. Periodic maintenance fees, renewal fees, annuity fees, and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we employ an outside firm and rely on our outside counsel to pay these fees due to non-U.S. patent agencies. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment, and other similar provisions during the patent application process. We employ law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market, which could have a material adverse effect on our business.

Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court.

If we initiated legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation.

Such mechanisms include re-examination, post grant review, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover our product candidates.

The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on one or more of our product candidates. Such a loss of patent protection could have a material adverse impact on our business. A defendant could also challenge our ownership of patents assigned to us. We cannot be certain that a third party would not challenge our rights to these patents and patent applications. Any legal proceeding or enforcement action can also be expensive and time-consuming.

Patent terms may be inadequate to protect our competitive position on our products for an adequate amount of time.

The term of any individual patent depends on applicable law in the country where the patent is granted. In the United States, provided all maintenance fees are timely paid, a patent generally has a term of 20 years from its application filing date or earliest claimed non-provisional filing date. Extensions may be available under certain circumstances, but the life of a patent and, correspondingly, the protection it affords is limited. Given the amount of time required for the development, testing, and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. For patents that are eligible for extension of patent term, we expect to seek extensions of patent terms in the United States and, if available, in other countries. In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent term extension of up to five years beyond the normal expiration of the patent, which is limited to the approved indication (or any additional indications approved during the period of extension). We might not be granted an extension because of, for example, failure to apply within applicable periods, failure to apply prior to the expiration of relevant patents or otherwise, or failure to satisfy any of the numerous applicable requirements. Moreover, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to obtain approval of competing products following our patent expiration by referencing our clinical and pre-clinical data and launch their product earlier than might otherwise be the case. If this were to occur, it could have a material adverse effect on our ability to generate revenue.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting, and defending our intellectual property in all countries throughout the world could be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. Therefore, we may choose not to pursue or maintain protection for certain intellectual property in certain jurisdictions. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent such competitors from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuit that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. In addition, many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties (for example, the patent owner has failed to “work” the invention in that country, or the third party has patented improvements) or limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of the patent.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our trademarks of interest and our business may be adversely affected.

While we seek to protect the trademarks we use in the United States and in other countries, we may be unsuccessful in obtaining registrations and/or otherwise protecting these trademarks. If that were to happen, we may be prevented from using our names, brands, and trademarks unless we enter into appropriate royalty, license, or coexistence agreements, which may not be available or may not be available on commercially reasonable terms. Over the long term, if we are unable to establish name recognition based on our trademarks, trade names, service marks, and domain names, then we may not be able to compete effectively, resulting in a material adverse effect on our business. Our registered or unregistered trademarks or trade names may be challenged, infringed, diluted, or declared generic, or determined to be infringing on other marks. We rely on both registration and common law protection for our trademarks. We may not be able to protect our rights

to these trademarks and trade names or may be forced to stop using these names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trademarks and trade names similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks. Over the long term, if we are unable to establish name recognition based on our trademarks, then we may not be able to compete effectively and our business may be adversely affected. During trademark registration proceedings, we may receive rejections. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. Effective trademark protection may not be available or may not be sought in every country in which our products are made available. Any name we propose to use for our products in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA objects to any of our proposed product names, we may be required to expend significant additional resources in an effort to identify a usable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties, and be acceptable to the FDA. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

Our proprietary rights may not adequately protect our technologies and product candidates, and do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- others may be able to make products that are the same as or similar to our product candidates but that are not covered by the claims of the patents that we own;
- others, including inventors or developers of our patented technologies who may become involved with competitors, may independently develop similar technologies that function as alternatives or replacements for any of our technologies without infringing our intellectual property rights;
- we might not have been the first to conceive and reduce to practice the inventions covered by our patents or patent applications;
- we might not have been the first to file patent applications covering certain of our patents or patent applications;
- it is possible that our pending patent applications will not result in issued patents;
- it is possible that there are prior public disclosures that could invalidate our patents;
- our issued patents may not provide us with any commercially viable products or competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- the Supreme Court of the United States, other U.S. federal courts, Congress, the USPTO, or similar foreign authorities may change the standards of patentability and any such changes could narrow or invalidate, or change the scope of, our or our collaboration partners' patents;
- patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time;
- our competitors might conduct research and development activities in countries where we do not have patent rights, or in countries where research and development safe harbor laws exist, and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;

- ownership, validity, or enforceability of our patents or patent applications may be challenged by third parties; and
- the patents of third parties or pending or future applications of third parties, if issued, may have an adverse effect on our business.

Risks Related to Employee Matters and Managing Growth

We will need to expand our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of product candidate development, regulatory affairs, and sales, marketing, and distribution. As of December 31, 2020, we had 38 full-time employees. To manage our growth activities, we must continue to implement and improve our managerial, operational, and financial systems, expand our facilities, and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. As we expand our organization, we may have difficulty identifying, hiring, and integrating new personnel. Future growth would impose significant additional responsibilities on our management, including the need to identify, recruit, maintain, motivate, and integrate additional employees, consultants, and contractors. Also, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees, and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenues could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

Many of the biotechnology and pharmaceutical companies that we compete against for qualified personnel and consultants have greater financial and other resources, different risk profiles, and a longer history in the industry than we do. If we are unable to continue to attract and retain high-quality personnel and consultants, the rate and success at which we can discover and develop product candidates and operate our business will be limited.

If we lose key management or scientific personnel, cannot recruit qualified employees, directors, officers, or other significant personnel, or experience increases in our compensation costs, our business may materially suffer.

We are highly dependent on our management and directors, including our chief executive officer, Maria Palasis, Ph.D., among others. Due to the specialized knowledge each of our officers and key employees possesses with respect to our product candidates and our operations, the loss of service of any of our officers or directors could delay or prevent the successful enrollment and completion of our clinical trials. We do not carry key person life insurance on our officers or directors. Although we have formal employment agreements with our executive officers, these agreements do not prevent them from terminating their employment with us at any time.

In addition, our future success and growth will depend in part on the continued service of our directors, employees, and management personnel and our ability to identify, hire, and retain additional personnel. If we lose one or more of our executive officers or key employees, our ability to implement our business strategy successfully could be seriously harmed. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of, and commercialize product candidates successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain, or motivate these additional key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be engaged by entities other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to develop and commercialize product candidates will be limited.

Many of our employees have become or will soon become vested in a substantial amount of our common stock or a number of common stock options. Our employees may be more likely to leave us if the shares they own have significantly appreciated in value relative to the original purchase prices of the shares, or if the exercise prices of the options that they hold are significantly below the market price of our common stock. Our future success also depends on our ability to continue to attract and retain additional executive officers and other key employees.

We may engage in acquisitions or strategic partnerships that could disrupt our business, cause dilution to our stockholders, reduce our financial resources, cause us to incur debt or assume contingent liabilities, and subject us to other risks.

In the future, we may enter into transactions to acquire other businesses, products, or technologies or enter into strategic partnerships, including licensing. If we do identify suitable acquisition or partnership candidates, we may not be able to make such acquisitions or partnerships on favorable terms, or at all. Any acquisitions or partnerships we make may not strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an acquisition or issue our common stock or other equity securities to the stockholders of the acquired company, which would reduce the percentage ownership of our existing stockholders. We could incur losses resulting from undiscovered liabilities of the acquired business or partnership that are not covered by the indemnification we may obtain from the seller or our partner. In addition, we may not be able to successfully integrate any acquired personnel, technologies, and operations into our existing business in an effective, timely, and non-disruptive manner. Acquisitions or partnerships may also divert management attention from day-to-day responsibilities, lead to a loss of key personnel, increase our expenses, and reduce our cash available for operations and other uses. We cannot predict the number, timing, or size of future acquisitions or partnerships or the effect that any such transactions might have on our operating results.

We or the third parties upon whom we depend may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Natural disasters could severely disrupt our operations and have a material adverse effect on our business, results of operations, financial condition, and prospects. If a natural disaster, power outage, or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities on which we rely, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business. For example, following Hurricane Maria, shortages in production and delays in a number of medical supplies produced in Puerto Rico resulted, and any similar interruption due to a natural disaster affecting us or any of our third-party manufacturers could materially delay our operations.

The global pandemic caused by COVID-19 could adversely impact our business and operations, including our clinical trials.

In December 2019, a disease caused by a novel strain of the coronavirus, COVID-19, was identified in Wuhan, China, and on March 11, 2020, the World Health Organization declared the outbreak of COVID-19 as a global pandemic. This virus has subsequently spread to a number of countries where we have planned or ongoing clinical trials and activities, including the United States, Australia, Austria, Czech Republic, New Zealand, and Poland, and continues to spread globally. The global pandemic and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen.

In light of developments relating to the COVID-19 pandemic and the focus of healthcare providers and hospitals on fighting the virus, and consistent with the FDA's updated industry guidance for conducting clinical trials issued on March 18, 2020, we discontinued enrollment at 67 patients in our Phase 2 LANTERN clinical trial and we did not open any sites in the United States. Ultimately, LYR-210 did not achieve the primary endpoint in our Phase 2 LANTERN clinical trial, we believe due primarily to the discontinuation of enrollment related to the COVID-19 pandemic. As a result of the decrease in the number of patients enrolled from planned (99 evaluable) to actually enrolled (67), a greater magnitude of change from baseline in 4CSS at week 4 and/or a smaller standard deviation associated with the change from baseline was required in order to achieve statistical significance for the primary endpoint at week 4.

Moreover, although we leveraged remote electronic data collection to enable us to complete certain clinical assessments and generate sufficient information to commence designing our Phase 3 clinical trial, we were unable to enroll patients in our Phase 2 LANTERN clinical trial in the United States from whom we intended to collect certain additional pharmacokinetic data, and as a result, we initiated a separate characterization study in September 2020 as a follow-on to our Phase 2 LANTERN clinical trial in order to collect such data. Furthermore, in response to the spread of COVID-19, we have closed our executive offices with our administrative employees continuing their work outside of our offices.

As a result of the COVID-19 pandemic, we may experience further disruptions that could severely impact our business and clinical trials, including:

- delays or difficulties in enrolling patients in our planned clinical trials;
- further delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by foreign, federal, or state governments, employers, and others or interruption of clinical trial subject visits and study procedures, which may impact the integrity of subject data and clinical study endpoints;
- interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines;
- interruption of, or delays in receiving, supplies of our product candidates from our contract manufacturing organizations due to staffing shortages, production slowdowns or stoppages, and disruptions in delivery systems;
- interruptions in planned pre-clinical studies due to restricted or limited operations at our laboratory facility;
- limitations on employee resources that would otherwise be focused on the conduct of our pre-clinical studies and clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people;
- risk that participants enrolled in our clinical trials will acquire COVID-19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events;
- refusal of the FDA to accept data from clinical trials in these affected geographies; and
- interruption or delays to our sourced discovery and clinical activities.

Additionally, certain third parties, including manufacturers, medical institutions, clinical investigators, CROs, and consultants with whom we conduct business are similarly adjusting their operations and assessing their capacity in light of the COVID-19 pandemic. If these third parties continue to experience shutdowns or business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively impacted. For example, as a result of the COVID-19 pandemic, there could be delays in the manufacturing supply chain for mometasone furoate, which could delay or otherwise impact the manufacturing of LYR-210. It is also likely that the disproportionate impact of COVID-19 on hospitals and clinical sites will have an impact on recruitment and retention for our planned clinical trials.

The COVID-19 pandemic continues to evolve. The extent to which the outbreak impacts our business and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of COVID-19, the duration of the pandemic, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions, and the effectiveness of actions taken and vaccines and other treatments developed in the United States and other countries to contain and treat COVID-19. The COVID-19 pandemic resulted in a widespread health crisis that adversely affected the economies and financial markets worldwide, resulting in an economic downturn that could continue to significantly impact our business, financial condition, and results of operations. To the extent the COVID-19 pandemic adversely affects our business, financial condition, and results of operations, it may also have the effect of heightening many of the other risks described in this "Risk Factors" section.

Litigation against us could be costly and time-consuming to defend and could result in additional liabilities.

We may from time to time be subject to legal proceedings and claims that arise in the ordinary course of business or otherwise, such as claims brought by our customers in connection with commercial disputes and employment claims made by our current or former employees. Claims may also be asserted by or on behalf of a variety of other parties, including government agencies, patients, or vendors of our customers, or stockholders.

Any litigation involving us may result in substantial costs, operationally restrict our business, and may divert management's attention and resources, which may seriously harm our business, overall financial condition, and results of operations. Insurance may not cover existing or future claims, be sufficient to fully compensate us for one or more of such claims, or continue to be available on terms acceptable to us. A claim brought against us that is uninsured or underinsured could result in unanticipated costs, thereby adversely impacting our results of operations and resulting in a reduction in the trading price of our stock.

Risks Related to Our Common Stock

The market price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock.

Our stock price may be volatile. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the purchase price. The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- actual or expected changes in our growth rate relative to our competitors;
- results of clinical trials of our product candidates or those of our competitors;
- developments related to our existing or any future collaborations;
- regulatory actions with respect to our product candidates or our competitors' products and product candidates;
- regulatory or legal developments in the United States and other countries;
- development of new product candidates that may address our markets and make our product candidates less attractive;
- changes in physician, hospital, or healthcare provider practices that may make our product candidates less useful;
- announcements by us, our partners, or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations, or capital commitments;

- developments or disputes concerning patent applications, issued patents, or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- failure to meet or exceed financial estimates and projections of the investment community or that we provide to the public;
- the results of our efforts to discover, develop, acquire, or in-license additional product candidates or products;
- actual or expected changes in estimates as to financial results, development timelines, or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- short selling activities;
- general economic, industry, and market conditions; and
- the other factors described in this "Risk Factors" section and elsewhere in this Annual Report on Form 10-K.

In addition, the trading prices for common stock of other biopharmaceutical companies have been highly volatile as a result of the COVID-19 pandemic. The COVID-19 outbreak continues to evolve. The extent to which the outbreak may impact our business, pre-clinical studies, and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence.

Our current executive officers, directors, and principal stockholders, if they choose to act together, will continue to have the ability to control or significantly influence all matters submitted to stockholders for approval.

Based on the number of shares of common stock outstanding as of December 31, 2020, our current executive officers, directors, and stockholders who own more than 5% of our outstanding common stock and their respective affiliates will, in the aggregate, hold shares representing approximately 48.2% of our outstanding voting stock. As a result, if these stockholders choose to act together, they would be able to control or significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control or significantly influence the election of directors, the composition of our management, and approval of any merger, consolidation, or sale of all or substantially all of our assets.

A significant portion of our total outstanding shares are eligible to be sold into the market in the near future, which could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Holders of approximately 5.4 million shares of our common stock have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders, until such shares can otherwise be sold without restriction under Rule 144 or until the rights terminate pursuant to the terms of the stockholders' agreement between us and such holders. We have also registered all shares of common stock that we may issue under our equity compensation plans, which can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates.

We are an "emerging growth company," and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act, and may remain an emerging growth company until December 31, 2025. However, if certain events occur prior to such date, including if we become a "large accelerated filer," our annual gross revenues exceed $1.07 billion, or we issue more than $1.0 billion of non-convertible debt in any three-year period, we will cease to be an emerging growth company prior to such date. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure in this Annual Report on Form 10-K;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We have taken advantage of reduced reporting burdens in this Annual Report on Form 10-K. In particular, in this Annual Report on Form 10-K, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be reduced or more volatile. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies.

If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline, even if our business is doing well.

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property, or our stock performance, or if our target pre-clinical studies or clinical trials and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

We are a "smaller reporting company" and the reduced disclosure requirements applicable to smaller reporting companies may make our common stock less attractive to investors.

We are considered a "smaller reporting company." We are therefore entitled to rely on certain reduced disclosure requirements, such as an exemption from providing selected financial data and executive compensation information. We are also exempt from the requirement to obtain an external audit on the effectiveness of internal control over financial reporting provided in Section 404(b) of the Sarbanes-Oxley Act. These exemptions and reduced disclosures in our SEC filings due to our status as a smaller reporting company may make it harder for investors to analyze our results of operations and financial prospects. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock prices may be more volatile.

Provisions in our restated certificate of incorporation and amended and restated bylaws and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our restated certificate of incorporation and our amended and restated bylaws may discourage, delay, or prevent a merger, acquisition, or other change in control of our company that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions include those establishing:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death, or removal of a director, which prevents stockholders from filling vacancies on our board of directors;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquirer;
- the ability of our board of directors to alter our bylaws without obtaining stockholder approval;
- the required approval of the holders of at least two-thirds of the shares entitled to vote at an election of directors to adopt, amend, or repeal our bylaws or repeal the provisions of our restated certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by the chairman of the board of directors, the chief executive officer, the president, or the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of us.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Our restated certificate of incorporation designates specific courts as the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us.

Our restated certificate of incorporation specifies that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for most legal actions involving claims brought against us by stockholders; provided that, the exclusive forum provision will not apply to suits brought to enforce any liability or duty created by the Securities Act, the Exchange Act, the rules and regulations thereunder, or any other claim for which the federal courts have exclusive jurisdiction; and provided further that, if and only if the Court of Chancery of the State of Delaware dismisses any such action for lack of subject matter jurisdiction, such action may be brought in another state or federal court sitting in the State of Delaware. Our restated certificate of incorporation further provides that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America shall, to the fullest extent permitted by law, be the sole and exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our restated certificate of incorporation described above.

We believe these provisions benefit us by providing increased consistency in the application of Delaware law by chancellors particularly experienced in resolving corporate disputes and in the application of the Securities Act by federal judges, as applicable, efficient administration of cases on a more expedited schedule relative to other forums, and protection against the burdens of multi-forum litigation. However, the provision may have the effect of discouraging lawsuits against our directors, officers, employees, and agents as it may limit any stockholder's ability to bring a claim in a judicial forum that such stockholder finds favorable for disputes with us or our directors, officers, employees, or agents. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any applicable action brought against us, a court could find the choice of forum provisions contained in our restated certificate of incorporation to be inapplicable or unenforceable in such action. If a court were to find the choice of forum provision contained in our restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business, financial condition, or results of operations.

General Risk Factors

We have incurred and expect to continue to incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, we have incurred significant legal, accounting, and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Market, and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and made some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors.

We are evaluating these rules and regulations, and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, engage outside consultants, adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to

improve control processes as appropriate, validate through testing whether such controls are functioning as documented, and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. We may discover significant deficiencies or material weaknesses, which we may not successfully remediate on a timely basis or at all. Any failure to remediate any significant deficiencies or material weaknesses identified by us or to implement required new or improved controls, or difficulties encountered in their implementation, could cause us to fail to meet our reporting obligations or result in material misstatements in our financial statements. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Because we do not anticipate paying any cash dividends on our common shares in the foreseeable future, capital appreciation, if any, would be your sole source of gain.

On March 20, 2012, we declared and paid a special cash dividend of $0.2630467 per share of our common stock, par value $0.001, which we refer to as the Special Dividend, which totaled approximately $42,115 in the aggregate. Other than the Special Dividend, we have never declared or paid any cash dividends on our common shares. We currently anticipate that we will retain future earnings for the development, operation, and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. As a result, capital appreciation, if any, of our common shares would be your sole source of gain on an investment in our common shares for the foreseeable future.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biopharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

Our ability to use our net operating losses and research and development credits to offset future taxable income may be subject to certain limitations.

As of December 31, 2020, we had net operating loss carryforwards, or NOLs, of $135.4 million for federal income tax purposes and $116.0 million for state income tax purposes, which may be available to offset our future taxable income, if any, and begin to expire at various dates through 2037. As of December 31, 2020, we also had federal and state research and development credit carryforwards of $5.6 million, which begin to expire at various dates through 2035. In general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an "ownership change," generally defined as a greater than 50% change by value in its equity ownership over a three-year period, is subject to limitations on its ability to utilize its pre-change NOLs and its research and development credit carryforwards to offset future taxable income. Our existing NOLs and research and development credit carryforwards may be subject to limitations arising from previous ownership changes. Future changes in our stock ownership, some of which might be beyond our control, could result in an ownership change under Section 382 of the Code. For these reasons, in the event we experience a change of control, we may not be able to utilize a material portion of the NOLs or research and development credit carryforwards even if we attain profitability.

The impact of the Tax Cuts and Jobs Act on our financial results is not entirely clear and could differ materially from the financial statements provided herein.

On December 22, 2017, the United States enacted the Tax Cuts and Jobs Act, or TCJA, that significantly reformed the Code. The TCJA, among other things, contained significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%; limitation of the tax deduction for interest expense; limitation of the deduction for NOLs and elimination of NOL carrybacks, in each case, for losses arising in taxable years beginning after December 31, 2017 (though any such tax losses may be carried forward indefinitely); and modifying or repealing many business deductions and credits. The financial statements contained herein reflect the effects of the TCJA based on current guidance. However, there remain uncertainties and ambiguities in the application of certain provisions of the TCJA, and, as a result, we made certain judgments and assumptions in the interpretation thereof. The U.S. Treasury Department and the Internal Revenue Service may issue further guidance on how the provisions of the TCJA will be applied or otherwise administered that differs from our current interpretation. In addition, the TCJA could be subject to potential amendments and technical corrections, any of which could materially lessen or increase certain adverse impacts of the legislation on us.

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 2. Properties.

We occupy office and laboratory space in Watertown, Massachusetts under a lease agreement, as amended, that terminates on April 30, 2023. We do not own any real property. We believe that our facilities are sufficient to meet our current needs and that suitable additional space will be available as and when needed.

