Filed pursuant to Rule 424(b)(4)
Registration No. 333-255583

1,883,487 Shares

Common Stock

Offered by the Selling Stockholders

This prospectus relates to the proposed resale or other disposition by the selling stockholders identified in this prospectus, or the selling stockholders, of 1,883,487 shares of our common stock, or the Shares. The Shares being offered were issued and sold in a private placement in connection with our acquisition of ZebiAI Therapeutics, Inc., which closed on April 22, 2021. We are not selling any Shares under this prospectus and will not receive any of the proceeds from the sale or other disposition of Shares by the selling stockholders.

The selling stockholders may sell the Shares on any national securities exchange or quotation service on which the securities may be listed or quoted at the time of sale, on the over-the-counter market, in one or more transactions otherwise than on these exchanges or systems, such as privately negotiated transactions, or using a combination of these methods, and 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. See the disclosure under the heading “Plan of Distribution” elsewhere in this prospectus for more information about how the selling stockholders may sell or otherwise dispose of their Shares hereunder.

The selling stockholders may sell any, all or none of the Shares offered by this prospectus and we do not know when or in what amount the selling stockholders may sell their Shares hereunder following the effective date of the registration statement of which this prospectus forms a part.

You should carefully read this prospectus, as well as any documents incorporated by reference, before you invest in any of the securities being offered.

Our common stock is listed on the Nasdaq Global Market under the symbol “RLAY.” The last reported sale price of our common stock on the Nasdaq Global Market on April 23, 2021 was $33.34.

We are an “emerging growth company” as that term is used in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and, as such, we have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings.

Investing in our common stock involves risks. See “Risk Factors” on page 10.

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 May 6, 2021.

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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 rely only on the information contained in or incorporated by reference in this prospectus or in any free writing prospectus we file with the Securities and Exchange Commission, or the SEC. Neither we nor the selling stockholders have authorized anyone to provide you with information other than that contained in or incorporated by reference in this prospectus or any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. The selling stockholders are offering to sell, and seeking offers to buy, common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date on the front cover page of this prospectus, or other earlier date stated in this prospectus, regardless of the time of delivery of this prospectus or of any sale of our common stock.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus, including our consolidated financial statements and the related notes incorporated by reference in this prospectus. You should also consider, among other things, the matters described under "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations," in our Annual Report on Form 10-K for the year ended December 31, 2020, in each case incorporated by reference in this prospectus. Unless the context otherwise requires, the terms "Relay," "Relay Therapeutics," "the Company," "we," "us," and "our" in this prospectus refer to Relay Therapeutics, Inc. and its subsidiary.

Overview

We are a clinical-stage precision medicines company transforming the drug discovery process with the goal of bringing life-changing therapies to patients. We are among the first of a new breed of biotech created at the intersection of disparate disciplines. Our Dynamo™ platform integrates an array of leading-edge computational and experimental approaches to effectively drug protein targets that have previously been intractable. Our initial focus is on enhancing small molecule therapeutic discovery in targeted oncology and genetic disease.

We are advancing a pipeline of medicines to address targets in precision oncology, including our lead product candidates, RLY-1971 and RLY-4008, as well as our PI3Kα mutant selective program, or the RLY-PI3K1047 program. We initiated a Phase 1 clinical trial for RLY-1971, our inhibitor of Src homology region 2 domain-containing phosphatase-2, or SHP2, in patients with advanced solid tumors in the first quarter of 2020. In December 2020, we entered into a global collaboration and license agreement, or the Genentech Agreement, with Genentech, Inc., a member of the Roche Group, or Genentech, for the development and commercialization of RLY-1971. We initiated a first-in-human clinical trial of RLY-4008, our inhibitor of fibroblast growth factor receptor 2, or FGFR2, enriched for patients with advanced solid tumors having oncogenic FGFR2 alterations in the third quarter of 2020. We anticipate the RLY-PI3K1047 program, our program for molecules targeting cancer-associated mutant variants of phosphoinostide 3-kinase alpha, or PI3Kα, to be in Investigational New Drug, or IND, enabling studies in 2021. While our initial focus is on precision oncology, we believe our Dynamo platform may also be broadly applied to other areas of precision medicine, such as genetic disease. In addition to the three product candidates described above, we have five discovery stage programs across precision oncology and genetic disease. We are focused on using the novel insights derived from our approach to transform the lives of patients suffering from debilitating and life-threatening diseases through the discovery, development and commercialization of our therapies.

Precision medicine emerged as an approach for disease treatment as the understanding of the link between genetic alterations, protein dysfunction and diseases evolved. Precision medicine aims to specifically and potently drug genetically validated target proteins (i.e., genetic variants potentially implicated in biology of disease). However, some target proteins thus far have been intractable using conventional drug discovery tools, such as structure-based drug design, or SBDD. While SBDD is well-suited to solving some drug discovery problems such as orthosteric site kinase inhibitors, its reliance on static images of protein fragments limits its ability to gain accurate insights into the dynamic behavior of proteins in their natural state, which in turn limits its ability to discover medicines with exquisite specificity. Our approach pivots the understanding of protein targets from the industry-standard, static view, to a novel paradigm based on fundamental insights into protein motion. We then apply these novel insights into protein motion to drug discovery and design, which we term Motion Based Drug Design™, or MBDD.

The confluence of three forces — the proliferation of readily available genomic data, the evolution of experimental techniques, and advancements in computational power and speed — led to the founding of Relay Therapeutics. We believe we are uniquely situated in our ability to consolidate these advances and, when combined with our world-class team of both experimental and computational experts, integrate these solutions into MBDD to create medicines that will make a transformative difference for patients.

