CALCULATION OF REGISTRATION FEE

| | | Proposed | Proposed | |
|---|---------------|----------------|------------------|---------------------|
| | Amount | Maximum | Maximum | |
| Title of Each Class of | to be | Offering Price | Aggregate | Amount of |
| Securities to be Registered | Registered(1) | Per Share | Offering Price | Registration Fee(2) |
| Common Stock, par value \$0.001 per share | 15,188,679 | \$26.50 | \$402,499,993.50 | \$37,311.75 |

- (1) Includes 1,981,132 shares of common stock, par value \$0.001 per share, which may be purchased by the underwriters upon exercise of the underwriters' option to purchase additional shares.
- (2) Calculated in accordance with Rule 456(b) and 457(r) of the Securities Act of 1933, as amended.

PROSPECTUS SUPPLEMENT (to Prospectus dated August 12, 2021)

13,207,547 Shares



Common Stock

We are offering 13,207,547 shares of our common stock.

Our common stock is listed on The Nasdaq Global Market under the symbol "RLAY". The last sale price as reported on The Nasdaq Global Market on October 12, 2021, was \$27.77 per share.

We are an "emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012 and, as such, have elected to comply with certain reduced public company disclosure and reporting requirements.

Investing in our common stock involves risks. See "Risk Factors" on page S-8 of this prospectus supplement.

Neither the Securities and Exchange Commission, any state securities commission nor any other regulatory body has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

| | Per S | Per Share | | Total | |
|----------------------------------|-------|-----------|----|-------------|--|
| Initial price to public | \$ | 26.50 | \$ | 349,999,996 | |
| Underwriting discount(1) | \$ | 1.325 | \$ | 17,500,000 | |
| Proceeds, before expenses, to us | \$ | 25.175 | \$ | 332,499,996 | |

⁽¹⁾ We refer you to "Underwriting" beginning on page S-24 of this prospectus supplement for additional information regarding underwriting compensation.

We have granted the underwriters a 30-day option to purchase up to an additional 1,981,132 shares of our common stock from us at the public offering price, less the underwriting discounts and commissions.

The underwriters expect to deliver the shares on or about October 15, 2021.

| Goldman Sachs & Co. LLC | J.P. Morgan | Cowen | Guggenheim Securities |
|----------------------------|----------------------------|---------------------|-----------------------|
| | Prospectus Supplement date | ed October 12, 2021 | |

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document contains two parts. The first part is this prospectus supplement, which describes the specific terms of this offering of common stock and also supplements and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part is the accompanying prospectus dated August 12, 2021, included in our registration statement on Form S-3ASR (File No. 333-258768), along with the documents incorporated by reference, which provides more general information, some of which may not apply to this offering. Generally, when we refer to this prospectus, we are referring to both parts of this document combined.

To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or in any document incorporated by reference that was filed with the Securities and Exchange Commission, or the SEC, before the date of this prospectus supplement, on the other hand, you should rely on the information contained in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in the accompanying prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

This prospectus supplement and the accompanying prospectus are part of a "shelf" registration statement that we filed with the SEC. Under the shelf registration process, we may offer from time to time various securities, of which this offering of shares of our common stock is a part. Such registration statement also includes exhibits that provide more detail on the matters discussed in this prospectus supplement and the accompanying prospectus. You should read this prospectus supplement, the accompanying prospectus, including the information incorporated by reference, the exhibits filed with the SEC, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision.

We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. For investors outside the United States, we have not done anything that would permit this offering or possession or distribution of this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we have authorized for use in connection with this offering in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering outside the United States.

You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus, along with the information contained in any free writing prospectus that we have authorized for use in connection with this offering. We have not, and the underwriters have not, authorized anyone to provide you with different or additional information. If anyone provides you with different or inconsistent information, you should not rely on it. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering is accurate only as of the respective dates of those documents, unless we indicate otherwise. Our business, financial condition, results of operations and prospects may have changed since those dates.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in this prospectus supplement or the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties and covenants were accurate only as of the date when made; therefore, such representations, warranties and covenants should not be relied on as accurate representations of the current state of our affairs.

Unless otherwise indicated or the context suggests otherwise, references in this prospectus supplement and the accompanying prospectus to "Relay Therapeutics," "Relay", the "company," "we," "us," and "our," and similar designations refer to Relay Therapeutics, Inc. and, where appropriate, our consolidated subsidiaries. When we refer to "you," we mean the potential purchasers of our common stock in this offering.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our common stock. For a more complete understanding of our company and this offering, we encourage you to read and consider carefully the more detailed information in this prospectus supplement and the accompanying prospectus, including our financial statements and related notes and the other information incorporated by reference into this prospectus supplement and the accompanying prospectus, and the information included in any free writing prospectus that we have authorized for use in connection with this offering, including the information referred to under the heading "Risk Factors" in this prospectus supplement beginning on page S-8 and in the documents incorporated herein by reference.

Company Overview

We are a clinical-stage precision medicines company transforming the drug discovery process by combining leading-edge computational and experimental technologies 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 designed to drug protein targets that have previously been intractable or inadequately addressed. Our initial focus is on enhancing small molecule therapeutic discovery in targeted oncology and genetic disease indications.

We are advancing a pipeline of medicines to address targets in precision oncology, including our lead product candidates, RLY-4008, RLY-2608 and RLY-1971. In the third quarter of 2020, we initiated a first-in-human clinical trial for RLY-4008, our inhibitor of fibroblast growth factor receptor 2, or FGFR2, focusing on patients with advanced solid tumors having oncogenic FGFR2 alterations. In October 2021, we announced initial clinical data from this trial, which is discussed below in "Recent Developments—RLY-4008." In 2021, we initiated Investigational New Drug, or IND, enabling studies for RLY-2608, our inhibitor of cancer-associated mutant variants H1047X, E542X, and E545X of phosphoinostide 3-kinase alpha, or PI3Kα. RLY-2608 is the lead program of multiple preclinical efforts to discover and develop mutant selective inhibitors of PI3Kα. In October 2021, we also announced preclinical data for RLY-2608, which is discussed below in "Recent Developments—RLY-2608." 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 with Genentech, Inc., a member of the Roche Group, or Genentech, for the development and commercialization of RLY-1971. In July 2021, Genentech initiated the cohort of RLY-1971 in combination with GDC-6036, its KRASG12C inhibitor, in a Phase 1b trial. 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 both precision oncology and genetic disease indications. 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 an

Precision medicine emerged as an approach for disease treatment as the understanding of the links 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 or inadequately addressed 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 DesignTM, 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.

Recent Developments

RLY-2608

On October 7, 2021, at the AACR-NCI-EORTC Molecular Targets Conference, we announced preclinical data for RLY-2608, our inhibitor of cancer-associated mutant PI3K α variants H1047X, E542X and E545X. RLY-2608 is the lead program of our multiple preclinical efforts to discover and develop mutant selective inhibitors of PI3K α .

The data show that in preclinical models, RLY-2608 preferentially binds mutant PI3K α at a novel allosteric site discovered by our Dynamo platform. In biochemical and cellular assays, RLY-2608 inhibited the three major classes of PI3K α oncogenic mutations (H1047X, E542X and E545X) while sparing wild-type PI3K α . The data further suggest that RLY-2608 is also highly selective against other PI3K family members and exquisitely selective across the kinome. The data suggest that projected clinically relevant doses of RLY-2608 achieved tumor regression in PIK3CA mutant in vivo xenograft models representing H1047R and E545K mutations with significantly reduced impact on glucose metabolism compared to non-mutant selective active site inhibitors. In higher species, dosing of RLY-2608 resulted in exposures exceeding 90% inhibition of mutant PI3K α in cells without resulting in elevated glucose levels or histopathological changes associated with dysregulation of glucose metabolism that are seen with non-mutant selective inhibitors.

We believe these results support advancement of RLY-2608 into clinical development as a differentiated mechanism of mutant PI3K α inhibition. In addition, we believe that due to the preclinical selectivity that RLY-2608 has shown against the PI3K α mutant variants H1047X, E542X, and E545X, RLY-2608 could potentially address over 100,000 patients per year in the United States. We expect to initiate a first-in-human clinical trial of RLY-2608 in the first half of 2022, subject to submission and acceptance of an IND by the U.S. Food and Drug Administration, or FDA.

RLY-4008

On October 8, 2021, at the AACR-NCI-EORTC Molecular Targets Conference, we also announced interim clinical data from our ongoing dose-escalation first-in-human clinical trial of RLY-4008, or the RLY-4008-101 Trial, in patients with FGFR2 altered tumors regardless of prior FGFR inhibitor treatment. The clinical trial is designed to determine the maximum tolerated dose and recommended Phase 2 dosing as well as assess initial safety and tolerability. Approximately 125 patients are planned to enroll in the trial, which is being conducted in two parts, a dose escalation (part 1) and a dose expansion (part 2).

We believe the interim clinical data suggest robust inhibition of FGFR2 in the first 49 subjects that was not shown to be limited by off-target toxicities, including hyperphosphatemia and diarrhea. The initial toxicity data suggest that certain dose levels administered can achieve >85% continuous inhibition of FGFR2. At those levels, acute toxicities that would limit dose intensity have generally not been observed to date. The interim clinical data included results from FGFR2-altered solid tumors, with approximately 80% of all patients treated having achieved reductions in tumor size as of September 9, 2021, or the Data Cut-off Date. In pan-FGFR inhibitor treatment-naïve cholangiocarcinoma patients, RLY-4008 demonstrated tumor shrinkage in all six pan-FGFR treatment-naïve FGFR2 fusion positive cholangiocarcinoma patients, with three achieving confirmed partial responses. Three of these six patients remain on study and a fourth patient went on to surgery with curative intent. We plan to select a once daily recommended Phase 2 dose and initiate expansion cohorts of the RLY-4008-101 Trial prior to the end of 2021.

As of the Data Cut-off Date, 48 of the 49 patients enrolled had a primary FGFR2 alteration, of which a majority were FGFR2 fusion cholangiocarcinoma. Most patients had high disease burden with multiple prior treatments including pan-FGFR inhibitors, and several had FGFR2 resistance mutations detected by circulating tumor DNA, or ctDNA, at baseline. Patients were treated at nine different once daily, or QD, or twice daily, or BID, dose levels, ranging from 20 mg QD to 70 mg QD and 20 mg BID to 100 mg BID. As of the Data Cut-off Date, duration of treatment ranged from 4 to 45 weeks.

Initial Safety Analysis

The interim clinical data of the RLY-4008-101 Trial indicate that RLY-4008 has generally been well tolerated in the 49 patients treated as of the Data Cut-Off Date. With regard to dosing, the QD dosing schedule has been prioritized due to its preferable tolerability (as only one dose limiting toxicity, or DLT, was observed across all dose levels) and high target coverage (lowest dose of 20 mg exceeded 85% receptor occupancy). Within the BID dosing schedule there were five DLTs observed, and receptor occupancy ranged from 90% to 98% across the BID doses.