Item 3. Legal Proceedings.

From time to time, we may become involved in litigation relating to claims arising from the ordinary course of business. Our management believes that there are currently no claims or actions pending against us, the ultimate disposition of which could have a material adverse effect on our results of operations or financial condition.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

Our common stock commenced trading under the symbol "LYRA" on The Nasdaq Global Market on May 1, 2020. Prior to that time, there was no public market for our common stock.

Holders

As of March 1, 2021, there were approximately 64 holders of record of our common stock. However, because many of our outstanding shares are held in accounts with brokers and other institutions, we believe we have more beneficial owners.

Dividend Policy

We currently intend to retain all available funds and future earnings, if any, for the operation and expansion of our business and do not anticipate declaring or paying any dividends in the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors after considering our financial condition, results of operations, capital requirements, contractual requirements, business prospects, and other factors the board of directors deems relevant, and subject to the restrictions contained in any future financing instruments.

On March 20, 2012, we declared and paid a special cash dividend of $0.2630467 per share of our common stock, par value $0.001, which we refer to as the Special Dividend, which totaled approximately $42,115 in the aggregate. Other than the Special Dividend, we have not declared or paid any cash dividends on our capital stock.

Recent Sales of Unregistered Securities; Purchases of Equity Securities by the Issuer or Affiliated Purchaser

In the quarter ended December 31, 2020, we did not repurchase any of our equity securities or issue any securities that were not registered under the Securities Act.

Use of Proceeds from Initial Public Offering of Common Stock

On May 5, 2020, we completed the sale of 4,025,000 shares of our common stock, including 525,000 shares pursuant to the full exercise of the underwriters' option to purchase additional shares, at a public offering price of $16.00 per share. The offer and sale of the shares in our initial public offering, or IPO, was registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-236962), which was declared effective by the SEC on April 30, 2020 (the "Registration Statement").

There has been no material change in the planned use of proceeds from our IPO as described in our final prospectus for our IPO dated April 30, 2020 and filed pursuant to Rule 424(b)(4) under the Securities Act on May 1, 2020. We invested the funds received in cash equivalents and other short-term investments in accordance with our investment policy.

Item 6. Selected Financial Data.

We are a smaller reporting company as defined in Rule 12b-2 of the Exchange Act and are not required to provide the information otherwise required under this Item 6.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

You should read the following discussion and analysis of our financial condition and results of operations together with the "Selected Consolidated Financial Data" section of this Annual Report on Form 10-K and our consolidated financial statements and the related notes included elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties.

Our actual results and timing of certain events may differ materially from the results discussed, projected, anticipated, or indicated in any forward-looking statements. We caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition, and liquidity, and the development of the industry in which we operate may differ materially from the forward-looking statements contained in this Annual Report on Form 10-K. In addition, even if our results of operations, financial condition, and liquidity, and the development of the industry in which we operate are consistent with the forward-looking statements contained in this Annual Report on Form 10-K, they may not be predictive of results or developments in future periods.

The following information and any forward-looking statements should be considered in light of factors discussed elsewhere in this Annual Report on Form 10-K, including those risks identified under Part I, Item 1A. Risk Factors.

We caution readers not to place undue reliance on any forward-looking statements made by us, which speak only as of the date they are made. We disclaim any obligation, except as specifically required by law and the rules of the SEC, to publicly update or revise any such statements to reflect any change in our expectations or in events, conditions, or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

Overview

We are a clinical-stage therapeutics company focused on the development and commercialization of novel integrated drug and delivery solutions for the localized treatment of patients with ear, nose and throat diseases. Our proprietary technology platform, XTreo, is designed to precisely and consistently deliver medicines directly to the affected tissue for sustained periods with a single administration. Our initial product candidates, LYR-210 and LYR-220, are bioresorbable polymeric matrices designed to be administered in a brief, non-invasive, in-office procedure and intended to deliver up to six months of continuous drug therapy to the sinonasal passages for the treatment of CRS. The therapeutic embedded within LYR-210 and LYR-220 is mometasone furoate, which is the active ingredient in various FDA approved drugs and has a well-established efficacy and safety profile. CRS is an inflammatory disease of the paranasal sinuses which leads to debilitating symptoms and significant morbidities and affects approximately 14 million people in the United States. We are advancing LYR-210 as a potential preferred alternative to surgery in our Phase 2 randomized, sham procedure-controlled, patient blinded LANTERN clinical trial, evaluating the safety and efficacy in surgically-naïve CRS patients who have failed previous medical management. The trial was designed to enroll 99 evaluable patients with the potential to increase to up to 150 patients and was initiated in May 2019 at sites in Australia, Austria, Czech Republic, New Zealand, and Poland. In December 2019, the FDA cleared our investigational new drug application, and, prior to the COVID-19 pandemic, we planned to enroll patients in the United States. However, in light of developments relating to the COVID-19 global pandemic we discontinued enrollment at 67 patients in our Phase 2 LANTERN clinical trial and did not enroll patients in the United States.

On December 7, 2020, we reported positive top-line results from our Phase 2 LANTERN clinical trial, including that the 7,500 µg dose of LYR-210 achieved statistically significant improvement in the composite four cardinal symptoms score, or 4CSS, in favor of the treatment arm as measured by the change from baseline at weeks 16, 20, and 24. However, although a strong treatment effect was observed at week 4, LYR-210 did not achieve the primary endpoint of change from baseline in 4CSS at week 4 at either the 7,500 µg dose or 2,500 µg dose. We believe this was due primarily to the discontinuation of enrollment related to the COVID-19 global pandemic. As a result of the decrease in the number of patients enrolled from planned (99 evaluable) to actually enrolled (67), a greater magnitude of change from baseline in 4CSS at week 4 and/or a smaller standard deviation associated with the change from baseline was required in order to achieve statistical significance for the primary endpoint at week 4. LYR-210 was observed to be safe and well-tolerated at all doses in the trial, and no treatment-related serious adverse events were reported.

In addition, although we collected certain pharmacokinetic data from all patients in our Phase 2 LANTERN clinical trial starting at week 4, our protocol contemplated utilizing a subset of U.S. patients to collect certain additional pharmacokinetic data in order to support the NDA for LYR-210. However, because we were unable to enroll patients in the United States due to the COVID-19 pandemic, we were unable to collect these additional pharmacokinetic data as planned. As a result, in September 2020, we initiated a separate characterization study in the United States to collect these additional data. This study is fully enrolled and all 24 patients have completed the study-required visits. We expect data lock and analysis activities to be completed by the second quarter of 2021.

In our Phase 1 clinical trial, LYR-210 met its primary safety endpoint, and we observed that patients generally experienced significant, rapid, clinically meaningful, and durable improvement in SNOT-22 scores, an established patient symptom severity scale, through week 25, which was the end of the trial. Secondary findings from our Phase 1 clinical trial showed that LYR-210 demonstrated significant reduction of sinonasal Type 2 inflammation in surgically-naïve patients with CRS. The reduction of Type 2 inflammation suggests a correlation with rhinologic symptom improvement in CRS and could be a potential measure of LYR-210's local anti-inflammatory effects at the site of inflammation in the sinonasal passages.

We are also developing LYR-220 for use in CRS patients who have an enlarged nasal cavity due to sinus surgery but continue to require treatment to manage CRS symptoms and, subject to the impact of COVID-19 on our business, we intend to initiate a Phase 2 clinical trial for LYR-220 by the end of 2021. Beyond CRS, we believe our XTreo platform has potential applications in other disease areas, which we are actively exploring to further broaden its therapeutic potential.

We were incorporated as a Delaware corporation on November 21, 2005, and our headquarters is located in Watertown, Massachusetts. On July 16, 2018, we formally changed our name to Lyra Therapeutics, Inc. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our technology, building our intellectual property portfolio, and conducting research and development activities for our product candidates. We do not have any products approved for sale and have not generated any revenue from product sales.

On May 5, 2020, we completed our IPO in which we issued and sold 4,025,000 shares of our common stock (including shares issued upon the underwriters' exercise in full of their option to purchase additional shares of our common stock) at a public offering price of $16.00 per share, par value $0.001, for aggregate gross proceeds of $64.4 million. We received approximately $57.3 million in net proceeds after deducting underwriting discounts and commissions and offering expenses paid by us. The shares began trading on The Nasdaq Global Market on May 1, 2020. Upon completion of our IPO, all of our outstanding shares of convertible preferred stock converted into 8,335,248 shares of our common stock, par value $0.001.

Prior to our IPO, we funded our operations primarily through private placements of redeemable convertible preferred stock and funding from government contracts. From inception through December 31, 2020, we have raised an aggregate of $236.5 million to fund our operations, of which $162.1 million were gross proceeds from sales of our redeemable convertible preferred stock, $57.3 million were net proceeds from our IPO (taking into account the issuance and sale of 4,025,000 shares of our common stock at a public offering price of $16.00 per share, par value $0.001, for aggregate gross proceeds of $64.4 million, after deducting $7.1 million of underwriting discounts and offering expenses paid by us), and $16.8 million were gross proceeds from government contracts.

We have incurred significant net operating losses in every year since our inception and expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. Our net losses may fluctuate significantly from quarter to quarter and year to year and could be substantial. Our net losses were $22.1 million and $16.3 million for the years ended December 31, 2020 and 2019, respectively. As of December 31, 2020, we had an accumulated deficit of $149.9 million. We anticipate that our expenses will increase significantly as we:

- conduct additional clinical trials of our most advanced product candidate, LYR-210, including one or more planned pivotal Phase 3 clinical trials of LYR-210;
- advance the development of LYR-220;
- continue to discover and develop additional product candidates;
- establish manufacturing and supply chain capacity sufficient to provide commercial quantities of any product candidates for which we may obtain marketing approval;
- seek regulatory and marketing approvals for product candidates that successfully complete clinical trials, if any;

- establish a sales, marketing, and distribution infrastructure to commercialize any products for which we may obtain regulatory approval in geographies in which we plan to commercialize our products ourselves;

- maintain, expand, and protect our intellectual property portfolio;

- hire additional staff, including clinical, scientific, technical, regulatory, operational, financial, commercial, and support personnel, to execute our business plan; and

- add clinical, scientific, operational, financial, and management information systems and personnel to support our product development and potential future commercialization efforts, and to enable us to operate as a public company.

We do not expect to generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for a product candidate. Additionally, we currently use contract research organizations, or CROs, to carry out our clinical development activities. We do not yet have a sales organization. If we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing, and distribution. Furthermore, we will continue to incur additional costs associated with operating as a public company. As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to fund our operations through public or private equity or debt financings or other sources, including strategic collaborations and licensing arrangements. We may, however, be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements as and when needed would have a negative impact on our financial condition and our ability to develop our current product candidates, or any additional product candidates, if developed.

Because of the numerous risks and uncertainties associated with therapeutics product development, we are unable to accurately predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate revenue from product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

COVID-19 Pandemic and the CARES Act

On January 30, 2020, the World Health Organization, or WHO, announced a global health emergency because of a new strain of coronavirus originating in Wuhan, China, or the COVID-19 outbreak, and the risks to the international community as the virus subsequently spread globally beyond its point of origin. On March 11, 2020, the WHO classified the COVID-19 outbreak as a pandemic, based on the rapid increase in exposure globally. The COVID-19 pandemic is affecting the United States and global economies and may affect our operations and those of third parties on which we rely, including by causing disruptions in the supply of our product candidates and the conduct of current and future clinical trials. In addition, the COVID-19 pandemic may affect the operations of the FDA and other health authorities, which could result in delays of reviews and approvals, including with respect to our product candidates. Additionally, while the potential economic impact brought by, and the duration of, the COVID-19 pandemic is difficult to assess or predict, the impact of the COVID-19 pandemic on the global financial markets may reduce our ability to access capital, which could negatively impact our short-term and long-term liquidity. The ultimate impact of the COVID-19 pandemic is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, financing, or clinical trial activities, or on healthcare systems or the global economy as a whole. However, these effects could have a material impact on our liquidity, capital resources, operations, and business and those of the third parties on which we rely.

On March 27, 2020, President Trump signed into law the “Coronavirus Aid, Relief, and Economic Security (CARES) Act.” The CARES Act, among other things, includes provisions relating to refundable payroll tax credits, deferment of employer side social security payments, net operating loss carryback periods, alternative minimum tax credit refunds, modifications to the net interest deduction limitations, increased limitations on qualified charitable contributions, and technical corrections to tax depreciation methods for qualified improvement property. We currently defer the employer side social security payments and also are evaluating whether we will take advantage of other provisions, if any. The CARES Act also appropriated funds for the Small Business Administration Paycheck Protection Program loans that are forgivable in certain situations to promote continued employment, as well as Economic Injury Disaster Loans to provide liquidity to small businesses harmed by the COVID-19 pandemic. On December 27, 2020, the Consolidated Appropriations Act, 2021 was signed into law in order to provide further stimulus and support to those affected by the COVID-19 pandemic. We have not and do not plan on obtaining funding from such loans. We do not believe the CARES Act or the Consolidated Appropriations Act, 2021 will have a material impact on our financial condition, results of operations, or liquidity.

As of December 31, 2020, we had cash and cash equivalents totaling $74.6 million. We believe that our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements into 2023. We have based these estimates on assumptions that may prove to be imprecise or incorrect, and we may use our available capital resources sooner than we currently expect. See "—Liquidity and Capital Resources." Because of the numerous risks and uncertainties associated with the development of our product candidates and any future product candidates, our platform, and technology, and because the extent to which we may enter into collaborations with third parties for development of any of our product candidates is unknown, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with completing the research and development of our product candidates.

If we raise additional funds through collaborations, strategic alliances, or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs, or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce, or terminate our product development programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Financial Operations Overview

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the foreseeable future. If our development efforts for our product candidates are successful and result in regulatory approval and successful commercialization efforts, we may generate revenue in the future from product sales. We cannot predict if, when, or to what extent we will generate revenue from the commercialization and sale of our product candidates. We may never succeed in obtaining regulatory approval for any of our product candidates.

Operating Expenses

Our operating expenses since inception have consisted solely of research and development costs and general and administrative costs.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including the development of and pursuit of regulatory approval of our most advanced product candidate, LYR-210, for the treatment of CRS, which include:

- employee-related expenses, including salaries, benefits, and stock-based compensation expense for personnel engaged in research and development functions;
- expenses incurred in connection with the preclinical and clinical development of our product candidates, including under agreements with CROs, investigative sites, and consultants;
- costs of manufacturing our product candidates for use in our preclinical studies and clinical trials as well as manufacturers that provide components of our product candidates for use in our preclinical and potential future clinical trials;
- consulting and professional fees related to research and development activities;
- costs related to compliance with clinical regulatory requirements; and
- facility costs and other allocated expenses, which include expenses for rent and maintenance of our facility, utilities, depreciation, and other supplies.

We expense research and development costs as incurred. We recognize costs for certain development activities, such as clinical trials, based on an evaluation of the progress to completion of specific tasks using data such as clinical site activations, patient enrollment, or information provided to us by our vendors and our clinical investigative sites. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and may be reflected in our consolidated financial statements as prepaid or accrued research and development expenses.

Our research and development expenses consist primarily of costs such as employee compensation, consulting fees, and CRO expenses in connection with our preclinical and clinical development activities. We typically use our employee and infrastructure resources across our development programs and we do not allocate personnel costs and other internal costs to specific product candidates or development programs with the exception of the costs to manufacture our product candidates.

Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will continue to increase for the foreseeable future as we initiate additional clinical trials, including one or more clinical trials for LYR-210 and LYR-220, scale our manufacturing processes, and continue to discover and develop additional product candidates.

The successful development of LYR-210, LYR-220, and other potential future product candidates is highly uncertain. Accordingly, at this time, we cannot reasonably estimate or know the nature, timing, and costs of the efforts that will be necessary to complete the development of these product candidates. We are also unable to predict when, if ever, we will generate revenue and material net cash inflows from the commercialization and sale of any of our product candidates for which we may obtain marketing approval. We may never succeed in achieving regulatory approval for any of our product candidates. The duration, costs, and timing of preclinical studies, clinical trials, and development of our product candidates will depend on a variety of factors, including:

- successful completion of clinical trials with safety, tolerability, and efficacy profiles for LYR-210, LYR-220, and any potential future product candidates that are satisfactory to the FDA or any comparable foreign regulatory authority;
- approval of an IND for LYR-220 and any potential future product candidate to commence planned or future clinical trials in the United States or foreign countries;
- significant and changing government regulation and regulatory guidance;
- timing and receipt of marketing approvals from applicable regulatory authorities;
- establishing arrangements with contract manufacturing organizations, or CMOs, for third-party clinical and commercial manufacturing to obtain sufficient supply of our product candidates;
- obtaining and maintaining patent and other intellectual property protection and regulatory exclusivity for our product candidates;
- commercializing the product candidates, if and when approved, whether alone or in collaboration with others;
- competition with other therapies; and
- business interruptions resulting from the COVID-19 pandemic.

A change in the outcome of any of these variables with respect to the development, manufacture, or commercialization enabling activities of any of our product candidates would significantly change the costs, timing, and viability associated with the development of that product candidate. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials beyond those that we anticipate will be required for the completion of clinical development of a product candidate, or if we experience significant delays in our clinical trials due to patient enrollment or other reasons, we may be required to expend significant additional financial resources and time on the completion of clinical development.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance, and administrative functions. General and administrative expenses also include direct and allocated facility-related costs as well as professional fees for legal, patent, consulting, investor, and public relations, accounting, auditing, tax services, and insurance costs.

We expect that our general and administrative expenses will increase in the future to support continued research and development activities and potential commercialization of our product candidates. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, attorneys, and accountants, among other expenses. Additionally, we will continue to incur increased expenses associated with being a public company, including costs of additional personnel, accounting, audit, legal, regulatory, and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, director and officer insurance costs, and investor and public relations costs.

Interest Income

Interest income consists of interest income earned on our cash and cash equivalents.

Critical Accounting Policies and Use of Estimates

Our management's discussion and analysis of financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States, or GAAP. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements during the reporting periods. These items are monitored and analyzed by us for changes in facts and circumstances, and material changes in these estimates could occur in the future. We base our estimates on historical experience, known trends and events, and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Changes in estimates are reflected in reported results for the period in which they become known. Actual results may differ materially from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies used in the preparation of our consolidated financial statements require the most significant judgments and estimates.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing purchase orders and open contracts, communicating with our personnel to identify services that have been performed on our behalf, and estimating the level of service performed and the associated cost incurred for the services when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed, on a pre-determined schedule, or when contractual milestones are met; however, some require advance payments. We make estimates of our accrued expenses as of each balance sheet date in our consolidated financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses include the following costs incurred for services in connection with research and development activities for which we have not yet been invoiced:

- vendors in connection with preclinical development activities;
- vendors in connection with the testing of preclinical and clinical trial materials;
- CROs in connection with preclinical and clinical studies; and
- investigative sites in connection with clinical trials.

We contract with CROs to conduct clinical and other research and development services on our behalf. We base our expenses related to CROs on our estimates of the services received and efforts expended pursuant to quotes and contracts with them. The financial terms of these agreements are subject to negotiation, vary from contract to contract, and may result in uneven payment flows. There may be instances in which payments made to our CROs will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or amount of prepaid expense accordingly. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

Stock-Based Compensation

We apply the fair value recognition provisions of ASC 718, *Compensation—Stock Compensation*, or ASC 718, for stock-based awards granted to employees and directors for their services on the board of directors. Determining the amount of stock-based compensation to be recorded requires us to develop estimates of the fair value of stock options as of their grant date. We estimate the fair value of each stock option grant using the Black-Scholes option-pricing model. Calculating the fair value of stock-based awards requires that we make subjective assumptions.

Pursuant to ASC 718, we measure stock-based awards granted to employees and members of the board of directors at fair value on the date of grant and recognize the corresponding stock-based compensation expense of those awards on a straight-line basis over the requisite service period, which is generally the vesting period of the respective award. We have historically granted stock options with exercise prices equivalent to the fair value of our common stock as of the date of grant.

We account for stock-based awards to non-employees in accordance with ASU No. 2018-07, *Compensation-Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting*, or ASU No. 2018-07, which simplifies the accounting for stock-based payments granted to non-employees for goods and services. Under ASU No. 2018-07, most of the guidance on such payments to non-employees would be aligned with the requirements for stock-based payments granted to employees. Prior to January 1, 2019, we accounted for stock-based payments to non-employees in accordance with ASC 505-50, *Equity-Based Payments to Non-Employees*, or ASC 505-50. Pursuant to ASC 505-50, we measured stock-based awards granted to non-employees at fair value as the awards vested and recognized the resulting value as expense during the period the related services were rendered, which was typically the vesting period. At the end of each financial reporting period prior to completion of the service, we re-measured the unvested portion of these awards using the then-current fair value of our common stock and updated assumption inputs in the Black-Scholes option-pricing model.