Key Drug Discovery Steps of Our Dynamo Platform

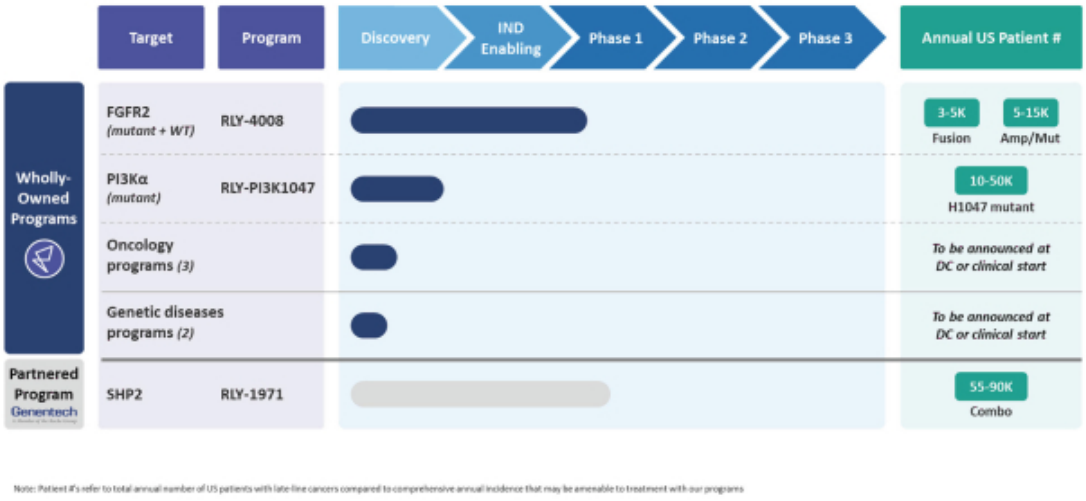
Our Dynamo platform puts protein motion at the center of drug discovery and design, integrating a broad and tailored array of leading-edge experimental and computational approaches, including deploying the Anton 2 supercomputer, which was custom-built by D. E. Shaw Research, LLC, or D. E. Shaw Research, to perform molecular dynamic simulations of proteins. We have access to the Anton 2 supercomputer, which we believe to be the only resource of computational power of its caliber, through our collaboration with D. E. Shaw Research, LLC, or D.E. Shaw Research, pursuant to which we collaborate with D. E. Shaw Research to rapidly develop various protein models. Our use of the Anton 2 supercomputer and our collaboration with D.E. Shaw Research is subject to the terms and conditions of the Amended and Restated Collaboration and License Agreement with D. E. Shaw Research, or the DESRES Agreement. We deploy the power of the platform in three key phases of MBDD discovery:

- **Target Modulation Hypothesis.** By generating fundamental insights into the structure and conformational dynamics of full-length proteins, our Dynamo platform enables us to model a target protein's function, to develop unique motion-based hypotheses for how to modulate the protein's behavior, and to identify potential novel binding sites for new therapeutic agents.
- **Hit Finding and Lead Generation.** The integration of our computational and experimental platforms affords a deeper functional understanding of our targets and enables the design of physiologically relevant activity-based, ligand-centric and computational screens. These highly differentiated screens have the ability to yield a larger number of chemical series and potential therapies to proceed into lead optimization than conventional experimental techniques alone.
- **Lead Optimization.** Our Dynamo platform uses advanced computational models in tight integration with our medicinal chemistry, structural biology, enzymology and biophysics capabilities to predict, design and experimentally evaluate compounds that will achieve the most desirable characteristics, including potency, selectivity, bioavailability, and drug-like properties. We believe our approach enables us to converge on optimized compounds with much greater efficiency than conventional approaches, which are typically highly iterative over an extended timeframe.

Our Dynamo platform has the potential to address a diverse range of disease targets, including those proteins that have not been addressed selectively and potently with existing therapies. While we have initially focused our Dynamo platform on small molecule drug discovery in the area of precision oncology, we believe it could be readily deployed across broader precision and genetic medicine areas as well as other therapeutic modalities, such as protein therapeutics and antibody design.

Our Programs

We have deployed our technology platform to build a pipeline of product candidates to address targets in precision oncology, where there is clear evidence linking target proteins to disease and where molecular diagnostics can unambiguously identify relevant patients for treatment. We believe this approach will increase the likelihood of successfully translating a specific pharmacological mechanism into clinical benefit. The targets associated with all of our current programs are Category 1 Targets under our DESRES Agreement.



Note: Patient #'s refer to total annual number of US patients with late-line cancers compared to comprehensive annual incidence that may be amenable to treatment with our programs

RLY-4008

RLY-4008 is designed to be an oral, small molecule, selective inhibitor of fibroblast growth factor receptor 2, or FGFR2, a receptor tyrosine kinase that is frequently altered in certain cancers. FGFR2 is one of four members of the FGFR family, a set of closely related proteins with highly similar protein sequences and properties. RLY-4008 demonstrates FGFR2-dependent killing in cancer cell lines, while showing minimal inhibition of other targets, including other members of the FGFR family. We initiated a first-in-human clinical trial of RLY-4008 enriched for patients with advanced solid tumors having oncogenic FGFR2 alterations in September 2020. We anticipate giving an initial clinical update on this trial in the second half of 2021. We believe FGFR2-mediated cancers affect approximately 8,000 late-line patients annually in the United States. In the future, if RLY-4008 advances to earlier lines of treatment, we believe it could potentially address approximately 20,000 patients annually in the United States.

Mutant-PI3Kα Inhibitor Program

RLY-PI3K1047 is a lead compound in our franchise of programs targeting cancer-associated mutant variants of phosphoinositide 3-kinase alpha, or PI3Kα. RLY-PI3K1047 is a small molecule inhibitor of PI3Kα that we designed specifically to target PI3Kα H1047X mutants via a previously undescribed allosteric mechanism. Oral dosing of RLY-PI3K1047 resulted in tumor growth inhibition in mouse xenograft models of PI3Kα H1047R mutant carcinoma. We expect to begin IND-enabling studies for a differentiated PI3Kα H1047X mutant-selective inhibitor in 2021. We believe PI3Kα H1047X mutant cancers affect approximately 10,000 late-line patients annually in the United States. In the future, if RLY-PI3K1047 advances to earlier lines of treatment, we believe it could potentially be suitable for use in approximately 50,000 patients annually in the United States.

Two additional mutations of interest for our PI3Kα franchise are E542X and E545X. We estimate there are approximately 15,000 late-line and 60,000 total patients annually in the United States who might benefit from a PI3Kα targeted inhibitor that targets the mutations at E542 and E545.

RLY-1971

RLY-1971 binds and stabilizes SHP2 in its inactive conformation. SHP2 promotes cancer cell survival and growth through the RAS pathway by transducing signals downstream from receptor tyrosine kinases, or RTKs.

Additionally, activating SHP2 mutations causes enhanced signaling in the absence of ligand stimulation and has been identified as an oncogenic driver in a range of tumors. As a critical signaling node and regulator, SHP2 drives cancer cell proliferation and plays a key role in the way cancer cells develop resistance to targeted therapies. We believe that inhibition of SHP2 could be effective as a monotherapy in cancers with specific alterations and could block a common path that cancer cells exploit to resist other antitumor agents, thus overcoming or delaying the onset of resistance to those therapies.

We are currently evaluating the safety and tolerability of RLY-1971 in a Phase 1 dose escalation study in patients with advanced or metastatic solid tumors. In December 2020, we entered into the Genentech Agreement, a global collaboration and license agreement with Genentech for the development and commercialization of RLY-1971. Future development for RLY-1971 will be governed by a joint development team between us and Genentech. We expect a combination trial of RLY-1971 and Genentech's $KRAS^{G12C}$ inhibitor, GDC-6036, to be initiated in 2021. Given the range of cancers that are related to SHP2 dependence, we believe RLY-1971 could serve as a backbone for compelling combination therapies. We believe SHP2-mediated cancers affect approximately 55,000 late-line patients annually in combination therapy settings in the United States. In the future, if RLY-1971 advances to earlier lines of treatment, we believe it could potentially have applicability to approximately 90,000 patients annually in the United States.