Across all QD doses only 16% of patients, all Grade 1 or 2, experienced hyperphosphatemia, a toxicity that has been shown to limit dose intensity for pan-FGFR inhibitors in other studies. These data indicate that RLY-4008 had little or no FGFR1 inhibition at the examined dose levels. Additionally, little or no diarrhea was observed with RLY-4008 treatment suggesting minimal or no FGFR4 inhibition in treated patients to date across dose levels. Together, the interim data suggest that RLY-4008 is a highly selective FGFR2 inhibitor in humans.

Most treatment emergent adverse events were low-grade adverse events and manageable. There have been no Grade 4 or 5 adverse events. Given that retinal toxicity has been observed with FGFR inhibitor treatment, the trial is designed to assess retinopathy and retinal pigment epithelial dystrophy adverse events, which have been observed in seven patients (14%), three of which occurred in the QD dosing regimen. All seven of these events were Grade 1-2, which were self-limiting or resolved upon treatment interruption.

Initial Efficacy Analysis

The interim clinical data of the RLY-4008-101 Trial indicate that RLY-4008 has the potential to provide tumor reduction across a number of FGFR2 alterations and lines of treatment. Key interim data include:

- Promising early activity in FGFR inhibitor naïve cholangiocarcinoma FGFR2 fusion patients, with confirmed RECISTv1.1 partial responses observed in 3 out of 6 patients with deep tumor regressions (-56% to -83%) and 3 out of 6 patients continuing on treatment and a fourth who went on to surgery with curative intent.
- Radiographic tumor shrinkage and complete clearance of ctDNA in 70% of patients with acquired resistance mutations (N=10), including
 molecular brake (N550) and gatekeeper (V565) mutations, suggesting the potential for RLY-4008 to treat or prevent on-target acquired
 resistance.
- Early signs of activity observed outside of FGFR2 fusion positive cholangiocarcinoma, including tumor reduction in 6 out of 8 evaluable patients with activating mutations (1 confirmed partial response, or PR, 1 unconfirmed PR, and 4 stable disease, or SD, (based on RECISTv1.1 criteria)) and 3 out of 3 patients with amplifications (all SD).
- Approximately 80% of all patients treated achieved radiographic tumor regressions; this was observed across all dose levels, tumor types and FGFR2 alterations, and in patients with prior FGFR inhibitor treatment.

Consistent with the preclinical profile of RLY-4008, these early clinical data support our belief that RLY-4008 has broad therapeutic potential across FGFR2 alterations and tumor types.

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 supplement, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus supplement.

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 supplement are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus supplement are referred to

without the ® and TM symbols, 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 will become a large accelerated filer for the fiscal year ending December 31, 2022, and as such we will lose emerging growth status on December 31, 2021. We have taken advantage of reduced reporting requirements in this prospectus supplement. Accordingly, the information contained herein and in the accompanying prospectus may be different from the information you receive from other public companies in which you hold stock.

We are also a "smaller reporting company" as defined in the Securities Exchange Act of 1934, as amended, or the Exchange Act. 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. We will lose smaller reporting company status on December 31, 2021.

THE OFFERING

Common stock offered by us 13,207,547 shares (or 15,188,679 shares if the underwriters exercise their option to purchase additional

shares in full).

Common stock to be outstanding immediately after this offering

105,760,192 shares (or 107,741,324 shares if the underwriters exercise their option to purchase additional

shares in full).

Option to purchase additional

shares

We have granted a 30-day option to the underwriters to purchase up to 1,981,132 additional shares of common stock from us at the public offering price, less underwriting discounts and commissions on the same

terms as set forth in this prospectus supplement.

Use of proceeds We estimate that the net proceeds to us from this offering, after deducting the underwriting discounts and

> commissions and estimated offering expenses payable by us, will be approximately \$332.0 million, or approximately \$381.9 million if the underwriters exercise their option to purchase additional shares from us in full. We intend to use the net proceeds from this offering to fund research and clinical development of current or additional pipeline candidates, working capital, capital expenditures and other general corporate

purposes. See "Use of Proceeds" on page S-16 of this prospectus supplement.

Risk factors Investing in our common stock involves a high degree of risk, See "Risk Factors" beginning on page S-8 of

> this prospectus supplement, as well as "Risk Factors" in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, for a discussion of factors you should consider

carefully before deciding to purchase any shares of our common stock.

Nasdaq Global Market symbol **RLAY**

All information in this prospectus supplement related to the number of shares of our common stock to be outstanding immediately after this offering is based on 92,552,645 shares of our common stock outstanding as of June 30, 2021. The number of shares outstanding as of June 30, 2021 as used throughout this prospectus supplement, unless otherwise indicated, excludes:

- 8,906,194 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2021 under our 2020 Stock Option and Incentive Plan, or 2020 Plan, at a weighted-average exercise price of \$13.16 per share;
- 505,393 shares of common stock issuable upon the vesting and settlement of restricted stock units outstanding as of June 30, 2021 under our 2020 Plan:
- 10,653,994 shares of common stock reserved for future issuance as of June 30, 2021 under our 2020 Plan; and
- 1,991,600 shares of common stock reserved for future issuance as of June 30, 2021 under our 2020 Employee Stock Purchase Plan.

Except as otherwise indicated, all information in this prospectus supplement reflects and assumes the following:

- no exercise of outstanding stock options after June 30, 2021; and
- no exercise by the underwriters of their option to purchase additional shares of our common stock.

In addition, the number of shares outstanding immediately after this offering does not include shares of common stock that we may offer and sell in the future pursuant to our sales agreement, or the Sales Agreement, with Cowen

and Company, LLC, as sales agent. After the expiration or waiver of the 90-day lock-up period applicable to us and described under the section of this prospectus supplement entitled "Underwriting," we may offer and sell shares of our common stock having an aggregate offering price of up to \$300.0 million from time to time in "at-the-market" offerings pursuant to the Sales Agreement.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before making an investment decision, you should carefully consider the risks described below and in our most recent Annual Report on Form 10-K and subsequent Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as well as any amendments thereto reflected in subsequent filings with the SEC, each of which are incorporated by reference in this prospectus supplement, and all of the other information in this prospectus supplement, including our financial statements and related notes incorporated by reference herein, and in any free writing prospectus that we have authorized for use in connection with this offering before acquiring any of our common stock. These risks could result in material and adverse impact on our business, financial condition, results of operations and prospects, which could cause the trading price of our common stock to decline, and you could lose part or all of your investment. Additional risks and uncertainties that are not yet identified or that we currently believe to be immaterial may also materially harm our business, financial condition, results of operations and prospects and could result in a complete loss of your investment. The risks discussed below also include forward-looking statements, and our actual results may differ substantially from those discussed in these forward-looking statements. See "Cautionary Statement Regarding Forward-Looking Statements."

Summary of Material Risks Associated with Our Business

- 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 data from preclinical or early clinical studies of our product candidates are not necessarily predictive of the results of later clinical studies and any future clinical trials of our product candidates. If we cannot replicate the positive data from our preclinical or early clinical studies of our product candidates in our future clinical trials, we will 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 or early clinical trial data and may result in a safety profile that would 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 delays occur 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 our Amended and Restated Collaboration and License Agreement, or the DESRES Agreement, with D. E. Shaw Research, LLC, or D. E. Shaw Research, 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 have and may enter into other 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 will 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.

Risks Related to this Offering and Our Common Stock

The trading price of our common stock historically has been volatile, which may affect the price at which you could sell any shares of our common stock.

The market price for our common stock historically has been volatile and could continue to be subject to wide fluctuations in response to various factors. Since shares of our common stock were sold in our IPO in July 2020 at a price of \$20.00 per share, our stock price has fluctuated significantly, ranging from an intraday low of \$25.72 to an intraday high of \$64.37 through October 12, 2021. This volatility may affect the price at which you could resell the common stock. Our stock price is likely to continue to be volatile and subject to significant price and volume fluctuations in response to market and other factors, including the factors described below. The stock market in general and Nasdaq and the market for biopharmaceutical companies in particular, have experienced extreme volatility that has often been unrelated or disproportionate to the operating performance of these companies.

The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- results of clinical trials of our product candidates or those of our competitors;
- regulatory or legal developments in the United States and other countries;
- · developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;

- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- · actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares:
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- · general economic, industry and market conditions; and
- the other factors described in this "Risk Factors" section as well as the "Risk Factors" section in the documents incorporated by reference into
 this prospectus supplement.

In the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

Our executive officers, directors, principal stockholders and their affiliates exercise significant control over our company, which will limit your ability to influence corporate matters and could delay or prevent a change in corporate control.

As of June 30, 2021, the holdings of our executive officers, directors, principal stockholders and their affiliates, including entities affiliated with SoftBank Vision Fund and FMR LLC represented beneficial ownership, in the aggregate, of approximately 40.1% of our outstanding common stock. As a result, these stockholders, if they act together, will be able to influence our management and affairs and control the outcome of matters submitted to our stockholders for approval, including the election of directors and any sale, merger, consolidation, or sale of all or substantially all of our assets. These stockholders may have interests, with respect to their common stock, that are different from those of our public market investors and the concentration of voting power among these stockholders may have an adverse effect on the price of our common stock. In addition, this concentration of ownership might adversely affect the market price of our common stock by:

- delaying, deferring or preventing a change of control of us;
- impeding a merger, consolidation, takeover or other business combination involving us; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

We have broad discretion in the use of the net proceeds from this offering as well as our cash, cash equivalents and investments and may invest or spend the proceeds in ways with which you do not agree or in ways that ultimately may not increase the value of your investment.

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in the section entitled "Use of Proceeds," as well as our existing cash, cash equivalents and investments, and you will be relying on the judgment of our management regarding such application. You will not have the opportunity, as part of your investment decision, to assess whether the proceeds from this offering and our existing cash, cash equivalents or investments are being used effectively. Our management might not apply the net proceeds or our existing cash, cash equivalents or investments in ways that ultimately increase the value of your investment. If we do not invest or apply the net proceeds from this offering or our existing cash, cash equivalents or investments in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline. Pending their use, we may invest the net proceeds from this offering in short- and intermediate-term, interest-bearing obligations, investment-grade

instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government. These investments may not yield a favorable return to our stockholders.

If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the book value of your shares.

Investors purchasing shares of common stock in this offering will pay a price per share that substantially exceeds the net tangible book value per share of our common stock before giving effect to this offering. As a result, investors purchasing shares of common stock in this offering will incur immediate dilution of \$17.53 per share based on the public offering price of \$26.50 per share. For information on how the foregoing amounts were calculated, see "Dilution."

This dilution is due to the substantially lower price paid by some of our investors who purchased shares prior to this offering as compared to the price offered to the public in this offering. In addition, we have a significant number of stock options and unvested restricted stock units outstanding. The exercise of any of these outstanding options and vesting and settlement of these restricted stock units would result in further dilution. As a result of the dilution to investors purchasing shares in this offering, investors may receive significantly less than the purchase price paid in this offering, if anything, in the event of our liquidation. For a further description of the dilution that you will experience immediately after this offering, see the section titled "Dilution."

