Use these links to rapidly review the document
Prospectus Supplement
TABLE OF CONTENTS

Table of Contents

Filed pursuant to Rule 424(b)(5)
Registration No. 333-253749

Calculation of Registration Fee

Title of Each Class of Securities To Be Registered	Maximum Aggregate Offering Price	Amount of Registration Fee(1)(2)
Ordinary Shares, par value €0.05 per share	$200,000,000	$2,350

(1) The registration fee is calculated in accordance with Rule 457(o) under the Securities Act of 1933, as amended (the "Securities Act"), based on the proposed maximum aggregate offering price, and Rule 457(r) under the Securities Act. In accordance with Rules 456(b) and 457(r) under the Securities Act, the registrant initially deferred payment of all of the registration fee for Registration Statement No. 333-253749, except with respect to unsold securities that have been previously registered.

(2) Pursuant to Rule 457(p) under the Securities Act, the registrant is offsetting the registration fee due under this prospectus supplement of $21,820 by the remaining unused registration fee of $19,470 previously paid by the registrant with respect to unsold securities registered on the registrant's registration statement on Form S-3 (No. 333-225636) filed with the SEC on June 14, 2018 and offered by means of a prospectus supplement dated March 2, 2020.

PROSPECTUS SUPPLEMENT
(To Prospectus dated March 1, 2021)

Up to $200,000,000

uniQure

Ordinary Shares

We have entered into a sales agreement with SVB Leerink LLC, or SVB Leerink, dated March 1, 2021, relating to the sale of our ordinary shares, nominal value €0.05 per share, offered by this prospectus supplement. In accordance with the terms of the sales agreement, under this prospectus supplement we may offer our ordinary shares having an aggregate offering price of up to $200,000,000 from time to time through SVB Leerink, acting as our agent.

Sales of our ordinary shares, if any, under this prospectus supplement and the accompanying base prospectus will be made in sales deemed to be "at-the-market offerings" as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, or the Securities Act. SVB Leerink is not required to sell any specific amount of securities, but will act as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices, on mutually agreed terms between SVB Leerink and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

The compensation to SVB Leerink for sales of ordinary shares sold on our behalf pursuant to the sales agreement will be an amount equal to 3% of the gross proceeds from the sales of ordinary shares sold under the sales agreement. See "Plan of Distribution" beginning on page S-24 for additional information regarding the compensation to be paid to SVB Leerink. In connection with the sale of the ordinary shares on our behalf, SVB Leerink will be deemed to be an "underwriter" within the meaning of the Securities Act, and the compensation paid to SVB Leerink will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to SVB Leerink with respect to certain liabilities, including liabilities under the Securities Act or the Exchange Act of 1934, as amended, or the Exchange Act.

Our ordinary shares are listed on The Nasdaq Global Select Market under the symbol "QURE". On February 26, 2021 the last reported sale price of our ordinary shares on The Nasdaq Global Select Market was $36.70 per share.

Investing in our ordinary shares involves a high degree of risk. See "Risk Factors" on page S-9 of this prospectus supplement and the risk factors contained or incorporated by reference in this prospectus supplement and the accompanying prospectus.

Neither the Securities and Exchange Commission nor any state securities commission 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.

SVB Leerink

This date of this prospectus supplement is March 1, 2021

Prospectus Supplement

Prospectus

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus relate to an offering of our ordinary shares. Before buying any of the ordinary shares that we are offering, we urge you to carefully read this prospectus supplement and the accompanying prospectus, together with the information incorporated by reference as described under the headings "Where You Can Find Additional Information" and "Incorporation of Certain Information by Reference" in this prospectus supplement. These documents contain important information that you should consider when making your investment decision.

Unless otherwise specified or required by context, references in this prospectus supplement to "uniQure", "we", "us" and "our" refer to uniQure N.V., a public company with limited liability (*naamloze vennootschap*) under the laws of the Netherlands, together with its subsidiaries.