Under the terms of the Genentech Agreement, we have received $75 million in an upfront payment and are eligible to receive $25 million in near-term payments; and, if we do not opt into a U.S. profit/cost share, up to $695 million in additional development, commercialization and sales-based milestones for RLY-1971; and tiered royalties on annual global net sales (on a country-by-country basis), in the low-to-mid-teens, subject to reduction in certain circumstances. Additionally, we are eligible to receive additional royalties in the event of regulatory approval of RLY-1971 and Genentech's compound, GDC-6036, that directly binds to and inhibits $KRAS^{G12C}$, in combination. We have the right to opt-in to a 50/50 U.S. profit/cost share and if we do opt into the U.S. profit/cost share, we are eligible to receive up to $410 million in additional commercialization and sales-based milestones for RLY-1971 outside of the U.S. and tiered royalties on annual net sales outside of the U.S. (on a country-by-country basis), in the low-to-mid-teens, subject to reduction in certain circumstances. We also retain the right to develop RLY-1971 in combination with our FGFR2 and PI3Kα programs. If we elect to opt-out of the profit/cost share, then the milestone and royalty payment obligations will revert to the financial terms that would be applicable if we had not opted into the profit/cost share, with certain adjustments.

Discovery Programs

We are deploying our Dynamo platform and MBDD approach to advance multiple discovery-stage precision oncology programs. As with our lead programs, these programs leverage insights into protein conformational dynamics to address high-value, genetically validated oncogenes that previously have been intractable to conventional drug-discovery approaches. Our Dynamo platform's protein visualization capabilities can be applied to multiple therapeutic areas beyond precision oncology. To further diversify our pipeline, we are leveraging our Dynamo platform to address validated targets in monogenic diseases, where genetic alterations lead to disease-causing defects in protein motion.

Our Strategy

Our mission is to leverage unique insights into protein motion to transform the lives of patients suffering from debilitating and life-threatening diseases through the discovery, development and commercialization of small molecule therapies. We believe that, by placing protein motion at the heart of MBDD discovery, our unique Dynamo platform has the potential to address previously intractable precision medicine targets. To accomplish this, we intend to continue building a team that shares our commitment to patients, to continue to enhance our

platform, and to rapidly advance our precision medicine pipeline of product candidates. The key elements of our strategy are to:

Rapidly advance our lead precision oncology programs, RLY-4008 and RLY-PI3K1047, through clinical development and regulatory approval. We believe our lead precision oncology programs have the potential to treat a wide variety of cancers either as monotherapy or in combination regimens. In September 2020, we initiated a first-in-human clinical trial of RLY-4008. In 2021, we expect to have early safety and efficacy data for RLY-4008 and to be in IND-enabling studies for our RLY-PI3K1047 program. For our wholly-owned programs, we plan to conduct our clinical studies in genetically-defined patient populations. To potentially mitigate development risks, we will leverage learnings from recently approved precision oncology drugs to inform the clinical and regulatory pathways for our lead oncology programs. If we are successful in achieving clinically meaningful anti-tumor activity across solid tumor types, we plan to meet with regulatory authorities to discuss expedited regulatory approval strategies.

Continue to enhance our unique drug-discovery platform. Our Dynamo platform uniquely integrates a broad range of leading-edge experimental and computational technologies and tools, providing us with fundamental insights into the conformational dynamics of target proteins. We are committed to continuously integrating new computational and experimental tools, technologies and capabilities to enhance the power of our Dynamo platform.

Harness the insights and data generated from our platform against intractable targets in oncology and other therapeutic areas. We have built a drug discovery process that leverages our collaboration with D. E. Shaw Research and their access to the Anton 2 supercomputer and our proprietary computational workflows. We are committed to deploying our Dynamo platform against targets in additional therapeutic areas beyond oncology. Our next focus, outside of oncology, is on rare genetic diseases where protein targets are genetically validated, where defects in protein conformational dynamics are abundant, and where we believe our approach is well-suited to identify therapies with the potential to have transformative impact for patients.

Selectively enter into strategic collaborations to maximize the value of our platform and pipeline. We have initiated a Phase 1 clinical trial for RLY-1971 in patients with advanced solid tumors in the first quarter of 2020 and have continued to advance the clinical development of RLY-1971. In December 2020, we entered into the Genentech Agreement, a global collaboration and license agreement with Genentech for the development and commercialization of RLY-1971. Other than our SHP2 program, we retain full development and commercialization rights to our current pipeline of precision medicine programs. We intend to build a fully integrated biopharmaceutical company and independently pursue the development and commercialization of our key product candidates. Given our potential to generate novel product candidates addressing a wide variety of therapeutic indications, we may enter into additional strategic partnerships around certain targets, product candidates, disease areas or geographies. If we believe these collaborations could accelerate the development and commercialization of our product candidates, and allow us to realize additional potential in our product candidates and our platform.

Recent Developments

Acquisition of ZebiAI Therapeutics

On April 15, 2021, we entered into an Agreement and Plan of Merger, or the Merger Agreement, to acquire ZebiAI Therapeutics, Inc., or ZebiAI. Pursuant to the terms of the Merger Agreement, at the closing of the acquisition on April 22, 2021, we paid the former stockholders, optionholders and warrant holders of ZebiAI, or the ZebiAI Holders, upfront consideration consisting of approximately $20.0 million in cash and 1,883,487 shares of our common stock, excluding customary purchase price adjustments. Under the terms of the Merger

Agreement, we agreed to register for resale the shares of our common stock that we issued as payment for the equity portion of the upfront consideration. The 1,883,487 shares of our common stock we issued as payment for the equity portion of the upfront consideration are the shares being registered for resale hereby.

In addition, (i) the ZebiAI Holders will be eligible to receive up to an additional $85.0 million in milestone payments upon the achievement of certain platform or program-related milestones, payable in our common stock valued using the volume-weighted average price over the five trading day period ending on the last trading day prior to the date on which the applicable milestone is achieved and (ii) we will pay the ZebiAI Holders 10% of the payments received by us within three years of the closing date of the Merger Agreement from partnering, collaboration or other agreements related to ZebiAI's platform, up to an aggregate maximum amount of $100.0 million, payable in cash.

With the closing of the Merger Agreement, we continue to expect that our current cash, cash equivalents and investments will enable us to fund our operating expenses and capital expenditure requirements into 2024.

Risks Associated with Our Business

Our ability to implement our business strategy is subject to numerous risks that you should be aware of before making an investment decision. These risks are described more fully in the section entitled "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2020 incorporated by reference in this prospectus. These risks include, among others:

- We have never successfully completed any clinical trials, and we may be unable to do so for any product candidates we develop. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.
- If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.
- Positive results from early preclinical studies of our product candidates are not necessarily predictive of the results of later preclinical studies and any future clinical trials of our product candidates. If we cannot replicate the positive results from our earlier preclinical studies of our product candidates in our later preclinical studies and future clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize our product candidates.
- Our current or future clinical trials may reveal significant adverse events not seen in our preclinical or nonclinical studies and may result in a safety profile that could inhibit regulatory approval or market acceptance of any of our product candidates.
- Although we intend to explore other therapeutic opportunities, in addition to the product candidates that we are currently developing, we may fail to identify viable new product candidates for clinical development for a number of reasons. If we fail to identify additional potential product candidates, our business could be materially harmed.
- The incidence and prevalence for target patient populations of our product candidates have not been established with precision. If the market opportunities for our product candidates are smaller than we estimate or if any approval that we obtain is based on a narrower definition of the patient population, our revenue and ability to achieve profitability will be adversely affected, possibly materially.
- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.
- If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our product candidates, we will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired.