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

Additional capital will be needed in the future to continue our planned operations. To the extent we issue additional equity securities to raise capital or pursuant to our equity incentive plans or other contractual obligations, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell or issue common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

In addition, sales of a substantial number of shares of our outstanding common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. Persons who were our stockholders prior to our initial public offering continue to hold a substantial number of shares of our common stock that many of them are now able to sell in the public market. Significant portions of these shares are held by a relatively small number of stockholders. Sales by our stockholders of a substantial number of shares, or the expectation that such sales may occur, could significantly reduce the market price of our common stock.

Further, because we expect we will need to raise additional capital to fund our future activities, we may in the future sell substantial amounts of common stock or securities convertible into or exchangeable for common stock. Future issuances of common stock or common stock-related securities, together with the exercise of outstanding stock options, the vesting and settlement of outstanding restricted stock units, and new equity awards granted under our equity incentive plans, if any, may result in further dilution. Pursuant to the Sales Agreement, we may offer and sell up to an aggregate amount of \$300.0 million of our common stock from time to time in "at-the-market" offerings, subject to the limitations thereof. As of October 12, 2021, no shares of common stock have been sold under the Sales Agreement. To the extent that we sell shares of our common stock in the future pursuant to the Sales Agreement, after the expiration or waiver of the 90-day lock-up period applicable to us and described under the section of this prospectus supplement entitled "Underwriting," investors purchasing shares of common stock in this offering could experience further dilution.

An active trading market for our common stock may not be sustained.

If an active market for our common stock does not continue, it may be difficult for our stockholders to sell their shares without depressing the market price for the shares or sell their shares at or above the prices at which they

acquired their shares or sell their shares at the time they would like to sell. Any inactive trading market for our common stock may also impair our ability to raise capital to continue to fund our operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

Commencing December 31, 2021, we will no longer be an "emerging growth company" or a "smaller reporting company" and the reduced disclosure requirements applicable to emerging growth companies will no longer apply to us.

We are currently an emerging growth company but because as of June 30, 2021, the market value of our common stock that was held by non-affiliates exceeded \$700 million, we will no longer qualify for such status commencing December 31, 2021. As a large-accelerated filer, we will be subject to certain disclosure requirements that are applicable to other public companies that have not been applicable to us as an emerging growth company. These requirements include:

- compliance with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- compliance with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- full disclosure obligations regarding executive compensation; and
- compliance with the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We are also currently a smaller reporting company, but based on the market value of our common stock that was held by non-affiliates as of June 30, 2021, we have determined that we will no longer be a smaller reporting company as of January 1, 2022. However, for so long as we remain a smaller reporting company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not smaller reporting companies. Similar to emerging growth companies, smaller reporting companies are able to provide simplified executive compensation disclosure and have certain other reduced disclosure obligations, including, among other things, being required to provide only two years of audited financial statements and not being required to provide selected financial data, supplemental financial information or risk factors. After January 1, 2022, we will no longer be able to rely on these reduced requirements.

Additional Risks Related to Clinical Development

We have never successfully completed any clinical trials, and we may be unable to do so for any product candidates we develop.

We have not yet demonstrated our ability to successfully complete any clinical trials, including large-scale, pivotal clinical trials, obtain regulatory approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. We have two product candidates, RLY-1971 and RLY-4008, in first-in-human clinical development. For RLY-2608, we initiated IND-enabling studies in 2021 and plan to initiate a first-in-human clinical study in the first half of 2022, subject to submission and acceptance of an IND by the FDA. We may not be able to file such IND or INDs for any of our other product candidates on the timelines we expect, if at all. For example, we may experience manufacturing delays with IND-enabling studies. Moreover, we cannot be sure that once we have submitted an IND, the FDA will allow clinical trials to begin, or that, once begun, issues will not arise that require us to suspend or terminate clinical trials. The FDA may impose a clinical hold before or after a trial begins for a number of reasons outlined in FDA regulations, including if the FDA believes the study drug raises a significant risk of illness or injury. If the FDA imposes a clinical hold, trials may not commence or recommence without FDA authorization and then only under terms authorized by the FDA. Accordingly, the submission of an IND does not mean the FDA will allow clinical trials to begin and, if and when clinical trials do commence under an active IND, issues may arise that require suspension or termination of such trials. Further, commencing each of these clinical trials is subject to finalizing the trial design based on discussions with the FDA and other regulatory authorities. Any guidance we receive from the FDA or other regulatory authorities is subject to change. Regulatory authorities could change their position,

including, on the acceptability of our trial designs or the clinical endpoints selected, which may require us to complete additional clinical trials or impose stricter approval conditions than we currently expect. Successful completion of our clinical trials is a prerequisite to submitting a new drug application, or NDA, to the FDA and a Marketing Authorization Application, or MAA, to the European Medicines Agency, or EMA, for each product candidate and, consequently, the ultimate approval and commercial marketing of each product candidate. Our RLY-1971 and RLY-4008 first-in-human clinical trials are ongoing, but we do not know whether any of our future clinical trials, including the planned first-in-human clinical trial for RLY-2608, will begin on time or ever be completed on schedule, if at all.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- be subject to post-marketing testing requirements; or
- · have the product removed from the market after obtaining marketing approval.

Positive results from preclinical or early clinical studies of our product candidates are not necessarily predictive of the results of later clinical studies and any future clinical trials of our product candidates. If we cannot replicate the positive results from our preclinical or earlier clinical studies of our product candidates in our future clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize our product candidates.

Any positive results from our preclinical or early clinical studies of our product candidates may not necessarily be predictive of the results of later clinical studies and clinical trials. Similarly, even if we are able to complete our planned preclinical and clinical studies or any future clinical trials of our product candidates according to our current development timeline, the positive results from such preclinical or earlier clinical studies and clinical trials of our product candidates may not be replicated in subsequent preclinical studies or clinical trial results.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical and other nonclinical findings made while clinical trials were underway, or safety or efficacy observations made in preclinical studies and clinical trials, including previously unreported adverse events. Moreover, preclinical, nonclinical and clinical data are often susceptible to varying interpretations and analyses and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA or EMA approval.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein, and any free writing prospectus that we have authorized for use in connection with this offering, contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Exchange Act of 1934, as amended, or the Exchange Act.

Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and are forward-looking. These statements are often, but are not always, made through the use of words or phrases such as "may," "will," "could," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "projects," "potential," "continue," and similar expressions, or the negative of these terms, or similar expressions. Accordingly, these statements are subject to risks and uncertainties that could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus supplement, and in particular those factors referenced in the section "Risk Factors."

This prospectus supplement contains forward-looking statements that relate to future events or our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements 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;
- the identification of research priorities and application of 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;
- · the potential safety and efficacy of our product candidates and the implications of clinical and preclinical data;
- the manufacture of our drug substances, delivery vehicles, and product candidates for preclinical use, for clinical trials and on a larger scale for commercial use, if approved;
- our relationships with our third-party strategic collaborators and their ability to continue research and development activities relating to our development candidates and product candidates;
- the funding for our operations necessary to complete further development and commercialization of our product candidates;
- our plans to seek regulatory approval of our product candidates;
- 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 for intellectual property rights covering our product candidates and technology;
- estimates of our future expenses, revenues and capital requirements and our needs for additional financing;
- the potential benefits of strategic collaboration agreements with 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 on our business and programs;
- 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, 2021.

These forward-looking statements are neither promises nor guarantees of future performance due to a variety of risks and uncertainties, many of which are beyond our control, which could cause actual results to differ materially from those indicated by these forward-looking statements, including, without limitation the risk factors and cautionary statements described in other documents that we file from time to time with the SEC, specifically under "Item 1A: Risk Factors" and elsewhere in our most recent Annual Report on Form 10-K for the period ended December 31, 2020 and our most recent Quarterly Reports on Form 10-Q for the quarters ended March 31, 2021 and June 30, 2021, and our Current Reports on Form 8-K, and in this prospectus supplement under the heading "Risk Factors."

While we may elect to update forward-looking statements at some point in the future, we assume no obligation to update or revise any forward-looking statements except to the extent required by applicable law.

This prospectus supplement and the documents incorporated by reference also contain estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. 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 reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data 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.

USE OF PROCEEDS

We estimate that we will receive net proceeds from this offering of approximately \$332.0 million, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, or approximately \$381.9 million if the underwriters exercise their option to purchase additional shares from us in full.

We intend to use the net proceeds from this offering, together with our existing cash, cash equivalents and investments, to fund research and clinical development of current or additional pipeline candidates, working capital, capital expenditures and other general corporate purposes. The expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures will depend on numerous factors, including the factors described under "Risk Factors" in this prospectus supplement, the accompanying prospectus and in the documents incorporated by reference herein, as well as the amount of cash used in our operations. We may find it necessary or advisable to use the net proceeds for other purposes, and we will have broad discretion in the application of the net proceeds. Pending the uses described above, we plan to invest the net proceeds from this offering in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends to our stockholders in the foreseeable future.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted to the extent of the difference between the public offering price per share of our common stock in this offering and the as adjusted net tangible book value per share of our common stock immediately after this offering. The net tangible book value of our common stock as of June 30, 2021 was approximately \$616.2 million, or approximately \$6.66 per share of common stock based upon 92,552,645 shares outstanding. Net tangible book value per share is equal to our total tangible assets (total assets less intangible assets), less our total liabilities, divided by the total number of shares of common stock outstanding as of June 30, 2021.

Net tangible book value dilution per share to investors participating in this offering represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the as adjusted net tangible book value per share of common stock immediately after completion of this offering. After giving effect to the issuance and sale by us of 13,207,547 shares of our common stock at the public offering price of \$26.50 per share, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of June 30, 2021 would have been \$948.2 million, or \$8.97 per share of our common stock. This represents an immediate increase in net tangible book value of \$2.31 per share to our existing stockholders and an immediate dilution in as adjusted net tangible book value of \$17.53 per share to new investors in this offering.

The following table illustrates this calculation on a per share basis without giving effect to the option to purchase additional shares granted to the underwriters:

| Public offering price per share | | \$ 26.50 |
|--|------------|-------------|
| Net tangible book value per share as of June 30, 2021 | \$ 6.66 | |
| Increase in net tangible book value per share attributable to | | |
| this offering | \$ 2.31 | |
| As adjusted net tangible book value per share after giving effect to | | |
| this offering | | \$ 8.97 |
| Dilution in net tangible book value per share to new investors in | | |
| this offering | | \$ 17.53 |

If the underwriters exercise in full their option to purchase additional shares of common stock, the as adjusted net tangible book value after this offering would be \$9.26 per share of our common stock, representing an increase of as adjusted net tangible book value of \$2.61 per share to our existing stockholders and an immediate dilution of \$17.24 per share to new investors purchasing shares in this offering.

The information above and in the foregoing table is based upon 92,552,645 shares of our common stock outstanding as of June 30, 2021. The information above and in the foregoing table excludes:

- 8,906,194 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2021 at a weighted-average exercise price of \$13.16 per share;
- 505,393 shares of common stock issuable upon the vesting and settlement of restricted stock units outstanding as of June 30, 2021;
- 10,653,994 shares of common stock reserved for future issuance as of June 30, 2021 under our 2020 Plan; and
- 1,991,600 shares of common stock reserved for future issuance as of June 30, 2021 under our 2020 Employee Stock Purchase Plan.