This document contains two parts. The first part is this prospectus supplement, which describes the terms of this offering of ordinary shares and also adds to, updates and changes information contained in the accompanying prospectus and the documents incorporated by reference. The second part is the accompanying prospectus, which gives more general information. To the extent the information contained in this prospectus supplement differs from or conflicts with the information contained in the accompanying prospectus or any document incorporated by reference, the information in this prospectus supplement will control. 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 into the accompanying prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

We are responsible for the information contained in or incorporated by reference in this prospectus supplement and the accompanying prospectus and in any free writing prospectus we prepare or authorize. We have not, and SVB Leerink has not, authorized anyone to provide you with information different from that which is contained in or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we have authorized for use in connection with this offering **and we take no responsibility for any other information others may give you. We are not, and SVB Leerink is not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted.** You should assume that the information contained in this prospectus supplement is accurate as of the date on the front cover of this prospectus supplement only and that any information we have incorporated by reference or included in the accompanying prospectus is accurate only as of the date given in the document incorporated by reference or as of the date of the prospectus, as applicable, regardless of the time of delivery of this prospectus supplement, the accompanying prospectus, any related free writing prospectus, or any sale of our ordinary shares. Our business, financial condition, results of operations and prospects may have changed since that date.

For investors outside the United States: neither we nor SVB Leerink have done anything that would permit this offering or possession or distribution of this prospectus supplement or the accompanying prospectus in any jurisdiction where action for that purpose is required, other than in the United States. You are required to inform yourselves about, and to observe any restrictions relating to, this offering and the distribution of this prospectus supplement and the accompanying prospectus.

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 into 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 or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

This prospectus supplement, the accompanying prospectus and the information incorporated herein and therein by reference include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus supplement and the accompanying prospectus are the property of their respective owners.

Information contained on, or that can be accessed through, our website does not constitute part of this prospectus supplement, the accompanying prospectus or any related free writing prospectus.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary does not contain all the information you should consider before investing in our ordinary shares. You should read and consider carefully the more detailed information in this prospectus supplement and the accompanying prospectus, including the factors described under the heading "Risk Factors" in this prospectus supplement and the financial and other information incorporated by reference in this prospectus supplement and the accompanying prospectus, as well as the information included in any free writing prospectus that we have authorized for use in connection with this offering, before making an investment decision.

Overview

General

We are a leader in the field of gene therapy, seeking to develop single treatments with potentially curative results for patients suffering from genetic and other devastating diseases. We are advancing a focused pipeline of innovative gene therapies, including product candidates for the treatment of hemophilia B, which we intend to license to CSL Behring pursuant to the CSL Behring Agreement described below, and Huntington's disease. We believe our validated technology platform and manufacturing capabilities provide us distinct competitive advantages, including the potential to reduce development risk, cost, and time to market. We produce our Adeno-associated virus, or AAV,-based gene therapies in our own facilities with a proprietary, commercial-scale, current good manufacturing practices, or cGMP,-compliant, manufacturing process. We believe our Lexington, Massachusetts-based facility is one of the world's most versatile gene therapy manufacturing facilities.

Key events

CSL Behring commercialization and license agreement

On June 24, 2020, uniQure biopharma B.V., a wholly-owned subsidiary of uniQure N.V., entered into a commercialization and license agreement, or the CSL Behring Agreement, with CSL Behring LLC, or CSL Behring, pursuant to which CSL Behring will receive exclusive global rights to etranacogene dezaparvovec, our investigational gene therapy for patients with hemophilia B which we refer to herein as Product.

Under the terms of the CSL Behring Agreement, we will receive a $450.0 million upfront cash payment upon the closing of the transactions contemplated by the CSL Behring Agreement and we will be eligible to receive up to $1.6 billion in additional payments based on the achievement of regulatory and commercial milestones. The CSL Behring agreement also provides that we will be eligible to receive tiered double-digit royalties in a range of up to a low-twenties percent of net sales of the Product based on sales thresholds.

