Filed Pursuant to Rule 424(b)(3)
Registration No. 333-265570

PROSPECTUS

3,865,491 shares of Common Stock

This prospectus relates to the resale by the selling securityholders identified in this prospectus of up to an aggregate of 3,865,491 shares of our common stock issuable upon the exercise of warrants to purchase 3,865,491 shares of our common stock (the "May 2022 Warrants"). We are registering these shares issuable upon exercise of the May 2022 Warrants ("warrant shares") on behalf of the selling securityholders, to be offered and sold by them from time to time.

We are not selling any shares of common stock and will not receive any proceeds from the sale of the warrant shares by the selling stockholders under this prospectus. Upon the exercise of the May 2022 Warrants for all 3,865,491 shares of our common stock by payment of cash, however, we will receive aggregate gross proceeds of approximately $2.7 million.

We have agreed to bear all of the expenses incurred in connection with the registration of these warrant shares. The selling securityholders will pay or assume brokerage commissions and similar charges, if any, incurred for the sale of the warrant shares.

Sales of the shares by the selling securityholders may occur at fixed prices, at market prices prevailing at the time of sale, at prices related to prevailing market prices, at negotiated prices and/or at varying prices determined at the time of sale. The selling securityholders may sell shares directly or through underwriters, broker-dealers or agents, who may receive compensation in the form of discounts, concessions or commissions from the selling securityholders, the purchasers of the shares, or both. The selling securityholders may sell any, all or none of the securities offered by this prospectus and we do not know when or in what amount the selling securityholders may sell their shares of common stock hereunder following the effective date of the registration statement of which this prospectus forms a part. We provide more information about how the selling securityholders may sell or otherwise dispose of their shares of common stock in the section titled "Plan of Distribution" on page 34.

Our common stock is listed on The Nasdaq Capital Market under the symbol "PALI." On June 27, 2022, the last reported sale price of our common stock was $0.4568 per share.

Investing in our common stock involves a high degree of risk. Before making an investment decision, please read the information under "Risk Factors" beginning on page 20 of this prospectus and under similar headings in any amendment or supplement to this prospectus or in any filing with the Securities and Exchange Commission that is incorporated by reference herein.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR DETERMINED IF THIS PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

The date of this prospectus is June 28, 2022.

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This prospectus is part of a registration statement on Form S-1 that we filed with the Securities and Exchange Commission (the "SEC"). Under this registration statement, the selling securityholders may sell from time to time in one or more offerings the common stock described in this prospectus. We incorporate by reference important information into this prospectus. You may obtain the information incorporated by reference without charge by following the instructions under "Where You Can Find More Information." You should carefully read this prospectus as well as additional information described under "Incorporation of Certain Information by Reference," before deciding to invest in our common shares.

We have not authorized anyone to provide you with information other than the information that we have provided or incorporated by reference in this prospectus and your reliance on any unauthorized information or representation is at your own risk. This prospectus may be used only in jurisdictions where offers and sales of these securities are permitted. You should assume that the information appearing in this prospectus is accurate only as of the date of this prospectus and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, or any sale of our common stock. Our business, financial condition and results of operations may have changed since those dates.

Unless otherwise stated, all references in this prospectus to "we," "us," "our," "Palisade," the "Company" and similar designations refer to Palisade Bio, Inc. This prospectus contains references to trademarks belonging to other entities. Solely for convenience, trademarks and trade names referred to in this prospectus, including logos, artwork and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to indicate, in any way, that the applicable licensor will not assert, to the fullest extent under applicable law, its rights to these trademarks and trade names. We do not intend our use or display of other companies' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

A prospectus supplement may add to, update or change the information contained in this prospectus. You should read both this prospectus and any applicable prospectus supplement together with additional information described below under the heading "Where You Can Find Additional Information."

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and any applicable prospectus supplement or free writing prospectus, including the documents that we incorporate by reference herein and therein, contain "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act). These statements relate to future events or to our future operating or financial performance and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Forward-looking statements may include, but are not limited to, statements about:

- estimates about the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- estimates about timing of initiation of the Phase 3 clinical trial, study enrollment, study completion, availability of results, and cessation of operations of Suzhou;
- the impact of the COVID-19 pandemic on our business, and operations, and supply;
- the rate and degree of market acceptance of our products;
- our ability to build and expand our sales organization to address effectively existing and new markets that we intend to target;
- future regulatory, judicial, and legislative changes or developments in the United States ("U.S.") and foreign countries and the impact of these changes;
- our ability to build a commercial infrastructure in the U.S. and other markets;
- our ability to compete effectively in a competitive industry;
- our ability to identify and qualify additional manufacturers to provide active pharmaceutical ingredients ("APIs") and manufacture drug product;
- our ability to enter into longer term commercial supply agreements;
- the success of competing technologies that are or may become available;
- our ability to attract and retain key scientific or management personnel;
- the accuracy of our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- our ability to obtain funding for our operations; and
- our ability to attract collaborators and strategic partnerships.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "intend," "should," "could," "would," "expects," "plans," "anticipates," "believes," "estimates," "projects," "predicts," "potential" and similar expressions intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and are subject to risks and uncertainties. As such, our actual results may differ significantly from those expressed in any forward-looking statements. Given these uncertainties, you should not place undue reliance on these forward-looking statements.

We discuss many of these risks in greater detail under the heading "Risk Factors" in this prospectus, in the "Business" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections incorporated by reference from our most recent Annual Report on Form 10-K and in our Quarterly Reports on Form 10-Q for the quarterly periods ended subsequent to our filing of such Annual Report on Form 10-K, as well as any amendments thereto reflected in subsequent filings with the SEC.

The discussion of risks and uncertainties set forth in those filings is not necessarily a complete or exhaustive list of all risks facing us at any particular point in time. As a result of these factors, we cannot assure you that the forward-looking statements in this prospectus will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame or at all. Forward-looking statements represent our estimates and assumptions only as of the date of the document containing the applicable statement. Unless required by law, we undertake no obligation to update or revise any forward-looking statements to reflect new information or future events or developments. Thus, you should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements. You should read this prospectus, any applicable prospectus supplement, together with the documents that we have filed with the SEC that are incorporated by reference and any free writing prospectus we have authorized for use in connection with this offering, completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements.

PROSPECTUS SUMMARY

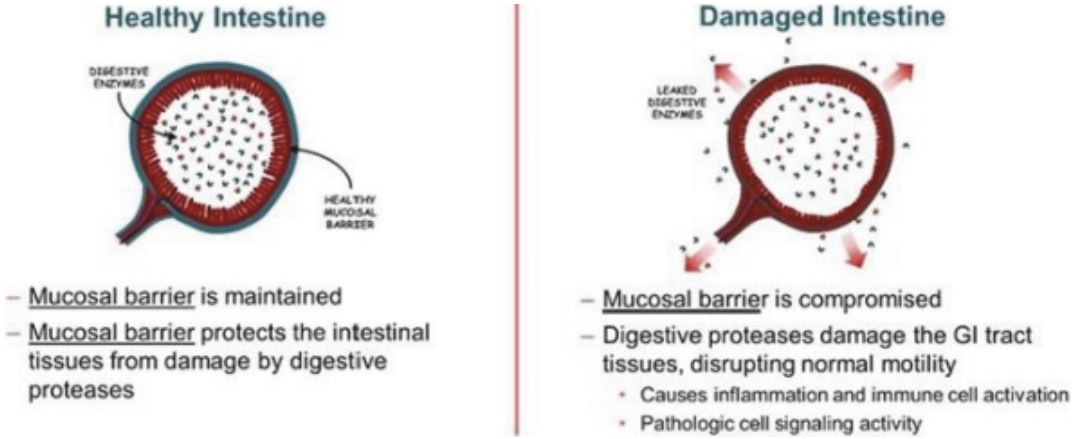
This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus. This summary is not complete and does not contain all of the information that you should consider before making an investment decision. For a more complete understanding of our company, you should read and consider carefully the more detailed information included or incorporated by reference in this prospectus and any applicable prospectus supplement, including the factors described under the heading "Risk Factors" beginning on page 20 *of this prospectus, as well as the information incorporated by reference from our most recent Annual Report on Form 10-K filed with the SEC on March 17, 2022 and our most recent Quarterly Report on Form 10-Q filed with the SEC on May 13, 2022, before making an investment decision. When used in this prospectus, except where the context otherwise requires, the terms the "Company," "we," "us," "our," "Palisade," or similar terms refer to Palisade Bio, Inc.*

Company Overview

We are a clinical-stage biopharmaceutical company focused on discovering, developing, and commercializing innovative oral therapies that target serious diseases associated with the breakdown of the mucosal barrier protecting the gastrointestinal ("GI") tract. Our goal is to be an industry leader in developing therapies to treat these diseases and to improve the lives of patients suffering from such diseases.

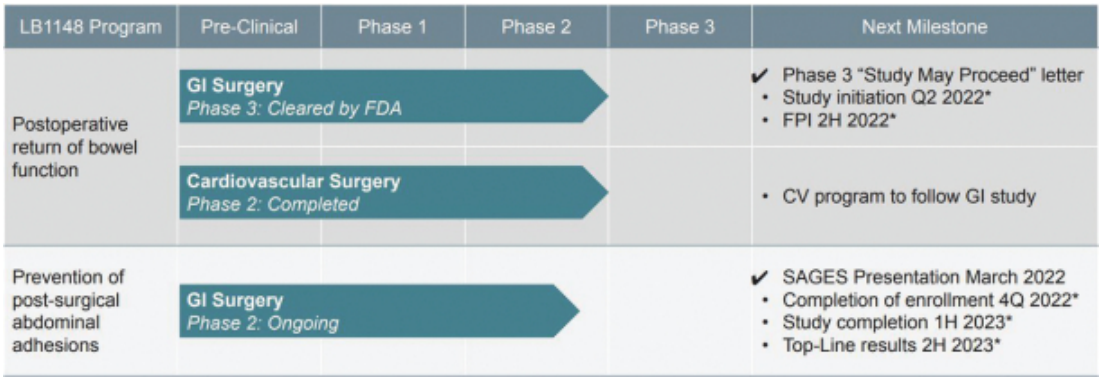
Our approach is founded on the discovery that damage to the intestinal epithelial barrier can result in the leakage of digestive enzymes from the GI tract that can damage tissues and promote inflammation, causing a broad array of acute and chronic conditions.

We are focused on developing a portfolio of oral product candidates to treat conditions driven by protease (intestinal enzymes) leakage through the intestinal epithelial barrier, including by surgical complications and inflammatory conditions. The below graphic illustrates the protease leakage resulting from a compromised intestinal epithelial barrier:



Our lead therapeutic candidate, LB1148, is an oral liquid formulation of the well-characterized digestive enzyme inhibitor, tranexamic acid, intended to inhibit digestive enzyme activity and preserve gut integrity during intestinal stress resulting from, among other things, reduced blood flow to the intestine, infections, or due to surgery. Peer reviewed publications of third-party research suggest that digestive enzyme leakage from the GI tract increases incidents of GI and organ dysfunction following these events.

Our pipeline of LB1148[(1)] is illustrated in this chart:



* Anticipated

(1) Commercial rights to LB1148 in Greater China (excluding Taiwan) have been out-licensed to Newsoara Biopharma Co., Ltd. ("Newsoara").

We are initially developing LB1148 to be administered to patients prior to major surgeries that risk disrupting the intestinal mucosal barrier. On July 20, 2021, we and our co-development partner Newsoara announced topline Phase 2 clinical trial data demonstrating that LB1148 had a statistically significant (p=0.0008) effect in accelerating the return of bowel function in patients undergoing elective bowel resection surgery.

Results from the trial include:

- A 1.1-day improvement in GI recovery in patients receiving LB1148 vs placebo. The median time to return of bowel function was 2.77 days in patients treated with LB1148 and 3.83 days in those receiving placebo (hazard ratio = 1.886; p = 0.0008).
- The difference between groups increased at the 3rd quartile (75th percentile), with LB1148 (3.4 days) demonstrating a 1.5-day faster recovery of bowel function compared to placebo (4.9 days).
- LB1148 was well tolerated with 10.9% and 4.8% of patients in the LB1148 group and placebo group, respectively, experiencing a drug-related adverse event.
- The most common drug-related adverse events were GI disorders (LB1148 4.7% vs. placebo 3.2%).
- No drug-related serious adverse events occurred in the trial.

We and Newsoara are advancing LB1148 to Phase 3 clinical trials for accelerating the return of bowel function for major surgical indications. As announced on March 22, 2022, we received the "Study May Proceed" letter from the U.S. Food and Drug Administration ("FDA") for a randomized, double-blind, parallel-group, placebo-controlled Phase 3 clinical trial evaluating LB1148 to accelerate the return of bowel function in adult patients undergoing bowel/abdominal surgery. The clinical trial will enroll approximately 600 subjects undergoing a scheduled bowel resection surgery that will include either laparotomy or laparoscopic surgical approaches. We intend to initiate the Phase 3 clinical trial in the second quarter of 2022.

On May 5, 2022, in partnership with Newsoara, we announced clearance from the Center for Drug Evaluation ("CDE") of the National Medical Products Administration ("NMPA") of the People's Republic of China to commence a randomized, multi-center, double-blind Phase 3 clinical trial evaluating LB1148 to accelerate the

return of bowel function following abdominal surgery. As described in the existing licensing agreement, Newsoara is responsible for development costs of LB1148 in China.