- Under the DESRES Agreement, we collaborate with D. E. Shaw Research to rapidly develop various protein models, a process that depends on D. E. Shaw Research's use of their proprietary supercomputer, Anton 2. A termination of the DESRES Agreement could have a material adverse effect on our business, financial condition, results of operations, and prospects.
- We rely on third parties to conduct our ongoing clinical trials of RLY-1971 and RLY-4008 and expect to rely on third parties to conduct future clinical trials, as well as investigator-sponsored clinical trials of our product candidates. If these third parties do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.
- We may enter into collaborations with third parties for the research, development, manufacture and commercialization of one or more of our programs or product candidates. If these collaborations are not successful, our business could be adversely affected.
- We are a biopharmaceutical company with a limited operating history. We have incurred significant operating losses since our inception and anticipate that we will incur continued losses for the foreseeable future. We have no products approved for commercial sale and have not generated any revenue from product sales.
- We will need to raise substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate some of our product development programs or commercialization efforts.
- A pandemic, epidemic, or outbreak of an infectious disease, such as COVID-19, may materially and adversely affect our business and our financial results and could cause a disruption to the development of our product candidates.
- If we are unable to adequately protect our proprietary technology or obtain and maintain patent protection for our technology and products or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be impaired.
- Even if we receive regulatory approval for any of our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to post-market study requirements, marketing and labeling restrictions, and even recall or market withdrawal if unanticipated safety issues are discovered following approval. In addition, we may be subject to penalties or other enforcement action if we fail to comply with regulatory requirements.
- We are an "emerging growth company" as defined in the JOBS Act and a "smaller reporting company" as defined in the Securities Exchange Act of 1934, as amended, or the Exchange Act, and may avail ourselves of reduced disclosure requirements applicable to emerging growth companies and smaller reporting companies, which could make our common stock less attractive to investors and adversely affect the market price of our common stock.

Corporate history

We were incorporated under the laws of the State of Delaware on May 4, 2015 under the name "Allostery, Inc." Our principal corporate office is located at 399 Binney Street, 2nd Floor, Cambridge, MA 02139, and our telephone number is (617) 370-8837. Our website address is www.relaytx.com. We do not incorporate the information on or accessible through our website into this prospectus, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus.

We own various U.S. federal trademark applications and unregistered trademarks, including our company name. All other trademarks or trade names referred to in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus are referred to without the symbols ® and ™, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

Implications of Being an Emerging Growth Company and a Smaller Reporting Company

We qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, as amended. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- being permitted to only two years of audited financial statements in addition to any required unaudited interim financial statements with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- reduced disclosure about our executive compensation arrangements;
- not being required to hold advisory votes on executive compensation or to obtain stockholder approval of any golden parachute arrangements not previously approved; and
- an exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting.

We may take advantage of these exemptions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company on the date that is the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more; (ii) the last day of our fiscal year following the fifth anniversary of the date of our initial public offering in July 2020, or IPO; (iii) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years; or (iv) the last day of the fiscal year in which we are deemed to be a large accelerated filer under the rules of the SEC, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th. We may choose to take advantage of some but not all of these exemptions. We have taken advantage of reduced reporting requirements in this prospectus. Accordingly, the information contained herein may be different from the information you receive from other public companies in which you hold stock. We are in the process of evaluating the benefits of relying on other exemptions and reduced reporting requirements under the JOBS Act. Subject to certain conditions, as an emerging growth company, we may rely on certain of these exemptions, including without limitation, providing an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act.

We are also a "smaller reporting company" as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies until the fiscal year following the determination that our voting and non-voting common stock held by non-affiliates is more than $250 million measured on the last business day of our second fiscal quarter, or our annual revenues are more than $100 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is more than $700 million measured on the last business day of our second fiscal quarter.

THE OFFERING

Common stock to be offered by the selling stockholders hereunder	1,883,487 shares of common stock
Use of proceeds	We will not receive any proceeds from the sale of our shares of common stock by the selling stockholders. See “Use of Proceeds.”
Plan of Distribution	The selling stockholders 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. Registration of the common stock covered by this prospectus does not mean, however, that such shares necessarily will be offered or sold. See “Plan of Distribution.”
Risk factors	This investment involves a high degree of risk. You should read the description of risks set forth under “Risk Factors” beginning on page 10 of this prospectus and the documents incorporated by reference herein for a discussion of factors to consider before deciding to purchase our securities.
Nasdaq Global Market Symbol	“RLAY”

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before investing in our common stock, you should consider carefully the risks and other information described in, or incorporated by reference into, this prospectus, including the risks and uncertainties discussed in the “Risk Factors” sections in this prospectus, our Annual Report on Form 10-K for the year ended December 31, 2020 and any subsequent Quarterly Reports on Form 10-Q, which are incorporated by reference herein in their entirety. Additional risks and uncertainties not presently known to us, or that we currently see as immaterial, may also harm our business. If any of the risks incorporated by reference herein occur, our business, financial condition and operating results could be harmed, the trading price of our common stock could decline and you could lose part or all of your investment.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the documents that we incorporate by reference, contains express or implied forward-looking statements that are based on our management's belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to future events or our future operational or financial performance, and involve known and unknown risks, uncertainties, and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements in this prospectus include, but are not limited to, statements about:

- the initiation, timing, progress, results, and cost of our research and development programs and our current and future preclinical and clinical studies, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available, and our research and development programs;
- our ability to identify research priorities and apply a risk-mitigated strategy to efficiently discover and develop product candidates, including by applying learnings from one program to other programs and from one modality to our other modalities;
- our ability and the potential to successfully manufacture our drug substances, delivery vehicles, and product candidates for preclinical use, for clinical trials and on a larger scale for commercial use, if approved;
- the ability and willingness of our third-party strategic collaborators to continue research and development activities relating to our development candidates and product candidates;
- our ability to obtain funding for our operations necessary to complete further development and commercialization of our product candidates;
- our ability to obtain and maintain regulatory approval of our product candidates;
- our ability to commercialize our products, if approved;
- the pricing and reimbursement of our product candidates, if approved;
- the implementation of our business model, and strategic plans for our business, product candidates, and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;
- estimates of our future expenses, revenues, capital requirements, and our needs for additional financing;
- the potential benefits of strategic collaboration agreements, our ability to enter into strategic collaborations or arrangements, and our ability to attract collaborators with development, regulatory and commercialization expertise;
- future agreements with third parties in connection with the commercialization of product candidates and any other approved product;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- our financial performance;
- the rate and degree of market acceptance of our product candidates;
- regulatory developments in the United States and foreign countries;

- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- our ability to produce our products or product candidates with advantages in turnaround times or manufacturing cost;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel;
- the impact of laws and regulations;
- developments relating to our competitors and our industry;
- the effect of the COVID-19 pandemic, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations, including but not limited to our preclinical studies and future clinical trials; and
- other risks and uncertainties, including those listed under the caption “Risk Factors” in our Annual Report on Form 10-K for the year ended December 31, 2020.