Pursuant to the CSL Behring Agreement, we will be responsible for the completion of our Phase III HOPE-B pivotal trial of etranacogene dezaparvovec, or the HOPE-B trial, manufacturing process validation, and the manufacturing supply of the Product until such time that these capabilities may be transferred to CSL Behring or its designated contract manufacturing organization. Concurrently with the execution of the CSL Behring Agreement, we and CSL Behring entered into a development and commercial supply agreement, pursuant to which, among other things, we will supply the Product to CSL Behring at an agreed-upon price. Clinical development and regulatory activities performed by us pursuant to the CSL Behring Agreement will be reimbursed by CSL Behring. CSL Behring will be responsible for global regulatory submissions and commercialization requirements for the Product.

Other than under the CSL Behring Agreement, neither we nor CSL Behring may perform any clinical trials, with the exception of trials required to extend the label or gain marketing authorization

outside the United States or the European Union, for any gene therapy product, gene-editing product, or any other product comprising an AAV vector to conduct nucleotide transfer (including deoxyribonucelic acid, or DNA, and ribonucleic acid, or RNA) for the treatment, prevention, or cure of hemophilia B for a period commencing on June 24, 2020 and continuing for a period of four years following the first commercial sale of the Product in the United States, and neither we nor CSL Behring may commercialize such a product for a period commencing as of June 24, 2020 and continuing for a period of seven years following the first commercial sale of the Product in the United States. This exclusivity commitment would not bind any party that acquirers us and that owns or controls such a product so long as certain precautions are followed to ensure that CSL Behring's confidential information and our proprietary technology related to the Product are not used or accessed by personnel of such acquirer who are developing or commercializing such competing product.

Unless earlier terminated as described below, the CSL Behring Agreement will continue on a country-by-country basis until expiration of the royalty term in a country. The royalty term expires in a country on the later of (a) 15 years after the first commercial sale of the Product in such country, (b) expiration of regulatory exclusivity for the Product in such country and (c) expiration of all valid claims of specific licensed patents covering the Product in such country. Either we or CSL Behring may terminate the CSL Behring Agreement for the other party's material breach if such breach is not cured within a specified cure period. In addition, if CSL Behring fails to commercialize the Product in any of a group of major countries for an extended period of time following the first regulatory approval of the Product in any of such group of countries (other than due to certain specified reasons) and such failure has not been cured within a specified cure period, then we may terminate the CSL Behring Agreement. CSL Behring may also terminate the CSL Behring Agreement for convenience.

The effectiveness of the transactions contemplated by the CSL Behring Agreement is contingent on completion of review under antitrust laws in the United States, Australia, and the United Kingdom, and certain provisions of the CSL Behring Agreement will not become effective until after we receive all such regulatory approvals.

On November 11, 2020, the Australian Competition and Consumer Commission, or the ACCC, determined, pursuant to section 50 of the Competition and Consumer Act 2010 of Australia, that it will not intervene in the CSL Behring Agreement. Thus, the ACCC has completed its review of the CSL Behring Agreement, and the transactions contemplated by the CSL Behring Agreement may close from the perspective of the Australian competition authority.

On November 24, 2020, the Competition and Markets Authority in the United Kingdom, or the CMA, adopted a decision not to refer the CSL Behring Agreement for proceedings under section 33 of the Enterprise Act 2002 of the United Kingdom. The decision was made public by the CMA on January 6, 2021. Thus, the CMA has completed its review of the CSL Behring Agreement, and the transactions contemplated by the CSL Behring Agreement may close from the perspective of the United Kingdom competition authority.

On December 3, 2020, we and CSL Behring filed a premerger notification and report form under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, or the HSR Act. On January 4, 2021, the United States Federal Trade Commission, or the FTC, issued to us a request for additional information and documentary material, or a Second Request, under the HSR Act. The FTC similarly issued a Second Request to CSL Behring also with respect to the antitrust review of the CSL Behring Agreement. The effect of the Second Request is to extend the waiting period imposed under the HSR Act until 30 days after all parties to the CSL Behring Agreement have substantially complied with the requests unless the waiting period is terminated earlier by the FTC or voluntarily extended by the parties. We do not believe that the FTC will determine that the consummation of the transaction contemplated by the CSL Behring Agreement will result in a violation of the HSR Act. However, there can be no assurance as to the outcome of the Second Request.