Adhesion prevalence is reported to be >90% in patients who have abdominal surgery and represents a significant contribution to serious complications such as small bowel obstruction, infertility, chronic abdominal pain, subsequent surgery, and other morbidities. On March 16, 2022 we announced data from a pooled-analysis of studies LBS-IST-POI-101 and LBS-POI-201-CN ("PROFILE-CN") at the Society of American Gastrointestinal and Endoscopic Surgeons ("SAGES") 2022 Annual Meeting. The results from the pooled analysis showed that 8/9 (89%) of subjects in the placebo group versus 2/8 (25%) in the LB1148 group had adhesions observed during a second follow-up surgery, representing a relative risk reduction of 72% ($p = 0.0152$). The mean total adhesion score which measures both the extent and severity of adhesions was 1.0 (8/8) for LB1148 and 14.3 (129/9) for placebo, representing relative risk reduction of 93% ($p = 0.0162$). We believe the reduction in the incidence of post-surgical intra-abdominal adhesions as well as the reduction in the extent and severity of adhesions provides preliminary evidence of the clinically meaningful efficacy of LB1148 to reduce post-surgical adhesions when compared to placebo. LB1148 has received Fast Track designation from the FDA for reduction of adhesions following abdominal and pelvic surgery.

We are currently conducting a randomized, double-blind, placebo-controlled, proof-of-concept Phase 2 clinical trial of LB1148 in patients undergoing elective bowel resection surgery in the United States. This trial will enroll up to 200 total patients, with approximately 70 of those patients having a planned adhesions evaluation. This trial will evaluate whether or not patients treated with LB1148 experience fewer postoperative intra-abdominal adhesions and quicker return of bowel function following surgery.

As announced in March 2020, a randomized, double-blind, parallel, placebo-controlled Phase 2 investigator-sponsored clinical trial of LB1148 in 120 patients undergoing coronary artery bypass grafting and/or heart valve replacement surgery requiring cardiopulmonary bypass was completed. Patients were randomized to receive LB1148 or placebo in conjunction with surgery. The trial's primary endpoint was time to return of bowel function. Secondary endpoints include Intensive Care Unit ("ICU") length of stay, hospital length of stay, organ function changes, inflammatory response and glucose control. LB1148 provided an approximately 30% improvement in the time to normal bowel function following cardiovascular ("CV") surgery ($p<0.001$) compared to placebo. The treatment group also had an average 1.0-day shorter length of stay in the ICU and an average 1.1-day shorter hospital stay. Generally, treatment with LB1148 was well tolerated. Adverse events were similar between the treatment groups and not considered unexpected for the subject population. None of the adverse events or serious adverse events reported were considered drug-related by the sponsor-investigator. One of the primary factors in discharging patients from the hospital following surgery is the return of bowel function. LB1148 has been granted Fast Track designation from the FDA for the treatment of postoperative GI dysfunction (which may present as feeding intolerance, ileus, necrotizing enterocolitis ("NEC"), etc.) associated with gut hypoperfusion injury in pediatric patients who have undergone congenital heart disease repair surgery.

LB1148 contains a broad-spectrum serine protease inhibitor, tranexamic acid ("TXA"), and is formulated as an aqueous solution for oral (or enteral) administration. In addition to TXA, the patented LB1148 formulation contains polyethylene glycol, carbohydrates, and electrolytes. The components of LB1148 are provided as dry powders for reconstitution in water prior to administration. Such reconstitution is carried out in an outpatient setting (by the patient) or may be carried out in pharmacy (by a pharmacist).

The potential of LB1148 relies on its formulation as a liquid composition for oral administration, which is designed to stop the downstream effects of a disruption of the intestinal mucosal barrier. We are not aware of any other approved oral TXA-containing liquid compositions in the marketplace suitable for such administration.

We believe that LB1148, if successfully developed and approved, may have the ability to become the standard of care across a broad range of acute and chronic conditions associated with GI barrier dysfunction.

Beyond our initial therapeutic focus on GI-related pathology triggered by major surgeries, we believe that protease-based therapeutics hold promise in meeting a number of unmet needs resulting from chronic protease leak. By leveraging our expertise in protease-mediated diseases and dysregulation of the intestinal epithelia barrier, our strategy is to create a broad portfolio of innovative oral therapeutics that target serious diseases associated with the breakdown of this barrier.

Regulatory Considerations for LB1148

LB1148 has been granted Fast Track designation from the FDA for reduction of adhesions following abdominal and pelvic surgery. Furthermore, LB1148 has received Fast Track designation from the FDA for the treatment of postoperative GI dysfunction (which may present as feeding intolerance, ileus, necrotizing enterocolitis, etc.) associated with gut hypoperfusion injury in pediatric patients who underwent congenital heart disease repair surgery. The LB1148 final drug product contains polyethylene glycol 3350 ("PEG"). In certain circumstances, in different countries and across different regulatory authorities, PEG may be regulated as an inactive ingredient, a medical device, or an active ingredient. We believe that there is ambiguity and risk regarding the PEG in LB1148 being classified as an active ingredient. From our communications with regulatory authorities including the FDA about our development of LB1148, there remains uncertainty about (1) whether regulatory agencies will classify LB1148 as a fixed-combination drug product and (2) consequential implications of, for example, FDA's fixed-combination drug product regulation concerning the evaluation of each active drug component's individual contribution to the overall treatment effect. The treatment of PEG and any regulatory requirements, if it is considered an active ingredient, may differ across regulatory authorities. If LB1148 is considered a fixed-combination drug product, then this may impact the design and overall number of required clinical trials as well as additional requirements for nonclinical studies. Even though we are proceeding with a Phase 3 trial for LB1148 as a single active ingredient drug product, we may be required to conduct additional trials, which could include the use of a factorial design, and nonclinical studies if, for example, FDA (1) concludes that PEG is an active ingredient in LB1148 and (2) is unwilling to provide a waiver from meeting their fixed-combination drug product regulation/requirements. It is important to note that before GI surgery, most patients undergo a mechanical bowel prep. Traditionally, the standard of care for a bowel prep includes PEG. Therefore, including a treatment arm of a clinical trial that would not allow for a standard bowel prep containing PEG may be impractical. As a result, we believe that it would be impractical, infeasible, and ultimately unethical to exclude the use of PEG as part of the mechanical bowel prep for GI surgery studies.

Our Strategy

Beyond our initial therapeutic focus on GI-related pathology triggered by major surgeries, we believe that protease-based therapeutics hold promise in meeting a number of unmet needs resulting from chronic protease leak. By leveraging our expertise in protease-mediated diseases and dysregulation of the intestinal epithelia barrier, our strategy is to create a broad portfolio of innovative oral therapeutics that target serious diseases associated with the breakdown of this barrier. The key components of our strategy are to:

- Pursue approval of our lead drug candidate LB1148 for its first indication to accelerate the return of bowel function following GI surgery and, if approved, commercialize LB1148 for this indication in the United States. GI hypomotility and delayed return of bowel function is expected after major surgery. This is associated with significant discomfort, nausea, vomiting, and the inability to advance the diet in the post-operative setting. If unresolved, this can predispose patients to nosocomial complications, infections, malnutrition, electrolyte derangements, and poor wound healing. Delayed return of bowel function is associated with a prolonged hospital length of stay, increased resource utilization, and risk for readmission due to GI dysmotility or bowel obstruction. In a retrospective study of colon resections, prolonged postoperative ileus was significantly associated with the serious complications of intra-abdominal infections, anastomotic leak and a significantly higher mortality risk. We believe

treating the root cause of GI hypomotility caused by abdominal surgery has the potential to lower the risk of morbidity and mortality for the over six million patients undergoing abdominal surgeries each year in the U.S.

- Pursue approval of LB1148 for the reduction of postoperative adhesions following major surgeries. Some studies have shown that postoperative intra-abdominal adhesions develop in up to 93% of surgery patients. Adhesions are a costly postoperative consequence of surgery for patients. They can cause bowel obstruction and can require hospitalization or even corrective surgery. Due to its oral route of administration and results from our preclinical and early-stage clinical trials, we believe LB1148 has the potential to be an oral agent for reducing postoperative surgical adhesions. To our knowledge there are no other oral drugs approved or pending approval for this indication. Results from animal studies demonstrated that LB1148 may reduce the number of postoperative adhesions. In addition, a pooled analysis of clinical trial results showed a reduction in the incidence of post-surgical intra-abdominal adhesions as well as the reduction in the extent and severity of adhesions. We believe this provides preliminary evidence of LB1148 to potentially reduce post-surgical adhesions when compared to placebo. We have amended the study design of the PROFILE-US clinical trial to ensure adequate enrollment of patients receiving an adhesions assessment to inform the design of future pivotal studies in this indication.
- Build sales and marketing capabilities to commercialize our product candidates in the United States and European Union. If approved, we intend to develop and commercialize our product candidates in major markets and establish distributor networks or strategic partnerships in smaller markets.
- Leverage our expertise in protease-mediated diseases and the GI tract to efficiently expand our product candidate pipeline to address chronic conditions. Many chronic endocrine and inflammatory diseases are associated with chronic proteolytic enzyme leak from the GI tract. Using our understanding of digestive protease biology of the GI tract, we have developed a proprietary whole-blood assay to measure the activity of specific proteases. In conjunction with the development of this whole-blood assay, we have acquired an exclusive license to synthetic protease substrates and methodologies for analyzing human clinical samples associated with a broad spectrum of conditions and disorders. Together, we believe these assets form a platform for novel drug discovery and highly efficient patient selection and measurement of ex vivo clinical response during drug development.

Manufacturing

We do not own or operate any manufacturing facilities. We rely on third-party contract manufacturing organizations (“CMOs”) to manufacture and supply our preclinical and clinical materials to be used during the development of our drug candidates, including our lead drug product. As our product candidates advance through development, we expect to enter into longer-term commercial supply agreements with key suppliers and manufacturers to fulfill and secure our production needs.

To that end, we have entered into an umbrella services agreement with a manufacturing company who we expect to lead our drug manufacturing efforts and under which we plan to enter into individual project agreements to meet our future drug manufacturing needs. Although we rely on CMOs, we have personnel and third-party consultants with extensive drug manufacturing experience to oversee the relationships with our CMOs. It is also our intent to identify and qualify additional manufacturers to provide API and drug product manufacturing.

Supply chain constraints associated with the COVID-19 pandemic have impacted the availability of the components needed in the manufacture of LB1148 and, depending on the duration and extent of the pandemic or new strains, could impact the components and production capacity required for a commercial scale-up of LB1148. We believe we have sufficient supply to meet our clinical and nonclinical development needs through

2022. Further, we believe we have plans for supply to meet our development needs through our submission of a new drug application to the FDA. However, depending on the duration and impact of the ongoing COVID-19 pandemic on local and global supply chains, our suppliers could be adversely impacted, which may result in delays or disruptions in our current or future supply chain.

LB1148 is a dry powder for reconstitution, consisting of the previously approved API (tranexamic acid) as well as other components. Drug product manufacturing is a relatively straightforward operation, involving the blending of dry components. To date, controlled stability experiments indicate that the active ingredient is highly stable and that the drug product has a long shelf life.

Sales and Marketing

We do not currently have any approved drugs. However, we intend to build a commercial infrastructure in the United States and potentially in other markets, that we believe will be necessary to effectively support the commercialization of LB1148, if approved, and any other products that we develop in the future, with a focus on high treating physicians and hospitals. In the U.S. we estimate that cardiovascular and abdominal surgeries collectively represent close to seven million addressable patients, which we believe, based on certain assumptions, could translate into over $2 billion in annual sales for LB1148. We believe that we may be able to address the market using our own targeted, specialty sales and marketing organization supported by internal sales personnel, an internal marketing group, and distribution support.

We plan to utilize a variety of marketing programs to promote LB1148, if approved, including sales promotional materials, speaker programs, journal advertising, industry publications, medical conferences, electronic media, and product sampling. Additional capabilities important to commercialization of LB1148, if approved, and any other products that we may develop in the future, include the management of key accounts, such as managed care organizations, hospital and specialty pharmacies, and government accounts – where formulary acceptance is necessary for product adoption and reimbursement.

Outside of the U.S., where we believe it is appropriate, we may utilize strategic partners, distributors, or contract sales forces to expand the commercial availability of LB1148, if approved, and other products, if approved. In addition, we believe the other indications that we may pursue with our product candidates can be addressed with a small, dedicated sales force. We currently do not expect that we will require large pharmaceutical partners for the commercialization of our product candidates, although we may consider partnering in certain territories or indications or for other strategic purposes. We intend to continuously evaluate our commercialization strategy as we advance our clinical and preclinical programs.

Competition

Drug development is highly competitive and subject to rapid and significant technological advancements. Our ability to compete will greatly depend upon our ability to complete necessary clinical trials and the related regulatory approval processes, and successfully market any product that we may successfully develop. The key competitive factors that will affect the commercial success of any product candidate for which we may receive marketing approval include efficacy, safety, tolerability, dosing convenience, price, coverage and reimbursement.

Our current and potential future competitors are diverse. There are many public and private biopharmaceutical companies, universities, governmental agencies and other research organizations actively engaged in the research and development of products that may be similar to our product candidates or address similar markets. In addition, the number of companies seeking to develop and commercialize products and therapies similar to our product candidates is likely to increase.

With regard to postoperative improvement of bowel function, we expect to face competition in the pharmacological therapy space from alvimopan, marketed as a branded product, ENTEREG®, by Merck, as well as in generic form. Alvimopan is currently the only approved therapeutic indicated to accelerate return for bowel function. However, the alvimopan label is restricted to those surgeries that include partial bowel resection with primary anastomosis. Other companies are currently developing, and may in the future develop, product candidates for postoperative improvement of bowel function that could pose future competition if approved for sale in overlapping territories.

With regard to the reduction or elimination of postoperative intra-abdominal adhesions, to our knowledge, there are no approved therapeutics for treating or preventing postoperative intra-abdominal adhesions. The only potential oral therapeutic in clinical development we are aware of is TTX 333 Evitar™ being developed by Temple Therapeutics based in the Netherlands. However, we face general competition from other medical interventions for adhesions, namely surgical procedures and adhesion barrier products. Adhesion barrier products approved for abdominal or pelvic surgery in the United States consist of SEPRAFILM, INTERCEED®, and ADEPT®. In addition, several products are used off-label for adhesion prevention in the United States, including EVICEL®, SURGIWRAP®, COSEAL™, and PRECLUDE™. Adhesion barrier products available outside the United States include HYALOBARRIER®, SPRAYSHIELD™, PREVADH™, and INTERCOAT™. Such products are used as adjunctive, have variable efficacy, and are not easily used with laparoscopic procedures, which are becoming increasingly common.