In addition, we may choose to raise additional capital in the future through the sale of equity or convertible debt securities due to market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. To the extent that any of our outstanding options are exercised, shares of common stock are issued upon the vesting and settlement of our restricted stock units outstanding, new equity awards are granted under our equity incentive plans, additional shares of common stock are issued pursuant to the Sales

Agreement with Cowen and Company, LLC or we otherwise issue additional shares of common stock or other equity or convertible debt securities in the future, there may be further dilution to investors participating in this offering.

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. 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 supplement 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 supplement. 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 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.

UNDERWRITING

We and the underwriters named below have entered into an underwriting agreement with respect to the shares being offered. Subject to certain conditions, each underwriter has severally agreed to purchase the number of shares indicated in the following table. Goldman Sachs & Co. LLC, J.P. Morgan Securities LLC, Cowen and Company, LLC and Guggenheim Securities, LLC are the representatives of the underwriters.

| <u>Underwriters</u> | Number of Shares |
|----------------------------|------------------|
| Goldman Sachs & Co. LLC | 4,688,679 |
| J.P. Morgan Securities LLC | 4,688,679 |
| Cowen and Company, LLC | 2,641,510 |
| Guggenheim Securities, LLC | 1,188,679 |
| Total | 13,207,547 |

The underwriters are committed to take and pay for all of the shares being offered, if any are taken, other than the shares covered by the option described below unless and until this option is exercised.

The underwriters have an option to buy up to an additional 1,981,132 shares from us. They may exercise that option for 30 days. If any shares are purchased pursuant to this option, the underwriters will severally purchase shares in approximately the same proportion as set forth in the table above.

The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters by us. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase 1,981,132 additional shares from us.

| Paid by Relay Therapeutics, Inc. | N | o Exercise |] | Full Exercise | |
|----------------------------------|----|------------|----|---------------|--|
| Per Share | \$ | 1.325 | \$ | 1.325 | |
| Total | \$ | 17,500,000 | \$ | 20,125,000 | |

Shares sold by the underwriters to the public will initially be offered at the public offering price set forth on the cover of this prospectus supplement. Any shares sold by the underwriters to securities dealers may be sold at a discount of up to \$0.795 per share from the public offering price. After the initial offering of the shares, the representatives may change the offering price and the other selling terms. The offering of the shares by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part.

We have agreed that, subject to certain limited exceptions, we will not (i) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, or submit to, or file with, the SEC a registration statement under the Securities Act relating to, any shares of our common stock or securities convertible into or exercisable or exchangeable for any shares of our common stock, or publicly disclose the intention to make any offer, sale, pledge, loan, disposition or filing, or (ii) enter into any swap or other arrangement that transfers all or a portion of the economic consequences associated with the ownership of any shares of common stock or any such other securities (regardless of whether any of these transactions are to be settled by the delivery of shares of common stock or such other securities, in cash or otherwise), in each case without the prior written consent of Goldman Sachs & Co. LLC and J.P. Morgan Securities LLC for a period of 90 days after the date of this prospectus supplement, other than the shares of our common stock to be sold in this offering.

Our directors and executive officers (such persons, the "lock-up parties") have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each lock-up party, with limited exceptions, for a period of 90 days after the date of this prospectus supplement (such period, the "restricted period"), may not (and may not cause any of their direct or indirect affiliates to), without the prior written consent of Goldman Sachs & Co. LLC and J.P. Morgan Securities LLC, (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise

transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock (including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by such lock-up parties in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant (collectively with the common stock, the "lock-up securities")), (2) enter into any hedging, swap or other agreement or transaction that transfers, in whole or in part, any of the economic consequences of ownership of the lock-up securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of lock-up securities, in cash or otherwise, (3) make any demand for, or exercise any right with respect to, the registration of any lock-up securities, or (4) publicly disclose the intention to do any of the foregoing. Such persons or entities have further acknowledged that these undertakings preclude them from engaging in any hedging or other transactions or arrangements (including, without limitation, any short sale or the purchase or sale of, or entry into, any put or call option, or combination thereof, forward, swap or any other derivative transaction or instrument, however described or defined) designed or intended, or which could reasonably be expected to lead to or result in, a sale or disposition or transfer (by any person or entity, whether or not a signatory to such agreement) of any economic consequences of ownership, in whole or in part, directly or indirectly, of any lock-up securities, whether any such transaction or arrangement (or instrument provided for thereunder) would be settled by delivery of lock-up securities, in cash or otherwise.

The restrictions described in the immediately preceding paragraph and contained in the lock-up agreements between the underwriters and the lockup parties do not apply, subject in certain cases to various conditions, to certain transactions, including (a) transfers of lock-up securities: (i) as a bona fide gift or gifts, or for bona fide estate planning purposes, (ii) by will or intestacy, (iii) to any trust for the direct or indirect benefit of the lock-up party or any immediate family member of the lock-up party, or, if the lock-up party is a trust, to a trustor or beneficiary of the trust or to the estate of a beneficiary of such trust, (iv) to a partnership, limited liability company or other entity of which the lock-up party and its immediate family members are the legal and beneficial owner of all of the outstanding equity securities or similar interests, (v) to a nominee or custodian of a person or entity to whom a disposition or transfer would be permissible under clauses (i) through (iv), (vi) in the case of a corporation, partnership, limited liability company, trust or other business entity, (A) to another corporation, partnership, limited liability company, trust or other business entity that is an affiliate of the lock-up party, or to any investment fund or other entity controlling, controlled by, managing or managed by or under common control with the lock-up party or its affiliates or (B) as part of a distribution to members or stockholders of the lock-up party; (vii) by operation of law, (viii) to us from an employee upon death, disability or termination of employment of such employee, (ix) as part of a sale of lock-up securities acquired in open market transactions after the completion of this offering, (x) to us in connection with the vesting, settlement or exercise of restricted stock units, options, warrants or other rights to purchase shares of our common stock (including "net" or "cashless" exercise), including for the payment of exercise price and tax and remittance payments, or (xi) pursuant to a bona fide third-party tender offer, merger, consolidation or other similar transaction approved by our board of directors and made to all stockholders involving a change in control, provided that if such transaction is not completed, all such lock-up securities would remain subject to the restrictions in the immediately preceding paragraph; (b) exercise of the options, settlement of RSUs or other equity awards, or the exercise of warrants granted pursuant to our equity incentive plans (including "net" or "cashless" exercise, vesting or settlement), provided that any lock-up securities received upon such exercise, vesting or settlement would be subject to restrictions similar to those in the immediately preceding paragraph; (c) the conversion of outstanding preferred stock, warrants to acquire preferred stock, or convertible securities into shares of our common stock or warrants to acquire shares of our common stock. provided that any common stock or warrant received upon such conversion would be subject to restrictions similar to those in the immediately preceding paragraph; (d) the establishment by lock-up parties of trading plans under Rule 10b5-1 under the Exchange Act, provided that such plan does not provide for the transfer of lock-up securities during the restricted period; and (e) the sale of lock-up securities (including following the exercise of options to purchase common stock) pursuant to existing trading plans under Rule 10b5-1 under the Exchange Act.

J.P. Morgan Securities LLC and Goldman Sachs & Co. LLC, in their sole discretion, may release the securities subject to any of the lock-up agreements with the underwriters described above, in whole or in part at any time.

In connection with the offering, the underwriters may purchase and sell shares of common stock in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of shares than they are required to

purchase in the offering, and a short position represents the amount of such sales that have not been covered by subsequent purchases. A "covered short position" is a short position that is not greater than the amount of additional shares for which the underwriters' option described above may be exercised. The underwriters may cover any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to cover the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase additional shares pursuant to the option described above. "Naked" short sales are any short sales that create a short position greater than the amount of additional shares for which the option described above may be exercised. The underwriters must cover any such naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of common stock made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Purchases to cover a short position and stabilizing transactions, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of our stock, and together with the imposition of the penalty bid, may stabilize, maintain or otherwise affect the market price of the common stock. As a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. The underwriters are not required to engage in these activities and may end any of these activities at any time. These transactions may be effected on The Nasdaq Global Market, in the over-the-counter market or otherwise.

We may enter into derivative transactions with third parties, or sell securities not covered by this prospectus supplement to third parties in privately negotiated transactions. In connection with those derivatives, the third parties may sell securities covered by this prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter or will be identified in a post-effective amendment.

We estimate that the total expenses of the offering, excluding underwriting discounts and commissions, will be approximately \$500,000. We have also agreed to reimburse the underwriters for certain of their expenses in an amount up to \$35,000.

We have agreed to indemnify the several underwriters against certain liabilities, including liabilities under the Securities Act.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their respective affiliates have provided, and may in the future provide, a variety of these services to the issuer and to persons and entities with relationships with the issuer, for which they received or will receive customary fees and expenses. For example, Cowen and Company, LLC is the sales agent under the Sales Agreement.

In the ordinary course of their various business activities, the underwriters and their respective affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively trade securities, derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own account and for the accounts of their customers, and such investment and trading activities may involve or relate to assets, securities and/or instruments of the issuer (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with the issuer. The underwriters and their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express

independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

European Economic Area and the United Kingdom

In relation to each Member State of the European Economic Area and the United Kingdom (each a "Member State"), no common shares (the "Shares") have been offered or will be offered pursuant to the offering to the public in that Member State prior to the publication of a prospectus in relation to the Shares which has been approved by the competent authority in that Member State or, where appropriate, approved in another Member State and notified to the competent authority in that Member State, all in accordance with the Prospectus Regulation), except that offers of Shares may be made to the public in that Member State at any time under the following exemptions under the Prospectus Regulation:

- (a) to any legal entity which is a qualified investor as defined under the Prospectus Regulation;
- (b) to fewer than 150 natural or legal persons (other than qualified investors as defined under the Prospectus Regulation), subject to obtaining the prior consent of the Representatives for any such offer; or
- (c) in any other circumstances falling within Article 1(4) of the Prospectus Regulation, provided that no such offer of Shares shall require the company or any Representative to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

United Kingdom

Each underwriter has represented and agreed that:

- (a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000 (FSMA)) received by it in connection with the issue or sale of the shares in circumstances in which Section 21(1) of the FSMA does not apply to the company; and
- (b) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares in, from or otherwise involving the United Kingdom.

Canada

The securities may be sold in Canada only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions, and Ongoing Registrant Obligations. Any resale of the securities must be made in accordance with an exemption form, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this offering memorandum (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Hong Kong

The shares may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32 of the Laws of Hong Kong) ("Companies (Winding Up and Miscellaneous Provisions) Ordinance") or which do not constitute an invitation to the public within the meaning of the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong) ("Securities and Futures Ordinance"), or (ii) to "professional investors" as defined in the Securities and Futures Ordinance and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance, and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" in Hong Kong as defined in the Securities and Futures Ordinance and any rules made thereunder.

Singapore

This prospectus supplement has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor (as defined under Section 4A of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA")) under Section 274 of the SFA, (ii) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to conditions set forth in the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor, the securities (as defined in Section 239(1) of the SFA) of that corporation shall not be transferable for 6 months after that corporation has acquired the shares under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer in that corporation's securities pursuant to Section 275(1A) of the SFA, (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore ("Regulation 32").