Closing of the transaction contemplated by the CSL Behring Agreement is expected to materially impact our profitability and cash flows. Receipt of the $450.0 million payment due on closing would extend the funding of our operations into the second half of 2024 (assuming a full repayment of funds borrowed from Hercules Capital Inc., or Hercules, under our term loan facility by 2023). However, we expect to continue to incur losses and to generate negative cash flows beyond the fiscal year in which we would close the transaction.

Hemophilia B program—Etranacogene dezaparvovec (AMT-061)

Etranacogene dezaparvovec is our lead gene therapy candidate and includes an AAV serotype 5, which we collectively refer to as AAV-5, vector incorporating the functional human Factor IX, or FIX, Padua variant. We are currently conducting a pivotal study in patients with severe and moderately-severe hemophilia B.

In August 2018, we initiated a Phase IIb dose-confirmation study of etranacogene dezaparvovec and in September 2018, we completed the dosing for that study. In February, May, July, and December 2019, and in December 2020, we presented updated data from the Phase IIb dose-confirmation study of etranacogene dezaparvovec. The most recent data that we announced from the Phase IIb study of etranacogene dezaparvovec show that all three patients experienced increasing and sustained FIX levels after a one-time administration of etranacogene dezaparvovec. Mean FIX activity was 44.2% of normal two years after administration, exceeding threshold FIX levels generally considered sufficient to significantly reduce the risk of bleeding events. The first patient achieved FIX activity of 44.7% of normal, the second patient was 51.6% of normal and the third patient was 36.3% of normal. The second and third patients had previously screen-failed and were excluded from another gene therapy study due to pre-existing neutralizing antibodies to a different AAV vector. At two years after dosing, two of the three participants remain free from bleeds and use of FIX replacement therapy. A single bleed has been reported in one participant, who has used a total of two FIX infusions (excluding surgery). All patients have remained free of prophylaxis in the two years since receiving etranacogene dezaparvovec.

In June 2018, we initiated the six-month lead-in period of our HOPE-B trial. The HOPE-B trial is a multinational, multi-center, open-label, single-arm study to evaluate the safety and efficacy of etranacogene dezaparvovec. After the six-month lead-in period, patients received a single intravenous administration of etranacogene dezaparvovec. Patients enrolled in the HOPE-B trial were tested for the presence of pre-existing neutralizing antibodies to AAV-5 but not excluded from the trial based on their titers.

The primary endpoints of the study are based on the FIX activity level achieved following the administration of etranacogene dezaparvovec after 26 weeks and 52 weeks after dosing as well as annualized bleed rates during the 52 weeks after dosing.

In March 2020, we completed dosing of the 54 patients in the HOPE-B trial. The targeted number of patients to be dosed per the clinical trial protocol was 50. As set forth below, we have implemented and continue to implement various measures to allow us to closely monitor the trial within the guidance provided by the U.S. Food and Drug Administration, or the FDA, regarding the impact of the COVID-19 coronavirus pandemic to minimize any risk or disruption in patient follow-up visits.

In December 2020, we announced top-line data from the HOPE-B trial. The 26-week follow-up date from the trial showed that FIX activity in the 54 patients increased after dosing from £ 2% to a mean of 37.2% at 26 weeks, meeting a first primary endpoint of the HOPE-B trial. No correlation between pre-existing neutralizing antibodies and FIX activity was found in patients with neutralizing antibody titers up to 678.2, a range expected to include more than 95% of the general population; one patient with a neutralizing antibody titer of 3,212.3 did not show an increase in FIX activity. Less than 1% of the general population is expected to have neutralizing antibody titers of greater than 3,000.