The Black-Scholes option-pricing model uses the following inputs: the fair value of our common stock, the expected volatility of our common stock, the expected term of our stock options, the risk-free interest rate for a period that approximates the expected term of our stock options, and our expected dividend yield. Following the closing of our IPO, the fair value of our common stock is determined based on the quoted market price of our common stock. We have historically been a private company and lack company-specific historical and implied volatility data. Therefore, we have based our computation of expected volatility on the historical volatility of a representative group of public companies with similar characteristics to us, including stage of product development, life science industry focus, length of trading history, and similar vesting provisions. The historical volatility data is calculated based on a period of time commensurate with the expected term assumption. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available or until circumstances change, such that the identified entities are no longer representative companies. In the latter case, more suitable, similar entities whose share prices are publicly available would be utilized in the calculation. We use the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, *Share-Based Payment*, to calculate the expected term for options granted to employees as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. Under this approach, the weighted-average expected option term is presumed to be the average of the contractual term (ten years) and the vesting term (generally four years) of our stock options. We utilize this method due to lack of historical exercise data and the “plain-vanilla” nature of our stock-based awards. The expected term is applied to the stock option grant group as a whole, as we do not expect substantially different exercise or post-vesting termination behavior among our employee population. For options granted to non-employees, we utilize the contractual term of the arrangement as the basis for the expected term assumption. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected term of the stock options. The expected dividend yield is assumed to be zero as we have never paid cash dividends, other than the Special Dividend, and have no current plans to pay any cash dividends on our common stock.

Recently Adopted Accounting Pronouncements

We have reviewed all recently issued standards and have determined that, other than as disclosed in Note 2 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K, such standards will not have a material impact on our consolidated financial statements or do not otherwise apply to our operations.

Results of Operations

Comparison of the Years Ended December 31, 2020 and 2019

The following table summarizes our results of operations for the years ended December 31, 2020 and 2019 (in thousands):

	Year Ended December 31,		Dollar
	2020	2019	Change
Operating expenses:			
Research and development	$ 12,522	$ 12,032	$ 490
General and administrative	9,687	4,487	5,200
Total operating expenses	22,209	16,519	5,690
Loss from operations	(22,209)	(16,519)	(5,690)
Other income:			
Interest income	82	213	(131)
Total other income	82	213	(131)
Net loss	$ (22,127)	$ (16,306)	$ (5,821)

Research and Development Expenses

Research and development expense increased by $0.5 million to $12.5 million for the year ended December 31, 2020 from $12.0 million for the year ended December 31, 2019.

The increase in research and development expense was primarily attributable to an increase of $1.9 million in employee related costs as we increased research and development headcount and an increase of $0.4 million in facility costs and other allocated expenses. The increase was partially offset by decreases of $1.0 million for product development and manufacturing expenses, $0.6 million for consulting expenses, and $0.3 million for clinical and regulatory expenses related to our LANTERN trial.

General and Administrative Expenses

General and administrative expense increased by $5.2 million to $9.7 million for the year ended December 31, 2020 from $4.5 million for the year ended December 31, 2019.

The increase in general and administrative expenses was primarily attributable to an increase in employee related costs of $2.3 million, including an increase of $1.4 million of stock-based compensation, an increase in costs associated with being a public company of $2.4 million, in particular an increase in the cost of directors and officers insurance of $2.2 million, an increase in professional and consulting expenses of $0.4 million, and a decrease in sublease income and expense reimbursements of $0.4 million related to the end of all subleases in June 2019. These increases were partially offset by a decrease of $0.2 million for a charge for uncollectible accounts in the year ended December 31, 2019 without a corresponding charge in the year ended December 31, 2020.

Interest Income

Interest income decreased $0.1 million to $82,000 for the year ended December 31, 2020 from $0.2 million for the year ended December 31, 2019. The decrease in interest income was attributable to lower average interest rates for the year ended December 31, 2020 due to changes in market conditions as compared to the year ended December 31, 2019.

Liquidity and Capital Resources

Sources of Liquidity

We have funded our operations from inception through December 31, 2020 primarily with gross proceeds of $162.1 million from sales of our redeemable convertible preferred stock, net proceeds of $57.3 million from our IPO, and $16.8 million from government contracts. The following table provides information regarding our total cash and cash equivalents at December 31, 2020 and 2019 (in thousands):

	As of December 31,	
	2020	2019
Cash and cash equivalents	$ 74,593	$ 9,808

Cash Flows

The following table provides information regarding our cash flows for the years ended December 31, 2020 and 2019 (in thousands):

	Year Ended December 31,	
	2020	2019
Net cash used in operating activities	$ (21,143)	$ (13,754)
Net cash used in investing activities	(1,775)	(211)
Net cash provided by (used in) financing activities	87,703	(115)
Net increase (decrease) in cash and cash equivalents	$ 64,785	$ (14,080)

Net Cash Used in Operating Activities

The cash used in operating activities resulted primarily from our net losses adjusted for non-cash charges and changes in components of working capital.

Net cash used in operating activities was $21.1 million for the year ended December 31, 2020 compared to $13.8 million for the year ended December 31, 2019. The increase in cash used in operating activities of $7.3 million was primarily attributable to:

- $5.8 million increase in net loss;
- $1.6 million increase in stock-based compensation; and
- $3.0 million decrease in changes in the components of working capital.

Net Cash Used in Investing Activities

Net cash used in investing activities was $1.8 million for the year ended December 31, 2020 compared to $0.2 million for the year ended December 31, 2019. The increase in cash used in investing activities of $1.6 million was attributable to an increase in cash used for the purchases of property and equipment as we invest in increasing our manufacturing capabilities.

Net Cash Provided by (Used in) Financing Activities

Net cash provided by financing activities was $87.7 million for the year ended December 31, 2020 compared to net cash used in financing activities of $0.1 for the year ended December 31, 2019. The increase in cash provided by financing activities of $87.8 million was attributable to:

- net proceeds of $30.2 million from the sale of our Series C redeemable convertible preferred stock in the year ended December 31, 2020; and

- completion of our IPO by issuing 4,025,000 shares of common stock, at an offering price of $16.00 per share, par value $0.001, for gross proceeds of $64.4 million and after deducting $6.9 million of underwriting discounts and commissions and offering expenses paid by us in the year ended December 31, 2020.

Funding Requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development for, begin the manufacturing scale up process for, initiate later stage clinical trials for, and seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing, and distribution. Furthermore, we will continue to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce, or eliminate our research and development programs or future commercialization efforts.

We expect that our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements into 2023. We have based this estimate on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Our future capital requirements will depend on many factors, including:

- the costs of conducting future clinical trials of LYR-210;
- the costs of manufacturing additional material for one or more pivotal Phase 3 clinical trials of LYR-210 and potential future clinical studies we might conduct for our other product candidates;
- the costs of scaling up our manufacturing process and supply chain capacity to provide sufficient quantities of LYR-210 for the potential commercialization of LYR-210 if our clinical development program is successful and we obtain marketing approval;
- the advancement of LYR-220;
- the scope, progress, results, and costs of discovery, preclinical development, laboratory testing, and clinical trials for other potential product candidates we may develop, if any;
- the costs, timing, and outcome of regulatory review of our product candidates;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under any collaboration agreements we might have at such time;
- the costs and timing of future commercialization activities, including product sales, marketing, manufacturing, and distribution, for any of our product candidates for which we receive marketing approval;
- the amount of revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval;
- the costs of preparing, filing, and prosecuting patent applications, obtaining, maintaining, and enforcing our intellectual property rights, and defending intellectual property-related claims;
- our headcount growth and associated costs as we expand our business operations, our research and development activities, and our manufacturing scale up;
- the costs of operating as a public company; and
- the cost of potential business interruptions resulting from the COVID-19 pandemic.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, and licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interests may be diluted, and the terms of these securities may include liquidation or other preferences that could adversely affect your rights as a common stockholder. Any debt financing, if available, may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends, that could adversely impact our ability to conduct our business.

If we raise funds through collaborations, strategic alliances, or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs, or product candidates, or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce, or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Off-Balance Sheet Arrangements

We did not have, during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable SEC rules.

Emerging Growth Company Status

The Jumpstart Our Business Startups Act of 2012, or the JOBS Act, permits an “emerging growth company” such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies. We have elected to use this extended transition period under the JOBS Act. As a result, our financial statements may not be comparable to the financial statements of issuers who are required to comply with the effective dates for new or revised accounting standards that are applicable to public companies, which may make comparison of our financials to those of other public companies more difficult.

We will remain an emerging growth company until the earliest to occur of: (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of our IPO, or December 31, 2025, (b) in which we have total annual gross revenues of $1.07 billion or more, or (c) in which we are deemed to be a large accelerated filer under the rules of the SEC, which means the market value of our outstanding common stock held by non-affiliates exceeds $700 million as of last business day of our most recently completed second fiscal quarter, and (2) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Quantitative and Qualitative Disclosures About Market Risk

We are a smaller reporting company as defined in Rule 12b-2 of the Exchange Act and are not required to provide the information otherwise required under this Item 7A.

Item 8. Financial Statements and Supplementary Data.

The consolidated financial statements required to be filed pursuant to this Item 8 are appended to this report and are incorporated herein by reference. An index to those financial statements is found in Item 15 of Part IV of this Annual Report on Form 10-K.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Management's Evaluation of Disclosure Controls and Procedures

Limitations on Effectiveness of Controls and Procedures

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated, as of the end of the period covered by this Annual Report on Form 10-K, the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act). Based on that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2020.

Management's Annual Report on Internal Control over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) or an attestation report of our independent registered accounting firm due to a transition period established by rules of the SEC for newly public companies. Additionally, our independent registered accounting firm will not be required to opine on the effectiveness of our internal control over financial reporting pursuant to Section 404 until we are no longer an "emerging growth company" as defined in the JOBS Act.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting identified in management's evaluation pursuant to Rules 13a-15(f) or 15d-15(f) of the Exchange Act during the quarter ended December 31, 2020 that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Information about our Directors

The following table presents information concerning our board of directors.

Name	Age	Position	In Current Position Since
Maria Palasis, Ph.D.	56	President and Chief Executive Officer and Director	January 2015
Michael Altman	39	Director	June 2018
Edward Anderson	71	Director	February 2019
C. Ann Merrifield	69	Director	September 2019
Konstantin Poukalov	37	Director	January 2020
W. Bradford Smith	65	Director	November 2019
Nancy Snyderman, M.D., FACS	68	Director	October 2020

The following are brief biographies describing the backgrounds of our directors.

Maria Palasis, Ph.D. has served as our President and Chief Executive Officer and a member of our board of directors since January 2015. Prior to her role with us as President and Chief Executive Officer, Dr. Palasis held positions of increasing responsibility, the most recent of which was Executive Vice President and Chief Technology Officer from 2011 to 2015. Before that, in 2008, Dr. Palasis joined Arsenal Medical, Inc., a biotechnology company, as Executive Vice President and subsequently served as President and Chief Executive Officer and a member of the board of directors of Arsenal Medical from January 2015 to June 2018. Before that, from November 1995 to January 2008, Dr. Palasis was employed with the title of Director at Boston Scientific Corporation, a medical device company, where she managed a portfolio of external biotech and medical device investments and led the development of several combination therapies. Dr. Palasis holds a B.S. and Ph.D. in Chemical Engineering from the University of Cincinnati, and she held a postdoctoral fellowship in molecular biology at the University of Cincinnati School of Medicine. We believe that Dr. Palasis' experience in the industry and knowledge of our company qualifies her to serve on our board of directors.

Michael Altman has served as a member of our board of directors since June 2018. Since 2007, Mr. Altman has been employed on the investment team at Perceptive Advisors, a life sciences focused investment firm, where he currently serves as Managing Director and focuses on medical devices, diagnostics, digital health and specialty pharmaceuticals investments. Since October 2018, Mr. Altman has also served as Chief Financial Officer and member of the board of directors of ARYA Sciences Acquisition Corp., a special purpose acquisition company. From October 2005 to October 2007, Mr. Altman served as a healthcare trader and analyst at First New York Securities. Mr. Altman has served on the board of directors of Vitruvius Therapeutics, Inc., a pharmaceutical company, since December 2017, and served on the board of directors of Vensun Pharmaceuticals, Inc., a pharmaceutical company, from November 2016 to January 2019. Mr. Altman holds a B.S. in Business Administration from the University of Vermont. We believe that Mr. Altman's broad operational and transactional experience qualifies him to serve on our board of directors.

Edward Anderson has served as a member of our board of directors since February 2019. Since June 1994, Mr. Anderson has served as the Founder and a Managing Partner at North Bridge Venture Partners & Growth Equity, a venture capital firm. Mr. Anderson holds a B.F.A. from the University of Denver and an M.B.A. from Columbia University Graduate School of Business. We believe that Mr. Anderson's extensive experience in venture capital investments qualifies him to serve on our board of directors.

C. Ann Merrifield has served as a member of our board of directors since September 2019. Ms. Merrifield has also served as a member of the boards of directors for a portfolio of public and private companies in the life sciences sector which include Flexion Therapeutics, Inc., since June 2014, InVivo Therapeutics Holdings Corp., since November 2014. From July 2015 to August 2018, she served as a director of Juniper Pharmaceuticals, Inc., a healthcare company, until it was acquired by Catalent, Inc. and from December 2016 to January 2019, she served as a director of Veritas Genetics, Inc. Ms. Merrifield also serves as a Trustee for MassMutual Premier, Select and MML Series Investment Funds, Partners Continuing Care (the post-acute care services division of Partners HealthCare), the Huntington Theatre Company and the YMCA of Greater Boston. From November 2012 to July 2014, Ms. Merrifield served as President, Chief Executive Officer and director of PathoGenetix Inc., a genomics company, which voluntarily filed for Chapter 7 bankruptcy in July 2014. Before that, Ms. Merrifield spent 18 years at Genzyme Corporation, serving in several leadership roles, including President of Genzyme Biosurgery, President of Genzyme Genetics and Senior Vice President, Business Excellence. Ms. Merrifield holds a B.A. in Zoology and a Master of Education from the University of Maine and an M.B.A. from the Tuck School of Business at Dartmouth College. We believe that Ms. Merrifield's extensive industry experience qualifies her to serve on our board of directors.

Konstantin Poukalov has served as a member of our board of directors since January 2020. Since March 2019, Mr. Poukalov has served as Managing Director at Perceptive Advisors, a life sciences focused investment firm. Since August 2019, Mr. Poukalov has also served on the board of directors of Landos Biopharma, Inc., a biopharmaceutical company. From July 2012 to October 2018, Mr. Poukalov served in roles of increasing responsibility at Kadmon Holdings, Inc., a biopharmaceutical company, most recently serving as Executive Vice President and Chief Financial Officer from July 2014 to October 2018. Mr. Poukalov holds a B.S. in Electrical Engineering from Stony Brook University. We believe that Mr. Poukalov's extensive financial and industry experience qualify him to serve on our board of directors.

W. Bradford Smith has served a member of our board of directors since November 2019. Mr. Smith has served as Chief Financial Officer and Treasurer of Homology Medicines, Inc., a genetic medicines company, since April 2017 and as Secretary since July 2017. From March 2014 to April 2017, Mr. Smith was Chief Financial Officer of Ocular Therapeutix, Inc., a biopharmaceutical company. Prior to joining Ocular Therapeutix, Mr. Smith served as Chief Financial Officer of OmniGuide, Inc., a medical device company, from July 2008 to March 2014. Mr. Smith holds a B.S. in Biology from Tufts University and an M.B.A. from the Whittemore School of Business and Economics at the University of New Hampshire. We believe that Mr. Smith's extensive financial and industry experience qualify him to serve on our board of directors.

Nancy Snyderman, M.D., FACS has served as a member of our board of directors since October 2020. Dr. Snyderman has also served on the boards of directors of Axonics Modulation Technologies, Inc., a medical device company, since April 2019 and Alkermes plc, a biopharmaceutical company, since May 2016. From 2006 to 2018, Dr. Snyderman served as an advisory board member to GE's Healthymagination, General Electric Company's healthcare initiative. From 2003 to 2008, Dr. Snyderman also served as a vice president for corporate communications at Johnson & Johnson. Dr. Snyderman is a board-certified head and neck surgeon and has had academic appointments at the University of Pennsylvania and the University of California-San Francisco. From 2016 to 2018, she served as a professor at the Center for Innovation for Global Health at Stanford University. Dr. Snyderman is an Emmy award winning medical correspondent, having worked at ABC News from 1987 to 2003 and later as chief medical editor at NBC News from 2004 to 2015. Dr. Snyderman holds a B.A. in Microbiology from Indiana University and a M.D. from the University of Nebraska and has completed residencies in Pediatrics and Otolaryngology Head and Neck Surgery at the University of Pittsburgh. We believe that Dr. Snyderman's extensive experience as a veteran healthcare journalist, a practicing physician, and an executive at a pharmaceutical company, as well as her roles in academia and as advisor to policy organizations, qualify her to serve on our board of directors.

Information about our Executive Officers

Name	Age	Position	In Current Position Since
Maria Palasis, Ph.D.	56	President and Chief Executive Officer and Director	January 2015
R. Don Elsey	68	Chief Financial Officer, Treasurer and Secretary	August 2019
Robert Richard, Ph.D.	64	Senior Vice President of Research and Development	June 2020
Pamela Nelson	51	Senior Vice President of Regulatory Affairs	August 2020
Corinne Noyes	53	Senior Vice President of Commercial Strategy and Market Development	September 2018

The following are brief biographies describing the backgrounds of our executive officers.

The biography for Dr. Palasis appears above on page 102.

R. Don Elsey has served as our Chief Financial Officer since August 2019 and as our Treasurer and Secretary since October 2019. Prior to joining our company, from February 2015 to February 2019, Mr. Elsey served as Chief Financial Officer at Senseonics, Inc., a medical device company. From May 2014 until February 2015, Mr. Elsey served as Chief Financial Officer of Regado Biosciences, Inc., a biopharmaceutical company. From December 2012 to February 2014, Mr. Elsey served as Chief Financial Officer of LifeCell Corporation, a privately held regenerative medicine company. Mr. Elsey holds a B.A. in economics and an M.B.A. in finance from Michigan State University.

Robert Richard, Ph.D. has served as our Senior Vice President of Research and Development since June 2020. Prior to joining our company, from February 2019 to May 2020 Dr. Richard served as Vice President of Research and Development at Anika Therapeutics, Inc., a therapeutics company. Prior to that, he held research and development leadership positions at Hyalex Orthopaedics, Inc., a medical device company, from November 2017 to February 2019, C.R. Bard, Inc., a medical device company, from June 2008 to November 2017, Boston Scientific Corporation, a global medical device company, from September 2000 to June 2008, and Johnson & Johnson, a global medical device, pharmaceutical and consumer product company, from September 1991 to August 2000. Dr. Richard holds a B.S. in chemistry and a B.S. in biology from University of Massachusetts at Dartmouth and a Ph.D. in polymer chemistry and plastics engineering from the University of Massachusetts at Lowell.

Pamela Nelson has served as our Senior Vice President of Regulatory Affairs since August 2020. Prior to joining our company, from January 2011 to July 2020, Ms. Nelson served as Vice President, Regulatory Affairs at Avedro, Inc., a medical technology company. Prior to that, she held regulatory positions at Alnara Pharmaceuticals, Inc., a biotechnology company from June 2009 to December 2010, Altus Pharmaceuticals Inc., a biopharmaceutical company from February 2006 to May 2009, Alkermes PLC, a global biopharmaceutical company July 1998 to January 2006 and Genzyme Corporation, a global biotechnology company January 1995 to June 1998. Ms. Nelson holds a B.A. in English and an M.A. in education administration from the University of Massachusetts at Amherst.

Corinne Noyes has served as our Senior Vice President of Commercial Strategy and Market Development since September 2018. Prior to joining our company, from January 2018 to August 2018, Ms. Noyes served as an independent contractor to our Company, providing biopharmaceutical consulting services. Before that, from January 2005 to August 2018, Ms. Noyes worked as a strategic advisor and independent biopharmaceutical consultant providing commercial leadership to emerging life sciences companies, including, among others, AMAG Pharmaceuticals, Inc., Avila Therapeutics, Inc. (Celgene Corporation), Adnexus Therapeutics Inc. (Bristol-Myers Squibb Company), Constellation Pharmaceuticals, Inc. and Editas Medicine, Inc. Before that, from 1997 to 2004, Ms. Noyes held various commercial leadership positions at Biogen Inc., a biotechnology company. Prior to joining Biogen Inc., from 1992 to 1996, Ms. Noyes worked as a health care strategy consultant at Deloitte & Touche LLP. Ms. Noyes holds a B.A. in Humanities and a B.B.A. in Business from St. Mary's College of Notre Dame and an M.B.A. in finance from University of Chicago Graduate School of Business.

Family Relationships

There are no family relationships among any of our executive officers or directors.

Code of Business Conduct and Ethics

The Board has adopted a written code of business conduct (the "Code of Business Conduct and Ethics") that applies to all of our directors, officers and employees, including our principal executive officer, principal financial officer and principal accounting officer. A copy of the code is available on our website at www.lyratherapeutics.com in the "Governance" section of the "Investors & News" page. In addition, we intend to post on our website all disclosures that are required by law or The Nasdaq Stock Market LLC concerning any amendments to, or waivers from, any provision of our Code of Business Conduct and Ethics.

Audit Committee and Audit Committee Financial Expert

We have a separately-designated standing audit committee ("Audit Committee") that consists of Edward Anderson, C. Ann Merrifield and Bradford Smith. Mr. Smith serves as the Chair of the Audit Committee. Our board of directors has determined that all members of the audit committee (Edward Anderson, C. Ann Merrifield and Bradford Smith) are independent directors under the Nasdaq rules and the additional independence standards applicable to audit committee members established pursuant to Rule 10A-3 under the Exchange Act. Our board of directors has also determined that each of Edward Anderson, C. Ann Merrifield and Bradford Smith meets the "financial literacy" requirement for audit committee members under the Nasdaq Stock Market rules and Bradford Smith is an "audit committee financial expert" within the meaning of the SEC rules.