Intellectual Property

Our commercial success depends in part on our ability to (i) obtain and maintain proprietary protection to protect our current and future product candidates, novel discoveries, product development technologies, improvements, and know-how; (ii) preserve the confidentiality of our trade secrets and confidential information; (iii) maintain our co- development agreements and licenses for exclusive commercial rights to intellectual property, including patent rights co-owned with third parties; (iv) defend and enforce our proprietary rights, including our patents; and (v) operate without infringing valid and enforceable patents and other proprietary rights of third parties.

We seek to protect our proprietary position by, among other methods, filing or in-licensing U.S. and foreign patents and patent applications related to technology, inventions and improvements that are important to the development and implementation of our business. As for the product candidates we develop and plan to commercialize, as a normal course of business, we generally have pursued, or intend to pursue, composition and therapeutic use patents, as well as patents directed to dosing regimens and additional prospective indications. We also rely, as needed, on trademarks, trade secrets, copyright protection, know-how, continuing technological innovation and confidential information to develop and maintain our proprietary position. We also will pursue data exclusivity, market exclusivity, and other regulatory exclusivities, as applicable and available.

Regardless of the coverage we seek under our existing patent families, there is always a risk that a third party or competitor could alter our products, methods, or processes in a manner that would provide sufficient basis for a competitor or third party to avoid infringement of our claims. In addition, the coverage claimed in a patent application can be significantly reduced before a patent is issued, and courts can reinterpret patent scope after issuance. Moreover, many jurisdictions, including the United States, permit third parties to challenge issued patents in administrative proceedings, which may result in further narrowing or even cancellation of patent claims. Moreover, we cannot provide any assurance that any patents will be issued from our pending or any future applications or that any current or future issued patents will adequately protect our intellectual property. While we seek broad coverage under our existing patent applications, there is always a risk that an alteration to the products or processes may provide sufficient basis for a competitor to avoid infringing our patent claims. In addition, patents, if granted, expire and we cannot provide any assurance that any patents will be issued from our pending or any future applications or that any potentially issued patents will adequately protect our products or product candidates.

Individual patents extend for varying periods depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, patents issued for regularly filed applications in the United States are granted a term of 20 years from the earliest effective non-provisional filing date. In addition, in certain instances, a patent term can be extended to recapture a period due to delay by the United States Patent and Trademark Office ("USPTO") in issuing the patent as well as a portion of the term effectively lost as a result of the FDA regulatory review period. However, as to the FDA component, the restoration period cannot be longer than five years and the total patent term including the restoration period must not exceed 14 years following FDA approval. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest effective non-provisional filing date. However, the actual protection afforded by a patent varies on a product-by-product basis, from country to country, and depends upon many factors, including the type of patent, whether there are any priority claims to earlier filed patents, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

Our commercial success will also depend in part on not infringing upon the proprietary rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies for our products, if approved, or processes, or to obtain licenses or cease certain activities. Our breach of any license agreements or failure to obtain a license to proprietary rights that we may require to develop or commercialize our future products may have an adverse impact on us. If third parties prepare and file patent applications in the United States that also claim technology to which we have rights, we may have to participate in interference or derivation proceed.

LB1148 Patent Portfolio

Currently, we solely own (or co-own with exclusive commercial rights) four patent families with claims directed to compositions covering components of LB1148, including the protease inhibitor tranexamic acid, or their therapeutic uses and dosing regimens:

The First Family is directed to compositions comprising four components of LB1148 and their therapeutic use in treating shock and other indications. As of June 16, 2022, this patent family includes three granted patents in the United States, two granted patents in Taiwan, granted patents in Australia, Europe, India, Japan, Korea and Mexico, and pending applications in Canada, Korea, and the U.S., all of which we solely own. In addition, this family includes a granted patent in China that we previously assigned to Newsoara to support our co-development agreement with Newsoara, as discussed below. The expected expiration date of the issued patents (or any patents that may issue from pending applications) is 2035, excluding any adjustments or extensions of patent term that may be available.

The Second Family, which we jointly own with the University of California, is directed to compositions comprising three (or fewer) components of LB1148 and their therapeutic use in treating shock and other indications. Under the 2015 License with the University of California (as discussed in the section entitled "License Agreements and Collaborations"), we have exclusive commercial rights to this family. As of June 16, 2022, this patent family includes three granted patents in the U.S., granted patents in China, Canada, and Korea, and pending applications in Europe and the U.S. The issued Chinese patent has been exclusively licensed to Newsoara. The expected expiration date of the issued patents (or any patents that may issue from pending applications) is 2031, excluding any adjustments or extensions of patent term that may apply.

The Third Family covers the use of LB1148 (or its active ingredient, tranexamic acid) in certain therapeutic indications, including POI and adhesions, which align with our current clinical and commercial strategy. This family also covers specific split-dose regimens of LB1148 that can apply to the current therapies. As of March 9, 2022, this patent family includes a recent patent in the United States (US 11,202,768) that was granted on December 21, 2021, as well as pending applications in Australia, Europe, Canada, Hong Kong, all of which we

solely own. In addition, this family includes a recent patent in China (CN 108883086) that was granted on October 26, 2021 and that we previously assigned to Newsoara to support our co-development agreement with Newsoara (as discussed in the section entitled "License Agreements and Collaborations"). The expected expiration date of any patents (or patents that may issue from pending applications) is 2037, excluding any adjustments or any extensions of patent term that may apply.

The Fourth Family, which we solely own, consists of a U.S. patent application with claims covering the use of LB1148 in methods of controlling glucose levels in diabetic patients in hospital and non-hospital settings. The expected expiration date of any patents that may issue from pending applications is 2038, excluding any adjustments or any extensions of patent term that may apply.

License Agreements and Collaborations

2015 License Agreement with the Regents of the University of California

In August 2015, Leading Biosciences, Inc. ("LBS") entered into a license agreement with the Regents of the University of California (the "Regents"), as amended in December 2019 (the "2015 UC License"). Pursuant to the 2015 UC License, LBS has an exclusive, sublicensable, worldwide license under certain patent rights to make, use, sell, offer for sale and import products and practice methods covered by the claims of the licensed patent rights in the field of the direct administration of protease inhibitors to the gastrointestinal tract via a tube, as well as oral administration of protease inhibitor, for therapeutic indications including, among others, uses in surgery generally, and the treatment of shock, sepsis, inflammatory disease and post-surgical ileus and adhesions, diabetes, glucose- and insulting mediated disorders, and related metabolic disorders, damage to the gastro- intestinal tract caused by radiation damage, and other gastrointestinal tract-related disorders, including chronic conditions resulting from digestive enzyme leak. LBS utilizes these licensed patent rights in certain compositions comprising components of LB1148, including the active ingredient, tranexamic acid.

Upon the execution of the 2015 UC License, LBS paid a one-time license issue fee of $3,500 and is obligated to pay an annual license maintenance fee in the mid four-digit dollar range until such time that we are commercially selling a licensed product. LBS is also obligated to make: (i) payments up to $250,000 in the aggregate upon achievement of certain regulatory milestones and (ii) tiered royalty payments in the low single-digit percentage range on annual net sales of licensed products by LBS, its affiliates, or its sublicensees. Upon commencement of commercial sales, LBS will become subject to a minimum annual royalty in the low five-digit dollar range. Further, LBS is obligated to pay a percentage of non-royalty licensing revenue LBS receives from our sublicensees under the 2015 UC License to the Regents.

Under the 2015 UC License, LBS is required, either directly or through its affiliates, to diligently proceed with the development, manufacture, regulatory approval, and sale of licensed products and is subject to a number of diligence obligations relating to developmental, regulatory and commercialization milestones for the licensed products. For the first three years of the 2015 UC License, LBS was subject to a minimum annual spend requirement in the low six-digit dollar range. If LBS fails to meet any milestones, the Regents will have the right to either terminate the license or convert the license to a nonexclusive commercial license. Additionally, LBS is subject to certain progress and royalty reporting obligations.

The 2015 UC License will expire upon the later of the expiration date of the longest-lived patent right licensed under the 2015 UC License. The Regents may terminate the 2015 UC License if: (i) a material breach by LBS is not cured within 60 days, (ii) LBS files a claim asserting the Regents licensed patent rights are invalid or unenforceable, or (iii) LBS files for bankruptcy. LBS has the right to terminate the 2015 UC License at any time upon at least 90 days' written notice.

2020 License Agreement with the Regents of the University of California

In April 2020, LBS entered into another license agreement with the Regents (the "2020 UC License"). Pursuant to the 2020 UC License Agreement, which extends to LBS's affiliates, LBS has an exclusive, sublicensable,

worldwide license under certain patent rights to make, use, sell, offer for sale and import products and practice methods covered by the claims of the licensed patent rights in the field of analysis of animal samples and human clinical samples (including microbial samples from an animal or human), including detecting and measuring proteases, enzymes, and biomolecules in bodily fluids, breath, and other sources but excluding analysis of human clinical samples associated with blood cancers, solid tumors, and other samples related to oncology conditions and diseases, and provision of sample testing services directed to such cancer, tumor, and oncology samples; and manufacture and sale of research (non-clinical testing) laboratory equipment for direct sale to research laboratories. We expect these licensed patent rights to support our pipeline activities, including those focused on identifying new drug targets and diagnostics. Under the 2020 UC License, there may be certain conditions under which LBS may be required to provide a sublicense or that the Regents may grant certain license rights that limit certain of LBS's exclusive rights.

Upon the execution of the 2020 UC License, LBS paid a one-time license issue fee of $5,000, agreed to reimburse the Regents for past patent costs and are obligated to pay an annual license maintenance fee in the mid four-digit dollar range until such time that it is commercially selling a licensed product. LBS is also obligated to make: (i) payments up to approximately $1.9 million in the aggregate upon achievement of certain development, regulatory and commercial milestones and (ii) royalty payments in the low- to mid-single-digit percentage range on annual net sales of licensed products by LBS, its affiliates, or its sublicensees, subject to adjustments to the royalty in certain events. Upon commencement of commercial sales, LBS will become subject to a minimum annual royalty in the low five-digit dollar range. Further, LBS is obligated to pay to the Regents a percentage of non-royalty licensing revenue it receives from its sublicensees under the 2020 UC License.

Under the 2020 UC License, LBS is required, either directly or through its affiliates, to diligently proceed with the development, manufacture, regulatory approval, and sale of licensed products and is subject to a number of diligence obligations relating to developmental, regulatory and commercialization milestones for the licensed products. For the first three years of the 2020 UC License, LBS is subject to a minimum annual spend requirement in the mid five-digit dollar range. If LBS fails to meet any milestones, the Regents will have the right to terminate the license or convert the license to a nonexclusive commercial license. Additionally, LBS is subject to certain progress and royalty reporting obligations.

The 2020 UC License will expire upon the later of the expiration date of the longest-lived patent right licensed under the 2020 UC License. The Regents may terminate the 2020 UC License if: (i) a material breach by LBS is not cured within 60 days, (ii) LBS files a claim asserting the Regents licensed patent rights are invalid or unenforceable, or (iii) LBS files for bankruptcy or becomes insolvent. LBS has the right to terminate the 2020 UC License at any time upon at least 90 days' written notice.

2021 License Agreement with the Regents of the University of California

In July 2021, we entered into a license agreement with the Regents (the "2021 UC License") to obtain exclusive rights to the cancer-related indications and uses that had been excluded under the 2020 UC License granted to LBS. Pursuant to the 2021 UC License Agreement, which extends to our affiliates, we have an exclusive, sublicensable, worldwide license under certain patent rights to make, use, sell, offer for sale and import products and practice methods covered by the claims of the licensed patent rights in the field of analysis of human clinical samples associated with blood cancers, solid tumors, and other samples related to oncology conditions and diseases, and provision of sample testing services directed to such cancer, tumor, and oncology samples. In conjunction with the 2020 UC License, which we are permitted to take advantage of as an affiliate of LBS, we expect these licensed patent rights to further enhance pipeline activities, including those focused on identifying new drug targets and diagnostics. Under the 2021 UC License, there may be certain conditions under which we may be required to provide a sublicense or that the Regents may grant certain license rights that limit certain of our exclusive rights.

Upon execution of the 2021 UC License, we paid a one-time license issue fee of $10,000 and are obligated to pay an annual license maintenance fee in the mid four-digit dollar range until such time that it is commercially selling

a licensed product. We are also obligated to make: (i) payments up to approximately $1.9 million in the aggregate upon achievement of certain development, regulatory and commercial milestones and (ii) royalty payments in the low- to mid-single-digit percentage range on annual net sales of licensed products us, our affiliates, or our sublicensees, subject adjustments to the royalty in certain events. Upon commencement of commercial sales, we will become subject to a minimum annual royalty in the low five-digit dollar range. Further, we are obligated to pay the Regents a percentage of non-royalty licensing revenue we receive from any sublicensees under the 2021 UC License.

Under the 2021 UC License, we are required, either directly or through our affiliates, to diligently proceed with the development, manufacture, regulatory approval, and sale of licensed products and we are subject to a number of diligence obligations relating to developmental, regulatory and commercialization milestones for the licensed products. For the first three years of the 2021 UC License, we are subject to as a minimum annual spend requirement in the mid five-digit dollar range. We presently expect to be in a position to meet our future milestone obligations. If we fail to meet any milestones, the Regents will have the right to terminate the license or convert the license to a nonexclusive commercial license. Additionally, we are subject to certain progress and royalty reporting obligations.