In some cases, you can identify forward-looking statements by terminology such as “may,” “should,” “expects,” “intends,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “potential,” “continue,” or the negative of these terms or other comparable terminology. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties and other factors, which are, in some cases, beyond our control and which could materially affect results. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under the section titled “Risk Factors” in our Annual Report on Form 10-K for the year ended December 31, 2020 and elsewhere in or incorporated by reference in this prospectus. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future performance. You should read this prospectus and the documents that we incorporate by reference in this prospectus and have filed with the Securities and Exchange Commission as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements.

The forward-looking statements in this prospectus represent our views as of the date of this prospectus. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should therefore not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this prospectus.

This prospectus also contains or incorporates by reference estimates, projections and other information concerning our industry, our business and the markets for our product candidates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market, and other data from our own internal estimates and research as well as from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. While we are not aware of any misstatements regarding any third-party information presented in or incorporated by reference in this prospectus, their estimates, in particular as they relate to projections, involve numerous assumptions, are subject to risks and uncertainties and are subject to change based on various factors.

USE OF PROCEEDS

The selling stockholders will make offers and sales pursuant to this prospectus. We will not receive any of the proceeds of such offerings. The selling stockholders will pay any underwriting discounts and commissions and expenses they incur for brokerage, accounting, tax or legal services, or any other expenses they incur in disposing of their shares. We will incur certain expenses in connection with the registration with the SEC of the shares of our common stock to be sold by the selling stockholders.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to fund the growth and development of our business. We do not intend to pay cash dividends to our stockholders in the foreseeable future. Any future determination to declare dividends will be made at the discretion of our board of directors and will depend on our financial condition, operating results, capital requirements, general business conditions, and other factors that our board of directors may deem relevant. Investors should not purchase our common stock with the expectation of receiving cash dividends.

SELLING STOCKHOLDERS

This prospectus relates to the resale of shares of our common stock held by the selling stockholders listed in the table below. The selling stockholders acquired these shares from us in a private offering pursuant to an exemption from registration afforded by Section 4(a)(2) of the Securities Act and/or Regulation D promulgated thereunder as partial consideration for our acquisition of ZebiAI Therapeutics, Inc. on April 22, 2021. Under the Merger Agreement and related Registration Rights Agreement, we agreed to file a registration statement or prospectus with the SEC for the purposes of registering for resale the shares of our common stock issued to the selling stockholders and to maintain the effectiveness of the registration statement until such time as all shares of common stock covered by the registration statement have been sold or may be sold under Rule 144 without manner of sale restrictions or volume limitations, subject to certain exceptions.

The following table sets forth the names of the selling stockholders, the number of shares of common stock owned beneficially by the selling stockholders as of April 22, 2021, and the number of shares of our common stock that may be offered by the selling stockholders pursuant to this prospectus. The table and the other information contained under the captions “Selling Stockholders” and “Plan of Distribution” has been prepared based upon information furnished to us by or on behalf of the selling stockholders. The following table sets forth, as to each of the selling stockholders, the number of shares beneficially owned, the number of shares being sold, the number of shares beneficially owned upon completion of the offering and the percentage beneficial ownership upon completion of the offering.

Beneficial ownership is determined in accordance with the rules of the SEC and includes voting or investment power with respect to the securities. The percentage of shares beneficially owned prior to and after the offering is based on 90,650,933 shares of our common stock outstanding as of April 22, 2021. Except as otherwise indicated, each of the selling stockholders has sole voting and investment power with respect to all shares of capital stock held by it.

Based upon information provided by the selling stockholders, unless otherwise set forth in the footnotes to the table below, none of the selling stockholders nor any of their affiliates, officers, directors or principal equity holders has had any positions or office or has had any material relationship with us within the past three years.

Name and Address of Selling Stockholder(1)	Shares Beneficially Owned Before Offering		Shares Offered by This Prospectus	Shares Beneficially Owned After Offering(3)	
	Number	Percentage		Number	Percentage
Patrick Walters(2)	345,367	*	3,338	342,029	*
Richard Wagner	501,057	*	501,057	0	*
Google LLC 1600 Amphitheatre Parkway Mountain View, CA 94043	231,971	*	231,971	0	*
X-Chem, Inc. 100 Beaver St., Suite 100 Waltham, MA 02453	204,135	*	204,135	0	*
Brant C. Binder	91,861	*	91,861	0	*
BCB Irrevocable 2015 Trust	75,159	*	75,159	0	*
BINDER TRUST, dated 15 July 2003	250,529	*	250,529	0	*
Anterra F&A Ventures II Coöperatief U.A. Herengracht 454, 1017 CA Amsterdam, The Netherlands	417,547	*	417,547	0	*
All other selling stockholders as a group holding less than 1% of outstanding shares in the aggregate (39 individuals)	107,890	*	107,890	0	*
Total	**2,225,516**	**2.46%**	**1,883,487**	**342,029**	*****

* Represents beneficial ownership of less than one percent (1%).
(1) Unless otherwise noted, the address of the selling stockholder is c/o Relay Therapeutics, Inc. 399 Binney St., 2nd Floor, Cambridge, MA 02139.
(2) Patrick Walters is our Senior Vice President, Computation.
(3) We do not know when or in what amounts a selling stockholder may offer shares for sale. The selling stockholders might not sell any or all of the shares offered by this prospectus. Because the selling stockholders may offer all or some of the shares pursuant to this offering, and because there are currently no agreements, arrangements or understandings with respect to the sale of any of the shares, we cannot estimate the number of the shares that will be held by the selling stockholders after completion of the offering. However, for purposes of this table, we have assumed that, after completion of the offering, none of the shares covered by this prospectus will be held by the selling stockholders.

Under the Merger Agreement and Registration Rights Agreement, we will indemnify each selling stockholder against any damages to which a selling stockholder may become subject by reason of any material misstatement or omission in this registration statement, except to the extent that such damages arise out of or are based upon information furnished to us in writing by such selling stockholder for use in this registration statement. Each selling stockholder will indemnify us and certain related persons against any damages to which such indemnified parties may become subject by reason of any material misstatement or omission in this registration statement or any violation or alleged violation of the Securities Act, the Exchange Act, or any state securities law, or any rule promulgated under any of the foregoing, in each case to the extent based upon any action or omission made in reliance upon information provided in writing by such selling stockholder for use in this registration statement.