Item 11. Executive Compensation.

This section discusses the material components of the executive compensation program for our executive officers who are named in the "2020 Summary Compensation Table" below. In 2020, our "named executive officers" and their positions were as follows:

- Maria Palasis, Ph.D., President and Chief Executive Officer;
- R. Don Elsey, Chief Financial Officer; and
- Robert Richard, Ph.D., Senior Vice President of Research and Development.

Dr. Richard commenced employment with us effective June 22, 2020.

2020 Summary Compensation Table

The following table sets forth information concerning the compensation of our named executive officers for the years shown.

Name and Principal Position	Year	Salary ($)	Option Awards(1) ($)	Non-Equity Incentive Plan Compensation(2) ($)	All Other Compensation ($)		Total ($)
Maria Palasis, Ph.D. *President and Chief Executive Officer*	2020	470,520	3,547,671	275,000	8,550	(3)	4,301,741
	2019	388,025	318,850	135,809	—		842,684
R. Don Elsey *Chief Financial Officer*	2020	362,558	224,350	150,000	23,778	(4)	760,686
	2019	130,625	501,247	41,671	64,235		737,778
Robert Richard, Ph.D.(5) *Senior Vice President of Research and Development*	2020	164,127	300,043	81,000	4,428	(3)	549,598

(1) Amounts represent the full grant date fair value of stock options granted during 2020 computed in accordance with ASC Topic 718, rather than the amounts paid to or realized by the named individual. We provide information regarding the assumptions used to calculate the value of all option awards made to named executive officers in Note 8 to the consolidated financial statements included in this Annual Report on Form 10-K.

(2) Amounts represent performance-based annual cash bonuses made by our board of directors for the named executive officers for fiscal year 2020.

(3) Amounts represent company 401(k) matching contributions.

(4) The amount represents company 401(k) matching contributions and use of a corporate apartment, commuting expenses and related tax gross-ups.

(5) Dr. Richard commenced employment with us in June 2020.

Narrative to Summary Compensation Table

2020 Salaries

The named executive officers receive a base salary to provide a fixed component of compensation reflecting the executive's skill set, experience, role and responsibilities. For 2020, the initial base salaries for Dr. Palasis and Mr. Elsey were $401,606 and $329,740, respectively. In connection with our initial public offering, our board of directors approved increasing the base salaries of Dr. Palasis and Mr. Elsey to $500,000 and $375,000, respectively, effective upon the closing of the offering in May 2020. Dr. Richard's base salary was set at $307,000 in connection with his commencement of employment with us in June 2020.

2020 Bonuses

We offer our named executive officers the opportunity to earn annual cash bonuses to compensate them for attaining short-term company goals as approved by our board of directors. For 2020, bonuses were based entirely on attaining clinical, research and development, strategic, capital raising and financial goals. The 2020 target bonuses for each of Dr. Palasis, Mr. Elsey and Dr. Richard were 55%, 40% and 35%, respectively, of his or her annual base salary. The target bonuses for Dr. Palasis and Mr. Elsey were increased from 35% and 30%, respectively, in connection with our initial public offering, and Dr. Richard's target bonus was set in connection with his commencement of employment with us in June 2020. Dr. Richard's bonus for 2020 was prorated to reflect his partial year of employment. The actual annual cash bonuses awarded to each named executive officer for 2020 performance are set forth above in the 2020 Summary Compensation Table in the column titled "Non-Equity Incentive Plan Compensation".

Equity Compensation

We offer stock options to our employees, including our named executive officers, as the long-term incentive component of our compensation program. Our stock options generally allow employees to purchase shares of our common stock at a price equal to the fair market value of our common stock on the date of grant. With respect to grants made in connection with the commencement of employment, our stock options typically vest as to 25% of the underlying shares on the first anniversary of the vesting commencement date and in equal monthly installments over the following three years, subject to the holder's continued service with us. From time to time, our board of directors may also construct alternate vesting schedules as it determines are appropriate to motivate particular employees. Historically, our stock options have been intended to qualify as "incentive stock options" to the extent permitted under the Internal Revenue Code.

The following table sets forth the stock options granted to our named executive officers in 2020.

Named Executive Officer	2020 Stock Options Granted
Maria Palasis, Ph.D.	326,303
R. Don Elsey	20,635
Robert Richard, Ph.D.	35,000

The stock option awards to Dr. Palasis and Mr. Elsey were made in connection with the initial public offering effective April 2020 and vest in 48 equal monthly installments following the effective date of grant, subject to the continued service of the applicable named executive officer. The stock option award to Dr. Richard was made in June 2020 in connection with his commencement of employment with us and is subject to our standard vesting schedule for grants made in connection with the commencement of employment described above.

Other Elements of Compensation

Retirement Plan

We maintain a 401(k) retirement savings plan for our employees, including our named executive officers, who satisfy certain eligibility requirements. Our named executive officers are eligible to participate in the 401(k) plan on the same terms as other full-time employees. We believe that providing a vehicle for tax-deferred retirement savings though our 401(k) plan adds to the overall desirability of our executive compensation package and further incentivizes our employees, including our named executive officers, in accordance with our compensation policies. For 2020, we made matching contributions of 50% of the first 6% of eligible compensation contributed under our 401(k) plan.

Employee Benefits and Perquisites

All of our full-time employees, including our named executive officers, are eligible to participate in our employee benefit plans and programs, including medical, dental, and vision benefits, health spending accounts, and short- and long-term disability, accidental death and dismemberment, and life insurance, to the same extent as our other full-time employees, subject to the terms and eligibility requirements of those plans.

Outstanding Equity Awards at 2020 Fiscal Year-End

The following table summarizes the number of shares of common stock underlying outstanding equity incentive plan awards for each named executive officer as of December 31, 2020.

Name	Vesting Commencement Date	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Equity Incentive Plan Awards: Number of Securities Underlying Unexercised Unearned Options (#)	Option Exercise Price ($)	Option Expiration Date
Maria Palasis, Ph.D.	11/16/2011	22,793	—	—	8.63	11/16/2021
	2/26/2013	24,358	—	—	21.73	6/26/2023
	1/1/2015	94,287	—	—	22.76	9/23/2025
	6/13/2017	31,429	—	31,429 (2)	1.73	6/13/2027
	3/6/2019	74,573	95,882 (1)	—	2.76	3/6/2029
	4/30/2020	54,383	271,920 (1)	—	16.00	4/29/2030
R. Don Elsey	7/29/2019	26,485	48,298 (3)	—	4.49	9/24/2029
	4/30/2020	3,439	17,196 (1)	—	16.00	4/29/2030
Robert Richard, Ph.D.	6/24/2020	—	35,000 (3)	—	12.33	6/24/2030

(1) Options vest and become exercisable in equal monthly installments over four years following the vesting commencement date, subject to the named executive officer's continued service with us on each applicable vesting date.

(2) Options vest and become exercisable at the end of any given three-month period occurring prior to six years from the vesting commencement date in which we recognize revenue from the commercial sale of an FDA-approved product each month and in amounts, with respect to the second and third months of such period that increase from the revenue recognized from such product sales in the immediately preceding month, subject to Dr. Palasis' continued employment with us on each applicable vesting date.

(3) Options vest and become exercisable as to 25% of the underlying shares on the first anniversary of the vesting commencement date and in 36 equal monthly installments over the following three years, subject to the named executive officer's continued service with us on each applicable vesting date.

Executive Employment Agreements

We entered into new employment agreements with Dr. Palasis and Mr. Elsey in connection with our initial public offering that superseded their prior employment arrangements with us, and we entered into an employment agreement with Dr. Richard in connection with his commencement of employment with us in June 2020. The employment agreements provide for the annual base salaries and annual target bonus opportunities described above under the headings "—Annual Base Salaries" and "—Target Bonuses". Through December 31, 2020, and subject to renewal by our board of directors thereafter, Mr. Elsey is also entitled to (i) reimbursement of reasonable travel expenses from his home to our offices in Massachusetts, (ii) use of a corporate apartment while working in Massachusetts and (iii) reimbursement for income and employment taxes incurred by Mr. Elsey as a result of these commuting payments and benefits. The total amount for (i) through (iii) may not exceed $75,000.

Under the employment agreements, if we terminate the employment of Dr. Palasis, Mr. Elsey or Dr. Richard without "cause" or the executive resigns for "good reason" (each as defined below), subject to the executive's timely execution of a release of claims and continued compliance with a separate restrictive covenant agreement (described below), the executive is entitled to receive (i) base salary continuation for a period of 12 months for Dr. Palasis, 9 months for Mr. Elsey and 6 months for Dr. Richard; (ii) payment of any annual bonus for the prior year earned but unpaid as of the date of termination and (iii) direct payment of or reimbursement for continued medical, dental or vision coverage pursuant to COBRA for up to 12 months for Dr. Palasis, 9 months for Mr. Elsey and 6 months for Dr. Richard, less the amount each named executive officer would have had to pay to receive such coverage as an active employee based on the cost sharing levels in effect on the named executive officer's termination date.

If we terminate Dr. Palasis, Mr. Elsey or Dr. Richard without "cause" or the executive resigns for "good reason," in either case, on or within three months prior to or 12 months following a change in control, then, in lieu of the severance benefits described above, subject to the executive's timely execution of a release of claims, the executive is entitled to receive (i) an amount equal in cash equal to 1.5 times for Dr. Palasis, one times for Mr. Elsey and 0.75 times for Dr. Richard the sum of the named executive officer's annual base salary plus target annual bonus for the year of termination, (ii) payment of any annual bonus for the prior year earned but unpaid as of the date of termination, (iii) direct payment of or reimbursement for continued medical, dental or vision coverage pursuant to COBRA for up to 18 months for Dr. Palasis, 12 months for Mr. Elsey and 9 months for Dr. Richard, less the amount each named executive officer would have had to pay to receive such coverage as an active employee based on the cost sharing levels in effect on the named executive officer's termination date, and (iv) accelerated vesting of all unvested equity or equity-based awards held by the named executive officer that vest solely based on the passage of time, with any such awards that vest based on the attainment of performance-vesting conditions being governed by the terms of the applicable award agreement.

Each of our named executive officers has agreed to refrain from competing with us while employed and following his or her termination of employment for any reason for a period of one year and to refrain from soliciting our employees or customers while employed and following his or her termination of employment for any reason for a period of two years in the case of Dr. Palasis and Mr. Elsey and one year in the case of Dr. Richard.

For purposes of the employment agreements, "cause" generally means the named executive officer's refusal to substantially perform the duties associated with his or her position with our company or to carry out the reasonable and lawful instructions of our board of directors concerning duties or actions consistent with his or her position, his or her breach of a material provision of the employment agreement which remains uncured (to the extent capable of cure) for a period of 30 days following written notice from our company, his or her conviction, plea of no contest or nolo contendere or imposition of unadjudicated probation for any felony or crime involving moral turpitude, his or her unlawful use (including being under the influence) or possession of illegal drugs on our premises or while performing his or her duties and responsibilities under the employment agreement, or his or her commission of any act of fraud, embezzlement, misappropriation, willful misconduct, or breach of fiduciary duty against us.

For purposes of the employment agreements, "good reason" generally means, subject to certain cure rights, the named executive officer's termination of employment due to a reduction in salary or target bonus (other than a reduction of 20% or less of the named executive officer's base salary implemented as part of an across the board, proportionate reduction of base salaries for other members of our management team), a material decrease in authority or areas of responsibility, our company's breach of any one or more of the material provisions of the employment agreement, or a relocation by our company of the named executive officer's primary office to a location more than 50 miles from the named executive officer's primary office on the date of the agreement.

Director Compensation

2020 Director Compensation Table

Name	Fees Earned or Paid in Cash ($)	Stock Awards ($)(1)	Option Awards ($)(1)	Total ($)
Robert Langer Sc.D.(2)	19,355	—	—	19,355
George Whitesides Ph.D.(2)	19,355	314,576	—	333,931
Michael Altman	26,667	—	156,163	182,830
C. Ann Merrifield	70,333	—	56,264	126,597
Edward Anderson	31,667	—	156,163	187,830
W. Bradford Smith	52,667	—	76,110	128,777
Konstantin Poukalov	26,667	—	156,163	182,830
Nancy Snyderman, M.D.(3)	7,204	—	118,264	125,468

(1) Amounts reflect the full grant-date fair value of stock awards and stock options granted during 2020 computed in accordance with ASC Topic 718, rather than the amounts paid to or realized by the named individual. We provide information regarding the assumptions used to calculate the value of all stock awards and option awards made to our directors in Note 8 to the consolidated financial statements included in this Annual Report on Form 10-K

(2) Dr. Langer and Dr. Whitesides resigned from our board of directors on October 26, 2020.

(3) Dr. Snyderman was appointed to our board of directors on October 27, 2020.

The table below shows the aggregate numbers of option awards (exercisable and unexercisable) held as of December 31, 2020 by each non-employee director. None of our non-employee directors held unvested stock awards as of December 31, 2020.

Name	Options Outstanding at Fiscal Year End
Robert Langer Sc.D.	121,584
George Whitesides Ph.D.	107,085
Michael Altman	14,500
C. Ann Merrifield	13,288
Edward Anderson	14,500
W. Bradford Smith	13,289
Konstantin Poukalov	14,500
Nancy Snyderman, M.D.	14,500

Non-Employee Director Compensation Program

In connection with our initial public offering, we adopted, and our stockholders approved, a compensation program for our non-employee directors under which each non-employee director receives the following amounts for their services on our board of directors:

- Upon the director's initial election or appointment to our board of directors, an option to purchase 14,500 shares of our common stock;
- If the director has served on our board of directors for at least six months as of the date of an annual meeting of stockholders and will continue to serve as a director immediately following such meeting, an option to purchase 7,250 shares of our common stock on the date of the annual meeting;
- An annual director fee of $40,000;
- If the director serves as lead independent director or chair or on a committee of our board of directors, an additional annual fee as follows:
    - Chair of the board or lead independent director: $25,000;
    - Chair of the audit committee: $20,000;
    - Audit committee member other than the chair, $7,500;
    - Chair of the compensation committee, $15,000;
    - Compensation committee member other than the chair, $5,000;
    - Chair of the nominating and corporate governance committee, $8,000; and
    - Nominating and corporate governance committee member other than the chair, $4,000.

Director fees under the program are payable in arrears in four equal quarterly installments not later than the fifteenth day following the final day of each calendar quarter, provided that the amount of each payment is prorated for any portion of a quarter that a director is not serving on our board of directors and no fee was payable in respect of any period prior to the effective date of the registration statement relating to our initial public offering.

Stock options granted to our non-employee directors under the program have an exercise price equal to the fair market value of our common stock on the date of grant and expire not later than ten years after the date of grant. The stock options granted upon a director's initial election or appointment vest in 36 substantially equal monthly installments following the date of grant. The stock options granted annually to directors vest in a single installment on the earlier of the day before the next annual meeting or the first anniversary of the date of grant. In addition, all unvested stock options vest in full upon the occurrence of a change in control.

IPO Grants to Non-Employee Directors under the 2020 Plan

In connection with our initial public offering, our board of directors approved the grant to each of Michael Altman, Edward Anderson, Robert Langer, Sc.D., Konstantin Poukalov and George Whitesides, Ph.D. of an option to purchase 14,500 shares of our common stock at an exercise price per share equal to the initial public offering price per share of our common stock. Each option vests in 36 substantially equal monthly installments following the date of grant, subject to such director's continued service through each applicable vesting date and accelerated vesting upon a change in control.

Whitesides Stock Award

In connection with our initial public offering, our board of directors granted to Dr. Whitesides an award of 19,661 vested shares of our common stock, effective as of May 1, 2020, the date of effectiveness of the registration statement on Form S-8 registering the issuance of the shares subject to the award.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

Securities Authorized for Issuance under Equity Compensation Plans (As of December 31, 2020)

Plan category:	Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants, and Rights		Weighted-Average Exercise Price of Outstanding Options, Warrants, and Rights		Number of Securities Available for Future Issuance Under Equity Compensation Plans (excludes securities Reflected in first column) (4)
Equity compensation plans approved by security holders(1)	1,428,886	(2)	$ 10.41	(3)	1,609,767
Equity compensation plans not approved by security holders	—		—		—
Total	1,428,886		$ 10.41		1,609,767

(1) Consists of the Lyra Therapeutics, Inc. 2020 Stock Incentive Plan, as amended (the "2020 Plan"), 2016 Equity Incentive Plan, as amended ("2016 Plan"), 2005 Equity Incentive Plan, as amended ("2005 Plan"), and the 2020 Employee Stock Purchase Plan ("2020 ESPP").

(2) Includes 219,460 shares of common stock issuable upon exercise of stock options under the 2005 Plan, 576,806 shares of common stock issuable upon exercise of stock options under the 2016 Plan, and 632,620 shares of common stock issuable upon exercise of stock options under the 2020 Plan.

(3) As of December 31, 2020, the weighted-average exercise price of outstanding options under the 2005 Plan was $16.60, the weighted-average exercise price of outstanding options under the 2016 Plan was $2.95, and the weighted-average exercise price of outstanding options under the 2020 Plan was $15.05.

(4) Includes 1,459,767 shares available for future issuance under the 2020 Plan and 150,000 shares available for issuance under the 2020 ESPP. We no longer make any grants under the 2016 Plan or the 2005 Plan, and we have not yet commenced offering periods under the 2020 ESPP. The 2020 Plan provides for an annual increase on the first day of each calendar year beginning January 1, 2021 and ending on and including January 1, 2030, equal to the lesser of (A) 4% of the aggregate number of shares of common stock outstanding on the final day of the immediately preceding calendar year, and (B) such smaller number of shares as is determined by the board of directors, provided that no more than 8,800,000 shares of our common stock may be issued pursuant to the exercise of incentive stock options. In addition, any shares that were subject to awards outstanding under the 2005 Plan and the 2016 Plan as of the effective date of the 2020 Plan which are forfeited, expire, lapse for any reason or are settled for cash without the issuance of shares will be added to the number of shares available for issuance under the 2020 Plan. The 2020 ESPP provides for an annual increase on the first day of each calendar year beginning January 1, 2021 and ending on and including January 1, 2030, equal to the lesser of (A) 0.5% of the aggregate number of shares of common stock outstanding on the final day of the immediately preceding calendar year, and (B) such smaller number of shares as is determined by the board of directors, provided that no more than 987,500 shares of our common stock may be issued under the 2020 ESPP.

Security Ownership of Certain Beneficial Owners and Management

The following table sets forth information with respect to the beneficial ownership of our common stock by (i) each person or group of affiliated persons known by us to beneficially own more than 5% of our common stock and (ii) each of our named executive officers, each of our directors and all of our current executive officers and directors as a group as of March 1, 2021, unless otherwise indicated.

The number of shares beneficially owned by each stockholder is determined under rules issued by the SEC. Under these rules, beneficial ownership includes any shares as to which the individual or entity has sole or shared voting power or investment power. Applicable percentage ownership is based on 12,947,572 shares of common stock outstanding as of March 1, 2021. In computing the number of shares beneficially owned by an individual or entity and the percentage ownership of that person, shares of common stock subject to options held by such person that are currently exercisable or will become exercisable within 60 days of March 1, 2021 are considered outstanding, although these shares are not considered outstanding for purposes of computing the percentage ownership of any other person. Unless noted otherwise, the address of all listed stockholders is 480 Arsenal Way, Watertown, MA 02472. Each of the stockholders listed has sole voting and investment power with respect to the shares beneficially owned by the stockholder unless noted otherwise, subject to community property laws where applicable.

Name of Beneficial Owner	Shares of Common Stock Beneficially Owned	Percentage
5% or Greater Stockholders		
Entities Affiliated with Perceptive Advisors, LLC(1)	3,222,561	24.9%
Entities Affiliated with North Bridge Venture Partners(2)	1,713,333	13.2%
Entities Affiliated with Polaris Venture Partners(3)	1,423,772	11.0%
RA Capital Healthcare Fund, L.P.(4)	815,849	6.3%
Ikarian Capital, LLC(5)	815,364	6.3%
Intersouth Partners VII, L.P.(6)	738,203	5.7%
Arrowmark Colorado Holdings, LLC(7)	648,321	5.0%
Named Executive Officers and Directors		
Maria Palasis, Ph.D.(8)	348,220	2.6%
R. Don Elsey(9)	39,750	*
Robert Richard, Ph.D.(10)	750	*
Edward Anderson(2)	1,718,166	13.3%
Michael Altman(1)	4,833	*
C. Ann Merrifield(11)	7,110	*
Nancy Snyderman, M.D., FACS(12)	3,441	*
W. Bradford Smith(13)	6,275	*
Konstantin Poukalov(1)	4,833	*
All current executive officers and directors as a group (11 persons)(14)	2,173,910	16.2%

* Less than 1%.