The 2021 UC License will expire upon the later of the expiration date of the longest-lived patent right licensed under the 2021 UC License. The Regents may terminate the 2021 UC License if: (i) a material breach by us is not cured within 60 days, (ii) we file a claim asserting the Regents licensed patent rights are invalid or unenforceable, or (iii) we file for bankruptcy or become insolvent. We have the right to terminate the 2021 UC License at any time upon at least 90 days' written notice.

Co-Development and Distribution Agreement with Newsoara

In February 2018, LBS entered into a co-development and distribution agreement with Newsoara, a joint venture established with Biolead Medical Technology Limited, as amended in November 2018 (the "Co-Development Agreement"). Pursuant to the Co-Development Agreement, LBS granted Newsoara an exclusive, non-transferrable co-development right under certain patents and know-how owned or controlled by us to develop, use, sell, offer to sell, import, and otherwise commercialize licensed products (the "Licensed Products") for any and all indications in the People's Republic of China, including the regions of Hong Kong and Macao, but excluding Taiwan (the "Territory"). The Licensed Products only include LB1148. The co-development right includes the right to grant sublicenses to third parties, subject to LBS' written consent, provided that both parties agreed that Newsoara would be permitted to use a certain partner for development purposes. The Co-Development Agreement obligates Newsoara to initially use LBS as the exclusive supplier for all of Newsoara's requirements for Licensed Products in the Territory. During the term of the Co-Development Agreement, Newsoara may request to manufacture the Licensed Product in the Territory, subject to satisfying certain conditions to our reasonable satisfaction. LBS is obligated to approve Newsoara manufacturing rights without undue refusal or delay.

The Co-Development Agreement obligates Newsoara to not (i) develop, seek approval for, sell, distribute, or otherwise commercialize any competing product within the Territory or (ii) sell or distribute the Licensed Products outside the Territory. The Co-Development Agreement obligates LBS to not (i) develop, seek approval for, sell, distribute, or otherwise commercialize any competing product within the Territory or (ii) sell or distribute the Licensed Products inside the Territory.

Under the Co-Development Agreement, Newsoara is responsible for meeting certain regulatory milestones and maintaining those approvals once achieved. Newsoara is also required to periodically demonstrate its financial capability to fulfill Newsoara's obligations under the Co-Development Agreement. Newsoara has met all of its milestone obligations to date and we presently expect Newsoara to meet its future milestone obligations. Newsoara's failure to meet any milestones may subject Newsoara to certain penalties, including the payment of extension fees. Each party is required to share with the other certain data and information it generates that

pertains to the Licensed Products. Further, Newsoara is providing LBS with a perpetual, non-exclusive, fully paid and royalty-free sublicensable right and license to use certain of Newsoara's data for regulatory and legal purposes.

Under the Co-Development Agreement, LBS is responsible for (i) maintaining, the regulatory or other approvals from the applicable authority required for our manufacturing, packaging, release and shipping of the Licensed Product and (ii) providing to Newsoara all necessary documentation to enable Newsoara to import the Licensed Product within the Territory.

LBS also obtained from Newsoara (i) an exclusive license under certain patents and know-how owned or controlled by Newsoara ("Newsoara Technology") to make, have made, use, sell, offer to sell, import, and otherwise develop and commercialize Licensed Products in any and all indications outside of the Territory, and (ii) a non-exclusive license under the Newsoara Technology to make, have made, use, sell, offer to sell, and import Licensed Product inside the Territory to the extent necessary to comply with certain of our obligations under the Co-Development Agreement.

In consideration of the rights granted to Newsoara under the Co-Development Agreement, Newsoara paid LBS a one-time upfront fee of $1.0 million. In addition, Newsoara is obligated to make (i) payments up to $6.75 million in the aggregate upon achievement of certain regulatory and commercial milestones, (ii) payments in the low six-digit range per licensed product upon achievement of a regulatory milestone and (iii) tiered royalty payments ranging from the mid-single-digit to low-double-digit percentage range on annual net sales of Licensed Products, subject to adjustment to the royalty percentage in certain events, including a change of control, the expiration of certain patents rights, and royalties paid by Newsoara third parties. To date, Newsoara has met all of its payment obligations under the Co-Development Agreement.

Under the Co-Development Agreement, if either of the parties experiences a change of control and the acquiring party is directly or indirectly involved in the development, marketing, or sale of a product that competes with the Licensed Product in the Territory, then the applicable party must require the acquiring party to agree in writing to certain provisions to protect the viability and marketability of the Product.

The Co-Development Agreement will expire upon the later of the expiration date of the last valid claim of any licensed patent covering the Licensed Products in the Territory. In addition, the Co-Development Agreement can be terminated (i) by either party for the other party's material breach that remains uncured for a specified time period after written notice or for events related to the other party's insolvency, (ii) by us if Newsoara challenges or attempts to interfere with any licensed patent rights and, (iii) by Newsoara for any reason upon specified prior written notice.

Trade Secrets and Confidentiality

We rely, in some circumstances, on trade secrets and other confidential information to protect our unpatented technology. However, trade secrets can be difficult to protect. We seek to protect our trade secrets and proprietary technology and processes, in part, by entering into non-disclosure and confidentiality agreements with our employees, consultants, collaborators, scientific advisors, suppliers, contractors and other third parties. In addition, we enter into employment agreements that require employees to assign to us any inventions, trade secrets or know-how that they develop while employed by us.

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 our trade secrets and other proprietary information may be disclosed. We may not have adequate remedies for any breach and could lose our trade secrets and other proprietary information through such a breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To

the extent that our consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting trade secrets, know-how and inventions.

Selected Risks Affecting Our Business

Below is a summary of the principal factors that make an investment in our securities speculative or risky. This summary does not address all of the risks that we face. Additional discussion of the risks and uncertainties summarized in this risk factor summary, and other risks and uncertainties that we face, are set forth below under the heading "Risk Factors" contained in this prospectus, any accompanying prospectus supplement or free writing prospectus, and under similar headings in the documents that are incorporated by reference into this prospectus.

- The Company's business depends on the successful clinical development, regulatory approval and commercialization of LB1148.
- Some of the initial indications in which the Company plans to pursue development of LB1148 are indications for which there are no FDA-approved therapies. This makes it difficult to predict the timing and costs of clinical development for LB1148 in these indications, as well as the regulatory approval path.
- The development and commercialization strategy for the Company's product candidate LB1148 depends, in part, on published scientific literature and the FDA's prior findings regarding the safety and efficacy of tranexamic acid. If the Company is not able to pursue this strategy, it may be delayed in receiving regulatory authority approval.
- Clinical drug development is very expensive, time-consuming and uncertain.
- The results of previous clinical trials may not be predictive of future results, and the results of the Company's current and planned clinical trials may not satisfy the requirements of the FDA or non-U.S. regulatory authorities.
- Even if the Company receives marketing approval for LB1148, or any future product candidate, it may not be able to successfully commercialize its product candidates due to unfavorable pricing regulations or third-party coverage and reimbursement policies, which could make it difficult for the Company to sell its product candidates profitably.
- The Company's product candidates may cause undesirable side effects or have other unexpected properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in post-approval regulatory action.
- The Company may in the future conduct clinical trials for its product candidates outside the United States, and the FDA and applicable foreign regulatory authorities may not accept data from such trials.
- The Company relies on and expects to continue to rely on third-party Contract Research Organizations ("CROs") and other third parties to conduct and oversee its clinical trials. If these third parties do not meet the Company's requirements or otherwise conduct the trials as required, the Company may not be able to satisfy its contractual obligations or obtain regulatory approval for, or commercialize, its product candidates.
- The Company will need to raise additional financing in the future to fund its operations, which may not be available to it on favorable terms or at all.
- The Company currently has no products approved for sale, and it may never obtain regulatory approval to commercialize any of its product candidate.
- The Company's or third party's clinical trials may fail to demonstrate the safety and efficacy of its product candidates, or serious adverse or unacceptable side effects may be identified during their

development, which could prevent or delay marketing approval and commercialization, increase the Company's costs or necessitate the abandonment or limitation of the development of the product candidate.

- The Company has expressed substantial doubt about its ability to continue as a going concern.
- The Company's product candidates, if approved, will face significant competition and their failure to compete effectively may prevent them from achieving significant market penetration.
- Any adverse developments that occur during any clinical trials conducted by Newsoara may affect the Company's ability to obtain regulatory approval or commercialize LB1148.
- The Company has a very limited operating history and has never generated any revenues from product sales.
- If the Company is not able to comply with the applicable continued listing requirements or standards of The Nasdaq Capital Market, Nasdaq could delist its common stock.
- The Company may not be able to protect its intellectual property rights throughout the world.
- The Board has broad discretion to issue additional securities, which might dilute the net tangible book value per share of our common stock for existing stockholders**.**
- The Company currently has no marketing capabilities and no sales organization. If the Company is unable to establish sales and marketing capabilities on its own or through third parties, the Company will be unable to successfully commercialize its product candidates, if approved, or generate product revenue.
- Failure to remediate a material weakness in internal accounting controls could result in material misstatements in the Company's consolidated financial statements.
- The Company may not be able to obtain, maintain or enforce global patent rights or other intellectual property rights that cover its product candidates and technologies that are of sufficient breadth to prevent third parties from competing against the Company.
- Obtaining and maintaining the Company's patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by governmental patent agencies, and its patent protection could be reduced or eliminated for non-compliance with these requirements.
- If the Company fails to comply with its obligations under its intellectual property license agreements, it could lose license rights that are important to its business. Additionally, these agreements may be subject to disagreement over contract interpretation, which could narrow the scope of its rights to the relevant intellectual property or technology or increase its financial or other obligations to its licensors.
- The Company's business could be adversely affected by the effects of health pandemics or epidemics, including the recent COVID-19 pandemic, in regions where it or third parties on which it relies have significant manufacturing facilities, concentrations of clinical trial sites or other business operations. The COVID-19 pandemic could materially affect the Company's operations, including at its headquarters in California, which has been in the past, and could be in the future, subject to a county-wide stay-at-home order, and at clinical trial sites, as well as the business or operations of manufacturers, CROs or other third parties with whom the Company conducts business.

Implications of Being a Smaller Reporting Company

We are a "smaller reporting company" as defined in Item 10(f)(1) of Regulation S-K. Smaller reporting companies may take advantage of certain reduced disclosure obligations, including, among other things,

providing only two years of audited financial statements. We will remain a smaller reporting company until the last day of any fiscal year for so long as either (1) the market value of our shares of common stock held by non-affiliates does not equal or exceed $250.0 million as of the prior June 30th, or (2) our annual revenues did not equal or exceed $100.0 million during such completed fiscal year and the market value of our shares of common stock held by non-affiliates did not equal or exceed $700.0 million as of the prior June 30th. To the extent we take advantage of any reduced disclosure obligations, it may make comparison of our financial statements with other public companies difficult or impossible.

Corporate Information

We were originally incorporated in 2001 in the State of Delaware under the name Neuralstem, Inc. In October 2019, we changed our name from Neuralstem, Inc. to Seneca Biopharma, Inc. In April 2021, we effected the Merger (described below). In April 2021, we changed our name from Seneca Biopharma, Inc. to Palisade Bio, Inc. Our principal executive offices are located at 5800 Armada Drive, Suite 210, Carlsbad, California 92008, our telephone number is (858) 704-4900 and our website address is www.palisadebio.com. The information contained in or accessible through our website does not constitute part of this prospectus.

Subsidiaries

We have two wholly-owned subsidiaries, Suzhou Neuralstem Biopharmaceutical Co., Ltd., organized under the laws of the People's Republic of China ("Suzhou"), and Leading Biosciences, Inc. ("LBS"). Suzhou was established by Seneca Biopharma, Inc. to sponsor a clinical trial of NSI-566 that was conducted between 2013 and 2016. At this time, Suzhou has limited operations and exists for the sole purpose of conducting observational follow-up for a small group of remaining patients from the completed clinical trial, which it does through the engagement of a consultant. Suzhou has no employees or other operations. We believe that all Suzhou operations will cease in 2022.

Merger Transaction

On April 27, 2021, pursuant to the Agreement and Plan of Merger (the "Merger Agreement"), dated as of December 16, 2020, by and among the Company, formerly known as Seneca Biopharma, Inc., LBS and Townsgate Acquisition Sub 1, Inc., a wholly owned subsidiary of the Company ("Merger Sub"), the Company completed the previously announced merger transaction with LBS, pursuant to which Merger Sub merged with and into LBS, with LBS surviving such merger as a wholly owned subsidiary of the Company (the "Merger"). In connection with the Merger, and immediately prior to the effective time of the Merger, the Company effected a reverse stock split of the Company Common Stock at a ratio of 1-for-6 (the "Reverse Stock Split"). Unless otherwise noted, all references to share and per share amounts in this Prospectus reflect the Reverse Stock Split. Also, in connection with the closing of the Merger, the Company changed its name from "Seneca Biopharma, Inc." to "Palisade Bio, Inc." and the business conducted by the Company became primarily the business conducted by LBS, which is a clinical-stage biopharmaceutical company focused on advancing LBS's clinical program and developing a therapeutic to combat the interruption of gastrointestinal function following major surgery for which there is currently a significant unmet need for safe and effective therapies.