DESCRIPTION OF CAPITAL STOCK

The following descriptions are summaries of the material terms of our fourth amended and restated certificate of incorporation and amended and restated bylaws. We refer in this section to our fourth amended and restated certificate of incorporation as our certificate of incorporation, and we refer to our amended and restated bylaws as our bylaws.

General

Our authorized capital stock consists of One Hundred Fifty Million (150,000,000) shares of common stock, par value $0.001 per share and Ten Million (10,000,000) shares of undesignated preferred stock, par value $0.001 per share.

Common stock

The holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of our common stock do not have any cumulative voting rights. Holders of our common stock are entitled to receive ratably any dividends declared by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. Our common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions. In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock.

Our common stock is listed on the Nasdaq Global Market under the trading symbol “RLAY.”

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

Preferred stock

Our board of directors has the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company or other corporate action. No shares of preferred stock are outstanding, and we have no present plan to issue any shares of preferred stock.

Registration rights

Certain holders of our common stock are entitled to rights with respect to the registration of these securities under the Securities Act. These rights are provided under the terms of a second amended and restated investors’ rights agreement between us and the holders of our preferred stock. The second amended and restated investors’ rights agreement includes demand registration rights, short-form registration rights, and piggyback registration rights. All fees, costs and expenses of underwritten registrations under this agreement will be borne by us and all selling expenses, including underwriting discounts and selling commissions, will be borne by the holders of the shares being registered.

Demand registration rights

Certain holders of our common stock, are entitled to demand registration rights. Under the terms of the second amended and restated investors' rights agreement, we will be required, upon the written request of a majority of holders of the registrable securities then outstanding that would result in an aggregate offering price of at least $7.5 million, to file a registration statement and to use commercially reasonable efforts to effect the registration of all or a portion of these shares for public resale.

Short-Form registration rights

Pursuant to our second amended and restated investors' rights agreement, if we are eligible to file a registration statement on Form S-3, upon the written request of at least 10% in interest of these holders to sell registrable securities at an aggregate price of at least $1.0 million, we will be required to use commercially reasonable efforts to effect a registration of such shares. We are required to effect only two registrations in any twelve-month period pursuant to this provision of the second amended and restated investors' rights agreement. The right to have such shares registered on Form S-3 is further subject to other specified conditions and limitations.

Piggyback registration rights

Pursuant to our second amended and restated investors' rights agreement, if we register any of our securities either for our own account or for the account of other security holders, the holders of these shares are entitled to include their shares in the registration. Subject to certain exceptions contained in the second amended and restated investors' rights agreement, we and the underwriters may limit the number of shares included in the underwritten offering to the number of shares which we and the underwriters determine in our sole discretion will not jeopardize the success of the offering.

Indemnification

Our second amended and restated investors' rights agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

Expiration of registration rights

The demand registration rights and short form registration rights granted under our second amended and restated investors' rights agreement will terminate on the fifth anniversary of the completion of our initial public offering.

Anti-Takeover effects of our certificate of incorporation and bylaws and Delaware law

Our certificate of incorporation and bylaws include a number of provisions that may have the effect of delaying, deferring or preventing another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board composition and filling vacancies

Our certificate of incorporation provides for the division of our board of directors into three classes serving staggered three-year terms, with one class being elected each year. Our certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of two-thirds or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only

be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum. The classification of directors, together with the limitations on removal of directors and treatment of vacancies, has the effect of making it more difficult for stockholders to change the composition of our board of directors.

No written consent of stockholders

Our certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our bylaws or removal of directors by our stockholders without holding a meeting of stockholders.

Meetings of stockholders

Our certificate of incorporation and bylaws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our bylaws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance notice requirements

Our bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days nor more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. Our bylaws specify the requirements as to form and content of all stockholders' notices. These requirements may preclude stockholders from bringing matters before the stockholders at an annual or special meeting.

Amendment to certificate of incorporation and bylaws

Any amendment of our certificate of incorporation must first be approved by a majority of our board of directors, and if required by law or our certificate of incorporation, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, board composition, and limitation of liability must be approved by not less than two-thirds of the outstanding shares entitled to vote on the amendment, and not less than two-thirds of the outstanding shares of each class entitled to vote thereon as a class. Our bylaws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the bylaws; and may also be amended by the affirmative vote of a majority of the outstanding shares entitled to vote on the amendment, voting together as a single class, except that the amendment of the provisions relating to notice of stockholder business and nominations and special meetings must be approved by not less than two-thirds of the outstanding shares entitled to vote on the amendment, and not less than two-thirds of the outstanding shares of each class entitled to vote.

Undesignated preferred stock

Our certificate of incorporation provides for 10,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due

exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Choice of forum

Our bylaws provide that, unless we consent in writing to the selection of an alternative form, the Court of Chancery of the State of Delaware (or, if the Chancery Court does not have jurisdiction, the federal district court for the District of Delaware or other state courts of the State of Delaware) will be the sole and exclusive forum for: (1) any derivative action or proceeding brought on our behalf; (2) any action asserting a claim of breach of a fiduciary duty or other wrongdoing by any of our directors, officers, employees or agents to us or our stockholders; (3) any action asserting a claim against us arising pursuant to any provision of the General Corporation Law of the State of Delaware or our certificate of incorporation or bylaws; (4) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws; or (5) any action asserting a claim governed by the internal affairs doctrine. Our bylaws also provide that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock will be deemed to have notice of and to have consented to this choice of forum provision. It is possible that a court of law could rule that the choice of forum provision contained in our restated certificate of incorporation is inapplicable or unenforceable if it is challenged in a proceeding or otherwise.

In addition, our bylaws provide that, unless we consent in writing to the selection of an alternative forum, the United States District Court in the District of Massachusetts will be the exclusive forum for any private action asserting violations by us or any of our directors or officers of the Securities Act or the Exchange Act, or the rules and regulations promulgated thereunder, and of all suits in equity and actions at law brought to enforce any liability or duty created by those statutes or the rules and regulations under such statutes. If any action the subject matter of which is within the scope of the preceding sentence is filed in a court other than the United States District of Massachusetts, the plaintiff or plaintiffs shall be deemed by this provision of the bylaws (i) to have consented to removal of the action by us to the United States District Court in the District of Massachusetts, in the case of an action filed in a state court, and (ii) to have consented to transfer of the action to the United States District Court in the District of Massachusetts.

Section 203 of the Delaware general corporation law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a “business combination” with an “interested stockholder” for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the

voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or

- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation; subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; and
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Nasdaq Global Market listing

Our common stock is listed on the Nasdaq Global Market under the trading symbol “RLAY.”

Transfer agent and registrar

The transfer agent and registrar for our common stock will be Computershare Trust Company, N.A. The transfer agent and registrar’s address is 250 Royall Street, Canton, Massachusetts 02021, and its telephone number is (800) 962-4284.