(1) Pursuant to a Schedule 13D filed with the SEC on June 1, 2020, Perceptive Life Sciences Master Fund, Ltd. (“Perceptive Life”) reported shared voting power and shared dispositive power over 1,934,115 shares of common stock; Perceptive LS (A), LLC (“Perceptive LS”) reported shared voting power and shared dispositive power over 1,288,446 shares of common stock; Joseph Edelman reported shared voting power and shared dispositive power over 3,223,561 shares of common stock; and Perceptive Advisors LLC reported shared voting power and shared dispositive power over 3,223,561 shares of common stock. Perceptive Advisors LLC serves as the investment advisor to Perceptive Life. Perceptive LS GP, LLC is the manager of Perceptive LS. Joseph Edelman is the managing member of Perceptive Advisors LLC and the sole member of Perceptive LS GP, LLC. Michael Altman and Konstantin Poukalov, two of our directors, are Managing Directors at Perceptive Advisors LLC. Messrs. Altman and Poukalov each have sole voting power and sole dispositive power over 4,833 shares of common stock that are or will be immediately exercisable within 60 days of March 1, 2021. The address of the aforementioned individuals and entities is c/o Perceptive Advisors, LLC, 51 Astor Place, 10th Floor, New York, New York 10003.

(2) Pursuant to a Schedule 13D filed with the SEC on May 15, 2020, North Bridge Venture Partners V-A, L.P. ("NBVP V-A") reported shared voting power and shared dispositive power over 778,592 shares of common stock; North Bridge Venture Partners V-B, L.P. ("NBVP V-B") reported shared voting power and shared dispositive power over 381,618 shares of common stock; and North Bridge Venture Partners VI, L.P. ("NBVP VI") reported shared voting power and shared dispositive power over 553,123 shares of common stock. North Bridge Venture Management V, L.P. ("NBVM V"), is the sole General Partner of NBVP V-A and NBVP V-B and may be deemed to have voting and dispositive power with respect to the shares held by those entities. NBVM GP, LLC, the General Partner of NBVM V, may be deemed to have voting and dispositive power over the shares held of record by NBVP VA and NBVP V-B. Shared voting and dispositive power of such shares are vested in Edward T. Anderson and Richard A. D'Amore. North Bridge Venture Management VI, L.P. ("NBVM VI"), is the sole General Partner of NBVP VI. NBVM GP, LLC, the General Partner of NBVM VI, and may be deemed to have voting and dispositive power over the shares held of record by NBVP VI. Shared voting and dispositive power of such shares are vested in Edward T. Anderson and Richard A. D'Amore. Mr. Anderson, a member of our board of directors and a manager of NBVM GP, LLC, disclaims beneficial ownership over such shares, except to the extent of his pecuniary interest therein. Mr. Anderson has sole voting power and sole dispositive power over 4,833 shares of common stock that are or will be immediately exercisable within 60 days of March 1, 2021. The address of all entities affiliated with North Bridge Venture Partners is 60 William Street, Suite 350, Wellesley, MA 02481.

(3) Pursuant to a Schedule 13G filed with the SEC on February 12, 2021, Polaris Venture Partners IV, L.P. ("PVP IV") reported shared voting power and shared dispositive power over 316,980 shares of common stock; Polaris Venture Partners Entrepreneurs' Fund IV, L.P. ("PVPEF IV" and, together with PVP IV, the "Polaris IV Funds") reported shared voting power and shared dispositive power over 5,940 shares of common stock; Polaris Venture Partners V, L.P. ("PVP V") reported shared voting power and shared dispositive power over 1,062,259 shares of common stock; Polaris Venture Partners Entrepreneurs' Fund V, L.P. ("PVPEF V") reported shared voting power and shared dispositive power over 20,701 shares of common stock; Polaris Venture Partners Founders' Fund V, L.P. ("PVPFF V") reported shared voting power and shared dispositive power over 7,274 shares of common stock; Polaris Venture Partners Special Founders' Fund V, L.P. ("PVPSFF V," and together with PVP V, PVPEF V and PVPFF V, the "Polaris V Funds" and the Polaris V Funds, together with the Polaris IV Funds, the "Polaris Funds") reported shared voting power and shared dispositive power over 10,618 shares of common stock; Polaris Venture Management Co., IV, L.L.C. ("PVM IV") reported shared voting power and shared dispositive power over 1,100,852 shares of common stock; and Polaris Venture Management Co. IV, L.L.C.. reported shared voting power and shared dispositive power over 322,920 shares of common stock. PVM IV is the sole general partner of each of the Polaris IV Funds and may be deemed to have sole voting and dispositive power with respect to the shares held by each of the Polaris IV Funds. Polaris Venture Management Co. V, L.L.C. ("PVM V") is the sole general partner of each of the Polaris V Funds and may be deemed to have sole voting and dispositive power with respect to the shares held by each of the Polaris V Funds. Jonathan A. Flint and Terrance G. McGuire are the managing members of each of PVM V and PVM IV. Each of Messrs. Flint and McGuire, as managing members of each of PVM V and PVM IV, may be deemed to have shared voting and dispositive power with respect to the shares held by each of the Polaris Funds. Each of PVM IV, PVM V and Messrs. Flint and McGuire expressly disclaim beneficial ownership of the shares held by the each of the Polaris Funds, except to the extent of their respective pecuniary interests therein, if any. The mailing address of the aforementioned individuals and entities is One Marina Park Drive, 10th Floor, Boston, MA 02210.

(4) Pursuant to a Schedule 13G filed with the SEC on February 16, 2021, each of RA Capital Management, L.P., R.A. Capital Healthcare Fund, L.P. ("RA Capital"), Peter Kolchinsky and Rajeev Shah reported shared voting power and shared dispositive power over 815,849 shares of common stock. RA Capital Management, L.P., is the investment advisor ("Adviser") of RA Capital and RA Capital Management GP, LLC ("Adviser GP") is the general partner of the Adviser. Dr. Kolchinsky and Rajeev Shah are the controlling persons of the Adviser GP. The Adviser, Dr. Kolchinsky, and Mr. Shah may be deemed to beneficially own the shares held by RA Capital. The address of RA Capital is c/o RA Capital Management, L.P., 200 Berkeley Street, 18th Floor, Boston, Massachusetts 02116.

(5) Pursuant to a Schedule 13G/A filed with the SEC on February 16, 2021, Ikarian Capital, LLC ("Ikarian Capital") reported shared voting power and shared dispositive power over 815,364 shares of common stock; each of Ikarian Healthcare Master Fund, L.P. (the "Fund") and Ikarian Healthcare Fund GP, L.P. (the "Ikarian GP") reported shared voting power and shared dispositive power over 654,626 shares of common stock; and each of Chart Westcott and Neil Shahrestani reported shared voting power and shared dispositive power over 815,364 shares of common stock. Ikarian Capital is the investment manager of, and may be deemed to indirectly beneficially own securities owned by, the Fund. Ikarian GP is the general partner of, and may be deemed to indirectly beneficially own securities owned by, the Fund. Ikarian Capital is also the general partner of, and may be deemed to indirectly beneficially own, securities beneficially owned by Ikarian GP. Ikarian Capital is a sub-advisor for certain separate managed accounts (collectively, the "Managed Accounts") and may be deemed to indirectly beneficially own securities owned by the Managed Accounts. Ikarian Capital is ultimately owned and controlled by Chart Westcott Living Trust, of which Mr. Westcott serves as the sole trustee (the "Trust"), and indirectly by Mr. Shahrestani. Accordingly, each of Mr. Westcott, as sole trustee of the Trust, and Mr. Shahrestani may be deemed to indirectly beneficially own securities beneficially owned by Ikarian Capital. The Fund disclaims beneficial ownership of the shares held by the Managed Accounts. The address of the principal business office of each of the aforementioned individuals and entities is c/o Ikarian Capital, LLC, 100 Crescent Court, Suite 1620, Dallas, Texas 75201.

(6) Pursuant to a Schedule 13G filed with the SEC on February 12, 2021, each of Intersouth Partners VII, L.P. ("ISP VII"), Intersouth Associates VII, LLC ("ISA VII, LLC"), Dennis Dougherty and Mitch Mumma reported shared voting power and shared dispositive power over 738,203 shares of common stock. ISA VII directly beneficially owns 738,203 shares of common stock. ISA VII, LLC, as the general partner of ISP VII, may be deemed to beneficially own the securities owned by ISP VII. Messrs. Dougherty and Mumma, as Member Managers of ISA VII, LLC, may be deemed to indirectly beneficially own the securities owned by ISP VII. Each of (i) ISP VII, (ii) ISP VII, LLC and (iii) Messrs. Dougherty and Mumma, may be deemed to share the power to vote or direct the voting of, and to dispose or direct the disposition of, the securities that are directly beneficially owned by ISP VII. Each of Messrs. Dougherty and Mumma disclaims beneficial ownership of all securities other than those he owns by virtue of his indirect pro rata interest as a member of ISA VII, LLC. The mailing address of the aforementioned individuals and entities is 4711 Hope Valley Road, Suite 4F-632, Durham NC 27707.

(7) Pursuant to a Schedule 13G filed with the SEC on February 16, 2021, ArrowMark Colorado Holdings, LLC reported sole voting power over 648,321 shares of common stock. The address of ArrowMark Colorado Holdings, LLC is 100 Fillmore Street, Suite 325, Denver, Colorado, 80206.

(8) Consists of options to purchase 348,220 shares of common stock that are or will be immediately exercisable within 60 days of March 1, 2021.

(9) Consists of options to purchase 39,750 shares of common stock that are or will be immediately exercisable within 60 days of March 1, 2021.

(10) Consists of options to purchase 750 shares of common stock that are or will be immediately exercisable within 60 days of March 1, 2021.

(11) Consists of options to purchase 7,110 shares of common stock that are or will be immediately exercisable within 60 days of March 1, 2021.

(12) Consists of 1,025 shares of common stock and 2,416 options to purchase shares of common stock that are or will be immediately exercisable within 60 days of March 1, 2021.

(13) Consists of options to purchase 6,275 shares of common stock that are or will be immediately exercisable within 60 days of March 1, 2021.

(14) Consists of 1,714,358 shares of common stock and 459,552 options to purchase shares of common stock that are or will be immediately exercisable within 60 days of March 1, 2021.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

Policies and Procedures for Approval of Related Person Transactions

Our board of directors recognizes the fact that transactions with related persons present a heightened risk of conflicts of interests (or the perception thereof) and has adopted a written related person transactions policy to comply with Section 404 of the Exchange Act. Under the policy, our finance team is primarily responsible for developing and implementing processes and procedures to obtain information regarding related persons with respect to potential related person transactions and then determining, based on the facts and circumstances, whether such potential related person transactions do, in fact, constitute related person transactions requiring compliance with the policy. In addition, any potential related person transaction that is proposed to be entered into by the Company must be reported to the Company's Chief Financial Officer, by both the related person and the person at the Company responsible for such potential related person transaction.

If our finance team determines that a transaction or relationship is a related person transaction requiring compliance with the policy, our Chief Financial Officer is required to present to the Audit Committee all relevant facts and circumstances relating to the related person transaction. Our Audit Committee must review the relevant facts and circumstances of each related person transaction, including if the transaction is on terms comparable to those that could be obtained in arm's length dealings with an unrelated third party and the extent of the related person's interest in the transaction, take into account the conflicts of interest and corporate opportunity provisions of our Code of Business Conduct and Ethics, and either approve or disapprove the related person transaction. If advance Audit Committee approval of a related person transaction requiring the Audit Committee's approval is not feasible, then the transaction may be preliminarily entered into by management upon prior approval of the transaction by the chair of the Audit Committee subject to ratification of the transaction by the Audit Committee at the Audit Committee's next regularly scheduled meeting; provided, that if ratification is not forthcoming, management will make all reasonable efforts to cancel or annul the transaction. If a transaction was not initially recognized as a related person transaction, then upon such recognition the transaction will be presented to the Audit Committee for ratification at the Audit Committee's next regularly scheduled meeting; provided, that if ratification is not forthcoming, management will make all reasonable efforts to cancel or annul the transaction.

Our management will update the Audit Committee as to any material changes to any approved or ratified related person transaction and will provide a status report at least annually of all then current related person transactions. No director may participate in approval of a related person transaction for which he or she is a related person.

The following are certain transactions, arrangements and relationships with our directors, executive officers and stockholders owning 5% or more of our outstanding common stock, or any member of the immediate family of any of the foregoing persons, since January 1, 2019."

Series C Preferred Stock Financing. At various closings between January 10, 2020 and January 31, 2020, we issued and sold to investors an aggregate of 78,306,611 shares of our Series C preferred stock at a price per share of $0.38811, for aggregate consideration of approximately $30.4 million. We also issued to such investors warrants to purchase up to an aggregate of 681,256 shares of common stock, at an exercise price per share equal to the fair market value of our common stock following January 10, 2020 (as determined by our board of directors, in good faith, based on the most recent independent third party valuation of our company available following January 10, 2020 performed pursuant to Section 409A of the Internal Revenue Code, and taking into account any changes to our business between the date of such third party valuation and January 10, 2020). In accordance with such terms, on February 6, 2020, our board of directors determined such fair market value of our common stock to be $8.63 per share. Certain holders of 5% or more of our common stock at the time of the transactions, on an as-converted basis, including entities affiliated with Polaris Venture Partners, North Bridge Venture Partners, Intersouth Partners VII, L.P., Perceptive Advisors, LLC, RA Capital Healthcare Fund, L.P., ArrowMark Partners and Soleus Private Equity Fund I, L.P., participated in the Series C preferred stock financing, including the issuance of the warrants to purchase common stock.

The following table sets forth the aggregate number of shares of our capital stock acquired by beneficial owners of more than 5% of our common stock at the time of the Series C preferred stock financing transaction described above. Each share of our Series C preferred stock identified in the following table converted into 0.0289998 shares of common stock immediately prior to the closing of our initial public offering.

Participants	Series C Preferred Stock	Warrants to Purchase Common Stock
5% or Greater Stockholders(1)		
Entities affiliated with Polaris Venture Partners(2)	2,061,271	17,932
Intersouth Partners VII, L.P.	1,030,635	8,966
Entities affiliated with North Bridge Venture Partners(3)	5,153,178	44,831
Entities affiliated with Perceptive Advisors, LLC(4)	55,267,836	480,825
RA Capital Healthcare Fund, L.P.	1,288,294	11,208
Entities Affiliated with ArrowMark Partners(5)	3,864,883	33,624
Soleus Private Equity Fund I, L.P.	3,607,224	31,382

(1) Additional details regarding certain of these stockholders and their equity holdings are provided in this Annual Report on Form 10-K under the caption "Security Ownership of Certain Beneficial Owners and Management."

(2) Represents securities acquired by (i) Polaris Venture Partners Entrepreneurs' Fund V, L.P., (ii) Polaris Venture Partners V, L.P., (iii) Polaris Venture Partners Founders' Fund V, L.P. and (iv) Polaris Venture Partners Special Founders' Fund V, L.P.

(3) Represents securities acquired by (i) North Bridge Venture Partners V-A, L.P., (ii) North Bridge Venture Partners V-B, L.P. and (iii) North Bridge Venture Partners VI, L.P.

(4) Represents securities acquired by (i) Perceptive Life Sciences Master Fund, Ltd. and (ii) Perceptive LS (A), LLC.

(5) Represents securities acquired by (i) ArrowMark Fundamental Opportunity Fund, L.P. and (ii) Meridian Small Cap Growth Fund.

Some of our directors are associated with our principal stockholders as indicated in the table below:

Director	Principal Stockholder
Michael Altman	Entities affiliated with Perceptive Advisors, LLC
Edward Anderson	Entities affiliated with North Bridge Venture Partners
Robert S. Langer Sc.D.(1)	Entities affiliated with Polaris Venture Partners
Konstantin Poukalov	Entities affiliated with Perceptive Advisors, LLC

(1) Robert S. Langer Sc.D. resigned as a director on October 26, 2020.

Agreements with Arsenal

In 2011, we entered into a Collaboration Agreement, a Technology License Agreement, a Trademark Coexistence Agreement and a Transition Services Agreement with Arsenal Medical, Inc., or Arsenal, a company in which certain of our principal stockholders are stockholders. In October 2018, we entered an Acknowledgment and Release Agreement with Arsenal with respect to the expiration of the Collaboration Agreement and certain other intellectual property matters. In November 2019, we entered into an amendment to the Acknowledgement and Release Agreement, which clarifies our and Arsenal's rights to each of our and Arsenal's respective patents and patent applications, including patents and patent applications existing as of the effective date of the Collaboration Agreement, the Technology License Agreement, the Trademark Coexistence Agreement and the Transition Services Agreement. The amendment to the Acknowledgment and Release Agreement also provides for a mutual release of all claims arising under such patents and patent applications. The Technology License Agreement is a non-exclusive in-license agreement covering certain intellectual property regarding in situ forming foam and nanofiber, which is unrelated to our current and future expected product candidates. The Technology License Agreement provides for no future payments by us and remains in effect. In addition, the Trademark Coexistence Agreement relates to certain trademarks around our previous corporate name, which we no longer use. The Transition Services Agreement expired in June 2019.

Consulting Agreement with George Whitesides, Ph.D.

In October 2005, we entered into a consulting agreement with George Whitesides, Ph.D., who was one of our directors between October 2005 and October 2020, pursuant to which Dr. Whitesides agreed to provide us certain consulting and advisory services. The agreement was subsequently amended in March 2006, February 2012, January 2015 and January 2017. Pursuant to the terms of the agreement, as amended, the agreement expired on January 1, 2019. In lieu of all compensation payable by us under the agreement, upon consummation of our IPO on May 5, 2020, we granted to Dr. Whitesides an award of 19,661 fully vested shares of common stock under our 2020 Plan.

Investor Rights Agreement

On January 10, 2020, we entered into an Eighth Amended and Restated Investor Rights Agreement with the holders of our then-outstanding preferred stock, including Perceptive Advisers, LLC, North Bridge Venture Partners, and Polaris Venture Partners, which are 5% or greater holders of our common stock and entities with which certain of our directors are related. The agreement provides for certain rights relating to the registration of such holders' common stock and a right of first refusal to purchase future securities sold by us.

Indemnification Agreements

We have entered into indemnification agreements with each of our directors and executive officers. These agreements, among other things, require us to indemnify each director (and in certain cases their related venture capital funds) and executive officer to the fullest extent permitted by Delaware law, including indemnification of expenses such as attorneys' fees, judgments, fines and settlement amounts incurred by the director or executive officer in any action or proceeding, including any action or proceeding by or in right of us, arising out of the person's services as a director or executive officer.

Independence of the Board of Directors

Our board of directors has determined that each of Michael Altman, Edward Anderson, C. Ann Merrifield, Konstantin Poukalov, W. Bradford Smith and Nancy Snyderman, M.D., FACS qualify as "independent" in accordance with the listing requirements of Nasdaq. Our board of directors previously determined that Robert S. Langer, Sc.D. qualified as "independent" while he served on the board, in accordance with the listing requirements of Nasdaq. The Nasdaq independence definition includes a series of objective tests, including that the director is not, and has not been for at least three years, one of our employees and that neither the director nor any of his family members has engaged in various types of business dealings with us. In addition, as required by Nasdaq rules, our board of directors has made a subjective determination as to each independent director that no relationships exist, which, in the opinion of our board of directors, would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In making these determinations, our board of directors reviewed and discussed information provided by the directors and us with regard to each director's business and personal activities and relationships as they may relate to us and our management, including that Mr. Altman, Mr. Anderson and Mr. Poukalov are affiliated with certain of our significant stockholders. Maria Palasis, Ph.D. is not independent and George Whitesides, Ph.D., who resigned from the board on October 26, 2020, was not independent while we served on the Board. There are no family relationships among any of our directors or executive officers.

Item 14. Principal Accountant Fees and Services.

The following table summarizes the fees of BDO USA, LLP, our independent registered public accounting firm, billed to us for each of the last two fiscal years.

Fee Category	2020	2019
Audit Fees(1)	$ 237,725	$ 350,000
Audit-Related Fees(2)	$ —	$ —
Tax Fees(3)	$ 8,700	$ 8,425
All Other Fees(4)	$ —	$ —
Total Fees	$ 246,425	$ 358,425

(1) Audit fees consist of fees for the audit of our financial statements, the review of the interim financial statements included in our quarterly reports on Form 10-Q, and other professional services provided in connection with statutory and regulatory filings or engagements. Audit fees also includes fees for services incurred in connection with our IPO.

(2) Audit-related fees consist of fees that are reasonably related to the performance of the audit and the review of our financial statements and which are not reported under “Audit Fees.”

(3) Tax fees consist of fees for tax-related services, including tax compliance and tax advice.

(4) All other fees consist of fees for all other services that are not reported above.

Pre-Approval Policies and Procedures

The Audit Committee has adopted a policy (the “Pre-Approval Policy”) that sets forth the procedures and conditions pursuant to which audit and non-audit services proposed to be performed by the independent auditor may be pre-approved. The Pre-Approval Policy generally provides that we will not engage BDO USA, LLP to render any audit, audit-related, tax or permissible non-audit service unless the service is either (i) explicitly approved by the Audit Committee (“specific pre-approval”) or (ii) entered into pursuant to the pre-approval policies and procedures described in the Pre-Approval Policy (“general pre-approval”). Unless a type of service to be provided by BDO USA, LLP has received general pre-approval under the Pre-Approval Policy, it requires specific pre-approval by the Audit Committee or by a designated member of the Audit Committee to whom the committee has delegated the authority to grant pre-approvals. Any proposed services exceeding pre-approved cost levels or budgeted amounts will also require specific pre-approval. For both types of pre-approval, the Audit Committee will consider whether such services are consistent with the SEC's rules on auditor independence. The Audit Committee will also consider whether the independent auditor is best positioned to provide the most effective and efficient service, for reasons such as its familiarity with the Company's business, people, culture, accounting systems, risk profile and other factors, and whether the service might enhance the Company's ability to manage or control risk or improve audit quality. All such factors will be considered as a whole, and no one factor should necessarily be determinative. The Audit Committee periodically reviews and generally pre-approves any services (and related fee levels or budgeted amounts) that may be provided by BDO USA, LLP without first obtaining specific pre-approvals from the Audit Committee or the Chair of the Audit Committee. The Audit Committee may revise the list of general pre-approved services from time to time, based on subsequent determinations.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

(a) Documents filed as part of this report:

(1) Financial Statements.