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is a trust (where the trustee is not an accredited investor (as defined in Section 4A of the SFA)) whose sole purpose is to hold investments and each beneficiary of the trust is an accredited investor, the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferable for 6 months after that trust has acquired the shares under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer that is made on terms that such rights or interest are acquired at a consideration of not less than \$\$200,000 (or its equivalent in a foreign currency) for each transaction (whether such amount is to be paid for in cash or by exchange of securities or other assets), (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32.

Singapore SFA Product Classification—In connection with Section 309B of the SFA and the Securities and Futures (Capital Markets Products) Regulations 2018 (the "CMP Regulations 2018"), the Company has determined, and hereby notifies all relevant persons (as defined in the CMP Regulations 2018), that the shares are "prescribed capital markets products" (as defined in the CMP Regulations 2018) and Excluded Investment Products (as defined in MAS

Notice SFA 04-N12: Notice on the Sale of Investment Products and MAS Notice FAA-N16: Notice on Recommendations on Investment Products).

Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Act of Japan (the "FIEA") (Act No. 25 of 1948, as amended). The securities may not be offered or sold, directly or indirectly, in Japan or to or for the benefit of any resident of Japan (including any person resident in Japan or any corporation or other entity organized under the laws of Japan) or to others for reoffering or resale, directly or indirectly, in Japan or to or for the benefit of any resident of Japan, except pursuant to an exemption from the registration requirements of the FIEA and otherwise in compliance with any relevant laws and regulations of Japan.

LEGAL MATTERS

Certain legal matters in connection with this offering will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts. Certain legal matters in connection with this offering will be passed upon for the underwriters by Ropes & Gray 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 supplement. 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

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at www.sec.gov.

Our web site address is *www.relaytx.com*. The information on our web site, however, is not, and should not be deemed to be, a part of this prospectus supplement or the accompanying prospectus.

This prospectus supplement and the accompanying prospectus is part of a registration statement on Form S-3 that we filed with the SEC and does not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided above. Statements in this prospectus supplement and the accompanying prospectus about any documents filed as exhibits to the registration statement are summaries, and each statement is qualified in all respects by reference to the document to which it refers. You should refer to the actual documents for a more complete description of the relevant matters. You may inspect a copy of the registration statement through the SEC's website, as provided above.

INCORPORATION 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 supplement, 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 (SEC File No. 001-39385), 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 this prospectus supplement, except as to any portion of any future report or document that is not deemed filed under such provisions until we sell all of the securities:

- Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on March 25, 2021;
- The information specifically incorporated by reference into our Annual Report on <u>Form 10-K</u> for the year ended December 31, 2020 from our definitive proxy statement on <u>Schedule 14A</u> (other than information furnished rather than filed), which was filed with the SEC on April 7, 2021;
- Quarterly Reports on Form 10-Q filed with the SEC for the quarters ended March 31, 2021 and June 30, 2021, filed with the SEC on <u>May 13, 2021</u> and <u>August 12, 2021</u>, respectively;
- Current Reports on Form 8-K filed with the SEC on <u>April 16, 2021</u>, <u>May 19, 2021</u> and <u>May 27, 2021</u>, and <u>October 8, 2021</u>, excluding, in each case, information "furnished" pursuant to Items 2.02, 7.01 or 9.01; and
- The description of our common stock contained in our Registration Statement on <u>Form 8-A</u> (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 <u>Form 10-K</u> for the year ended December 31, 2020, as filed with the SEC on March 25, 2021.

Upon request, we will provide, without charge, to each person, including any beneficial owner, to whom a copy of this prospectus supplement is delivered, a copy of the documents incorporated by reference into this prospectus supplement but not delivered with the prospectus supplement. You may request a copy of these filings, and any exhibits we have specifically incorporated by reference as an exhibit in this prospectus supplement, at no cost by writing or telephoning us at the following address: Relay Therapeutics, Inc., 399 Binney Street, 2nd Floor, Cambridge, Massachusetts 02139, telephone: (617) 370-8837. You may also access these documents, free of charge on the SEC's website at www.sec.gov or on our website at www.relaytx.com. Information contained on our website is not incorporated by reference into this prospectus supplement, and you should not consider any information on, or that can be accessed from, our website as part of this prospectus supplement or any accompanying prospectus supplement.

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 supplement or the registration statement of which this prospectus supplement is a part.

This prospectus supplement and the accompanying prospectus are part of a registration statement we filed with the SEC. We have incorporated exhibits into the registration statement. You should read the exhibits carefully for provisions that may be important to you.

You should rely only on the information incorporated by reference or provided in this prospectus supplement and the accompanying prospectus. We have not authorized anyone to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus supplement, the accompanying prospectus or in the documents incorporated by reference is accurate as of any date other than the date on the front of this prospectus supplement or those documents.

Any statement contained in a document that is incorporated by reference will be modified or superseded for all purposes to the extent that a statement contained in this prospectus, or in any other document that is subsequently filed with the SEC and incorporated by reference into this prospectus supplement and the accompanying prospectus, modifies or is contrary to that previous statement. Any statement so modified or superseded will not be deemed a part of this prospectus supplement and the accompanying prospectus, except as so modified or superseded. Since information that we later file with the SEC will update and supersede previously incorporated information, you should look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any documents previously incorporated by reference have been modified or superseded.



Common Stock Preferred Stock Debt Securities Warrants Units

| We may from time to time issue, in one or more series or classes, our common stock, preferred stock, debt securities, warrants and/or units. We may offer hese securities separately or together in units. We will specify in the applicable accompanying prospectus supplement the terms of the securities being offered. We may sell these securities to or through underwriters and also to other purchasers or through agents. We will set forth the names of any underwriters or agents, and any fees, conversions or discount arrangements, in the applicable accompanying prospectus supplement. We may not sell any securities under this prospectus without delivery of the applicable prospectus supplement. |
|--|
| You should read this document and any prospectus supplement or amendment carefully before you invest in our securities. |
| Our common stock is listed on the Nasdaq Global Market under the symbol "RLAY." On August 9, 2021, the closing price for our common stock, as reported on the Nasdaq Global Market, was \$33.50 per share. Our principal executive office is located at 399 Binney Street, 2nd Floor, Cambridge, MA |

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties referenced under the heading "Risk Factors" contained in this prospectus beginning on page 2 and any applicable prospectus supplement, and under similar headings in the other documents that are incorporated by reference into this prospectus.

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 August 12, 2021.

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ABOUT THIS PROSPECTUS

This prospectus is part of an automatic shelf registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the SEC, as a "well-known seasoned issuer" as defined in Rule 405 under the Securities Act. Under the shelf registration, we and/or selling stockholders may offer or sell shares of our common stock and preferred stock, various series of warrants to purchase common stock or preferred stock, debt securities or any combination thereof, from time to time in one or more offerings.

This prospectus provides you with a general description of the securities we and/or selling stockholders may offer or sell. Each time we sell securities, we will provide one or more prospectus supplements that will contain specific information about the terms of the offering. The applicable prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and any accompanying prospectus supplement together with the additional information described under the heading "Where You Can Find More Information" beginning on page 26 of this prospectus.

You should rely only on the information contained in or incorporated by reference in this prospectus, the accompanying prospectus supplement or in any related free writing prospectus filed by us with the SEC. We have not authorized anyone to provide you with different information. This prospectus and the accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in the accompanying prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

Unless the context suggests otherwise, all references to "us," "our," "Relay Therapeutics," "we," the "Company" and similar designations refer to Relay Therapeutics, Inc. and, where appropriate, our consolidated subsidiaries.

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully consider the risks referenced below and described in the documents incorporated by reference in this prospectus and any applicable prospectus supplement, as well as other information we include or incorporate by reference into this prospectus and any applicable prospectus supplement, before making an investment decision. Our business, financial condition or results of operations could be materially adversely affected by the materialization of any of these risks. The trading price of our securities could decline due to the materialization of any of these risks, and you may lose all or part of your investment. This prospectus and the documents incorporated herein by reference also contain forward-looking statements that involve risks and uncertainties. Actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks referenced below and described in the documents incorporated herein by reference, including (i) our annual report on Form 10-K for the fiscal year ended December 31, 2020, which is on file with the SEC and is incorporated herein by reference, (ii) our quarterly reports on Form 10-Q for the quarters ended March 31, 2021 and June 30, 2021, which are on file with the SEC and incorporated herein by reference, and (iii) other documents we file with the SEC that are deemed incorporated by reference into this prospectus.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, any applicable prospectus supplement, any related free writing prospectus and the documents that we incorporate by reference herein or therein contain forward-looking statements within the meaning of Section 27A of the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but are not always,made through the use of words or phrases such as "may," "will," "could," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "projects," "potential," "continue," and similar expressions, or the negative of these terms, or similar expressions. Accordingly, these statements involve estimates, assumptions, risks and uncertainties which could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus, and in particular those factors referenced in the section "Risk Factors."

This prospectus contains forward-looking statements that are based on our management's belief and assumptions and on information currently available to our management. These statements relate to future events or our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements 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;
- the identification of research priorities and application of 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;
- the manufacture of our drug substances, delivery vehicles, and product candidates for preclinical use, for clinical trials and on a larger scale for commercial use, if approved;
- our relationships with our third-party strategic collaborators and their ability to continue research and development activities relating to our development candidates and product candidates;
- the funding for our operations necessary to complete further development and commercialization of our product candidates;
- our plans to seek regulatory approval of our product candidates;
- 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 for intellectual property rights covering our product candidates and technology;
- estimates of our future expenses, revenues and capital requirements and our needs for additional financing;
- the potential benefits of strategic collaboration agreements with 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 on our business and programs;
- 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, 2021.

These forward-looking statements are neither promises nor guarantees of future performance due to a variety of risks and uncertainties, many of which are beyond our control, which could cause actual results to differ materially from those indicated by these forward-looking statements, including, without limitation the risk factors and cautionary statements described in other documents that we file from time to time with the SEC, specifically under "Item 1A: Risk Factors" and elsewhere in our most recent Annual Report on Form 10-K for the period ended December 31, 2020 and our most recent Quarterly Reports on Form 10-Q for the quarters ended March 31, 2021 and June 30, 2021, and our Current Reports on Form 8-K, and the section of any accompanying prospectus supplement entitled "Risk Factors."

The forward-looking statements in this prospectus and the documents incorporated by reference represent our views as of their respective dates. 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 assume no obligation to update or revise any forward-looking statements 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 dates on which they were made.

This prospectus and the documents incorporated by reference also contain estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. 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 reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data 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.

THE COMPANY

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, RLY4008, RLY-2608 and RLY-1971. We initiated a first-in-human clinical trial for 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. In 2021, we initiated Investigational New Drug, or IND, enabling studies for RLY-2608, our inhibitor of cancer-associated mutant variants H1047X, E542X, and E545X of phosphoinostide 3-kinase alpha, or PI3Ka. RLY-2608 is the lead program of multiple preclinical efforts to discover and develop mutant selective inhibitors of PI3Ka. 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. In July 2021, Genentech initiated the cohort of RLY-1971 in combination with GDC-6036, its KRASG12C inhibitor, in a phase 1b trial. 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 both 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 DesignTM, 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.