At the Effective Time:

a) Each outstanding share of LBS's common stock, par value $0.001 per share ("LBS Common Stock"), and each outstanding non-voting share of LBS's Series 1 preferred stock, par value $0.001 per share ("LBS Series 1 Preferred"), issued in the Pre-Merger Financing (as defined below) was converted into the right to receive 0.02719 (the "Exchange Ratio") shares of Company Common Stock, as set forth in the Merger Agreement. The Exchange Ratio was determined based on the total number of outstanding

shares of Company Common Stock and LBS Common Stock, in each case as calculated on an adjusted fully diluted treasury stock method basis, after giving effect to the Pre-Merger Financing, including 50% of the shares subject to the Equity Warrants (as defined below), and taking into account certain adjustments based on the proceeds of the Pre-Merger Financing and the net cash of the Company at the Closing in accordance with the Merger Agreement.

b) Each option to purchase shares of LBS Common Stock (each, an "LBS Option") that was outstanding and unexercised immediately prior to the Effective Time under LBS's 2013 Equity Incentive Plan (the "LBS Plan"), whether or not vested, was converted into and became an option to purchase shares of Company Common Stock, and the Company assumed the LBS Plan and each such LBS Option in accordance with the terms of the LBS Plan (the "Assumed Options"). The number of shares of Company Common Stock subject to each Assumed Option was determined by multiplying (i) the number of shares of LBS Common Stock that were subject to such Assumed Option, as in effect immediately prior to the Effective Time, by (ii) the Exchange Ratio, and rounding the resulting number down to the nearest whole number of shares of Company Common Stock, and the per share exercise price for the Company Common Stock issuable upon exercise of each Assumed Option was determined by dividing (A) the per share exercise price of such Assumed Option, as in effect immediately prior to the Effective Time, by (B) the Exchange Ratio and rounding the resulting per share exercise price up to the nearest whole cent.

c) Each warrant to purchase shares of LBS Common Stock (each, an "LBS Warrant") outstanding immediately prior to the Effective Time was assumed by the Company and converted into a warrant to purchase shares of Company Common Stock (the "Assumed Warrants") and thereafter (i) each Assumed Warrant may be exercised solely for shares of Company Common Stock; (ii) the number of shares of Company Common Stock subject to each Assumed Warrant was determined by multiplying (A) the number of shares of LBS Common Stock that were subject to such LBS Warrant, as in effect immediately prior to the Effective Time, by (B) the Exchange Ratio, and rounding the resulting number down to the nearest whole number of shares of Company Common Stock; (iii) the per share exercise price for the Company Common Stock issuable upon exercise of each Assumed Warrant was determined by dividing (A) the exercise price per share of the LBS Common Stock subject to such LBS Warrant, as in effect immediately prior to the Effective Time, by (B) the Exchange Ratio, and rounding the resulting exercise price up to the nearest whole cent.

Pre-Merger Financing

Securities Purchase Agreement (Bridge Financing)

In connection with signing the Merger Agreement, LBS entered into a securities purchase agreement, dated as of December 16, 2020 (the "Bridge SPA") with Altium Growth Fund, LP (the "Investor" or "Altium"), pursuant to which the Investor purchased senior secured promissory notes (the "Bridge Notes") and warrants to purchase such number of shares of LBS Common Stock equal to the aggregate principal amount of the Bridge Notes issued divided by the initial per share exercise price of $0.4816 (the "Bridge Warrants"), subject to adjustment as disclosed below. The Bridge Warrants have a term of five years from the date all of the shares underlying the Bridge Warrants are registered for resale, and the exercise price shall be subject to price-only full ratchet anti-dilution protection upon the issuance of any shares of LBS Common Stock or securities convertible into LBS Common Stock for a period of two years from the effective date of the registration statement covering such shares. The Bridge Warrants also contain certain participation rights with regard to asset distributions and fundamental transactions. As a result of the Merger, at the Effective Time, each Bridge Warrant was automatically converted into a warrant to purchase that number of shares of the Company's common stock equal to the number of shares underlying the Bridge Warrants immediately prior to the closing of the Merger multiplied by the Exchange Ratio and the exercise price was proportionately adjusted. At the Effective Time,

there were 188,192 shares of the Company's common stock issuable upon exercise of the Bridge Warrants. The Bridge Warrants were Assumed Warrants pursuant to the Merger Agreement, as described above.

Securities Purchase Agreement (Equity Financing)

In connection with signing the Merger Agreement, on December 16, 2020, LBS, Seneca and the Investor entered into a Securities Purchase Agreement (the "Equity SPA"), pursuant to which, among other things, the Investor agreed to invest $20.0 million in cash and cancel any outstanding principal and interest on the Bridge Notes immediately prior to the closing of the Merger (the aggregate amount of such cash investment and the cancellation of the outstanding principal and interest on the Bridge Notes, the "Purchase Price" and the financing arrangement described herein, the "Pre-Merger Financing") to fund the combined company following the Merger. In return, LBS issued an amount of shares (the "Initial Shares") of LBS Series 1 Preferred Stock to the Investor equal to the Purchase Price divided by the per share purchase price of $0.4816 and the Company agreed to issue to the Investor, warrants to purchase shares of the Company's Common stock (the "Equity Warrants"). The Equity Warrants were issued on the 17th trading day following the closing of the Merger, and had an initial exercise price per share equal to $4.70 and were exercisable for up to 4,995,893 shares of the Company's common stock, and are immediately exercisable and will have a term of five years from the date of issuance.

The Bridge Warrants and Equity Warrants provide that, until the second anniversary of the date on which all shares of Company's common stock issued to the Investor (including any shares underlying the Equity Warrants) are registered on one or more registration statements, if the Company publicly announces, issues or sells, enters into a definitive, binding agreement pursuant to which the Company is required to issue or sell or is deemed, pursuant to the provisions of the Bridge Warrants and Equity Warrants, to have issued or sold, any shares of the Company's common stock for a price per share lower than the exercise price then in effect, subject to certain limited exceptions, then the exercise price of the Bridge Warrants and Equity Warrants shall be reduced to such lower price per share. Further, on preset reset dates, the exercise price of the Bridge Warrants and Equity Warrants was to be adjusted downward (but not increased) (the "Resets"). Further, the Equity Warrants include a provision such that, beginning six months after the closing of the Merger, if the volume weighted average price of Company Common Stock is less than the then-applicable exercise price for five consecutive trading days, the holder of the Equity Warrant shall be entitled to receive 1.0 share of Company Common Stock for each share underlying the Equity Warrants being exercised thereunder in a cashless exercise. The exercise price and the number of shares of Company Common Stock issuable upon exercise of the Bridge Warrants and Equity Warrants will also be subject to adjustment in the event of any stock splits, dividends or distributions or other similar transactions as well as fundamental transactions. Prior to the effectiveness of the Waiver and Amendment Agreement (described below), two Resets occurred and the two Bridge Warrants and the Equity Warrants were exercisable for up to 429,446, 429,446, and 5,303,568 shares, respectively, each at an exercise price of $3.88 per share, and two potential Resets remained.

Waiver and Amendment Agreements

July 2021

Effective July 21, 2021 (the "July Effective Time"), the Investor entered into a Waiver and Amendment Agreement with the Company (the "2021 Waiver Agreement"). Pursuant to the 2021 Waiver Agreement, the Investor and the Company agreed to waive certain rights, waive the reset provisions with respect to the exercise price and number of shares subject to the outstanding Bridge Warrants and Equity Warrants, eliminate certain financing restrictions, and accelerate registration rights for the shares underlying the warrants. As consideration for the foregoing, pursuant to the 2021 Waiver Agreement, the Company issued to the Investor an additional warrant to purchase up to 1,100,000 shares of the Company's common stock (the "July Warrant" and together with the Bridge Warrants and the Equity Warrants, the "Warrants"). The July Warrant is exercisable beginning

on January 21, 2022 and expires on the later of (x) five years from the date that the underlying shares are registered for resale and (y) January 21, 2027. The per share exercise price for the July Warrant is $3.631, subject to certain adjustments. Pursuant to the 2021 Waiver Agreement, Investor agreed to waive the reset provisions in the outstanding Bridge Warrants and Equity Warrants such that the number of shares and exercise price in effect immediately prior to the July Effective Time (as described above) shall no longer be subject to price-based resets.

January 2022

Effective January 31, 2022 (the "2022 Effective Time"), the Investor entered into a Waiver and Amendment Agreement with the Company (the "2022 Waiver Agreement"). Pursuant to the 2022 Waiver Agreement, the Investor and the Company agreed to irrevocably waive any adjustment to the exercise price of the existing warrants held by the Investor from and after the 2022 Effective Time for the Company's issuances of equity or equity-linked securities at a price below the exercise price of the warrants. The 2022 Waiver Agreement also includes agreement by the parties to, among other things, (i) restrict the Investor's ability to sell the Company's securities through a "leak out" provision whereby sales are restricted by applying a volume limitation, (ii) shorten the notice period for the Investor's participation rights related to certain future securities offerings, (iii) restrict the Company's ability to conduct a primary offering of its securities for a specified period of time, and (iv) provide registration rights for the shares underlying the January Warrant (defined below). As consideration for the foregoing, pursuant to the 2022 Waiver Agreement, the Company issued the Investor an additional warrant to purchase up to 2,250,000 shares of the Company's common stock (the "January 2022 Warrant"). The January 2022 Warrant is exercisable beginning six months following the 2022 Effective Time. The exercise price for the January Warrant is $1.10 (the closing price of the Company's common stock on January 28, 2022), subject to customary adjustments for stock splits, stock dividends, stock combinations, reclassifications and similar transactions.

May 2022 Private Placement

On May 6, 2022, we entered into securities purchase agreements (the "Securities Purchase Agreement") with certain institutional and accredited investors pursuant to which we agreed to sell and issue, in a registered direct offering (the "Registered Offering"), an aggregate of 3,646,690 shares of our common stock, par value $0.01 per share, at a purchase price per share of $0.55 and, in a concurrent private placement, we also agreed to sell and issue to such purchasers warrants (the "purchase warrants") to purchase up to 3,646,690 shares of common stock at an exercise price of $0.7105 per share, the closing bid price of our common stock on May 5, 2022 (collectively, the "May 2022 Offering"). The purchase warrants are not exercisable until six months following the date of issuance and expire five and a half years from the date of issuance.

Pursuant to a placement agency agreement dated as of May 6, 2022, we engaged Ladenburg Thalmann & Co. Inc. (the "placement agent"), to act as the exclusive placement agent in connection with the Registered Direct Offering and concurrent private placement transaction. We issued placement agent warrants ("placement agent warrants") to purchase an aggregate of 218,801 shares of our common stock. The placement agent warrants have an exercise price of $0.7105 per share and a five-and-a-half year term. The placement agent warrants are not exercisable until six months following the date of issuance. The shares of common stock underlying the placement agent warrants and the purchase warrants are referred to collectively as the warrant shares.

The registration statement of which this prospectus is a part relates to the resale of the shares of common stock that may be issued to the selling securityholders in connection with the exercise of the purchase warrants and placement agent warrants (collectively, the "May 2022 Warrants") issued in the foregoing transaction.

THE OFFERING

Common stock offered by the selling securityholders	3,865,491 shares
Terms of the offering	Each selling securityholder will determine when and how it will sell the common stock offered in this prospectus, as described in "Plan of Distribution."
Use of proceeds	We will not receive any proceeds from the sale of shares of our common stock by the selling securityholders.
Risk factors	See "Risk Factors" beginning on page 20, for a discussion of factors you should carefully consider before deciding to invest in our common stock.
Nasdaq Capital Market symbol	PALI

The selling securityholders named in this prospectus may offer and sell up to 3,865,491 shares of our common stock.

Each selling securityholder is prohibited, subject to certain exceptions, from exercising the May 2022 Warrants to the extent that immediately prior to or after giving effect to such exercise, the selling securityholder, together with its affiliates and other attribution parties, would own more than 4.99% or 9.99%, as indicated on such selling securityholder's warrant, of the total number of shares of the Company's common stock then issued and outstanding, which percentage may be changed at the selling securityholder's election to a lower percentage at any time or to a higher percentage not to exceed 9.99% upon 61 days' notice to the Company.

Our common stock is currently listed on The Nasdaq Capital Market under the symbol "PALI."

Shares of common stock that may be offered under this prospectus will be fully paid and non-assessable. We will not receive any of the proceeds of sales by the selling securityholders of any of the common stock covered by this prospectus. Throughout this prospectus, when we refer to the shares of our common stock being registered on behalf of the selling securityholders for offer and resale, we are referring to the shares of common stock issued to the selling securityholders in connection with the exercise of the May 2022 Warrants. When we refer to the selling securityholders in this prospectus, we are referring to the selling securityholders identified in this prospectus and, as applicable, their permitted transferees or other successors-in-interest that may be identified in a supplement to this prospectus or, if required, a post-effective amendment to the registration statement of which this prospectus is a part.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before making an investment decision, you should carefully consider the risks described below and described in the sections entitled "Risk Factors" in our most recent Annual Report on Form 10-K filed with the SEC on March 17, 2022, our most recent Quarterly Report on Form 10-Q, as filed with the SEC on May 13, 2022, and our subsequent Quarterly Reports on Form 10-Q, as filed with the SEC, which are incorporated herein by reference in their entirety, as well as any amendment or updates to our risk factors reflected in subsequent filings with the SEC, including any applicable prospectus supplement. Our business, financial condition, results of operations or prospects could be materially adversely affected by any of these risks. The trading price of our stock could decline due to any of these risks, and you may lose all or part of your investment. This prospectus and the documents incorporated herein by reference also contain forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks mentioned elsewhere in this prospectus. For more information, see the section entitled "Where You Can Find Additional Information." Please also read carefully the section entitled "Special Note Regarding Forward-Looking Statements." Below are material changes to our risk factors since the filing of our Quarterly Report on Form 10-Q, as filed with the SEC on May 13, 2022.

If the Company is not able to comply with the applicable continued listing requirements or standards of The Nasdaq Capital Market, Nasdaq could delist its common stock.

The Company's ability to publicly or privately sell equity securities and the liquidity of its common stock could be adversely affected if is delisted from The Nasdaq Capital Market or if it is unable to transfer its listing to another stock market. In order to maintain this listing, it must satisfy minimum financial and other continued listing requirements and standards, including a requirement to maintain a minimum bid price of the Company's common stock of $1.00 per share.

For example, on May 20, 2022, the Company received notice (the "Notice") from The Nasdaq Stock Market LLC ("Nasdaq") advising the Company that for 30 consecutive trading days preceding the date of the Notice, the bid price of the Company's common stock had closed below the $1.00 per share minimum required for continued listing on The Nasdaq Capital Market pursuant to Nasdaq Listing Rule 5550(a)(2).