The following documents are included on pages F-1 through F-22 attached hereto and are filed as part of this Annual Report on Form 10-K.

(2) Financial Statement Schedules.

No financial statement schedules have been submitted because they are not required or are not applicable or because the information required is included in the financial statements or the notes thereto.

(3) List of Exhibits.

Exhibit Number	Description of Exhibit	Form or Schedule	Exhibit No.	Filing Date with SEC	SEC File Number
3.1	Restated Certificate of Incorporation of the Registrant	8-K	3.1	May 5, 2020	001-39273
3.2	Amended and Restated Bylaws of the Registrant	8-K	3.2	May 5, 2020	001-39273
4.1	Eighth Amended and Restated Investor Rights Agreement, dated as of January 10, 2020, as amended	S-1	4.1	March 6, 2020	333-236962
4.2	Specimen Stock Certificate evidencing the shares of Common Stock of the Registrant	S-1/A	4.2	April 27, 2020	333-236962
4.3	Form of Warrants to Purchase Common Stock, dated various dates, issued by the Registrant to various investors, together with a schedule of warrants and warrantholders	S-1/A	4.3	April 27, 2020	333-236962
4.4*	Description of Securities				
10.1#	2005 Equity Incentive Plan, as amended, and form of agreements thereunder	S-1	10.1	March 6, 2020	333-236962
10.2#	2016 Equity Incentive Plan, as amended, and form of agreements thereunder	S-1	10.2	March 6, 2020	333-236962
10.3#	2020 Incentive Award Plan and form of agreements thereunder	S-1/A	10.3	April 27, 2020	333-236962
10.4#	Non-Employee Director Compensation Program	S-1/A	10.4	April 27, 2020	333-236962
10.5#	2020 Employee Stock Purchase Plan	S-1/A	10.5	April 27, 2020	333-236962
10.6#	Form of Indemnification Agreement for directors and officers of the Registrant	S-1/A	10.6	April 27, 2020	333-236962

Exhibit Number	Description of Exhibit	Form or Schedule	Exhibit No.	Filing Date with SEC	SEC File Number
10.7	Lease Agreement between the Registrant and ARE-480 Arsenal St, LLC, dated August 14, 2007, as amended	S-1	10.7	March 6, 2020	333-236962
10.8#	Employment Agreement between the Registrant and Maria Palasis, Ph.D., dated as of April 27, 2020	S-1/A	10.8	April 27, 2020	333-236962
10.9#	Offer Letter between the Registrant and R. Don Elsey, dated as of April 27, 2020	S-1/A	10.9	April 27, 2020	333-236962
10.10#	Offer Letter between the Registrant and Laura Edgerly-Pflug, dated as of April 27, 2020	S-1/A	10.10	April 27, 2020	333-236962
10.11#	Separation Agreement and Release between the Registrant and Laura Edgerly-Pflug, dated as of July 24, 2020	10-Q	10.8	August 5, 2020	001-39273
21.1	Subsidiaries of the Registrant	S-1	21.1	March 6, 2020	333-236962
23.1*	Consent of BDO USA, LLP				
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				
32.1+	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				
32.2+	Certification of Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				
101.INS	XBRL Instance Document				
101.SCH	XBRL Taxonomy Extension Schema Document				
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document				
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document				
101.LAB	XBRL Taxonomy Extension Label Linkbase Document				
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document				

# Indicates management contract or compensatory plan.

* Filed herewith.

+ Furnished herewith.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

LYRA THERAPEUTICS, INC.

Date: March 9, 2021

By: /s/ Maria Palasis, Ph.D.
Maria Palasis, Ph.D.
President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Maria Palasis, Ph.D. Maria Palasis, Ph.D.	President, Chief Executive Officer and Director (principal executive officer)	March 9, 2021
/s/ R. Don Elsey R. Don Elsey	Chief Financial Officer (principal financial officer and principal accounting officer)	March 9, 2021
/s/ Michael Altman Michael Altman	Director	March 9, 2021
/s/ Edward T. Anderson Edward T. Anderson	Director	March 9, 2021
/s/ C. Ann Merrifield C. Ann Merrifield	Director	March 9, 2021
/s/ Konstantin Poukalov Konstantin Poukalov	Director	March 9, 2021
/s/ W. Bradford Smith W. Bradford Smith	Director	March 9, 2021
/s/ Nancy Snyderman, M.D., FACS Nancy Snyderman, M.D., FACS	Director	March 9, 2021

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Board of Directors and Stockholders
Lyra Therapeutics, Inc.
Watertown, MA

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Lyra Therapeutics, Inc. (the "Company") and subsidiary as of December 31, 2020 and 2019, the related consolidated statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders' equity (deficit), and cash flows for the years then ended, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2020 and 2019, and the results of its operations and its cash flows for each of the years then ended, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ BDO USA, LLP

We have served as the Company's auditor since 2013.
Boston, Massachusetts
March 9, 2021

LYRA THERAPEUTICS, INC.
CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share data)

	December 31, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 74,593	$ 9,808
Prepaid expenses and other current assets	1,324	311
Total current assets	75,917	10,119
Property and equipment, net	2,165	237
Operating lease right-of-use assets	2,301	3,182
Restricted cash	329	329
Other assets	118	1,096
Total assets	$ 80,830	$ 14,963
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$ 922	$ 1,069
Accrued expenses and other current liabilities	2,977	3,240
Operating lease liabilities	985	899
Total current liabilities	4,884	5,208
Operating lease liabilities, net of current portion	1,454	2,427
Total liabilities	6,338	7,635
Commitments and contingencies (Note 11)		
Series A-1 redeemable convertible preferred stock, $0.001 par value; no shares issued, authorized or outstanding at December 31, 2020; 34,017,033 shares authorized, issued and outstanding at December 31, 2019	—	39,742
Series A-2 redeemable convertible preferred stock, $0.001 par value; no shares issued, authorized or outstanding at December 31, 2020; 26,680,202 shares authorized, issued and outstanding at December 31, 2019	—	18,393
Series A-3 redeemable convertible preferred stock, $0.001 par value; no shares issued, authorized or outstanding at December 31, 2020; 30,070,487 shares authorized, issued and outstanding at December 31, 2019	—	38,114
Series A-4 redeemable convertible preferred stock, $0.001 par value; no shares issued, authorized or outstanding at December 31, 2020; 19,999,999 shares authorized, issued and outstanding at December 31, 2019	—	6,000
Series B redeemable convertible preferred stock, $0.001 par value; no shares issued, authorized or outstanding at December 31, 2020; 100,018,619 shares authorized and 98,351,953 shares issued and outstanding at December 31, 2019	—	28,417
Series C redeemable convertible preferred stock, $0.001 par value; no shares authorized, issued or outstanding at December 31, 2020 and 2019	—	—
Total redeemable convertible preferred stock	—	130,666
Stockholders' equity (deficit):		
Common stock, $0.001 par value; 200,000,000 and 275,000,000 shares authorized at December 31, 2020 and 2019, respectively; 12,932,377 and 230,860 shares issued and outstanding at December 31, 2020 and 2019, respectively	13	—
Additional paid-in capital	224,363	4,419
Accumulated deficit	(149,884)	(127,757)
Total stockholders' equity (deficit)	74,492	(123,338)
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$ 80,830	$ 14,963

See accompanying notes to consolidated financial statements.

LYRA THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(in thousands, except share and per share data)

	Year Ended December 31,	
	2020	2019
Operating expenses:		
Research and development	$ 12,522	$ 12,032
General and administrative	9,687	4,487
Total operating expenses	22,209	16,519
Loss from operations	(22,209)	(16,519)
Other income:		
Interest income	82	213
Total other income	82	213
Net loss	$ (22,127)	$ (16,306)
Comprehensive loss	$ (22,127)	$ (16,306)
Net loss per share attributable to common stockholders—basic and diluted	$ (2.59)	$ (82.23)
Weighted-average common shares outstanding—basic and diluted	8,590,205	202,093

See accompanying notes to consolidated financial statements.

LYRA THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)
(in thousands, except share amounts)

	Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-In	Accumulated	Total Stockholders' Equity
	Shares	Value	Shares	Amount	Capital	Deficit	(Deficit)
Balance at December 31, 2018	209,119,674	$ 130,353	170,156	$ —	$ 4,377	$ (111,451)	$ (107,074)
Exercise of common stock options	—	—	60,704	—	111	—	111
Accretion of convertible preferred stock to redemption value	—	313	—	—	(313)	—	(313)
Stock-based compensation	—	—	—	—	244	—	244
Net loss	—	—	—	—	—	(16,306)	(16,306)
Balance at December 31, 2019	209,119,674	130,666	230,860	—	4,419	(127,757)	(123,338)
Issuance of Series C redeemable convertible preferred stock, net of issuance costs of $201	78,306,611	29,446	—	—	—	—	—
Accretion of convertible preferred stock to redemption value	—	115	—	—	(115)	—	(115)
Issuance of common stock warrants in conjunction with sale of Series C redeemable convertible preferred stock	—	—	—	—	740	—	740
Conversion of redeemable convertible preferred stock to common stock upon closing of initial public offering	(287,426,285)	(160,227)	8,335,248	8	160,219	—	160,227
Issuance of common stock from initial public offering, net of issuance costs of $7,116	—	—	4,025,000	4	57,280	—	57,284
Vesting of restricted common stock	—	—	24,661	—	—	—	—
Issuance of common stock upon exercise of warrants	—	—	313,794	1	(1)	—	—
Exercise of common stock options	—	—	2,814	—	8	—	8
Stock-based compensation	—	—	—	—	1,813	—	1,813
Net loss	—	—	—	—	—	(22,127)	(22,127)
Balance at December 31, 2020	—	$ —	12,932,377	$ 13	$ 224,363	$ (149,884)	$ 74,492

See accompanying notes to consolidated financial statements.

LYRA THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,	
	2020	2019
Cash flows from operating activities:		
Net loss	$ (22,127)	$ (16,306)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	1,813	244
Depreciation expense	95	27
Reserve for uncollectible accounts	—	167
Gain on disposal of assets	(45)	—
Changes in assets and liabilities:		
Prepaid expenses and other current assets	(1,013)	561
Operating lease right-of-use assets	894	864
Other assets	(118)	—
Accounts payable	345	(205)
Accrued expenses and other current liabilities	(87)	1,734
Operating lease liabilities	(900)	(840)
Net cash used in operating activities	(21,143)	(13,754)
Cash flows from investing activities:		
Purchases of property and equipment	(1,775)	(211)
Net cash used in investing activities	(1,775)	(211)
Cash flows from financing activities:		
Proceeds from the sale of Series C redeemable convertible preferred stock	30,392	—
Payment of offering costs related to sale of Series C redeemable convertible preferred stock	(206)	—
Proceeds from initial public offering, net of underwriting discount	59,892	—
Payment of initial public offering costs	(2,383)	(226)
Proceeds from exercise of stock options	8	111
Net cash provided by (used in) financing activities	87,703	(115)
Net increase (decrease) in cash and cash equivalents	64,785	(14,080)
Cash and cash equivalents and restricted cash, beginning of period	10,137	24,217
Cash and cash equivalents and restricted cash, end of period	$ 74,922	$ 10,137
Supplemental disclosure of non-cash financing and investing activities:		
Property and equipment purchases included in accounts payable	$ 205	$ 2
Conversion of redeemable convertible preferred stock	$ 160,227	$ —
Allocation of Series C redeemable convertible preferred stock to common stock warrant	$ 740	$ —
Accretion of redeemable convertible preferred stock to redemption value	$ 115	$ 313
Right-of-use asset obtained in exchange of operating lease obligation	$ 13	$ 4,046
Deferred offering costs included in accounts payable and accrued expense	$ —	$ 870

See accompanying notes to consolidated financial statements.

1. Organization and Basis of Presentation

Lyra Therapeutics, Inc. (the "Company") is a clinical-stage therapeutics company focused on the development and commercialization of novel integrated drug and delivery solutions for the localized treatment of patients with ear, nose and throat ("ENT") diseases. The Company's proprietary technology platform, XTreo, is designed to precisely and consistently deliver medicines directly to the affected tissue for sustained periods with a single administration. The Company's initial product candidates, LYR-210 and LYR-220, are bioresorbable polymeric matrices designed to be administered in a brief, non-invasive, in-office procedure and intended to deliver up to six months of continuous drug therapy to the sinonasal passages for the treatment of chronic rhinosinusitis ("CRS"). The Company was incorporated as a Delaware corporation on November 21, 2005 and is located in Watertown, Massachusetts. On July 16, 2018, the Company formerly changed its name from 480 Biomedical, Inc. to Lyra Therapeutics, Inc.

The Company is subject to risks common to companies in the therapeutics and pharmaceutical industry, including but not limited to, risks of failure of preclinical studies and clinical trials, the need to obtain marketing approval for any drug product candidate that it may identify and develop, the need to successfully commercialize and gain market acceptance of its product candidates, dependence on key personnel, protection of proprietary technology, compliance with government regulations, development by competitors of technological innovations, reliance on third party manufacturers, ability to transition from pilot-scale manufacturing to large-scale production of products and the need to obtain adequate additional financing to fund the development of its product candidates.

Since inception, the Company has funded its operations with proceeds from sales of redeemable convertible preferred stock and funding from government contracts. The Company has incurred recurring net losses since inception and had net losses of approximately $22.1 million and $16.3 million for the years ended December 31, 2020 and 2019, respectively. In addition, the Company has an accumulated deficit of approximately $149.9 million at December 31, 2020. The Company expects to continue to generate operating losses for the foreseeable future. At December 31, 2020, the Company had approximately $74.6 million of cash and cash equivalents.

On May 5, 2020, the Company completed its initial public offering ("IPO"), in which the Company issued and sold 4,025,000 shares of its common stock, including 525,000 shares pursuant to the full exercise of the underwriters' option to purchase additional shares, at a public offering price of $16.00 per share, for aggregate gross proceeds of $64.4 million. The Company received approximately $57.3 million in net proceeds after deducting underwriting discounts and offering expenses paid by the Company.

The Company believes that its cash and cash equivalents as of December 31, 2020 will be sufficient to fund the Company's operating plan for a period of at least one year from the issuance date of the consolidated financial statements. The Company will need additional financing to support its continuing operations and pursue its growth strategy. Until such time as the Company can generate significant revenue from product sales, if ever, it expects to finance its operations through a combination of equity or debt financings, collaboration agreements, strategic alliances and licensing arrangements. The Company may be unable to raise additional funds or enter into such other agreements when needed on favorable terms or at all. The inability to obtain funding as and when needed would have a negative impact on the Company's financial condition and ability to pursue its business strategies. If the Company is unable to obtain funding when needed, the Company could be forced to delay, reduce or eliminate some or all of its research and development programs, product portfolio expansion or commercialization efforts, which could adversely affect its business prospects, or the Company may be unable to continue operations. The Company will need to generate significant revenue to achieve profitability, and it may never do so.

Upon the completion of the IPO of its common stock in May 2020, all outstanding redeemable convertible preferred stock of the Company converted into shares of common stock and all outstanding warrants to purchase common stock were automatically cashless exercised.

COVID-19 Pandemic and CARES Act

On January 30, 2020, the World Health Organization ("WHO") announced a global health emergency because of a new strain of coronavirus originating in Wuhan, China (the "COVID-19 outbreak") and the risks to the international community as the virus subsequently spread globally beyond its point of origin. On March 11, 2020, the WHO classified the COVID-19 outbreak as a pandemic, based on the rapid increase in exposure globally. The COVID-19 pandemic is affecting the United States and global economies and may affect the Company's operations and those of third parties on which the Company relies, including by causing disruptions in the supply of the Company's product candidates and the conduct of current and future clinical trials. In addition, the COVID-19 pandemic may affect the operations of the Food and Drug Administration and other health authorities, which could result in delays of reviews and approvals, including with respect to the Company's product candidates. In light of developments relating to the COVID-19 pandemic, the Company discontinued enrollment at 67 patients in its Phase 2 LANTERN clinical trial and did not enroll patients in the United States. Additionally, while the potential economic impact brought by, and the duration of, the COVID-19 pandemic is difficult to assess or predict, the impact of the COVID-19 pandemic on the global financial markets may reduce the Company's ability to access capital, which could negatively impact the Company's short-term and long-term liquidity. The ultimate impact of the COVID-19 pandemic is highly uncertain and subject to change. The Company does not yet know the full extent of potential delays or impacts on its business, financing or clinical trial activities or on healthcare systems or the global economy as a whole. However, these effects could have a material impact on the Company's liquidity, capital resources, operations and business and those of the third parties on which the Company relies.

On March 27, 2020, President Trump signed into law the "Coronavirus Aid, Relief, and Economic Security (CARES) Act." The CARES Act, among other things, includes provisions relating to refundable payroll tax credits, deferment of employer side social security payments, net operating loss carryback periods, alternative minimum tax credit refunds, modifications to the net interest deduction limitations, increased limitations on qualified charitable contributions, and technical corrections to tax depreciation methods for qualified improvement property. The Company currently defers the employer side social security payments and also is evaluating whether it will take advantage of other provisions, if any. The CARES Act also appropriated funds for the SBA Paycheck Protection Program loans that are forgivable in certain situations to promote continued employment, as well as Economic Injury Disaster Loans to provide liquidity to small businesses harmed by COVID-19. On December 27, 2020, the Consolidated Appropriations Act, 2021 was signed into law in order to provide further stimulus and support to those affected by the COVID-19 pandemic. The Company has not and does not plan on obtaining funding from such loans. The Company does not believe the CARES Act or the Consolidated Appropriations Act, 2021 will have a material impact on its financial condition, results of operations, or liquidity.

Basis of Presentation

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standard Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB").

2. Summary of Significant Accounting Policies

Principles of Consolidation

The consolidated financial statements include the accounts of Lyra Therapeutics, Inc. and its wholly owned subsidiary Lyra Therapeutics Security Corporation, which was incorporated in December 2018. All intercompany transactions and balances have been eliminated.

The accompanying consolidated financial statements reflect the application of certain significant accounting policies as described in this note and elsewhere in the accompanying consolidated financial statements and notes.

Use of Estimates

The preparation of the Company's consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, expenses and related disclosure of contingent assets and liabilities at the date of the consolidated financial statements and reported amounts of expenses during the reporting period. On an ongoing basis, the Company's management evaluates its estimates, which include but are not limited to management's judgments of accrued expenses, fair value of common stock, valuation of share-based awards warrants to purchase common stock and deferred income taxes. Due to the uncertainty inherent in such estimates, actual results may differ from these estimates.

The Company utilizes significant estimates and assumptions in determining the fair value of its common stock. The Company has utilized various valuation methodologies to estimate the fair value of its common stock. Each valuation methodology includes estimates and assumptions that require the Company's judgment. These estimates and assumptions include a number of objective and subjective factors, including external market conditions, the prices at which the Company sold shares of preferred stock, the superior rights and preferences of securities senior to the Company's common stock at the time of, and the likelihood of, achieving a liquidity event, such as an initial public offering or sale. Significant changes to the key assumptions used in the valuations could result in different fair values of common stock at each valuation date.

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision-maker in deciding how to allocate resources and assess performance. The Company and the Company's chief operating decision-maker, the Company's chief executive officer, views the Company's operations and manages its business as a single operating segment, which is the business of developing targeted medicines to address ENT diseases.

Comprehensive Income (Loss)

Comprehensive income (loss) is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. As the Company did not have any element of other comprehensive income (loss), its comprehensive loss is equal to its net loss for all periods presented.

Cash and Cash Equivalents

The Company considers all highly liquid investments with a maturity of three months or less when purchased to be cash equivalents. Cash and cash equivalents include cash held in banks and amounts held in money market funds. Cash equivalents are stated at cost, which approximates market value.

Cash and cash equivalents consist of cash held in banks at December 31, 2020 and 2019.

Restricted Cash

The Company had restricted cash of approximately $0.3 million as of December 31, 2020 and 2019, which was held in certificates of deposit at the Company's financial institution to secure the Company's letter of credit for its facility lease.

Concentrations of Credit Risk and Off-Balance Sheet Risk

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash and cash equivalents. The Company maintains all its cash and cash equivalents at a single accredited financial institution, in amounts that exceed federally insured limits.

The Company has no significant off-balance sheet risk such as foreign exchange contracts, option contracts, or other foreign exchange hedging arrangements.

Significant Suppliers

The Company is dependent on third-party manufacturers to supply products for research and development activities in its programs. In particular, the Company relies and expects to continue to rely on a small number of manufacturers to supply it with its requirements for the drug product and associated applicator related to these programs. These programs could be adversely affected by a significant interruption in the supply of the materials required to manufacture the drug product and associated applicator.

Fair Value of Financial Instruments

Fair value is defined as the price that would be received upon sale of an asset or paid to transfer a liability between market participants at a measurement date. ASC Topic 820, *Fair Value Measurements* ("ASC 820"), establishes a three-level valuation hierarchy for instruments measured at fair value that prioritizes the inputs used to measure fair value that maximizes the use of observable inputs and minimizes the use of unobservable inputs by requiring that the observable inputs be used when available. Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability and are developed based on the best information available in the circumstances. The fair value hierarchy applies only to the valuation inputs used in determining the reported or disclosed fair value of the financial instruments and is not a measure of the investment credit quality. The three levels of the fair value hierarchy established by ASC 820 in order of priority are as follows:

Level 1 -Quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date.