During the 26-week period after dosing, 15 patients (28%) reported a total of 21 bleeding events, representing a reduction of 83% compared to the 123 bleeding events reported by 38 patients (70%) during the observational lead-in phase of the trial. Total bleeds include any bleeding event reported after the treatment of etranacogene dezaparvovec, including spontaneous, traumatic, and those associated with unrelated medical procedures, whether or not FIX treatment was required. Of the total bleeding events reported during the 26-week period after dosing, only three were classified as spontaneous bleeds requiring treatment, representing a reduction of 92% compared to the 37 such bleeding events reported during the observational lead-in phase. Mean annualized usage of FIX replacement therapy, a secondary endpoint in the clinical trial, declined by 96% during the 26-week period after dosing compared to the observational lead-in phase. Etranacogene dezaparvovec was generally well-tolerated. As of the November 2020 cut-off date, most adverse events were classified as mild (81.5%). The most common events included transaminase elevation treated with steroids per protocol (9 patients; 17%), infusion-related reactions (7 patients; 13%), headache (7 patients; 13%) and influenza-like symptoms (7 patients; 13%). Liver enzyme elevations resolved with a tapering course of corticosteroids and FIX activity remained in the mild range in the steroid treated patients. No relationship between safety and neutralizing antibody titers was observed. Based on interactions with the FDA and the European Medicines Agency, or the EMA, we plan to incorporate FIX activity and bleeding rates at 52 weeks as additional co-primary endpoints in the study.

On December 21, 2020, our clinical trials of etranacogene dezaparvovec, including our HOPE-B trial, were placed on clinical hold by the FDA. The clinical hold was initiated following the submission of a safety report in mid-December 2020 relating to a possibly related serious adverse event associated with a preliminary diagnosis of hepatocellular carcinoma, or HCC, a form of liver cancer, in one patient in the HOPE-B trial that was treated with etranacogene dezaparvovec in October 2019. The patient has multiple risk factors associated with HCC, including a twenty-five-year history of hepatitis C, hepatitis B virus, evidence of non-alcoholic fatty liver disease and advanced age. Chronic infections with hepatitis B and C have been associated with approximately 80% of HCC cases.

The liver lesion was detected during a routine abdominal ultrasound conducted as part of the required study assessments in patients at one-year post dosing. A surgical resection of the lesion has occurred, and an analysis of the tissue samples was initiated in early 2021. On February 19, 2021, we reported initial results from this analysis to the FDA in accordance with pharmacovigilance requirements. We are gathering final data from these molecular analyses and will be preparing a detailed response to the FDA's clinical hold questions regarding this event. currently, we do not have adequate data to determine a possible causal relationship, especially in the context of the other known risk factors. We currently do not anticipate any impact on our regulatory submission timelines, including the filing of a BLA.

No other cases of HCC have been reported in our clinical trials conducted in more than 67 patients in hemophilia B, with some patients dosed more than 5 years ago.

Etranacogene dezaparvovec has been granted Breakthrough Therapy Designation by the FDA and access to the current priority medicines ("PRIME") initiative by the EMA.

Huntington's disease program (AMT-130)

AMT-130 is our novel gene therapy candidate for the treatment of Huntington's disease. AMT-130 utilizes our proprietary, gene-silencing miQURE platform and incorporates an AAV vector carrying an miRNA specifically designed to silence the huntingtin gene and the potentially highly toxic exon 1 protein fragment. AMT-130 has received orphan drug and Fast Track designations from the FDA and Orphan Medicinal Product Designation from the EMA.

In June 2020, we announced the completion of the first two patient procedures in the Phase I/II clinical trial of AMT-130 for the treatment of Huntington's disease. These procedures occurred after a

postponement that resulted from the COVID-19 pandemic and the associated states of emergency declarations in the United States. The Phase I/II protocol is a randomized, imitation surgery-controlled, double-blinded study conducted at three surgical sites, and multiple referring, non-surgical sites in the U.S. The primary objective of the study is to evaluate the safety, tolerability, and efficacy of AMT-130 at two doses.