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 $^{\mathbb{R}}$ and $^{\text{TM}}$, 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.

USE OF PROCEEDS

We intend to use the net proceeds from the sale of any securities offered under this prospectus for general corporate purposes unless otherwise indicated in the applicable prospectus supplement. General corporate purposes may include research and clinical development of current or additional pipeline candidates, working capital, capital expenditures and other general corporate purposes. We may temporarily invest the net proceeds in a variety of capital preservation instruments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities, or may hold such proceeds as cash, until they are used for their stated purpose. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds.

SECURITIES WE AND/OR SELLING STOCKHOLDERS MAY OFFER OR SELL

This prospectus contains summary descriptions of the securities we and/or selling stockholders may offer or sell from time to time. These summary descriptions are not meant to be complete descriptions of each security. The particular terms of any security will be described in the applicable prospectus supplement. This prospectus provides you with a general description of the securities we may offer. Each time we sell securities described herein, we will provide prospective investors with a supplement to this prospectus that will contain specific information about the terms of that offering, including the specific amounts, prices and terms of the securities offered.

We may sell the securities to or through underwriters, dealers or agents, directly to purchasers or through a combination of any of these methods of sale or as otherwise set forth below under "Plan of Distribution." We, as well as any agents acting on our behalf, reserve the sole right to accept and to reject in whole or in part any proposed purchase of securities. Any prospectus supplement will set forth the names of any underwriters, dealers, agents or other entities involved in the sale of securities described in that prospectus supplement and any applicable fee, commission or discount arrangements with them.

DESCRIPTION OF CAPITAL STOCK

The following description of our common stock and preferred stock, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the common stock and preferred stock that we may offer under this prospectus. The following description of our capital stock does not purport to be complete and is subject to, and qualified in its entirety by, our certificate of incorporation and bylaws, which are exhibits to the registration statement of which this prospectus forms a part, and by applicable law. The terms of our common stock and preferred stock may also be affected by Delaware law.

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 orother 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 at the time of the agreement. 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.

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 entitled to vote on the amendment, and not

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.

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 P.O. Box 505000, Louisville, Kentucky 40233, and its telephone number within the U.S. is (800) 736-3001 and outside the U.S. is (781) 575-3100.

DESCRIPTION OF DEBT SECURITIES

We may offer debt securities which may be senior or subordinated. We refer to senior debt securities and subordinated debt securities collectively as debt securities. Each series of debt securities may have different terms. The following description summarizes the general terms and provisions of the debt securities. We will describe the specific terms of the debt securities and the extent, if any, to which the general provisions summarized below apply to any series of debt securities in the prospectus supplement relating to the series and any applicable free writing prospectus that we authorize to be delivered.

We may issue senior debt securities from time to time, in one or more series under a senior indenture to be entered into between us and a senior trustee to be named in a prospectus supplement, which we refer to as the senior trustee. We may issue subordinated debt securities from time to time, in one or more series, under a subordinated indenture to be entered into between us and a subordinated trustee to be named in a prospectus supplement, which we refer to as the subordinated trustee. The forms of senior indenture and subordinated indenture are filed as exhibits to the registration statement of which this prospectus forms a part. Together, the senior indenture and the subordinated indenture are referred to as the indentures and, together, the senior trustee and the subordinated trustee are referred to as the trustees. This prospectus briefly outlines some of the provisions of the indentures. The following summary of the material provisions of the indentures is qualified in its entirety by the provisions of the indentures, including definitions of certain terms used in the indentures. Wherever we refer to particular sections or defined terms of the indentures, those sections or defined terms are incorporated by reference in this prospectus or the applicable prospectus supplement. You should review the indentures that are filed as exhibits to the registration statement of which this prospectus forms a part for additional information. As used in this prospectus, the term "debt securities" includes the debt securities being offered by this prospectus and all other debt securities issued by us under the indentures.

General

The indentures:

- do not limit the amount of debt securities that we may issue;
- allow us to issue debt securities in one or more series;
- do not require us to issue all of the debt securities of a series at the same time; and
- allow us to reopen a series to issue additional debt securities without the consent of the holders of the debt securities of such series.

Unless otherwise provided in the applicable prospectus supplement, the senior debt securities will be unsubordinated obligations and will rank equally with all of our other unsecured and unsubordinated indebtedness. Payments on the subordinated debt securities will be subordinated to the prior payment in full of all of our senior indebtedness, as described under "—Subordination" and in the applicable prospectus supplement.

Each indenture provides that we may, but need not, designate more than one trustee under an indenture. Any trustee under an indenture may resign or be removed and a successor trustee may be appointed to act with respect to the series of debt securities administered by the resigning or removed trustee. If two or more persons are acting as trustee with respect to different series of debt securities, each trustee shall be a trustee of a trust under the applicable indenture separate and apart from the trust administered by any other trustee. Except as otherwise indicated in this prospectus, any action described in this prospectus to be taken by each trustee may be taken by each trustee with respect to, and only with respect to, the one or more series of debt securities for which it is trustee under the applicable indenture.

The prospectus supplement for each offering will provide the following terms, where applicable:

• the title of the debt securities and whether they are senior or subordinated;

- any limit upon the aggregate principal amount of the debt securities of that series;
- the date or dates on which the principal of the debt securities of the series is payable;
- the price at which the debt securities will be issued, expressed as a percentage of the principal and, if other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof or, if applicable, the portion of the principal amount of such debt securities that is convertible into another security of ours or the method by which any such portion shall be determined:
- the rate or rates at which the debt securities of the series shall bear interest or the manner of calculation of such rate or rates, if any;
- the date or dates from which interest will accrue, the interest payment dates on which such interest will be payable or the manner of determination of such interest payment dates, the place(s) of payment, and the record date for the determination of holders to whom interest is payable on any such interest payment dates or the manner of determination of such record dates;
- the right, if any, to extend the interest payment periods and the duration of such extension;
- the period or periods within which, the price or prices at which and the terms and conditions upon which debt securities of the series may be redeemed, converted or exchanged, in whole or in part;
- our obligation, if any, to redeem or purchase debt securities of the series pursuant to any sinking fund, mandatory redemption, or analogous provisions (including payments made in cash in satisfaction of future sinking fund obligations) or at the option of a holder thereof and the period or periods within which, the price or prices at which, and the terms and conditions upon which, debt securities of the series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;
- the form of the debt securities of the series including the form of the Certificate of Authentication for such series;
- if other than minimum denominations of one thousand U.S. dollars (\$1,000) or any integral multiple of \$1,000 thereof, the denominations in which the debt securities of the series shall be issuable;
- whether the debt securities of the series shall be issued in whole or in part in the form of a global debt security or global debt securities; the terms and conditions, if any, upon which such global debt security or global debt securities may be exchanged in whole or in part for other individual debt securities; and the depositary for such global debt security or global debt securities;
- whether the debt securities will be convertible into or exchangeable for common stock or other securities of ours or any other Person and, if so, the terms and conditions upon which such debt securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or how it will be calculated and may be adjusted, any mandatory or optional (at our optionor the holders' option) conversion or exchange features, and the applicable conversion or exchange period;
- any additional or alternative events of default to those set forth in the indenture;
- any additional or alternative covenants to those set forth in the indenture;
- the currency or currencies including composite currencies, in which payment of the principal of (and premium, if any) and interest, if any, on such debt securities shall be payable (if other than the currency of the United States of America), which unless otherwise specified shall be the currency of the United States of America as at the time of payment is legal tender for payment of public or private debts;
- if the principal of (and premium, if any), or interest, if any, on such debt securities is to be payable, at our election or at the election of any holder thereof, in a coin or currency other than that in which such debt securities are stated to be payable, then the period or periods within which, and the terms and conditions upon which, such election may be made;

- whether interest will be payable in cash or additional debt securities at our or the holders' option and the terms and conditions upon which the
 election may be made;
- the terms and conditions, if any, upon which we will pay amounts in addition to the stated interest, premium, if any and principal amounts of the debt securities of the series to any holder that is not a "United States person" for federal tax purposes;
- additional or alternative provisions, if any, related to defeasance and discharge of the offered debt securities than those set forth in the indenture;
- the applicability of any guarantees;
- any restrictions on transfer, sale or assignment of the debt securities of the series; and
- any other terms of the debt securities (which may supplement, modify or delete any provision of the indenture insofar as it applies to such series).

We may issue debt securities that provide for less than the entire principal amount thereof to be payable upon declaration of acceleration of the maturity of the debt securities. We refer to any such debt securities throughout this prospectus as "original issue discount securities."

We will provide you with more information in the applicable prospectus supplement regarding any deletions, modifications, or additions to the events of default or covenants that are described below, including any addition of a covenant or other provision providing event risk or similar protection.

Payment

Unless otherwise provided in the applicable prospectus supplement, the principal of, and any premium or make-whole amount, and interest on, any series of the debt securities will be payable by mailing a check to the address of the person entitled to it as it appears in the applicable register for the debt securities or by wire transfer of funds to that person at an account maintained within the United States.

All monies that we pay to a paying agent or a trustee for the payment of the principal of, and any premium, or interest on, any debt security will be repaid to us if unclaimed at the end of two years after the obligation underlying payment becomes due and payable. After funds have been returned to us, the holder of the debt security may look only to us for payment, without payment of interest for the period which we hold the funds.

Merger, Consolidation or Sale of Assets

The indentures provide that we may, without the consent of the holders of any outstanding debt securities, (i) consolidate with, (ii) sell, lease or convey all or substantially all of our assets to, or (iii) merge with or into, any other entity provided that:

- either we are the continuing entity, or the successor entity, if other than us, assumes the obligations (a) to pay the principal of, and any premium, and interest on, all of the debt securities and (b) to duly perform and observe all of the covenants and conditions contained in the applicable indenture; and in the event the debt securities are convertible into or exchangeable for common stock or other securities of ours, such successor entity will, by such supplemental indenture, make provision so that the holders of debt securities of that series shall thereafter be entitled to receive upon conversion or exchange of such debt securities the number of securities or property to which a holder of the number of common stock or other securities of ours deliverable upon conversion or exchange of those debt securities would have been entitled had such conversion or exchange occurred immediately prior to such consolidation, merger, sale, conveyance, transfer or other disposition; and
- an officers' certificate and legal opinion covering such conditions are delivered to each applicable trustee.

Events of Default, Notice and Waiver

Unless the applicable prospectus supplement states otherwise, when we refer to "events of default" as defined in the indentures with respect to any series of debt securities, we mean:

- default in the payment of any installment of interest on any debt security of such series continuing for 90 days unless such date has been
 extended or deferred;
- default in the payment of principal of, or any premium on, any debt security of such series when due and payable unless such date has been
 extended or deferred;
- default in the performance or breach of any covenant or warranty in the debt securities or in the indenture by us continuing for 90 days after written notice described below;
- · bankruptcy, insolvency or reorganization, or court appointment of a receiver, liquidator or trustee of us; and
- any other event of default provided with respect to a particular series of debt securities.