Level 2 -Inputs other than quoted prices included within Level 1 that are either directly or indirectly observable, such as quoted market prices, interest rates and yield curves.

Level 3 -Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

An entity may elect to measure many financial instruments and certain other items at fair value at specified election dates. Subsequent unrealized gains and losses on items for which the fair value option has been elected will be reported in net loss. The Company did not elect to measure any financial instruments or other items at fair value.

Derivative Liabilities

In connection with certain debt and equity financings, the Company may issue financial instruments in which a derivative instrument is "embedded." Upon issuing the financial instrument, the Company assesses whether the economic characteristics of the embedded derivative are clearly and closely related to the economic characteristics of the remaining component of the financial instrument (i.e., the host contract) and whether a separate, non-embedded instrument with the same terms as the embedded instrument would meet the definition of a derivative instrument. When it is determined that (1) the embedded derivative possesses economic characteristics that are not clearly and closely related to the economic characteristics of the host contract, and (2) a separate, stand-alone instrument with the same terms would qualify as a derivative instrument, the embedded derivative is separated from the host contract and carried at fair value until the derivative is settled. Changes in the fair value of the derivative liabilities are recognized as other income (expense) in the consolidated statement of operations and comprehensive loss.

Classification and Accretion of Redeemable Convertible Preferred Shares

The Company has classified the redeemable convertible preferred stock outside of stockholders' deficit in the accompanying consolidated balance sheets in accordance with authoritative guidance for the classification and measurement of redeemable securities as the redeemable convertible preferred stock is redeemable at a determinable price on a fixed date or upon the occurrence of a deemed liquidation event. The carrying values of the redeemable convertible preferred shares are accreted to their redemption values from the date of issuance through the earliest date of redemption.

Property and Equipment

Property and equipment are stated at cost, less accumulated depreciation. Depreciation expense is recognized using the straight-line method over the estimated useful life of each asset as follows:

	Estimated Useful Life
Laboratory equipment	5 years
Computer software and equipment	3 years
Office furniture and fixtures	7 years
Leasehold improvements	Shorter of useful life or remaining term of related lease

Costs for capital assets not yet placed into service are capitalized as construction in progress and are depreciated in accordance with the above guidelines once placed into service. Upon retirement or sale, the cost of the assets disposed of and the related accumulated depreciation are eliminated from the balance sheet and related gains or losses are reflected in the consolidated statement of operations and comprehensive loss. Repairs and maintenance that do not improve or extend the lives of the respective assets are expensed as incurred, while costs of major additions and betterments are capitalized.

Impairment of Long-Lived Assets

Long-lived assets consist of property and equipment. The Company continually evaluates long-lived assets for potential impairment when events or changes in circumstances indicate the carrying value of the assets may not be recoverable. Recoverability is measured by comparing the book values of the assets to the expected future net undiscounted cash flows that the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the book values of the assets exceed their fair value. The Company did not record any impairment losses on long-lived assets during the years ended December 31, 2020 and 2019.

Leases

ASU No. 2016-02, *Leases (Topic 842)* ("ASU No. 2016-02"), became effective January 1, 2019. As of the effective date of ASU No. 2016-02, the Company determines at the inception of an arrangement whether the arrangement contains a lease. If a lease is identified in an arrangement, the Company recognizes a right-of-use asset and liability on its balance sheet and determines whether the lease should be classified as a finance or operating lease. The Company does not recognize assets or liabilities for leases with lease terms of less than 12 months.

A lease qualifies as a finance lease if any of the following criteria are met at the inception of the lease: (i) there is a transfer of ownership of the leased asset to the Company by the end of the lease term, (ii) the Company holds an option to purchase the leased asset that it is reasonably certain to exercise, (iii) the lease term is for a major part of the remaining economic life of the leased asset, (iv) the present value of the sum of lease payments equals or exceeds substantially all of the fair value of the leased asset, (v) the nature of the leased asset is specialized to the point that it is expected to provide the lessor no alternative use at the end of the lease term. All other leases are recorded as operating leases.

Finance and operating lease assets and liabilities are recognized at the lease commencement date based on the present value of the lease payments over the lease term using the discount rate implicit in the lease. If the rate implicit in the lease is not readily determinable, the Company utilizes its incremental borrowing rate at the lease commencement date. Operating lease assets are further adjusted for prepaid or accrued lease payments. Operating lease payments are expensed using the straight-line method as an operating expense over the lease term. Finance lease assets are amortized to depreciation expense using the straight-line method over the shorter of the useful life of the related asset or the lease term. Finance lease payments are bifurcated into (i) a portion that is recorded as imputed interest expense and (ii) a portion that reduces the finance liability associated with the lease.

The Company separates lease and non-lease components when determining which lease payments to include in the calculation of its lease assets and liabilities. Variable lease payments are expensed as incurred. If a lease includes an option to extend or terminate the lease, the Company reflects the option in the lease term if it is reasonably certain it will exercise the option.

Operating leases are recorded in “Operating lease right-of use assets,” “Operating lease liabilities” and “Operating lease liabilities, net of current portion” in the Company’s consolidated balance sheets. The Company did not have any finance leases recorded in its consolidated balance sheet as of December 31, 2020.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development expenses include salaries and benefits, materials and supplies, preclinical and clinical trial expenses, manufacturing expenses, stock-based compensation expense, depreciation of equipment, contract services and other outside expenses. Costs of certain development activities, such as clinical trials, are recognized based on an evaluation of the progress to completion of specific tasks. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the consolidated financial statements as prepaid or accrued research and development costs. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

The Company has entered into various research and development contracts with companies both inside and outside of the United States. These agreements are generally cancelable, and related payments are recorded as research and development expenses as incurred. The Company records accruals for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies or trials, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company’s estimates. The Company’s historical accrual estimates have not been materially different from the actual costs.

Patent Costs

The Company expenses patent application and related legal costs as incurred and classifies such costs as general and administrative expenses in the accompanying consolidated statements of operations and comprehensive loss.

Accounting for Stock-Based Compensation

The Company accounts for its stock-based compensation in accordance with ASC Topic 718, *Compensation—Stock Compensation* (“ASC 718”). ASC 718 requires all stock-based payments to employees and directors to be recognized as expense in the consolidated statements of operations and comprehensive loss based on their grant date fair values. The Company estimates the fair value of options granted using the Black-Scholes option pricing model for stock option grants to both employees and non-employees. The Company believes the fair value of the stock options granted to non-employees is more reliably determinable than the fair value of the services provided.

The Black-Scholes option-pricing model uses the following inputs: the fair value of the Company’s common stock, the expected volatility of the Company’s common stock, the expected term of the Company’s stock options, the risk-free interest rate for a period that approximates the expected term of the Company’s stock options, and the Company’s expected dividend yield. Following the closing of the Company’s IPO, the fair value of the Company’s common stock is determined based on the quoted market price of its common stock. The Company has historically been a private company and lacks company-specific historical and implied volatility data. Therefore, the Company has based its computation of expected volatility on the historical volatility of a representative group of public companies with similar characteristics to it, including stage of product development, life science industry focus, length of trading history, and similar vesting provisions. The historical volatility data is calculated based on a period of time commensurate with the expected term assumption. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available or until circumstances change, such that the identified entities are no longer representative companies. In the latter case, more suitable, similar entities whose share prices are publicly available would be utilized in the calculation. The Company uses the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, *Share-Based Payment*, to calculate the expected term for options granted to employees as it does not have sufficient historical

exercise data to provide a reasonable basis upon which to estimate the expected term. The expected term is applied to the stock option grant group as a whole, as the Company does not expect substantially different exercise or post-vesting termination behavior among its employee population. For options granted to non-employees, the Company utilizes the contractual term of the share-based payment as the basis for the expected term assumption. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected term of the stock options. The expected dividend yield is assumed to be zero as the Company has never paid cash dividends and has no current plans to pay any cash dividends on its common stock.

The Company has elected as a policy to recognize forfeitures as they occur as described in ASU No. 2016-09, *Compensation—Stock Compensation* ("ASU No. 2016-09").

The Company expenses the fair value of its stock-based compensation awards to employees on a straight-line basis over the requisite service period, which is generally the vesting period. The Company records the expense for stock-based compensation awards subject to performance-based milestone vesting when management determines that achievement of the milestone is probable. Management evaluates when the achievement of a performance-based milestone is probable based on the expected satisfaction of the performance conditions as of the reporting date.

The Company follows the provisions of ASU No. 2018-07, *Compensation-Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting* ("ASU No. 2018-07") which permits the Company to recognize non-employee stock-based compensation costs over the requisite period based on a measurement of fair value on the grant date for each stock-based award.

Income Taxes

The Company accounts for income taxes using the liability method in accordance with ASC Topic 740, *Income Taxes* ("ASC 740"). The difference between the financial statement and tax basis of the assets and liabilities is determined annually. Deferred income tax assets and liabilities are computed using the tax laws and rates that are expected to apply for periods in which such differences reverse. Valuation allowances are established, if necessary, to reduce the deferred tax asset to the amount that will more likely than not be realized.

The Company recognizes the effect of income tax positions only if those positions are more likely than not of being sustained. Recognized income tax positions are measured at the largest amount that is greater than 50% likely of being realized. Changes in recognition or measurement are reflected in the period in which the change in judgment occurs.

Contingencies

In accordance with ASC Topic 450, *Contingencies*, the Company records accruals for contingencies and legal proceedings expected to be incurred in connection with a loss contingency when it is probable that a liability has been incurred and the amount can be reasonably estimated.

If a loss contingency is not probable but is reasonably possible, or is probable but cannot be estimated, the nature of the contingent liability, together with an estimate of the range of possible loss if determinable and material, would be disclosed.

Guarantees

The Company has identified the guarantees described below as disclosable, in accordance with ASC Topic 460, *Guarantees*.

As permitted under Delaware law, the Company indemnifies its officers and directors for certain events or occurrences while the officer or director is, or was, serving at the Company's request in such capacity. The maximum potential amount of future payments the Company could be required to make is unlimited; however, the Company has directors' and officers' insurance coverage that should limit its exposure and enable it to recover a portion of any future amounts paid.

The Company is a party to a number of agreements entered into in the ordinary course of business that contain typical provisions that obligate the Company to indemnify the other parties to such agreements upon the occurrence of certain events. Such indemnification obligations are usually in effect from the date of execution of the applicable agreement for a period equal to the applicable statute of limitations. The aggregate maximum potential future liability of the Company under such indemnification provisions is uncertain.

The Company leases office space under a noncancelable operating lease. The Company has standard indemnification arrangements under the lease that requires it to indemnify the landlord against all costs, expenses, fines, suits, claims, demands, liabilities, and actions directly resulting from any breach, violation, or nonperformance of any covenant or condition of the lease.

As of December 31, 2020 and 2019, the Company had not experienced any losses related to these indemnification obligations, and no material claims with respect thereto were outstanding. The Company does not expect significant claims related to these indemnification obligations and, consequently, concluded that the fair value of these obligations is negligible, and no related reserves have been established.

Deferred Offering Costs

The Company capitalizes certain legal, professional, accounting and other third-party fees that are directly associated with in-process equity financings as deferred offering costs until such financings are consummated. After consummation of the equity financing, these costs are recorded in stockholders' deficit as a reduction of additional paid-in capital generated as a result of the offering. Should the planned equity financing be abandoned, the deferred offering costs will be expensed immediately as a charge to operating expenses in the consolidated statement of operations and comprehensive loss. Deferred offering costs of $0 and $1.1 million are included in other assets in the consolidated balance sheets at December 31, 2020 and 2019, respectively.

Net Loss per Share

The Company has reported losses since inception and has computed basic net loss per share attributable to common stockholders by dividing net loss attributable to common stockholders by the weighted-average number of common shares outstanding for the period, without consideration for potentially dilutive securities. The Company has computed diluted net loss per common share after giving consideration to all potentially dilutive common shares, including options to purchase common stock, warrants to purchase common stock and redeemable convertible preferred stock, outstanding during the period determined using the treasury-stock and if-converted methods, except where the effect of including such securities would be antidilutive. Because the Company has reported net losses since inception, these potential common shares have been anti-dilutive and basic and diluted loss per share have been the same.

Basic and diluted net loss per share attributable to common stockholders was calculated as follows (in thousands, except share and per share data):

	Year Ended December 31,	
	2020	2019
Numerator:		
Net loss	$ (22,127)	$ (16,306)
Accretion of redeemable convertible preferred stock	(115)	(313)
Net loss attributable to common stockholders	$ (22,242)	$ (16,619)
Denominator:		
Weighted-average common shares—basic and diluted	8,590,205	202,093
Net loss per share attributable to common stockholders—basic and diluted	$ (2.59)	$ (82.23)

The following table sets forth the potentially dilutive securities that have been excluded from the calculation of diluted net loss per share because to include them would be anti-dilutive (in common stock equivalent shares retroactively adjusted):

	Year Ended December 31,	
	2020	2019
Series A-1 redeemable convertible preferred stock	—	986,466
Series A-2 redeemable convertible preferred stock	—	773,712
Series A-3 redeemable convertible preferred stock	—	872,031
Series A-4 redeemable convertible preferred stock	—	579,993
Series B redeemable convertible preferred stock	—	2,852,177
Stock options	1,428,886	792,439
Total	1,428,886	6,856,818

Recently Adopted Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the FASB or other standard setting bodies and adopted by the Company as of the specified effective date.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework-Changes to the Disclosure Requirements for Fair Value Measurement* ("ASU No. 2018-13"), which modifies the disclosure requirements on fair value measurements. The Company adopted ASU No. 2018-13 on January 1, 2020. The adoption of ASU 2018-13 did not have a material impact on the Company's consolidated financial position, results of operations or cash flows.

In August 2018, the FASB issued ASU No. 2018-15, *Intangibles—Goodwill and Other—Internal-Use Software (Subtopic 350-40): Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract* ("ASU No. 2018-15"), which clarifies the accounting for implementation costs in cloud computing arrangements. The Company adopted ASU No. 2018-15 on January 1, 2020 on a prospective basis. The adoption of ASU 2018-15 did not have a material impact on the Company's consolidated financial position, results of operations or cash flows.

Recently Issued Accounting Pronouncements

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* ("ASU No. 2019-12"), which makes a number of changes meant to add or clarify guidance on accounting for income taxes. The new guidance will become effective for the Company on January 1, 2022. Early adoption is permitted. The Company currently is evaluating the impact the adoption of ASU 2019-12 will have on its consolidated financial statements.

3. Fair Value Measurements

The Company did not have financial assets and liabilities measured at fair value at December 31, 2020 and 2019.

There have been no changes to the valuation methods used during the years ended December 31, 2020 and 2019. There were no transfers within the fair value hierarchy during the years ended December 31, 2020 and 2019.

The carrying values of the Company's accounts payable and accrued expenses approximate their fair values due to the short-term nature of these liabilities.

In connection with the Company's sale of Series C redeemable convertible preferred stock ("Series C Preferred Stock"), the Company issued to investors warrants for the purchase of common stock ("Warrants"). The proceeds from the issuance of the Series C Preferred Stock were allocated between the Series C Preferred Stock and Warrants based on their relative fair values at the time of issuance.

4. Property and Equipment

Property and equipment consist of the following at December 31, 2020 and 2019 (in thousands):

	December 31,	
	2020	2019
Property and equipment:		
Laboratory equipment	$ 3,277	$ 1,715
Computer software and equipment	650	595
Office furniture and fixtures	301	301
Leasehold improvements	317	317
Construction in progress	498	138
	$ 5,043	$ 3,066
Accumulated depreciation	(2,878)	(2,829)
Property and equipment, net	$ 2,165	$ 237

The Company recognized approximately $0.1 million and $27,000 of depreciation expense for the years ended December 31, 2020 and 2019, respectively.

5. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consist of the following at December 31, 2020 and 2019 (in thousands):

	December 31,	
	2020	2019
Payroll and employee related expenses	$ 1,892	$ 885
Third-party research and development expenses	381	1,344
Professional and consulting fees	555	901
Other	149	110
Total accrued expenses and other current liabilities	$ 2,977	$ 3,240

6. Redeemable Convertible Preferred Stock

On January 10, 2020, the Company filed an amended and restated certificate of incorporation which authorized its Board of Directors to issue up to 299,300,288 shares of preferred stock, par value $0.001 per share.

In January 2020, the Company issued 78,306,611 shares of Series C Preferred Stock for $0.38811 per share, in exchange for gross cash proceeds of approximately $30.4 million.

Upon the completion of the IPO of its common stock in May 2020, all outstanding redeemable convertible preferred stock of the Company converted into shares of common stock.

7. Preferred and Common Stock

On January 10, 2020, the Company filed an amended and restated certificate of incorporation which authorized its Board of Directors to issue up to 400,000,000 shares of common stock, par value $0.001 per share.

On May 5, 2020, the Company filed a restated certificate of incorporation which authorizes its Board of Directors to issue up to 200,000,000 shares of common stock, par value $0.001 per share and 10,000,000 shares of undesignated preferred stock, par value $0.001 per share.

The holders of common stock are entitled to one vote for each share held. Common stockholders are not entitled to receive dividends, unless declared by the Board of Directors.

The Company's Board of Directors approved a one-for-34.483 reverse stock split of its issued and outstanding common stock and stock options and a proportional adjustment to the existing conversion ratios for the Company's redeemable convertible preferred stock pursuant to an amendment to the Company's amended and restated certificate of incorporation effective as of April 27, 2020. Accordingly, all common stock shares, per share amounts, and additional paid in capital amounts for all periods presented in the accompanying consolidated financial statements and notes thereto have been retroactively adjusted, where applicable, to reflect the reverse stock split.

In May 2020, the Company completed its IPO in which the Company issued and sold 4,025,000 shares of its common stock, including 525,000 shares pursuant to the full exercise of the underwriters' option to purchase additional shares, at a public offering price of $16.00 per share, for aggregate gross proceeds of $64.4 million. The Company received approximately $57.3 million in net proceeds after deducting underwriting discounts and offering expenses paid by the Company. In connection with this financing, all outstanding shares of redeemable convertible preferred stock converted into 8,335,248 shares of the Company's common stock, all outstanding Warrants were automatically cashless exercised resulting in the issuance of 313,794 shares of the Company's stock and the issuance to one of our directors, in lieu of compensation payable by the Company under a consulting agreement, of 19,661 fully vested shares of the Company's common stock.

In December 2020, the Company issued as non-employee compensation 5,000 fully vested shares of the Company's common stock.

The Company has reserved for future issuances the following shares of common stock as of December 31, 2020:

	As of December 31, 2020
Stock options	2,888,653
Employee stock purchase plan	150,000
Total	3,038,653

Warrants

In conjunction with the issuance of the Series C Preferred Stock, the Company issued Warrants to purchase 681,256 shares of common stock at an exercise price of $8.63 per share.

The Company classified the Warrants as equity in the consolidated balance sheets in accordance with the guidance in ASC 815, *Derivatives and Hedging*. The Company allocated the net proceeds from the issuance of the Series C Preferred Stock based on the relative fair values of the Series C Preferred Stock and Warrants, which resulted in approximately $0.7 million of the net proceeds being allocated to the Warrants.

Upon the completion of the IPO of the Company's common stock in May 2020, all outstanding Warrants were automatically cashless exercised resulting in the issuance of 313,794 shares of the Company's common stock.

8. Stock-Based Compensation Expense

The Company adopted the 2016 Equity Incentive Plan ("2016 Plan") in February 2016 and amended it in June 2017 and June 2018. Upon adoption of the 2016 Plan, no further grants were made under the 2005 Equity Incentive Plan ("2005 Plan").

In April 2020, the Company's Board of Directors adopted the Company's 2020 Incentive Award Plan ("2020 Plan", and together with the 2016 Plan and 2005 Plan, the "Plans"), and upon effectiveness of the 2020 Plan, the Company ceased granting equity-based awards under the 2016 Plan. The 2020 Plan provides for grant of incentive stock options and nonqualified stock options, stock appreciation rights, restricted stock, dividend equivalents, restricted stock units, performance awards and other share and cash-based awards to employees and consultants and members of the Board of Directors of the Company and its subsidiaries.

The initial number of shares of the Company's common stock that may be issued under the 2020 Plan is 2,100,000 shares plus the number of shares of the Company's common stock underlying outstanding awards under the 2005 Plan and 2016 Plan as of the effective date of the 2020 Plan that expire, lapse or are terminated, exchanged for cash, surrendered, repurchased, canceled or forfeited following the effective date of the 2020 Plan. The number of shares available under the 2020 Plan will automatically increase on January 1st of each year from 2021 to 2030 by the lesser of (i) 4% of the number of shares of common stock outstanding on the final day of the immediately preceding calendar year and (ii) a smaller number of shares determined by the Company's Board of Directors. However, no more than 8,800,000 shares may be issued under the 2020 Plan pursuant to the exercise of incentive stock options. As of December 31, 2020, the Company had 1,459,767 shares available for issuance under the 2020 Plan.