On September 25, 2020, we announced that the independent Data Safety Monitoring Board, or the DSMB, overseeing the Phase I/II clinical trial of AMT-130 for the treatment of Huntington's disease had met and reviewed 90-day safety data from the first two patients enrolled in the trial. No significant safety concerns were noted to prevent further dosing.

On October 13, 2020, we announced the completion of the third and fourth patient procedures in the Phase I/II clinical trial.

On February 8, 2020, we announced that the DSMB had met and reviewed the six-month safety data from the first two enrolled patients and the 90-day safety data from the next two enrolled patients in the study. No significant safety concerns were noted to prevent further dosing, and the final six patients in the first cohort are now cleared for enrollment.

BMS collaboration

We and Bristol-Myers Squibb, or BMS, entered into a collaboration and license agreement in May 2015, or the BMS CLA. BMS had initially designated four Collaboration Targets in 2015 and in accordance with the terms of the BMS CLA could have designated a fifth to tenth Collaboration Target.

In February 2019, BMS requested a one-year extension of the initial research term. In April 2019, following an assessment of the progress of this collaboration and our expanding proprietary programs, we notified BMS that we did not intend to agree to an extension of the initial research term. Accordingly, the initial four-year research term under the collaboration terminated on May 21, 2019.

On December 1, 2020, we and BMS amended the BMS CLA, or the amended BMS CLA. Following the amendment BMS is no longer entitled to designate a fifth to tenth Collaboration Target and as such we are no longer entitled to receive an aggregate $16.5 million in target designation payments for research, development, and regulatory milestone payments related to the fifth and tenth Collaboration Targets. For a period of one-year from the effective date of the amended BMS CLA, BMS may replace up to two of the four active Collaboration Targets with two new targets in the field of cardiovascular disease. We continue to be entitled to receive up to $217.0 million for each of the four Collaboration Targets if defined milestones are achieved, as well as royalties on net sales associated with any Collaboration Target. On December 17, 2020, BMS designated one of the four Collaboration Targets as a candidate to advance into IND-enabling studies entitling us to receive a $4.4 million research milestone payment. We recorded the $4.4 million as License Revenue in the twelve months period ended December 31, 2020.

The amended BMS CLA does not extend the initial research term. BMS may place purchase orders to provide limited services primarily related to analytical and development efforts in respect of the four Collaboration Targets. BMS may request such services for a period not to exceed the earlier of (i) the completion of all activities under a Research Plan and (ii) either (A) three years after the last replacement target has been designated by BMS during the one-year replacement period following the amended BMS CLA effective date or (B) three years if no replacement targets are designated during this one-year period and BMS continues to reimburse us for these services.

For as long as any of the four Collaboration Targets are being advanced, BMS may place a purchase order to be supplied with research, clinical and commercial supplies. Subject to the terms of the amended BMS CLA, BMS has the right to terminate the research, clinical and commercial supply

relationships, and has certain remedies for failures of supply, up to and including technology transfer for any such failure that otherwise cannot be reasonably resolved. Both we and BMS may agree to a technology transfer of manufacturing capabilities pursuant to the terms of the amended BMS CLA.

We have agreed to certain restrictions on our ability to work independently of the collaboration, either directly or indirectly through any affiliate or third party, on certain programs that would be competitive with a Collaboration Target. We have agreed to indication exclusivity for the current four Collaboration Targets. BMS may add or change the exclusive indications in the process of replacing Collaboration Targets as described above. We can opt out of the indication exclusivity by giving up certain economic rights under the amended BMS CLA for each such indication that is affected by us opting out. If we opt out of an exclusive indication, we could pursue other targets for such indication other than a Collaboration Target.