The Company cannot assure you that, in the future, its securities will meet the continued listing requirements to be listed on Nasdaq. If the Company's common stock is delisted by Nasdaq, it could lead to a number of negative implications, including an adverse effect on the price of its common stock, increased volatility in its common stock, reduced liquidity in its common stock, a limited availability of market quotations for the Company's common stock, the loss of federal preemption of state securities laws and greater difficulty in obtaining financing. In addition, delisting of the Company's common stock could deter broker-dealers from making a market in or otherwise seeking or generating interest in its common stock, could result in a loss of current or future coverage by certain sell-side analysts and might deter certain institutions and persons from investing in the Company's securities at all. Delisting could also cause a loss of confidence of the Company's collaborators, vendors, suppliers and employees, which could harm its business and future prospects.

If the Company's common stock is delisted by Nasdaq, its common stock may be eligible to trade on the OTC Bulletin Board, OTC-QB or another over-the-counter market. Any such alternative would likely result in it being more difficult for the Company to raise additional capital through the public or private sale of equity securities and for investors to dispose of or obtain accurate quotations as to the market value of, the Company's common stock. In addition, there can be no assurance that the Company's common stock would be eligible for trading on any such alternative exchange or markets. Moreover, if the Company's common stock is delisted, it may come within the definition of "penny stock" under the Exchange Act, which imposes additional sales practice requirements on broker-dealers who sell securities to persons other than established customers and accredited investors. For example, the Company and/or broker-dealers are required to make a special suitability

determination for purchases of such securities and must receive a purchaser's written consent to the transaction prior to any purchase. Additionally, unless exempt, prior to a transaction involving a penny stock, the penny stock rules require the delivery of a disclosure schedule prescribed by the SEC relating to the penny stock market. The broker-dealer must also disclose the commissions payable to the broker-dealer, current quotations for the securities and, if the broker-dealer is the sole market-maker for the security, the fact that they are the sole market-maker and their presumed control over the market. Finally, monthly statements disclosing recent price information on the limited market in penny stocks must be sent to holders of such penny stocks. These requirements may reduce trading activity in the secondary market for the Company's common stock and may impact the ability or willingness of broker-dealers to sell our securities which could limit the ability of stockholders to sell their securities in the public market and limit our ability to attract and retain qualified employees or raise additional capital in the future.

Global, market and economic conditions may negatively impact our business, financial condition and share price.

Concerns over inflation, geopolitical issues, the U.S. financial markets, foreign exchange rates, capital and exchange controls, unstable global credit markets and financial conditions and the COVID-19 pandemic, have led to periods of significant economic instability, declines in consumer confidence and discretionary spending, diminished expectations for the global economy and expectations of slower global economic growth going forward, and increased unemployment rates. Our general business strategy may be adversely affected by any such economic downturns, volatile business environments and continued unstable or unpredictable economic and market conditions. If these conditions continue to deteriorate or do not improve, it may make any necessary debt or equity financing more difficult to complete, more costly and more dilutive. In addition, there is a risk that one or more of our current or future service providers, manufacturers, suppliers and other partners could be negatively affected by difficult economic times, which could adversely affect our ability to attain our operating goals on schedule and on budget or meet our business and financial objectives.

In addition, we face several risks associated with international business and are subject to global events beyond our control, including war, public health crises, such as pandemics and epidemics, trade disputes, economic sanctions, trade wars and their collateral impacts and other international events. Any of these changes could have a material adverse effect on our reputation, business, financial condition or results of operations. There may be changes to our business if there is instability, disruption or destruction in a significant geographic region, regardless of cause, including war, terrorism, riot, civil insurrection or social unrest; and natural or man-made disasters, including famine, flood, fire, earthquake, storm or disease. In February 2022, armed conflict escalated between Russia and Ukraine. The sanctions announced by the U.S. and other countries, following Russia's invasion of Ukraine against Russia to date include restrictions on selling or importing goods, services or technology in or from affected regions and travel bans and asset freezes impacting connected individuals and political, military, business and financial organizations in Russia. The U.S. and other countries could impose wider sanctions and take other actions should the conflict further escalate. It is not possible to predict the broader consequences of this conflict, which could include further sanctions, embargoes, regional instability, geopolitical shifts and adverse effects on macroeconomic conditions, currency exchange rates and financial markets, all of which could impact our business, financial condition and results of operations.

USE OF PROCEEDS

We are filing the registration statement of which this prospectus forms a part to permit the holders of the May 2022 Warrants to purchase shares of our common stock described in the section titled "Selling Securityholders" to resell such shares of common stock issuable upon exercise of such warrants, or the warrant shares. The selling securityholders will receive all of the net proceeds from sales of the warrant shares sold pursuant to this prospectus and we will not receive any proceeds from the resale of any warrant shares offered by this prospectus by the selling stockholders. However, upon the exercise of the warrants for 3,865,491 shares of our common stock by payment of cash, we will receive aggregate gross proceeds of approximately $2.7 million. Any proceeds from the exercise of the warrants will be used for working capital and general corporate purposes. We cannot predict when or if the warrants will be exercised, and it is possible that the warrants may expire and never be exercised. We will bear the out-of-pocket costs, expenses and fees incurred in connection with the registration of shares of our common stock to be sold by the selling securityholders, including registration, listing and qualifications fees, printers and accounting fees, and fees and disbursements of counsel, or collectively, the Registration Expenses. Other than Registration Expenses, the selling securityholders will bear underwriting discounts, commissions, placement agent fees or other similar expenses payable with respect to sales of shares.

MARKET INFORMATION

Our common stock is listed on The Nasdaq Capital Market under the symbol "PALI." On June 27, 2022, the last reported sale price for our common stock on The Nasdaq Capital Market was $0.4568 per share. As of May 31, 2022, we had approximately 226 stockholders of record.

DIVIDEND POLICY

We do not anticipate declaring or paying, in the foreseeable future, any cash dividends on our capital stock. We intend to retain all available funds and future earnings, if any, to fund the development and expansion of our business, and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination regarding the declaration and payment of dividends, if any, will be at the discretion of our Board and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our Board may deem relevant.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

Other than compensation arrangements, including employment, termination of employment and change in control arrangements, with our directors and executive officers, and the other transactions discussed in the sections titled “Executive Compensation” and “Certain Relationships and Related Party Transactions” in our Definitive Proxy Statement on Schedule 14A filed with the SEC on April 21, 2022 and incorporated by reference herein, the following is a description of each transaction since January 1, 2019 and each currently proposed transaction in which:

- the amounts involved exceeded or will exceed the lesser of (a) $120,000 or (b) 1% of the average of our total assets for the fiscal years ended December 31, 2021 or 2020; and
- any of our directors, executive officers or holders of more than 5% of our capital stock, or any member of the immediate family of, or person sharing the household with, the foregoing persons, had or will have a direct or indirect material interest.

Pursuant to the Registered Offering, we agreed to sell and issue an aggregate of 3,646,690 shares of our common stock, par value $0.01 per share, at a purchase price per share of $0.55 to certain of the selling securityholders. In a concurrent private placement, we also agreed to sell and issue to purchase warrants to such purchasers to purchase up to 3,646,690 shares of common stock at an exercise price of $0.7105 per share, the closing bid price of our common stock on May 5, 2022. Altium, a holder of greater than 5% of our common stock, purchased 900,000 shares.

In a concurrent private placement, we also agreed to sell and issue to such purchasers warrants to purchase up to 3,646,690 shares of common stock at an exercise price of $0.7105 per share, the closing bid price of our common stock on May 5, 2022. We issued Altium a warrant to purchase 900,000 shares of our common stock. The warrants are not exercisable until six months following the date of issuance and expire five and a half years from the date of issuance.

SELLING SECURITYHOLDERS

On May 6, 2022, we entered into securities purchase agreements with certain institutional and accredited investors, pursuant to which we agreed to sell and issue, in a registered direct offering, offered pursuant to an effective shelf registration statement on Form S-3 an aggregate of 3,646,690 shares of common stock, for aggregate gross proceeds of approximately $2.0 million, before deducting fees to the placement agents and other estimated offering expenses payable by us.

In a concurrent private placement, pursuant to the purchase agreement, we offered and sold to the investors common stock purchase warrants to purchase an aggregate of 3,646,690 shares of our common stock. The purchase warrants have an exercise price per share equal to $0.7105, are not exercisable until six months following the date of issuance and expire five-and-half years from the issuance date.

Pursuant to placement agency agreement dated as of May 6, 2022, we engaged the placement agent, to act as the exclusive placement agent in connection with the registered direct and private placement transaction. We issued placement agent warrants to purchase an aggregate of 218,801 shares of our common stock, or the placement agent warrants. The placement agent warrants have an exercise price of $0.7105 per share and a five-and-a-half year term. The placement agent warrants are not exercisable until six months following the date of issuance. The shares of common stock underlying the placement agent warrants and the purchase warrants are referred to collectively as the warrant shares. The purchase warrants and placement agent warrants are referred to collectively as the May 2022 Warrants.

Pursuant to the purchase agreements, we agreed to file the registration statement of which this prospectus is a part to cover the resale of the shares of common stock underlying the purchase warrants and to keep such registration statement effective until no selling securityholder owns any warrants or warrant shares issuable upon exercise of the purchase warrants.

We are registering the resale of 3,865,491 shares of common stock which are issuable upon the exercise of the May 2022 Warrants held by the selling securityholders identified below to permit such selling securityholders, or their permitted transferees or other successors-in-interest that may be identified in a supplement to this prospectus or, if required, a post-effective amendment to the registration statement of which this prospectus is a part, to resell or otherwise dispose of these shares in the manner contemplated under the section entitled “Plan of Distribution” in this prospectus (as may be supplemented and amended).

The selling securityholders may sell some, all or none of their shares. We do not know how long each of the selling securityholder will hold their shares before selling them, and we currently have no agreements, arrangements or understandings with the selling securityholders regarding the sale or other disposition of any of the shares. The shares covered hereby may be offered from time to time by the selling securityholders. As a result, we cannot estimate the number of shares of common stock each of the selling securityholders will beneficially own after termination of sales under this prospectus. In addition, the selling securityholders may have sold, transferred or otherwise disposed of all or a portion of their shares of common stock since the date on which it provided information for this table.

The following table sets forth the name of each selling securityholder, the number of our outstanding shares of common stock beneficially owned by the selling securityholder as of May 31, 2022, the number of warrant shares that may be offered under this prospectus, and the number and percentage of our outstanding shares of common stock beneficially owned by the selling securityholder assuming all of the warrant shares covered hereby are sold. Beneficial ownership is determined in accordance with the rules of the SEC and includes voting or investment power with respect to our common stock. Generally, a person “beneficially owns” shares of our common stock if the person has or shares with others the right to vote those shares or to dispose of them, or if the person has the right to acquire voting or disposition rights within 60 days.

Under the terms of the May 2022 Warrants and certain other warrants held by the Investor, each selling securityholder may not exercise the May 2022 Warrant or such other warrants held by the Investor to the extent such exercise would cause the selling securityholder, together with its affiliates, to beneficially own a number of shares of common stock which would exceed 4.99% or 9.99%, as indicated in such selling securityholder's warrant, of our then outstanding common stock following such exercise, excluding, for purposes of such determination, common stock issuable upon exercise of the May 2022 Warrants and such other warrants held by the Investor, which have not been exercised. The number of shares in the second and fourth columns and the percentage in the fourth column reflect this limitation.

The information in the table below and the footnotes thereto regarding shares of common stock to be beneficially owned after the offering assumes the exercise of the May 2022 Warrants by the selling securityholders and sale of all shares being offered by the selling securityholders under this prospectus. Information contained in the table below and the footnotes thereto is based upon information provided to us by the selling securityholders. The selling securityholders may have sold or transferred, in transactions exempt from the registration requirements of the Securities Act, some or all of their warrant shares or other securities since the date on which the information in the table below is presented. Information about the selling securityholders may change over time. The percentage of shares owned after the offering is based on 21,880,169 shares of common stock outstanding as of May 31, 2022.

			After Offering	
Name and Address	Before Offering Number of Shares Beneficially Owned	Number of Shares Offered	Number of Shares Beneficially Owned(1)	Percentage of Shares Beneficially Owned
Altium Growth Fund, LP(2) 152 West 57th Street, 20th Floor New York, NY 10019	2,464,599(3)	900,000(4)	2,464,599	4.99%
District 2 Capital Fund LP 14 Wall Street Huntington, NY 11743	549,338(5)	549,338(6)	549,338	2.4%
FGP Protective Opportunity Master Fund SP, a segregated portfolio of FGP Protective Opportunity Master Fund SPC 94 Solaris Avenue, 2nd Floor, Camana Bay P.O. Box 30 745, Grand Cayman	549,338(7)	549,338(8)	549,338	2.4%
Hudson Bay Master Fund Ltd.(9) 28 Havemeyer Place, 2nd Floor Greenwich, CT 06830	641,930(10)	549,338(11)	641,930	2.9%
Lincoln Park Capital Fund LLC(12) 440 N. Wells St., Suite 410 Chicago, IL 60654	549,338(13)	549,338(14)	549,338	2.4%
Lind Global Fund II LP 444 Madison Ave, 41st Floor New York, NY 10022	549,338(15)	549,338(16)	549,338	2.4%
Ladenburg Thalmann & Co. Inc. 640 Fifth Avenue, 4th Floor New York, New York 10019	—	218,801(17)	—	—

(1) Assumes the exercise of the May 2022 Warrants and sale of all shares available for sale under this prospectus and no further acquisitions of shares by the selling securityholder.

(2) Altium Capital Management, LP, the investment manager of Altium Growth Fund, LP, has voting and investment power over these securities. Jacob Gottlieb is the managing member of Altium Capital Growth GP, LLC, which is the general

partner of Altium Growth Fund, LP. Each of the Altium Growth Fund, LP and Jacob Gottlieb disclaims beneficial ownership over these securities. The principal address of Altium Capital Management, LP is 152 West 57th Street, 20th Floor, New York, NY 10019.