If an event of default (other than an event of default described in the fourth bullet point above) occurs and is continuing with respect to debt securities of any series outstanding, then the applicable trustee or the holders of 25% or more in principal amount of the debt securities of that series will have the right to declare the principal amount of, and accrued interest on, all the debt securities of that series to be due and payable. If an event of default described in the fourth bullet point above occurs, the principal amount of, and accrued interest on, all the debt securities of that series will automatically become and will be immediately due and payable without any declaration or other act on the part of the trustee or the holders of the debt securities. However, at any time after such a declaration of acceleration has been made, but before a judgment or decree for payment of the money due has been obtained by the applicable trustee, the holders of at least a majority in principal amount of outstanding debt securities of such series or of all debt securities then outstanding under the applicable indenture may rescind and annul such declaration and its consequences if:

- we have deposited with the applicable trustee all required payments of the principal, any premium, interest and, to the extent permitted by law, interest on overdue installment of interest, plus applicable fees, expenses, disbursements and advances of the applicable trustee; and
- all events of default, other than the non-payment of accelerated principal, or a specified portion thereof, and any premium, have been cured or waived.

The indentures provide that holders of debt securities of any series may not institute any proceedings, judicial or otherwise, with respect to such indenture or for any remedy under the indenture, unless the trustee fails to act for a period of 90 days after the trustee has received a written request to institute proceedings in respect of an event of default from the holders of 25% or more in principal amount of the outstanding debt securities of such series, as well as an offer of indemnity reasonably satisfactory to the trustee. However, this provision will not prevent any holder of debt securities from instituting suit for the enforcement of payment of the principal of, and any premium, and interest on, such debt securities at the respective due dates thereof.

The indentures provide that, subject to provisions in each indenture relating to its duties in the case of a default, a trustee has no obligation to exercise any of its rights or powers at the request or direction of any holders of any series of debt securities then outstanding under the indenture, unless the holders have offered to the trustee reasonable security or indemnity. The holders of at least a majority in principal amount of the outstanding debt securities of any series or of all debt securities then outstanding under an indenture shall have the right to direct the time, method and place of conducting any proceeding for any remedy available to the applicable trustee, or of exercising any trust or power conferred upon such trustee. However, a trustee may refuse to follow any direction which:

• is in conflict with any law or the applicable indenture;

- may involve the trustee in personal liability; or
- may be unduly prejudicial to the holders of debt securities of the series not joining the proceeding.

Within 120 days after the close of each fiscal year, we will be required to deliver to each trustee a certificate, signed by one of our several specified officers, stating whether or not that officer has knowledge of any default under the applicable indenture. If the officer has knowledge of any default, the notice must specify the nature and status of the default.

Modification of the Indentures

Subject to certain exceptions, the indentures may be amended with the consent of the holders of a majority in aggregate principal amount of the outstanding debt securities of all series affected by such amendment (including consents obtained in connection with a tender offer or exchange for the debt securities of such series).

We and the applicable trustee may make modifications and amendments of an indenture without the consent of any holder of debt securities for any of the following purposes:

- · to cure any ambiguity, defect, or inconsistency in the applicable indenture or in the Securities of any series;
- to comply with the covenant described above under "—Merger, Consolidation or Sale of Assets;"
- · to provide for uncertificated debt securities in addition to or in place of certificated debt securities;
- to add events of default for the benefit of the holders of all or any series of debt securities;
- to add the covenants, restrictions, conditions or provisions relating to us for the benefit of the holders of all or any series of debt securities (and if such covenants, restrictions, conditions or provisions are to be for the benefit of less than all series of debt securities, stating that such covenants, restrictions, conditions or provisions are expressly being included solely for the benefit of such series), to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default, or to surrender any right or power in the applicable indenture conferred upon us;
- to add to, delete from, or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication, and delivery of debt securities, as set forth in the applicable indenture;
- to make any change that does not adversely affect the rights of any holder of notes under the applicable indenture in any material respect;
- to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided in the applicable indenture, to establish the form of any certifications required tobe furnished pursuant to the terms of the applicable indenture or any series of debt securities under the applicable indenture, or to add to the rights of the holders of any series of debt securities;
- to evidence and provide for the acceptance of appointment under the applicable indenture by a successor trustee or to appoint a separate trustee with respect to any series;
- to comply with any requirements of the SEC or any successor in connection with the qualification of the indenture under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act; or
- to conform the applicable indenture to this "—Description of Debt Securities" or any other similarly titled section in any prospectus supplement or other offering document relating to a series of debt securities.

Subordination

Payment by us of the principal of, premium, if any, and interest on any series of subordinated debt securities issued under the subordinated indenture will be subordinated to the extent set forth in an indenture supplemental to the subordinated indenture relating to such series.

Discharge, Defeasance and Covenant Defeasance

Unless otherwise provided in the applicable prospectus supplement, the indentures allow us to discharge our obligations to holders of any series of debt securities issued under any indenture when:

- either (i) all securities of such series have already been delivered to the applicable trustee for cancellation; or (ii) all securities of such series have not already been delivered to the applicable trustee for cancellation but (a) have become due and payable, (b) will become due and payable within one year, or (c) if redeemable at our option, are to be redeemed within one year, and we have irrevocably deposited with the applicable trustee, in trust, funds in such currency or currencies, or governmental obligations in an amount sufficient to pay the entire indebtedness on such debt securities in respect of principal and any premium, and interest to the date of such deposit if such debt securities have become due and payable or, if they have not, to the stated maturity or redemption date; and
- we have paid or caused to be paid all other sums payable.

Unless otherwise provided in the applicable prospectus supplement, the indentures provide that, upon our irrevocable deposit with the applicable trustee, in trust, of an amount, in such currency or currencies in which such debt securities are payable at stated maturity, or government obligations, or both, applicable to such debt securities, which through the scheduled payment of principal and interest in accordance with their terms will provide money in an amount sufficient to pay the principal of, and any premium or make-whole amount, and interest on, such debt securities, and any mandatory sinking fund or analogous payments thereon, on the scheduled due dates therefor, the issuing company shall be released from its obligations with respect to such debt securities under the applicable indenture or, if provided in the applicable prospectus supplement, its obligations with respect to any other covenant, and any omission to comply with such obligations shall not constitute an event of default with respect to such debt securities.

The applicable prospectus supplement may further describe the provisions, if any, permitting such defeasance or covenant defeasance, including any modifications to the provisions described above, with respect to the debt securities of or within a particular series.

Conversion Rights

The terms and conditions, if any, upon which the debt securities are convertible into common stock or other securities of ours will be set forth in the applicable prospectus supplement. The terms will include whether the debt securities are convertible into shares of common stock or other securities of ours, the conversion price, or manner of calculation thereof, the conversion period, provisions as to whether conversion will be at the issuing company's option or the option of the holders, the events requiring an adjustment of the conversion price and provisions affecting conversion in the event of the redemption of the debt securities and any restrictions on conversion.

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements, summarizes the material terms and provisions of the warrants that we may offer under this prospectus and the related warrant agreements and warrant certificates. While the terms summarized below will apply generally to any warrants that we may offer, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. If we indicate in the prospectus supplement, the terms of any warrants offered under that prospectus supplement may differ from the terms described below. Specific warrant agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement, which includes this prospectus.

General

We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from these securities.

We will evidence each series of warrants by warrant certificates that we will issue under a separate warrant agreement. We will enter into the warrant agreement with a warrant agent. We will indicate the name and address of the warrant agent in the applicable prospectus supplement relating to a particular series of warrants.

We will describe in the applicable prospectus supplement the terms of the series of warrants, including:

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreement and the warrants;
- the terms of any rights to redeem or call the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the periods during which, and places at which, the warrants are exercisable;
- the manner of exercise;
- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrant agreement and warrants may be modified;
- federal income tax consequences of holding or exercising the warrants;
- the terms of the securities issuable upon exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

DESCRIPTION OF UNITS

We may issue units comprised of shares of common stock, shares of preferred stock, debt securities and warrants in any combination. We may issue units in such amounts and in as many distinct series as we wish. This section outlines certain provisions of the units that we may issue. If we issue units, they will be issued under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. The information described in this section may not be complete in all respects and is qualified entirely by reference to the unit agreement with respect to the units of any particular series. The specific terms of any series of units offered will be described in the applicable prospectus supplement. If so described in a particular prospectus supplement, the specific terms of any series of units may differ from the general description of terms presented below. We urge you to read any prospectus supplement related to any series of units we may offer, as well as the complete unit agreement and unit certificate that contain the terms of the units. If we issue units, forms of unit agreements and unit certificates relating to such units will be incorporated by reference as exhibits to the registration statement, which includes this prospectus.

Each unit that we may issue will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date. The applicable prospectus supplement may describe:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions of the governing unit agreement;
- the price or prices at which such units will be issued;
- the applicable United States federal income tax considerations relating to the units;
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units; and
- any other terms of the units and of the securities comprising the units.

The provisions described in this section, as well as those described under "Description of Capital Stock," "Description of Debt Securities" and "Description of Warrants" will apply to the securities included in each unit, to the extent relevant and as may be updated in any prospectus supplements.

Issuance in Series

We may issue units in such amounts and in as many distinct series as we wish. This section summarizes terms of the units that apply generally to all series. Most of the financial and other specific terms of a particular series of units will be described in the applicable prospectus supplement.

Unit Agreements

We will issue the units under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. We may add, replace or terminate unit agents from time to time. We will identify the unit agreement under which each series of units will be issued and the unit agent under that agreement in the applicable prospectus supplement.

The following provisions will generally apply to all unit agreements unless otherwise stated in the applicable prospectus supplement:

Modification without Consent

We and the applicable unit agent may amend any unit or unit agreement without the consent of any holder:

- to cure any ambiguity, including modifying any provisions of the governing unit agreement that differ from those described below;
- to correct or supplement any defective or inconsistent provision; or
- to make any other change that we believe is necessary or desirable and will not adversely affect the interests of the affected holders in any material respect.

We do not need any approval to make changes that affect only units to be issued after the changes take effect. We may also make changes that do not adversely affect a particular unit in any material respect, even if they adversely affect other units in a material respect. In those cases, we do not need to obtain the approval of the holder of the unaffected unit; we need only obtain any required approvals from the holders of the affected units.

Modification with Consent

We may not amend any particular unit or a unit agreement with respect to any particular unit unless we obtain the consent of the holder of that unit, if the amendment would:

- impair any right of the holder to exercise or enforce any right under a security included in the unit if the terms of that security require the consent of the holder to any changes that would impair the exercise or enforcement of that right; or
- reduce the percentage of outstanding units or any series or class the consent of whose holders is required to amend that series or class, or the applicable unit agreement with respect to that series or class, as described below.

Any other change to a particular unit agreement and the units issued under that agreement would require the following approval:

- If the change affects only the units of a particular series issued under that agreement, the change must be approved by the holders of a majority of the outstanding units of that series; or
- If the change affects the units of more than one series issued under that agreement, it must be approved by the holders of a majority of all
 outstanding units of all series affected by the change, with the units of all the affected series voting together as one class for this purpose.