CERTAIN MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS OF COMMON STOCK

The following discussion is a summary of certain material U.S. federal income tax considerations applicable to non-U.S. holders (as defined below) with respect to their ownership and disposition of shares of our common stock issued pursuant to this offering. For purposes of this discussion, a non-U.S. holder means a beneficial owner of our common stock that is, for U.S. federal income tax purposes:

- a non-resident alien individual;
- a foreign corporation or any other foreign organization taxable as a corporation for U.S. federal income tax purposes; or
- a foreign estate or trust, the income of which is not subject to U.S. federal income tax on a net income basis.

This discussion does not address the tax treatment of partnerships or other entities or arrangements that are treated as pass-through entities for U.S. federal income tax purposes or persons that hold their shares of our common stock through partnerships or such other pass-through entities. The tax treatment of a partner in a partnership or other entity or arrangement that is treated as a pass-through entity for U.S. federal income tax purposes generally will depend upon the status of the partner and the activities of the partnership. A partner in a partnership or an investor in any other pass-through entity that will hold our common stock should consult his, her or its tax advisor regarding the tax consequences of acquiring, holding and disposing of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based on current provisions of the Internal Revenue Code of 1986, as amended, or the Code, existing and proposed U.S. Treasury regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus and, all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any such change or differing interpretation could alter the tax consequences to non-U.S. holders described in this prospectus. There can be no assurance that the Internal Revenue Service, or the IRS, will not challenge one or more of the tax consequences described herein. We assume in this discussion that a non-U.S. holder holds shares of our common stock as a capital asset, which is generally property held for investment.

This discussion does not address all aspects of U.S. federal income taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances, including the alternative minimum tax, the Medicare tax on net investment income or the rules relating to "qualified small business stock." Any U.S. federal tax other than the income tax (including, for example, the estate tax), and it does not nor does it address any aspects of U.S. state, local or non-U.S. taxes. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

1. insurance companies;
2. tax-exempt or governmental organizations;
3. financial institutions;
4. brokers or dealers in securities;
5. regulated investment companies;
6. pension plans;
7. "controlled foreign corporations," "passive foreign investment companies," and corporations that accumulate earnings to avoid U.S. federal income tax;
8. "qualified foreign pension funds," or entities wholly owned by one or more "qualified foreign pension funds";

9. partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and partners and investors therein);
10. persons that have a functional currency other than the U.S. dollar;
11. persons deemed to sell our common stock under the constructive sale provisions of the Code;
12. persons that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment;
13. persons that hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation;
14. investors in pass-through entities (or entities that are treated as disregarded entities for U.S. federal income tax purposes); and
15. U.S. expatriates.

This discussion is for general information only and is not tax advice. Accordingly, all prospective non-U.S. holders of our common stock should consult their tax advisors with respect to the U.S. federal, state, local, estate and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock.

Distributions on our common stock

As described in the "Dividend Policy" section above, we do not intend to pay any cash dividends on our common stock to our stockholders stock in the foreseeable future. Distributions, if any, on shares of our common stock generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such holder's tax basis in the shares of common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in "Gain on sale or other taxable disposition of our shares of common stock." Any such distributions will also be subject to the discussion below under the section titled "Withholding and information reporting requirements—FATCA."

Subject to the discussion in the following two paragraphs in this section, dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate specified by an applicable income tax treaty between the United States and such holder's country of residence.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional "branch profits tax" at a 30% rate or such lower rate as specified by an applicable income tax treaty between the United States and such holder's country of residence.

A non-U.S. holder of shares of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or a successor form) to the applicable withholding agent and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty. A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim with the IRS.

Gain on sale, exchange or other taxable disposition of shares of our common stock

Subject to the discussion below under "Withholding and information reporting requirements—FATCA," a non-U.S. holder generally will not be subject to any U.S. federal income tax on any gain realized upon such holder's sale, exchange or other taxable disposition of shares of our common stock unless:

1. the gain is effectively connected with the non-U.S. holder's conduct of a U.S. trade or business and, if an applicable income tax treaty so provides, is attributable to a permanent establishment or a fixed-base maintained by such non-U.S. holder in the United States, in which case the non-U.S. holder generally will be taxed on a net income basis at the graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in "Distributions on our common stock" also may apply;

2. the non-U.S. holder is a nonresident alien individual who is present in the United States for a period or periods aggregating 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence) on the net gain derived from the disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder, if any (even though the individual is not considered a resident of the United States), provided that the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses; or

3. we are, or have been, at any time during the five-year period preceding such sale or other taxable disposition (or the non-U.S. holder's holding period, if shorter) a "U.S. real property holding corporation," unless our common stock is regularly traded on an established securities market, within the meaning of the relevant provisions of the Code, and the non-U.S. holder holds no more than 5% of our outstanding common stock, directly or indirectly, actually or constructively, during the shorter of the five-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. Generally, a corporation is a "U.S. real property holding corporation" only if the fair market value of its "U.S. real property interests" (as defined in the Code and applicable U.S. Treasury regulations) equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are, or have been, a "U.S. real property holding corporation" for U.S. federal income tax purposes, or that we are likely to become one in the future. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above.

Backup withholding and information reporting

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on shares of our common stock paid to such holder and the tax withheld, if any, with respect to such distributions.

Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a United States person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on shares of our common stock. Generally, a non-U.S. holder will comply with such procedures if it provides a properly executed IRS Form W-8BEN or W-8BEN-E (or other applicable IRS Form W-8), or otherwise meets documentary evidence requirements for establishing that it is a non-U.S. holder, or otherwise establishes an exemption. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above in "Distributions on our common stock," generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding will generally apply to the proceeds of a disposition of shares of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or non-U.S., unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment

of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their tax advisors regarding the application of the information reporting and backup withholding rules to them. Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement. Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is filed with the IRS in a timely manner.

Withholding and information reporting requirements—FATCA

The Foreign Account Tax Compliance Act, or FATCA, generally imposes a U.S. federal withholding tax at a rate of 30% on payments of dividends on our common stock paid to a foreign entity unless (i) if the foreign entity is a "foreign financial institution," such foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a "foreign financial institution," such foreign entity identifies certain of its U.S. investors, if any, or (iii) the foreign entity is otherwise exempt under FATCA. Such withholding may also apply to payments of gross proceeds of sales or other dispositions of shares of our common stock, although under proposed U.S. Treasury regulations (the preamble to which specifies that taxpayers, including withholding agents, are generally permitted to rely on them pending finalization), no withholding will apply to payments of gross proceeds. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of this withholding tax. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this paragraph. Non-U.S. holders should consult their tax advisors regarding the possible implications of this legislation on their investment in our common stock and the entities through which they hold our shares of common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30% withholding tax under FATCA.