All stock option grants are nonqualified stock options except option grants to employees and officers intended to qualify as incentive stock options under the Internal Revenue Code of 1986, as amended. Stock options may not be granted at less than the fair market value of the Company's common stock on the date of grant. Vesting periods of awards are determined by the Board of Directors or its compensation committee. Vesting periods of awards granted to date range from vesting upon grant to vesting over a four-year period. Vesting conditions are generally based on continued service. Additionally, the Company has granted certain awards which vest upon the achievement of certain financing and revenue milestones. Stock options granted under the Plans expire no more than 10 years from the date of grant.

Stock-based compensation expense included in the Company's consolidated statements of operations and comprehensive loss was as follows (in thousands):

	Year Ended December 31,	
	2020	2019
Research and development	$ 229	$ 26
General and administrative	1,584	218
Total	$ 1,813	$ 244

The Company did not record any stock-based compensation associated with milestone-based awards in the years ended December 31, 2020 and 2019.

The fair value of each stock option granted to employees, directors and non-employees was estimated on the date of grant using the Black-Scholes option-pricing model, with the following weighted-average assumptions:

	Year Ended December 31,	
	2020	2019
Risk-free interest rate	0.6%	2.2%
Expected dividend yield	—%	—%
Expected term (in years)	6.0	6.1
Expected volatility	80.7%	76.8%

A summary of the stock option activity under the Plans for the year ended December 31, 2020 was as follows:

	Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding December 31, 2019	792,439	$ 6.59	7.3	$ 3,363
Granted	763,505	14.16		
Exercised	(2,814)	2.92		
Cancelled	(124,244)	9.30		
Outstanding at December 31, 2020	1,428,886	$ 10.41	7.7	$ 5,165
Exercisable at December 31, 2020	626,578	$ 9.30	6.0	$ 3,099
Vested and expected to vest at December 31, 2020	1,428,886	$ 10.41	7.7	$ 5,165

The weighted-average fair value of options granted to employees, directors and non-employees during the years ended December 31, 2020 and 2019 was $9.66 and $3.45, respectively.

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common stock for those stock options that had exercise prices lower than the fair value of the Company's common stock. The aggregate intrinsic value of stock options exercised during the years ended December 31, 2020 and 2019 was approximately $27,000 and $0.2 million, respectively.

As of December 31, 2020, total unrecognized stock-based compensation expense relating to unvested stock options was approximately $6.2 million. This amount is expected to be recognized over a weighted-average period of 3.2 years. Additionally, as of December 31, 2020, there was approximately $36,000 of unrecognized stock-based compensation related to a stock option award related to the achievement of a revenue-based milestone. As the Company believes the achievement of the revenue-based milestone is currently not probable, it has not recorded any stock-based compensation related to this award. The Company will continue to assess the probability of achieving the revenue-based milestone at each reporting period.

2020 Employee Stock Purchase Plan

In April 2020, the Company's Board of Directors adopted the Company's 2020 Employee Stock Purchase Plan ("2020 ESPP"). The 2020 ESPP is structured as a qualified employee stock purchase plan under Section 423 of the Internal Revenue Code of 1986, as amended, and is not subject to the provisions of the Employee Retirement Income Security Act of 1974. The Company initially reserved 150,000 shares of common stock for issuance under the 2020 ESPP. In addition, the number of shares available for issuance under the 2020 ESPP will be annually increased on January 1st of each year from 2021 to 2030 by the lesser of (i) 0.5% of the number of shares of common stock outstanding on the final day of the immediately preceding calendar year and (ii) such smaller number of shares as is determined by the Company's Board of Directors, provided that no more than 987,500 shares of common stock may be issued under the 2020 ESPP. The 2020 ESPP permits eligible participants to purchase common stock through payroll deductions of up to a specified percentage of their eligible compensation. On the first trading day of each offering period, each participant will automatically be granted an option to purchase shares of the Company's common stock. The option will expire at the end of the applicable offering period, and will be exercised at that time to the extent of the payroll deductions accumulated during the offering period, subject to the limits set forth in the 2020 ESPP. The purchase price of the shares, in the absence of a contrary designation, will be 85% of the lower of the fair market value of the Company's common stock on the first trading day of the offering period or on the purchase date. As of December 31, 2020, no shares have been issued under the 2020 ESPP.

9. Related Parties

The Company had consulting agreements that expired in January 2020 with two of its founders who resigned as directors of the Company in October 2020. Total consulting expense related to these consulting agreements was $0 and $50,000 for the years ended December 31, 2020 and 2019, respectively.

In 2011, the Company entered into a Contribution Agreement, Transition Services Agreement (as amended), Collaboration Agreement, Technology License Agreement and Trademark Coexistence Agreement with Arsenal Medical, Inc. ("Arsenal"), a company which shares certain common owners with the Company. During the year ended December 31, 2019, the Company invoiced Arsenal for an aggregate of $0.3, primarily for its share of rent and other overhead costs. The Transition Services Agreement expired in June 2019. All amounts receivable from Arsenal were collected as of December 31, 2019.

10. Income Taxes

The Company records a provision or benefit for income taxes on pre-tax income or loss based on its estimated effective tax rate for the year. During the years ended December 31, 2020 and 2019, the Company recorded net losses of approximately $22.1 million and $16.3 million, respectively, and, since it maintains a full valuation allowance on its deferred tax assets, the Company did not record an income tax benefit for the years ended December 31, 2020 and 2019.

A reconciliation of income tax expense computed at the statutory federal income tax rate to income taxes reflected in the consolidated financial statements is as follows:

	Year Ended December 31,	
	2020	2019
Income tax computed at federal statutory tax rate	21.0%	21.0%
Permanent differences	(2.0)%	(0.2)%
State taxes, net of federal benefit	5.4%	6.2%
Research and development and other tax credits	2.6%	3.8%
Change in deferred tax asset valuation allowance	(28.4)%	(30.7)%
Other	1.4%	(0.1)%
	—%	—%

Net deferred tax assets as of December 31, 2020 and 2019 consist of the following (in thousands):

	December 31,	
	2020	2019
Deferred tax assets:		
Net operating loss carryforwards	$ 35,729	$ 30,006
Research and development credits	5,223	4,652
Stock-based compensation	322	173
Operating lease liabilities	661	909
Other	140	280
Total gross deferred tax assets	42,075	36,020
Less: Valuation allowance	(41,451)	(35,150)
Total deferred tax assets	624	870
Deferred tax liabilities:		
Operating lease right-of-use assets	(624)	(870)
Total deferred tax liabilities	(624)	(870)
Net deferred taxes	$ —	$ —

As of December 31, 2020, the Company had U.S. federal net operating loss carryforwards of approximately $91.4 million which may be able to offset future income tax liabilities and expire at various dates through 2037 and approximately $44.0 million of federal net operating loss carryforwards that may be carried forward indefinitely. As of December 31, 2020, the Company also had state net operating loss carryforwards of approximately $116.0 million which may be available to offset future income tax liabilities and expire at various dates through 2040.

As of December 31, 2020 and 2019, the Company had federal research and development tax credit carryforwards of approximately $3.6 million and $3.2 million, respectively, available to reduce future tax liabilities which expire at various dates through 2040. As of December 31, 2020 and 2019, the Company had state research and development tax credit carryforwards of approximately $2.0 million and $1.8 million, respectively, available to reduce future tax liabilities which expire at various dates through 2035. The Company has generated research credits but has not conducted a study to document the qualified activity. This study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the deferred tax asset established for the research and development credit carryforwards and the valuation allowance.

Under the provisions of the Internal Revenue Code, the net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating loss and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has not conducted a study to assess whether a change of control has occurred or whether there have been multiple changes of control since inception due to the significant complexity and cost associated with such a study. If the Company has experienced a change of control, as defined by Section 382, at any time since inception, utilization of the net operating loss carryforwards or research and development tax credit carryforwards would be subject to an annual limitation under Section 382, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional adjustments, as required. Any limitation may result in expiration of a portion of the net operating loss carryforwards or research and development tax credit carryforwards before utilization. Further, until a study is completed by the Company and any limitation is known, no amounts are being presented as an uncertain tax position.

ASC 740 requires a valuation allowance to reduce the deferred tax assets reported if, based on the weight of the evidence, it is more likely than not that some portion or all of the deferred tax assets will not be realized. After consideration of all the evidence, both positive and negative, the Company has recorded a valuation allowance against its deferred tax assets at December 31, 2020 and 2019 because the Company's management has determined that it is more likely than not that the Company will not recognize the benefits of its federal and state deferred tax assets primarily due to its history of cumulative net losses incurred since inception and its lack of commercialization of any products or generation of any revenue from product sales since inception and, as a result, a valuation allowance of approximately $41.5 million and $35.2 million, respectively, has been established at December 31, 2020 and 2019. Management reevaluates the positive and negative evidence at each reporting period. The valuation allowance increased by approximately $6.3 million and $5.1 million, respectively, during the years ended December 31, 2020 and 2019 due primarily to the generation of net operating losses.

The Company has recorded adjustments to deferred tax assets for unrecognized tax benefits as of December 31, 2020 and 2019. The Company's policy is to record interest and penalties related to uncertain tax positions as part of its income tax provision. As of December 31, 2020 and 2019, the Company had no accrued interest or penalties related to uncertain tax positions and no such amounts have been recognized in the Company's statement of operations and comprehensive loss. In many cases, the Company's uncertain tax positions are related to years that remain subject to examination by relevant tax authorities. The statute of limitations for federal and state tax authorities is closed for years prior to December 31, 2017. However, since the Company is in a loss carryforward position, the Company is generally subject to examination by the U.S. federal, state and local income tax authorities for all tax years in which a loss carryforward is available.

11. Leases

In August 2007, the Company entered into an operating lease, as amended, for approximately 22,343 square feet of office and laboratory space in Watertown, Massachusetts. In November 2017, the Company amended its lease ("2017 Amendment") and extended the lease term through April 2023. Initial base rent under the 2017 Amendment was approximately $1.0 million per year. The 2017 Amendment includes annual rent escalations over the term of the operating lease. The Company maintains a letter of credit of approximately $0.3 million securing its obligations under the operating lease which is secured by approximately $0.3 million of certificate of deposits, which are included as restricted cash in the consolidated balance sheets. Rent expense is recognized on a straight-line basis over the terms of occupancy.

In addition to the lease discussed above, the Company is party to an April 2020 lease for office equipment that expires in June 2024. The equipment lease is accounted for as an operating lease.

The components of lease cost recorded in the Company's consolidated financial statements were as follows (in thousands):

	Year Ended December 31,	
	2020	2019
Lease Cost:		
Operating lease cost	$ 1,055	$ 1,053
Variable lease cost	726	727
Sublease income	—	(368)
Total lease cost, net	$ 1,781	$ 1,412

Variable lease payments include the Company's allocated share of costs incurred and expenditures made by the landlord in the operation and management of the building. The Company's sublease income during the year ended December 31, 2019 related to subleases for a portion of the Company's office and lab space.

The weighted-average remaining lease term and discount rate related to the Company's operating leases were as follows:

	As of December 31, 2020
Weighted-average remaining lease term (in years)	2.3
Weighted-average discount rate	5.5%

Maturity of the Company's operating lease liabilities in accordance with ASC 842 as of December 31, 2020 were as follows (in thousands):

Year ending December 31,	
2021	$ 1,095
2022	1,127
2023	382
2024	2
Total maturities	2,606
Less: Amount representing interest	(167)
Present value of operating lease liability	2,439
Less: Current portion of operating lease liability	(985)
Total operating lease liability, net of current portion	$ 1,454

12. Retirement Plan

The Company has a defined-contribution plan under Section 401(k) of the Internal Revenue Code ("401(k) Plan"). The 401(k) Plan covers all employees who meet defined minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pre-tax basis. As currently established, the Company is not required to make any contributions to the 401(k) Plan. For the year ended December 31, 2020, the Company made a discretionary match that matches 50% of employee contributions up to a maximum of 3% of employees' salary. Matching contributions are fully vested at the time of contribution. During the year ended December 31, 2020, matching contribution costs incurred by the Company were $0.1 million. The Company did not make any matching contributions during the year ended December 31, 2019.

Exhibit 4.4

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

As of December 31, 2020, Lyra Therapeutics, Inc. had one class of securities registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). References herein to "we," "us," "our" and the "Company" refer to Lyra Therapeutics, Inc. and not to any of its subsidiaries.

General

The following description summarizes some of the terms of our amended and restated certificate of incorporation and amended and restated bylaws. Because it is only a summary, it does not contain all the information that may be important to you. For a complete description, you should refer to our amended and restated certificate of incorporation, amended and restated bylaws and investor rights agreement, copies of which have been filed with the Securities and Exchange Commission, as well as the relevant provisions of the General Corporation Law of the State of Delaware.

Our authorized capital stock consists of 200,000,000 shares of common stock, par value $0.001 per share, and 10,000,000 shares of preferred stock, par value $0.001 per share.

Common Stock

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Subject to the supermajority votes for some matters, other matters shall be decided by the affirmative vote of our stockholders having a majority in voting power of the votes cast by the stockholders present or represented and voting on such matter. Our amended and restated certificate of incorporation and amended and restated bylaws also provide that our directors may be removed only for cause and only by the affirmative vote of the holders of at least two-thirds in voting power of the outstanding shares of capital stock entitled to vote thereon. In addition, the affirmative vote of the holders of at least two-thirds in voting power of the outstanding shares of capital stock entitled to vote thereon is required to amend or repeal, or to adopt any provision inconsistent with, several of the provisions of our amended and restated certificate of incorporation. See below under "—Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws—Amendment of Charter Provisions." Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of any series of preferred stock that we may designate and issue in the future.

In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately our net assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption or conversion rights. Our outstanding shares of common stock are validly issued, fully paid and nonassessable. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Preferred Stock

Under the terms of our amended and restated certificate of incorporation, our board of directors is authorized to direct us to issue shares of preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock.

The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions, future financings and other corporate purposes, could

have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a majority of our outstanding voting stock. There are no shares of preferred stock outstanding, and we have no present plans to issue any shares of preferred stock.

Registration Rights

Certain holders of our common stock are entitled to certain rights with respect to the registration of such shares for public resale under the Securities Act, pursuant to the investor rights agreement, until the rights otherwise terminate pursuant to the terms of the investor rights agreement. The registration of shares of common stock as a result of the following rights being exercised would enable holders to trade these shares without restriction under the Securities Act when the applicable registration statement is declared effective.

Form S-1 Registration Rights

If at any time the holders of at least 30% of the registrable securities then outstanding request in writing that we effect a registration with respect to all or part of such registrable securities then outstanding having an anticipated aggregate offering price that would exceed $5,000,000, we may be required to register their shares. We are obligated to effect at most two registrations in response to these demand registration rights. If the holders requesting registration intend to distribute their shares by means of an underwriting, the managing underwriter of such offering will have the right to limit the numbers of shares to be underwritten for reasons related to the marketing of the shares.

Piggyback Registration Rights

If at any time we propose to register any shares of our common stock under the Securities Act, subject to certain exceptions, the holders of registrable securities then outstanding will be entitled to notice of the registration and to include their shares of registrable securities in the registration. If our proposed registration involves an underwriting, the managing underwriter of such offering will have the right to limit the number of shares to be underwritten for reasons related to the marketing of the shares.

Form S-3 Registration Rights

If, at any time after we become entitled under the Securities Act to register our shares on a registration statement on Form S-3, the holders of the registrable securities then outstanding request in writing that we effect a registration with respect to all or part of such registrable securities having an anticipated aggregate offering price to the public in the offering of at least $2,000,000, we will be required to effect such registration; provided, however, that we will not be required to effect such a registration if, within any twelve month period, we have already effected two registrations on Form S-3 for the holders of registrable securities.

Expenses and Indemnification

Ordinarily, other than underwriting discounts and commissions, we will be required to pay all expenses incurred by us related to any registration effected pursuant to the exercise of these registration rights. These expenses may include all registration and filing fees, printing expenses, fees and disbursements of our counsel, reasonable fees and disbursements of a counsel for the selling securityholders and blue sky fees and expenses. Additionally, we have agreed to indemnify selling stockholders for damages, and any legal or other expenses reasonably incurred, arising from or based upon any untrue statement of a material fact contained in any registration statement, an omission or alleged omission to state a material fact in any registration statement or necessary to make the statements therein not misleading, or any violation or alleged violation by the indemnifying party of securities laws, subject to certain exceptions.

Termination of Registration Rights

The registration rights terminate upon the earlier of the date on which no stockholder holds any registrable securities, the closing of a company sale, as defined in the investor rights agreement, at such time as SEC Rule 144

or another similar exemption under the Securities Act is available for the sale of all of a stockholder's shares without limitation during a three-month period without registration or May 5, 2025.

Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws

Some provisions of Delaware law, our restated certificate of incorporation and our restated bylaws could make the following transactions more difficult: an acquisition of us by means of a tender offer; an acquisition of us by means of a proxy contest or otherwise; or the removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interest or in our best interests, including transactions which provide for payment of a premium over the market price for our shares.

These provisions, summarized below, are intended to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of the increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Undesignated Preferred Stock

The ability of our board of directors, without action by the stockholders, to issue up to 10,000,000 shares of undesignated preferred stock with voting or other rights or preferences as designated by our board of directors could impede the success of any attempt to change control of us. These and other provisions may have the effect of deferring hostile takeovers or delaying changes in control or management of our company.

Stockholder Meetings

Our restated bylaws provide that a special meeting of stockholders may be called only by our chairman of the board, chief executive officer or president (in the absence of a chief executive officer), or by a resolution adopted by a majority of our board of directors.

Requirements for Advance Notification of Stockholder Nominations and Proposals

Our restated bylaws establish advance notice procedures with respect to stockholder proposals to be brought before a stockholder meeting and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors.

Elimination of Stockholder Action by Written Consent

Our restated certificate of incorporation eliminates the right of stockholders to act by written consent without a meeting.

Staggered Board

Our board of directors is divided into three classes. The directors in each class serve for a three-year term, one class being elected each year by our stockholders. This system of electing and removing directors may tend to discourage a third-party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

Removal of Directors

Our restated certificate of incorporation provides that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of

the holders of at least two-thirds in voting power of the outstanding shares of stock entitled to vote in the election of directors.

Stockholders Not Entitled to Cumulative Voting

Our restated certificate of incorporation does not permit stockholders to cumulate their votes in the election of directors. Accordingly, the holders of a majority of the outstanding shares of our common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they choose, other than any directors that holders of our preferred stock may be entitled to elect.

Delaware Anti-Takeover Statute

We are subject to Section 203 of the General Corporation Law of the State of Delaware, which prohibits persons deemed to be "interested stockholders" from engaging in a "business combination" with a publicly held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an "interested stockholder" is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status did own, 15% or more of a corporation's voting stock. Generally, a "business combination" includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors.

Choice of Forum

Our restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative form, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for: (1) any derivative action or proceeding brought on our behalf; (2) any action asserting a claim of breach of a fiduciary duty or other wrongdoing by any of our directors, officers, employees or agents to us or our stockholders; (3) any action asserting a claim against us arising pursuant to any provision of the General Corporation Law of the State of Delaware or our certificate of incorporation or bylaws; (4) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws; or (5) any action asserting a claim governed by the internal affairs doctrine. Under our amended and restated certificate of incorporation, this exclusive forum provision will not apply to claims which are vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery of the State of Delaware, or for which the Court of Chancery of the State of Delaware does not have subject matter jurisdiction. For instance, the provision would not apply to actions arising under federal securities laws, including suits brought to enforce any liability or duty created by the Securities Act, Exchange Act, or the rules and regulations thereunder. Our restated certificate of incorporation further provides that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America shall, to the fullest extent permitted by law, be the sole and exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act. Our restated certificate of incorporation also provides that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock will be deemed to have notice of and to have consented to these choice of forum provisions. It is possible that a court of law could rule that either or both of the choice of forum provisions contained in our restated certificate of incorporation is inapplicable or unenforceable if it is challenged in a proceeding or otherwise.

Amendment of Charter Provisions

The amendment of any of the above provisions, except for the provision making it possible for our board of directors to issue preferred stock and the provision prohibiting cumulative voting, would require approval by holders of at least two-thirds in voting power of the outstanding shares of stock entitled to vote thereon.

The provisions of Delaware law, our restated certificate of incorporation and our restated bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in the composition of our board

and management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Stock Exchange Listing

Our common stock is listed on The Nasdaq Global Market under the symbol “LYRA.”

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

Lyra Therapeutics, Inc.
Watertown, Massachusetts

We hereby consent to the incorporation by reference in the Registration Statement on Form S-8 (333-237973) of Lyra Therapeutics, Inc. of our report dated March 9, 2021 relating to the consolidated financial statements, which appears in this Annual Report on Form 10-K.

/s/ BDO USA, LLP

Boston, Massachusetts

March 9, 2021

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Maria Palasis, certify that:

1. I have reviewed this Annual Report on Form 10-K of Lyra Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) [Intentionally omitted];

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 9, 2021

By: /s/ Maria Palasis, Ph.D.
Maria Palasis, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, R. Don Elsey, certify that:

1. I have reviewed this Annual Report on Form 10-K of Lyra Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) [Intentionally omitted];

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 9, 2021

By: /s/ R. Don Elsey
R. Don. Elsey
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Lyra Therapeutics, Inc. (the "Company") for the period ended December 31, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 9, 2021

By: /s/ Maria Palasis, Ph.D.
Maria Palasis, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Lyra Therapeutics, Inc. (the "Company") for the period ended December 31, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 9, 2021

By: /s/ R. Don Elsey
R. Don. Elsey
Chief Financial Officer
(Principal Financial and Accounting Officer)