These provisions regarding changes with majority approval also apply to changes affecting any securities issued under a unit agreement, as the governing document.

In each case, the required approval must be given by written consent.

Unit Agreements Will Not Be Qualified under Trust Indenture Act

No unit agreement will be qualified as an indenture, and no unit agent will be required to qualify as a trustee, under the Trust Indenture Act. Therefore, holders of units issued under unit agreements will not have the protections of the Trust Indenture Act with respect to their units.

Mergers and Similar Transactions Permitted; No Restrictive Covenants or Events of Default

The unit agreements will not restrict our ability to merge or consolidate with, or sell our assets to, another corporation or other entity or to engage in any other transactions. If at any time we merge or consolidate with, or sell our assets substantially as an entirety to, another corporation or other entity, the successor entity will succeed to and assume our obligations under the unit agreements. We will then be relieved of any further obligation under these agreements.

The unit agreements will not include any restrictions on our ability to put liens on our assets, nor will they restrict our ability to sell our assets. The unit agreements also will not provide for any events of default or remedies upon the occurrence of any events of default.

Governing Law

The unit agreements and the units will be governed by Delaware law.

Form, Exchange and Transfer

We will issue each unit in global—i.e., book-entry—form only. Units in book-entry form will be represented by a global security registered in the name of a depositary, which will be the holder of all the units represented by the global security. Those who own beneficial interests in a unit will do so through participants in the depositary's system, and the rights of these indirect owners will be governed solely by the applicable procedures of the depositary and its participants. We will describe book-entry securities, and other terms regarding the issuance and registration of the units in the applicable prospectus supplement.

Each unit and all securities comprising the unit will be issued in the same form.

If we issue any units in registered, non-global form, the following will apply to them. The units will be issued in the denominations stated in the applicable prospectus supplement. Holders may exchange their units for units of smaller denominations or combined into fewer units of larger denominations, as long as the total amount is not changed.

- Holders may exchange or transfer their units at the office of the unit agent. Holders may also replace lost, stolen, destroyed or mutilated units at that office. We may appoint another entity to perform these functions or perform them ourselves.
- Holders will not be required to pay a service charge to transfer or exchange their units, but they may be required to pay for any tax or other
 governmental charge associated with the transfer or exchange. The transfer or exchange, and any replacement, will be made only if our transfer
 agent is satisfied with the holder's proof of legal ownership. The transfer agent may also require an indemnity before replacing any units.
- If we have the right to redeem, accelerate or settle any units before their maturity, and we exercise our right as to less than all those units or other securities, we may block the exchange or transfer of those units during the period beginning 15 days before the day we mail the notice of exercise and ending on the day of that mailing, in order to freeze the list of holders to prepare the mailing. We may also refuse to register transfers of or exchange any unit selected for early settlement, except that we will continue to permit transfers and exchanges of the unsettled portion of any unit being partially settled. We may also block the transfer or exchange of any unit in this manner if the unit includes securities that are or may be selected for early settlement.

Only the depositary will be entitled to transfer or exchange a unit in global form, since it will be the sole holder of the unit.

Payments and Notices

In making payments and giving notices with respect to our units, we will follow the procedures as described in the applicable prospectus supplement.

PLAN OF DISTRIBUTION

We may sell securities:

- through underwriters;
- through dealers;
- · through agents;
- · directly to purchasers; or
- through a combination of any of these methods or any other method permitted by law.

In addition, we may issue the securities as a dividend or distribution or in a subscription rights offering to our existing security holders.

We may directly solicit offers to purchase securities, or agents may be designated to solicit such offers. In the prospectus supplement relating to such offering, we will name any agent that could be viewed as an underwriter under the Securities Act and describe any commissions that we must pay to any such agent. Any such agent will be acting on a best efforts basis for the period of its appointment or, if indicated in the applicable prospectus supplement, on a firm commitment basis. This prospectus may be used in connection with any offering of our securities through any of these methods or other methods described in the applicable prospectus supplement.

The distribution of the securities may be effected from time to time in one or more transactions:

- at a fixed price, or prices, which may be changed from time to time;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions.

The prospectus supplement with respect to the securities of a particular series will describe the terms of the offering of the securities, including the following:

- the name of the agent or any underwriters;
- · the public offering or purchase price;
- any discounts and commissions to be allowed or paid to the agent or underwriters;
- all other items constituting underwriting compensation;
- any discounts and commissions to be allowed or paid to dealers; and
- any exchanges on which the securities will be listed.

If any underwriters or agents are used in the sale of the securities in respect of which this prospectus is delivered, we will enter into an underwriting agreement, sales agreement or other agreement with them at the time of sale to them, and we will set forth in the prospectus supplement relating to such offering the names of the underwriters or agents and the terms of the related agreement with them.

In connection with the offering of securities, we may grant to the underwriters an option to purchase additional securities with an additional underwriting commission, as may be set forth in the accompanying prospectus supplement. If we grant any such option, the terms of such option will be set forth in the prospectus supplement for such securities.

If a dealer is used in the sale of the securities in respect of which the prospectus is delivered, we will sell such securities to the dealer, as principal. The dealer, who may be deemed to be an "underwriter" as that term is defined in the Securities Act, may then resell such securities to the public at varying prices to be determined by such dealer at the time of resale.

If we offer securities in a subscription rights offering to our existing security holders, we may enter into a standby underwriting agreement with dealers, acting as standby underwriters. We may pay the standby underwriters a commitment fee for the securities they commit to purchase on a standby basis. If we do not enter into a standby underwriting arrangement, we may retain a dealer-manager to manage a subscription rights offering for us. Agents, underwriters, dealers and other persons may be entitled under agreements which they may enter into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not beless nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and
- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Offered securities may also be offered and sold, if so indicated in the prospectus supplement, in connection with a remarketing upon their purchase, in accordance with a redemption or repayment pursuant to their terms, or otherwise, by one or more remarketing firms, acting as principals for their own accounts or as agents for us. Any remarketing firm will be identified and the terms of its agreement, if any, with us and its compensation will be described in the applicable prospectus supplement. Remarketing firms may be deemed to be underwriters in connection with their remarketing of offered securities.

Certain agents, underwriters and dealers, and their associates and affiliates, may be customers of, have borrowing relationships with, engage in other transactions with, or perform services, including investment banking services, for us or one or more of our respective affiliates in the ordinary course of business.

In order to facilitate the offering of the securities, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities or any other securities the prices of which may be used to determine payments on such securities. Specifically, any underwriters may overallot in connection with the offering, creating a short position for their own accounts. In addition, to cover overallotments or to stabilize the price of the securities or of any such other securities, the underwriters may bid for, and purchase, the securities orany such other securities in the open market. Finally, in any offering of the securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the securities above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities at any time.

We may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act. In addition, we may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement so indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be named in the applicable prospectus supplement (or a post- effective amendment). In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus and an applicable prospectus supplement. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

Under Rule 15c6-1 of the Exchange Act, trades in the secondary market generally are required to settle in two business days, unless the parties to any such trade expressly agree otherwise. The applicable prospectus supplement may provide that the original issue date for your securities may be more than two scheduled business days after the trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the second business day before the original issue date for your securities, you will be required, by virtue of the fact that your securities initially are expected to settle in more than two scheduled business days after the trade date for your securities, to make alternative settlement arrangements to prevent a failed settlement. The securities may be new issues of securities and may have no established trading market. The securities may or may not be listed on a national securities exchange. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

The specific terms of any lock-up provisions in respect of any given offering will be described in the applicable prospectus supplement.

The underwriters, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business for which they receive compensation.

The anticipated date of delivery of offered securities will be set forth in the applicable prospectus supplement relating to each offer.

LEGAL MATTERS

Certain legal matters in connection with this offering will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts. Any underwriters will also be advised about the validity of the securities and other legal matters by their own counsel, which will be named in the prospectus supplement.

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. We are subject to the information requirements of the Exchange Act and, in accordance therewith, file annual, quarterly and current reports, proxy statements and other information with the SEC. These documents also may be accessed through the SEC's electronic data gathering, analysis and retrieval system, or EDGAR, via electronic means, including the SEC's home page on the Internet (www.sec.gov). We also maintain a website at www.relaytx.com. The information contained in or accessible from our website is not incorporated into this prospectus, and you should not consider it part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

We have the authority to designate and issue more than one class or series of stock having various preferences, conversion and other rights, voting powers, restrictions, limitations as to dividends, qualifications, and terms and conditions of redemption. See "Description of Capital Stock." We will furnish a full statement of the relative rights and preferences of each class or series of our stock which has been so designated and any restrictions on the ownership or transfer of our stock to any stockholder upon request and without charge. Written requests for such copies should be directed to Relay Therapeutics, Inc., 399 Binney Street, 2nd Floor, Cambridge, Massachusetts 02139, telephone: (617) 370-8837. Information contained on our website is not incorporated by reference into this prospectus and you should not consider any information on, or that can be accessed from, our website as part of this prospectus or any accompanying prospectus supplement.

INCORPORATION 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 (SEC File No. 001-39385), 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 until we sell all of the securities:

- Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on March 25,2021;
- The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2020 from our definitive <u>proxy statement</u> on Schedule 14A (other than information furnished rather than filed), which was filed with the SEC on April 7, 2021:
- Quarterly Reports on Form 10-Q filed with the SEC for the quarters ended March 31, 2021 and June 30, 2021, filed with the SEC on <u>May 13</u>, 2021 and <u>August 12, 2021</u>, respectively;
- Current Reports on Form 8-K filed with the SEC on <u>April 16, 2021</u>, <u>May 19, 2021</u> and <u>May 27, 2021</u>; and
- The description of our common stock contained in our Registration Statement on <u>Form 8-A</u> (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 <u>Exhibit 4.3</u> to our Annual Report on Form 10-K for the year ended December 31, 2020, as filed with the SEC on March 25, 2021.

Upon request, we will provide, without charge, to each person, including any beneficial owner, to whom a copy of this prospectus is delivered, a copy of the documents incorporated by reference into this prospectus but not delivered with the prospectus. You may request a copy of these filings, and any exhibits we have specifically incorporated by reference as an exhibit in this prospectus, at no cost by writing or telephoning us at the following address: Relay Therapeutics, Inc., 399 Binney Street, 2nd Floor, Cambridge, Massachusetts 02139, telephone: (617) 370-8837.

You may also access these documents, free of charge on the SEC's website at www.relaytx.com. Information contained on our website is not incorporated by reference into this prospectus, and you should not consider any information on, or that can be accessed from, our website as part of this prospectus or any accompanying prospectus supplement.

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.

This prospectus is part of a registration statement we filed with the SEC. We have incorporated exhibits into this registration statement. You should read the exhibits carefully for provisions that may be important to you.

You should rely only on the information incorporated by reference or provided in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus or in the documents incorporated by reference is accurate as of any date other than the date on the front of this prospectus or those documents.

13,207,547 Shares

Relay Therapeutics, Inc.

Common Stock



PROSPECTUS SUPPLEMENT

Goldman Sachs & Co. LLC

J.P. Morgan

Cowen

Guggenheim Securities