(3) Consists of (a) 214,599 shares of common stock and (b) 2,250,000 shares of common stock that may be acquired pursuant to the exercise of outstanding warrants, without regard to certain beneficial ownership limitations.

(4) Consists of 900,000 shares of common stock issuable upon the exercise of May 2022 Warrant held by the Altium Growth Fund, LP.

(5) Consists of 549,338 shares of common stock.

(6) Consists of 549,338 shares of common stock issuable upon the exercise of May 2022 Warrant held by District 2 Capital Fund LP.

(7) Consists of 549,338 shares of common stock.

(8) Consists of 549,338 shares of common stock issuable upon the exercise of May 2022 Warrant held by FGP Protective Opportunity Master Fund SP, a segregated portfolio of FGP Protective Opportunity Master Fund SPC.

(9) Hudson Bay Capital Management LP, the investment manager of Hudson Bay Master Fund Ltd., has voting and investment power over these securities. Sander Gerber is the managing member of Hudson Bay Capital GP LLC, which is the general partner of Hudson Bay Capital Management LP. Each of Hudson Bay Master Fund Ltd. and Sander Gerber disclaims beneficial ownership over these securities.

(10) Consists of 549,338 shares of common stock and 92,592 shares underlying warrants to purchase common stock expiring in January 2025.

(11) Consists of 549,338 shares of common stock issuable upon the exercise of May 2022 Warrant held by Hudson Bay Master Fund Ltd.

(12) Joshua Scheinfeld and Jonathan Cope, the principals of Lincoln Park Capital Fund LLC, are deemed to be beneficial owners of all the common stock of Lincoln Park Capital Fund LLC. Messrs. Scheinfeld and Cope have shared voting and disposition power.

(13) Consists of 549,338 shares of common stock.

(14) Consists of 549,338 shares of common stock issuable upon the exercise of May 2022 Warrant held by Lincoln Park Capital Fund LLC.

(15) Consists of 549,338 shares of common stock.

(16) Consists of 549,338 shares of common stock issuable upon the exercise of May 2022 Warrant held by Lind Global Fund II LP.

(17) Consists of 218,801 shares of common stock issuable upon the exercise of May 2022 Warrant held by Ladenburg Thalmann & Co. Inc.

Relationship with Selling Securityholders

As discussed in greater detail above under the section entitled “Prospectus Summary” we entered into agreements with the selling securityholders pursuant to which they acquired the May 2022 Warrants, and agreed with the selling securityholders to file a registration statement to enable the resale of the shares of common stock issuable upon the exercise of the May 2022 Warrants.

Except as discussed in the table above, none of the selling securityholders nor any persons having control over such selling securityholders have held any position or office with us or our affiliates within the last three years nor has had a material relationship with us or any of our predecessors or affiliates within the past three years, other than as a result of the ownership of our shares or other securities

SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The following table sets forth information regarding beneficial ownership of our capital stock as of May 31, 2022 by:

- each person, or group of affiliated persons, known by us to beneficially own more than 5% of our common stock;
- each of our directors;
- each of our named executive officers; and
- all of our current executive officers and directors as a group.

The information in the following table is calculated based on 21,880,169 shares of our common stock outstanding as of May 31, 2022 and does not take into account the issuance of 3,865,491 warrant shares.

Beneficial ownership is determined according to the rules of the SEC. Beneficial ownership means that a person has or shares voting or investment power of a security and includes any securities that person or group has the right to acquire within 60 days after the measurement date, including upon the exercise of common stock purchase options or warrants.

Name of Beneficial Owner[1]	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned
Greater than 5% Stockholders		
Altium Capital Management, LP[2]	2,464,599	4.99%
Yuma Regional Medical Center[3]	2,251,229	10.09%
Directors and Named Executive Officers[4]		
James R. Neal[5]	40,571	*
Thomas Hallam, Ph.D.[6]	315,407	1.42%
Stephanie C. Diaz[7]	38,779	*
Donald Williams[8]	38,779	*
Mary Ann Gray, Ph.D.[9]	28,212	*
Cristina Csimma, Pharm.D., MHP[10]	26,408	*
Robert J. Trenschel, D.O.[11]	2,306,284	10.32%
Binxian Wei[12]	26,170	*
J.D. Finley[13]	256,763	1.16%
Michael Dawson, M.D.[14]	59,224	*
Kenneth Carter, Ph.D.[15]	—	*
Dane Saglio[15]	—	*
Matthew Kalnik, Ph.D.[15]	—	*
All directors and executive officers as a group (10 persons)[16]	3,136,597	13.59%

* Represents less than one percent.

(1) Except as otherwise indicated in the footnotes to this table, this table is based upon information supplied by officers, directors and principal stockholders and Schedules 13D and 13G, and Form 4s, filed with the SEC. Unless otherwise indicated in the footnotes to this table and subject to community property laws where applicable, we believe that each of the stockholders named in this table has sole voting and investment power with respect to the shares indicated as beneficially owned. Shares of our common stock underlying options, warrants and convertible securities that are currently exercisable or exercisable within 60 days of May 31, 2022 are deemed to be outstanding for the purpose of computing the number of shares held and the percent of total ownership of the person holding those options, warrants or convertible securities, but are not treated as outstanding for the purpose of computing the percent of total ownership of any other person. Applicable percentages are based on 21,880,169 shares of common stock outstanding on May 31,

2022, adjusted as required by rules promulgated by the SEC. Unless otherwise indicated, the address of the beneficial owner is c/o Palisade Bio, Inc. 5800 Armada Drive, Suite 210, Carlsbad, CA 92008.

(2) Includes (a) 214,599 shares of common stock and (b) 2,250,000 shares of common stock that may be acquired pursuant to the exercise of outstanding warrants, without regard to certain beneficial ownership limitations. The shares of common stock set forth in (b) cannot be acquired upon exercise of the warrants to the extent that Altium Growth Fund, LP, Altium Capital Management, LP and Altium Growth GP, LLC would collectively own more than 4.99% of the outstanding shares of common stock of the Company. The percentage set forth in the table gives effect to this beneficial ownership limitation. Altium Capital Management, LP, the investment manager of Altium Growth Fund, LP, has voting and investment power over these securities. Jacob Gottlieb is the managing member of Altium Capital Growth GP, LLC, which is the general partner of Altium Growth Fund, LP. Each of the Altium Growth Fund, LP and Jacob Gottlieb disclaims beneficial ownership over these securities. The principal address of Altium Capital Management, LP is 152 West 57th Street, 20th Floor, New York, NY 10019.

(3) Includes (a) 1,814,375 shares of common stock and (b) 436,854 shares of common stock that may be acquired within 60 days pursuant to the exercise of outstanding warrants held by Yuma Regional Medical Center. The board of directors of Yuma Regional Medical Center, acting by a majority vote, has the authority to direct the vote and/or disposition of any and all shares of common stock and warrants held by Yuma Regional Medical Center. The address of Yuma Regional Medical Center is 2400 South Avenue A, Yuma, Arizona, 85364.

(4) In accordance with the Merger Agreement and effective as of the effective time of the Merger, the board of directors of Seneca (the “Seneca Board”) appointed Thomas Hallam, Ph.D., James R. Neal, Stephanie Diaz, Robert J. Trenschel, D.O. and Don Williams to the Board. Cristina Csimma, PharmD, M.H.P., Mary Ann Gray, Ph.D. and Binxian Wei, each an existing director of Seneca, remained on the Board. Mr. Neal was appointed as the chair of the Board. In accordance with the Merger Agreement and an action of the Seneca Board taken at a meeting duly called and held on April 26, 2021, the Board appointed Thomas Hallam, Ph.D. as the Company’s Chief Executive Officer (principal executive officer), J.D. Finley as the Company’s Chief Financial Officer (principal financial and accounting officer) and Michael Dawson, M.D. as the Company’s Chief Medical Officer, each effective as of the Closing and to serve at the discretion of the Board.

(5) Includes 40,571 shares of common stock underlying stock options which are exercisable as of July 30, 2022.

(6) Includes 17,592 shares of common stock, and 297,815 shares of common stock underlying stock options which are exercisable as of July 30, 2022.

(7) Includes 38,779 shares of common stock underlying stock options which are exercisable as of July 30, 2022.

(8) Includes 38,779 shares of common stock underlying stock options which are exercisable as of July 30, 2022.

(9) Includes 4,042 shares of common stock, and 24,170 shares of common stock underlying stock options which are exercisable as of July 30, 2022.

(10) Includes 2,238 shares of common stock, and 24,170 shares of common stock underlying stock options which are exercisable as of July 30, 2022.

(11) Includes (a) 14,999 shares of common stock, and 40,056 shares of common stock underlying stock options which are exercisable as of July 30, 2022 and (b) the shares described in footnote (3) above. Dr. Trenschel is the President, Chief Executive Officer and member of the board of directors of Yuma Regional Medical Center and shares voting and investment power over the shares held by Yuma Regional Medical Center.

(12) Includes 2,000 shares of common stock, 24,170 shares of common stock underlying stock options which are exercisable as of July 30, 2022.

(13) Consists of (a)(i) 2,312 shares of common stock held by Pensco Trust Co, Custodian FBO J.D. Finley IRA and (ii) 195 shares of common stock that may be acquired pursuant to the exercise of outstanding warrants held by Pensco Trust Co, Custodian FBO J.D. Finley IRA, (b)(i) 38,867 shares of common stock held by FCW Investments LLC and (ii) 1,682 shares of common stock that may be acquired pursuant to the exercise of outstanding warrants held by FCW Investments LLC, (c)(i) 19,584 shares of the common stock, (ii) 339 shares of common stock that may be acquired pursuant to the exercise of outstanding warrants held by Mr. Finley and (iii) 193,784 shares of common stock underlying stock options which are exercisable as of July 30, 2022. The address for Pensco Trust Co, Custodian FBO J.D. Finley IRA is PO Box 173859, Denver, CO 80217. The address for FCW Investments LLC is 19 Cherrymoor Dr, Englewood, CO 80113. Mr. Finley has sole investment and voting power over the shares held by Pensco Trust Co, Custodian FBO J.D. Finley IRA and FCW Investments LLC.

(14) Includes 15,000 shares of common stock, and 44,224 shares of common stock underlying stock options which are exercisable as of July 30, 2022.

(15) Based on information available to the Company as of the Closing. In connection with the Merger, the options held by Dr. Carter, Dr. Kalnik and Mr. Saglio were cancelled immediately prior to the Closing in exchange for cash consideration.

(16) Includes the shares described in footnotes (5)-(14) above.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock, certain provisions of our Amended and Restated Certificate of Incorporation ("Certificate of Incorporation"), Amended and Restated Bylaws ("Bylaws"), Certificate of Designation of Preferences, Rights and Limitations of Series A 4.5% Convertible Preferred Stock ("Certificate of Designation"), and certain provisions of Delaware law are summaries. The following description is not complete and is subject to and qualified in its entirety by our Certificate of Incorporation, Bylaws and Certificate of Designation, which are filed as exhibits to the registration statement of which this prospectus is a part, as well as the relevant provisions of the Delaware General Corporation Law ("DGCL").

As of the date of this prospectus, our authorized capital stock consists of 300,000,000 shares of common stock, par value $0.01 per share, and 7,000,000 shares of preferred stock, par value $0.01 per share.

Common Stock

Fully Paid and Non-Assessable

All outstanding shares of common stock are duly authorized, validly issued, fully paid, and nonassessable. All authorized but unissued shares of our common stock are available for issuance by our Board without any further stockholder action, except as required by the listing standards of the Nasdaq Stock Market.

Voting Rights

Our common stock is entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders, including the election of directors, and does not have cumulative voting rights. Our Bylaws establish a classified Board that is divided into three classes with staggered three-year terms. Only the directors in one class will be subject to election by a plurality of the votes cast at each annual meeting of our stockholders, with the directors in the other classes continuing for the remainder of their respective three-year terms.

Economic Rights

Except as otherwise expressly provided in our Certificate of Incorporation or required by applicable law, all shares of common stock have the same rights and privileges and rank equally, share ratably, and are identical in all respects for all matters, including those described below.

Dividends and Distributions. Subject to preferences that may be applicable to any then outstanding preferred stock, holders of our common stock are entitled to receive ratably those dividends, if any, as may be declared from time to time by the Board out of funds legally available for that purpose.

Liquidation Rights. In the event of our liquidation, dissolution or winding up, the holders of our common stock will be entitled to share ratably in the assets remaining after payment of liabilities, subject to prior distribution rights of preferred stock then outstanding.

Holders of our common stock have no preemptive or conversion rights or other subscription rights and there are no redemption or sinking funds provisions applicable to our common stock. 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 Certificate of Incorporation, our Board has the authority, without further action by our stockholders, to issue up to 7,000,000 shares of preferred stock in one or more series pursuant to a resolution or

resolutions providing for such issue duly adopted by our Board. Our Board is further authorized, subject to limitations prescribed by law, to fix by resolution or resolutions the designations, powers, preferences and rights, and the qualifications, limitations or restrictions thereof, of any wholly unissued series of preferred stock, including without limitation authority to fix by resolution or resolutions the dividend rights, dividend rate, conversion rights, voting rights, rights and terms of redemption (including sinking fund provisions), redemption price or prices, and liquidation preferences of any such series, and the number of shares constituting any such series and the designation thereof, or any of the foregoing.

Our Board may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of our common stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in our control and may adversely affect the market price of the common stock and the voting and other rights of the holders of our common stock.

Series A 4.5% Convertible Preferred Stock

In December 2016, a series of our preferred stock was designated as Series A 4.5% Convertible Preferred Stock consisting of 1,000,000 designated shares (which is subject to increase without the consent of all of the holders of the Series A 4.5% Convertible Preferred Stock in the event such additional shares of Series A 4.5% Convertible Preferred Stock are issued solely to the holders as payment of accrued dividends).