PLAN OF DISTRIBUTION

The selling stockholders and any of their pledgees, donees, assignees and successors-in-interest may, from time to time, sell any or all of their shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions or by gift. These sales may be made at fixed or negotiated prices. The selling stockholders may use any one or more of the following methods when selling or otherwise transferring shares:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which a 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;
- sales to a broker-dealer as principal and the resale by the broker-dealer of the shares for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions, including gifts;
- covering short sales made after the date of this prospectus;
- an over-the-counter distribution in accordance with the rules of the Nasdaq Global Market;
- in options transactions;
- a combination of any such methods of sale; and
- any other method of sale permitted pursuant to applicable law.

The selling stockholders may also sell shares under Rule 144 of the Securities Act, if available, rather than pursuant to this prospectus. The selling stockholders shall have the sole and absolute discretion not to accept any purchase offer or make any sale of shares if it deems the purchase price to be unsatisfactory at any particular time.

The selling stockholders and their pledgees, donees, transferees or other successors in interest, may also sell the shares directly to market makers acting as principals and/or broker-dealers acting as agents for themselves or their customers. Such broker-dealers may receive compensation in the form of discounts, concessions or commissions from the selling stockholder and/or the purchasers of shares for whom such broker-dealers may act as agents or to whom they sell as principal or both, which compensation as to a particular broker-dealer might be in excess of customary commissions. Market makers and block purchasers purchasing the shares will do so for their own account and at their own risk. It is possible that the selling stockholder will attempt to sell shares of common stock in block transactions to market makers or other purchasers at a price per share which may be below the then existing market price. We cannot assure that all or any of the shares offered in this prospectus will be issued to, or sold by, the selling stockholders. The selling stockholders and any brokers, dealers or agents, upon effecting the sale of any of the shares offered in this prospectus, may be deemed to be an “underwriters” as that term is defined under the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act.

We are required to pay all fees and expenses incident to the registration of the shares, but excluding brokerage commissions.

The selling stockholders, alternatively, may sell all or any part of the shares offered in this prospectus through an underwriter. The selling stockholders have not entered into any agreement with a prospective underwriter and there is no assurance that any such agreement will be entered into. If the selling stockholders propose to sell shares to an underwriter, we will be required to amend this prospectus to reflect the terms of the underwritten offering.

The selling stockholders may pledge shares to brokers under the margin provisions of customer agreements. If the selling stockholders defaults on a margin loan, the broker may, from time to time, offer and sell the pledged

shares. The selling stockholders and any other persons participating in the sale or distribution of the shares will be subject to applicable provisions of the Securities Exchange Act of 1934, as amended, and the rules and regulations under such Act, including, without limitation, Regulation M. These provisions may restrict certain activities of, and limit the timing of purchases and sales of any of the shares by, the selling stockholder or any other such person. In the event a selling stockholder is deemed an affiliated purchaser or distribution participant within the meaning of Regulation M, then the selling stockholder will not be permitted to engage in short sales of common stock. Furthermore, under Regulation M, persons engaged in a distribution of securities are prohibited from simultaneously engaging in market making and certain other activities with respect to such securities for a specified period of time prior to the commencement of such distributions, subject to specified exceptions or exemptions. In addition, if a short sale is deemed to be a stabilizing activity, then the selling stockholder will not be permitted to engage in a short sale of our common stock. All of these limitations may affect the marketability of the shares.

We have agreed to indemnify the selling stockholders against certain liabilities, including certain liabilities under the Securities Act.

We have agreed with the selling stockholders to keep the Registration Statement of which this prospectus constitutes a part effective until such time as all of the shares covered by this prospectus have been disposed of pursuant to and in accordance with the Registration Statement or may be sold under Rule 144 without manner of sale restrictions or volume limitations, subject to certain exceptions.

If a selling stockholder notifies us that it has a material arrangement with a broker-dealer for the resale of the common stock, then we would be required to amend the registration statement of which this prospectus is a part, and file a prospectus supplement to describe the agreement between the selling stockholder and the broker-dealer.

LEGAL MATTERS

The validity of the shares of common stock offered by this prospectus will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2020, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement that we have filed with the SEC. Certain information in the registration statement has been omitted from this prospectus in accordance with the rules of the SEC. For further information, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. Statements contained in this prospectus or incorporated by reference concerning the contents of any contract or any other document are not necessarily complete. If a contract or document has been filed or incorporated by reference as an exhibit to the registration statement, we refer you to the copy of the contract or document that has been filed. Each statement in this prospectus or incorporated by reference relating to a contract or document filed as an exhibit is qualified in all respects by the filed exhibit. The SEC maintains a web site (http://www.sec.gov) that contains reports, proxy and information statements and other information regarding issuers like us that file electronically with the SEC.

We are subject to the reporting and information requirements of the Exchange Act and, as a result, we file periodic reports, proxy statements and other information with the SEC. These periodic reports, proxy statements and other information will be available for inspection on the web site of the SEC referred to above.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information and reports we file with it, which means that we can disclose important information to you by referring you to these 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 the information already incorporated by reference. We are incorporating by reference the documents listed below, which we have already filed with the SEC, and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, including all filings made after the date of the filing of this registration statement and prior to the effectiveness of this registration statement, except as to any portion of any future report or document that is not deemed filed under such provisions, after the date of this prospectus and prior to the termination of this offering:

- Annual Report on Form 10-K for the year ended December 31, 2020, as filed with the SEC on March 25, 2021;
- The information specifically incorporated by reference in our Annual Report on Form 10-K for the year ended December 31, 2020, from our Definitive Proxy Statement on Schedule 14(a), as filed with the SEC on April 7, 2021;
- Current Report on Form 8-K (other than information furnished rather than filed) filed with the SEC on April 16, 2021; and

- The description of our common stock contained in our Registration Statement on Form 8-A (File No. 001-39385) as filed with the SEC on July 13, 2020, including any amendments or reports filed for the purpose of updating this description, including Exhibit 4.3 to our Annual Report on Form 10-K for the year ended December 31, 2020, as filed with the SEC on March 25, 2021.

Notwithstanding the foregoing, unless specifically stated to the contrary, information that we furnish (and that is not deemed "filed" with the SEC) under Items 2.02 and 7.01 of any Current Report on Form 8-K, including the related exhibits under Item 9.01, is not incorporated by reference into this prospectus or the registration statement of which this prospectus is a part.

We will furnish without charge to you, on written or oral request, a copy of any or all of the documents incorporated by reference in this prospectus, including exhibits to these documents. You should direct any requests for documents to Relay Therapeutics, Inc., 399 Binney Street, 2nd Floor, Cambridge, Massachusetts 02139, telephone: (617) 370-8837.

You also may access these filings on our website at *www.relaytx.com.* We do not incorporate the information on our website into this prospectus or any supplement to this prospectus and you should not consider any information on, or that can be accessed through, our website as part of this prospectus or any supplement to this prospectus (other than those filings with the SEC that we specifically incorporate by reference into this prospectus or any supplement to this prospectus).

Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus will be deemed modified, superseded or replaced for purposes of this prospectus to the extent that a statement contained in this prospectus modifies, supersedes or replaces such statement.

1,883,487
Common Stock
Offered by the Selling Stockholders

PROSPECTUS

May 6, 2021