As of March 31, 2022, we had outstanding 200,000 shares of Series A 4.5% Convertible Preferred Stock with a stated value of $12.79 per share held by one holder and which are immediately convertible into an aggregate of 6,479 shares of common stock. The Series A 4.5% Convertible Preferred Stock have no provisions regarding subsequent securities issuances or so called “price protection provisions.” The holders of Series A 4.5% Convertible Preferred Stock shall be entitled to receive dividends in cash or additional shares of Series A 4.5% Convertible Preferred Stock if and when declared by our Board in preference to the payment of any dividends on our common stock. The holders of Series A 4.5% Convertible Preferred Stock shall have no voting rights but shall be entitled to appoint one member to our Board. This right to appoint a member of the Board will terminate when there are less than 200,000 shares of Series A 4.5% Convertible Preferred Stock outstanding. As long as any shares of Series A 4.5% Convertible Preferred Stock are outstanding, we shall not, without the affirmative vote of the holders of a majority of the then outstanding shares of the Series A 4.5% Convertible Preferred Stock, alter or change adversely the powers, preferences or rights given to the Series A 4.5% Convertible Preferred Stock or alter or amend the Certificate of Designation, other than to authorize and issue additional shares of Series A 4.5% Convertible Preferred Stock. In addition, holders of Series A 4.5% Convertible Preferred Stock are subject to beneficial ownership limitations.

Options

As of March 31, 2022, stock options to purchase an aggregate of 796,719 shares of common stock were outstanding under the 2013 Plan. No further awards will be made under the 2013 Plan. As of March 31, 2022, stock options to purchase an aggregate of 1,409,736 shares of common stock were outstanding under the 2021 Plan and (ii) 662,414 shares remained available for future issuance under the 2021 Plan.

As of March 31, 2022, stock options to purchase an aggregate of 250,000 shares of common stock were outstanding under our 2021 Inducement Plan, and (ii) 500,000 shares remained available for future issuance under the 2021 Inducement Plan.

Warrants

As of March 31, 2022, our outstanding warrants consist of warrants to purchase 5,347,517 shares of common stock, each with an exercise price ranging from $1.10 to $694.80 per share and generally expire between five and ten years after the date of issuance.

Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws

Some provisions of Delaware law, our Certificate of Incorporation and our Bylaws contain provisions that 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. 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.

Section 203 of the DGCL

We are subject to Section 203 of the DGCL, which prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years after the date that such stockholder became an interested stockholder, subject to certain exceptions.

Amended and Restated Bylaws

Board Composition and Filling Vacancies. Our Bylaws provide for our Board to be divided into three classes with staggered three-year terms. Only one class of directors is elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms. Because our stockholders do not have cumulative voting rights, the holders of a plurality of the voting power of the shares present in person or represented by proxy at the meeting and entitled to vote on the election of directors, can elect all of the directors standing for election, if they so choose, other than any directors that holders of any preferred stock we have or may issue may be entitled to elect. Our Bylaws also provide that subject to the rights of the holders of any series of preferred stock then outstanding, any director or the entire Board may be removed from office at any time, with or without cause, by the affirmative vote of the holders of at least a majority of the voting power of the issued and outstanding shares of capital stock of the Company then entitled to vote in the election of directors.

Special Meeting of Stockholders. Our Bylaws also provides that a special meeting of stockholders may be called only by our chairperson of the Board, chief executive officer or president, the secretary or any two directors.

Advance Notice Requirements. Our Bylaws also establishes advance notice procedures with respect to certain stockholder proposals to be brought before a stockholder meeting and the nomination of candidates for election as directors.

Amendment to Bylaws. The Board is expressly empowered to adopt, amend or repeal the Bylaws. The stockholders shall also have power to adopt, amend or repeal the Bylaws; provided, however, that, in addition to any vote of the holders of any class or series of stock of the Company required by law or by the Certificate of Incorporation, the affirmative vote of the holders of at least a majority of the voting power of all of the then outstanding shares of capital stock of the Company entitled to vote generally in the election of directors, voting together as a single class, shall be required to adopt, amend or repeal any provision of the Bylaws.

The provisions of Delaware law, our Certificate of Incorporation and our 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.

Choice of Forum

Our Bylaws provide that unless we consent in writing to the selection of an alternative forum, the sole and exclusive forum for (i) any derivative action or proceeding brought on behalf of the Company, (ii) any action asserting a claim of breach of a fiduciary duty owed by any director, officer or other employee of the Company to the Company or the Company's stockholders, (iii) any action asserting a claim arising pursuant to any provision of the DGCL or the Certificate of Incorporation or Bylaws (as either may be amended from time to time), or (iv) any action asserting a claim governed by the internal affairs doctrine shall be the Court of Chancery in the State of Delaware (or, if the Court of Chancery does not have jurisdiction, the federal district court for the District of Delaware). If any action the subject matter of which is within the scope of the preceding sentence is filed in a court other than a court located within the State of Delaware (a "Foreign Action") in the name of any stockholder, such stockholder shall be deemed to have consented to (i) the personal jurisdiction of the state and federal courts located within the State of Delaware in connection with any action brought in any such court to enforce the preceding sentence and (ii) having service of process made upon such stockholder in any such action by service upon such stockholder's counsel in the Foreign Action as agent for such stockholder.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC. We act as the transfer agent and registrar for our Series A 4.5% Convertible Preferred Stock.

Listing on the Nasdaq Capital Market

Our common stock is listed on The Nasdaq Capital Market under the symbol "PALI."

DESCRIPTION OF SECURITIES OFFERED

The selling securityholders are offering 3,865,491 shares of our common stock issuable upon exercise of the May 2022 Warrants.

Common Stock

The material terms and provisions of our common stock and each other class of our securities which qualifies or limits our common stock are described under the caption “Description of Capital Stock” in this prospectus.

PLAN OF DISTRIBUTION

We are registering the shares of common stock issued and issuable upon exercise of the May 2022 Warrants to permit the resale of these shares of common stock by the holders of the May 2022 Warrants from time to time after the date of this prospectus. We will not receive any of the proceeds from the sale by the selling securityholders of the shares of common stock. We will bear all fees and expenses incident to our obligation to register the shares of common stock.

The selling securityholders may sell all or a portion of the shares of common stock beneficially owned by them and offered hereby from time to time directly or through one or more underwriters, broker-dealers or agents. If the shares of common stock are sold through underwriters or broker-dealers, the selling securityholders will be responsible for underwriting discounts or commissions or agent's commissions. The shares of common stock may be sold in one or more transactions at fixed prices, at prevailing market prices at the time of the sale, at varying prices determined at the time of sale, or at negotiated prices. These sales may be effected in transactions, which may involve crosses or block transactions,

- on any national securities exchange or quotation service on which the securities may be listed or quoted at the time of sale;
- in the over-the-counter market;
- in transactions otherwise than on these exchanges or systems or in the over-the-counter market;
- through the writing or settlement of options or other hedging transactions, whether such options are listed on an options exchange or otherwise;
- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales;
- sales pursuant to Rule 144;
- broker-dealers may agree with the selling securityholders to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of sale; and
- any other method permitted pursuant to applicable law.

If the selling securityholders effect such transactions by selling shares of common stock to or through underwriters, broker-dealers or agents, such underwriters, broker-dealers or agents may receive commissions in the form of discounts, concessions or commissions from the selling securityholders or commissions from purchasers of the shares of common stock for whom they may act as agent or to whom they may sell as principal (which discounts, concessions or commissions as to particular underwriters, broker-dealers or agents may be in excess of those customary in the types of transactions involved). In connection with sales of the shares of common stock or otherwise, the selling securityholders may enter into hedging transactions with broker-dealers, which may in turn engage in short sales of the shares of common stock in the course of hedging in positions they assume. The selling securityholders may also sell shares of common stock short and deliver shares of common stock covered by this prospectus to close out short positions and to return borrowed shares in connection with such short sales. The selling securityholders may also loan or pledge shares of common stock to broker-dealers that in turn may sell such shares.

The selling securityholders may pledge or grant a security interest in some or all of the May 2022 Warrant or shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock from time to time pursuant to this prospectus or any amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act of 1933, as amended, amending, if necessary, the list of selling securityholders to include the pledgee, transferee or other successors in interest as selling securityholders under this prospectus. The selling securityholders also may transfer and donate the shares of common stock in other circumstances in which case the transferees, donees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

The selling securityholders and any broker-dealer participating in the distribution of the shares of common stock may be deemed to be "underwriters" within the meaning of the Securities Act, and any commission paid, or any discounts or concessions allowed to, any such broker-dealer may be deemed to be underwriting commissions or discounts under the Securities Act. At the time a particular offering of the shares of common stock is made, a prospectus supplement, if required, will be distributed which will set forth the aggregate amount of shares of common stock being offered and the terms of the offering, including the name or names of any broker-dealers or agents, any discounts, commissions and other terms constituting compensation from the selling securityholders and any discounts, commissions or concessions allowed or reallowed or paid to broker-dealers.

Under the securities laws of some states, the shares of common stock may be sold in such states only through registered or licensed brokers or dealers. In addition, in some states the shares of common stock may not be sold unless such shares have been registered or qualified for sale in such state or an exemption from registration or qualification is available and is complied with.

There can be no assurance that any selling securityholder will sell any or all of the shares of common stock registered pursuant to the registration statement, of which this prospectus forms a part.

The selling securityholders and any other person participating in such distribution will be subject to applicable provisions of the Securities Exchange Act of 1934, as amended, and the rules and regulations thereunder, including, without limitation, Regulation M of the Exchange Act, which may limit the timing of purchases and sales of any of the shares of common stock by the selling securityholders and any other participating person. Regulation M may also restrict the ability of any person engaged in the distribution of the shares of common stock to engage in market-making activities with respect to the shares of common stock. All of the foregoing may affect the marketability of the shares of common stock and the ability of any person or entity to engage in market-making activities with respect to the shares of common stock.

We will pay all expenses of the registration of the shares of common stock pursuant to the registration rights agreement, estimated to be $70,000 in total, including, without limitation, Securities and Exchange Commission filing fees and expenses of compliance with state securities or "blue sky" laws; provided, however, that a selling securityholder will pay all underwriting discounts and selling commissions, if any. We will indemnify the selling securityholders against liabilities, including some liabilities under the Securities Act, in accordance with the registration rights provisions of the Securities Purchase Agreement, or the selling securityholders will be entitled to contribution.

Once sold under the registration statement, of which this prospectus forms a part, the shares of common stock will be freely tradable in the hands of persons other than our affiliates.

EXPERTS

The consolidated financial statements of Palisade Bio, Inc. as of December 31, 2021 and 2020 and for the years then ended incorporated by reference in this Prospectus and in the Registration Statement have been so incorporated in reliance on the report of BDO USA, LLP, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting. The report on the consolidated financial statements contains an explanatory paragraph regarding the Company's ability to continue as a going concern.

LEGAL MATTERS

Certain legal matters, including the validity of the shares of common stock offered pursuant to the registration statement of which this prospectus forms a part, will be passed upon for us by Cooley LLP, San Diego, California.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of the registration statement on Form S-1 we filed with the SEC under the Securities Act and does not contain all the information set forth or incorporated by reference in the registration statement. Whenever a reference is made in this prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference into this prospectus for a copy of such contract, agreement or other document. Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at www.sec.gov. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, including any amendments to those reports, and other information that we file with or furnish to the SEC pursuant to Section 13(a) or 15(d) of the Exchange Act can also be accessed free of charge on the Investor section of our website. These filings will be available as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Our website address is www. palisadebio.com. Information contained on or accessible through our website is not a part of this prospectus and is not incorporated by reference herein, and the inclusion of our website address in this prospectus is an inactive textual reference only.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" the information we file with it, which means that we can disclose important information to you by referring to those documents. The information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede this information.

We incorporate by reference the following documents we filed with the SEC pursuant to Section 13 of the Exchange Act and any future filings we will make with the SEC under Sections 13(a), 13(c), 14, or 15(d) of the Exchange Act after the date of this prospectus until the termination of the offering of the shares covered by this prospectus (other than information furnished under Item 2.02 or Item 7.01 of Form 8-K):

- our Annual Report on Form 10-K for the year ended December 31, 2021, filed with the SEC on March 17, 2022, including the information that is incorporated by reference therein upon the filing of our Definitive Proxy Statement on Schedule 14A to be filed with the SEC;
- our Quarterly Report on Form 10-Q for the quarter ended March 31, 2022, filed with the SEC on May 13, 2022;

- our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 21, 2022 (other than the portions thereof which are furnished and not filed);
- our Current Reports on Form 8-K filed on February 1, 2022, February 24, 2022 (with respect to Item 5.02), April 20, 2022, May 6, 2022 and May 6, 2022 (both Current Reports on Form 8-K filed on May 6, 2022 are incorporated by reference), May 20, 2022 and June 10, 2022; and
- the description of our common stock which is registered under Section 12 of the Exchange Act, in our registration statement on Form 8-A filed with the SEC on July 1, 2015, including any amendments or reports filed for the purpose of updating such description, including Exhibit 4.2 to our Annual Report on Form 10-K for the year ended December 31, 2021, filed with the SEC on March 17, 2022.

You may access Annual Report on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, Proxy Statement, and amendments, if any, to those documents filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act with the SEC free of charge at the SEC's website (www.sec.gov) or our website (www.palisadebio.com) as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The reference to our website does not constitute incorporation by reference of the information contained in our website. We do not consider information contained on, or that can be accessed through, our website to be part of this prospectus or the related registration statement.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, without charge upon written or oral request, a copy of any or all of the information that is incorporated by reference into this prospectus but not delivered with the prospectus, including exhibits which are specifically incorporated by reference into such documents. You should direct any requests for documents to Palisade Bio, Inc. at 5800 Armada Drive, Suite 210, Carlsbad, CA 92008, Attn: Secretary, or by telephone (858) 704-4900.