The amended BMS CLA also terminated two warrants to increase BMS ownership in the Company up to 19.9% through purchasing a specific number of our ordinary shares following the designation of a seventh, and a tenth Collaboration Target, respectively. We and BMS agreed that upon the consummation of a change of control transaction of uniQure that occurs prior to the earlier of (i) December 1, 2026 and (ii) BMS' delivery of a target cessation notice for all four Collaboration Targets, uniQure (or its third party acquirer) shall pay to BMS a one-time, non-refundable, non-creditable cash payment of $70.0 million, provided that (x) if $70.0 million is greater than five percent of the net proceeds (as contractually defined) from such change of control transaction, the payment shall be an amount equal to five percent of such net proceeds, and (y) if $70.0 million is less than one percent of such net proceeds, the change of control payment shall be an amount equal to one percent of such net proceeds. We have not consummated any change of control transaction as of December 31, 2020 that would obligate us to make a payment to BMS.

The amended BMS CLA did not change any of the provisions of the Investor Agreement with BMS that we entered into in 2015. We have granted BMS certain registration rights that allow BMS to require us to register our securities beneficially held by BMS under the U.S. Securities Exchange Act of 1934, as amended, or the Exchange Act. BMS may make up to two such demands for us to register the shares, provided that we may deny such demand if (i) the market value of the shares to be registered is less than $10.0 million (provided however, if BMS holds less than $10.0 million worth of our shares, we must comply with their demand for registration), (ii) we certify to BMS that we plan to effect a registration within 120 days of their demand or we are engaged in a transaction that would be required to be disclosed in a registration statement and that is not reasonably practicable to be disclosed at that time, or (iii) we have already effected one registration statement within the twelve months preceding BMS's demand for registration. In addition, independent of their demand registration rights, upon the occurrence of certain events, we must also provide BMS the opportunity to include their ordinary shares in any registration statement that we effect.

We also continue to grant BMS certain information rights under the Investor Agreement, although these requirements may be satisfied by our public filings required by U.S. securities laws.

BMS also continues to be subject to a lock up pursuant to the Investor Agreement for as long as BMS holds more than 4.9% of our ordinary shares (as of December 31, 2020 BMS holds 5.3%). Without our prior consent, BMS may not sell or dispose any of its current ordinary shares.

The Investor Agreement also continues to require BMS to vote all of our ordinary shares it beneficially holds in favor of all items on the agenda for the relevant general meeting of shareholders of our company as proposed on behalf of our company, unless, in the context of a change of control or similar transaction, BMS has itself made an offer to our company or our board in connection with the transaction that is the subject of the vote, in which case it is free to vote its shares at its discretion. This voting provision will terminate upon the later of the date on which BMS no longer beneficially owns at least 4.9% of our outstanding ordinary shares, the closing of a transaction that provides BMS

exclusive and absolute discretion to vote our shares it beneficially holds, or the termination of the amended BMS CLA for breach by us.

Term loan facility

As of December 31, 2020, a $35.0 million term loan was outstanding in accordance with the Second Amended and Restated Loan and Security Agreement, or the 2018 Amended Facility, between us and Hercules.

On January 29, 2021 we and Hercules entered into amendments to the 2018 Amended Facility, or the 2021 Amended Facility. Pursuant to the 2021 Amended Facility, Hercules agreed to make additional term loans in the maximum aggregate amount of $100.0 million, or the 2021 Term Loan, increasing the aggregate principal amount of the term loan facility from $35.0 million to up to $135.0 million. On January 29, 2021 we drew down $35.0 million of the 2021 Term Loan. We may draw down the remaining $65.0 million under the 2021 Term Loan in a series of one or more advances of not less than $20.0 million each until December 15, 2021. Advances under the 2021 Term Loan bear interest at a rate equal to the greater of (i) 8.25% or (ii) 8.25% plus the prime rate, less 3.25% per annum. The principal balance and all accrued but unpaid interest on advances under the 2021 Term Loan is due on June 1, 2023, which such date may be extended by us by up to two twelve-month periods. Advances under the 2021 Term Loan may not be prepaid until six-months after the Closing Date, following which we may prepay all such advances without charge.

In addition to the 2021 Term Loan, the amendment also extends the interest only payment period of the previously funded $35.0 million term loan from January 1, 2022 to June l, 2023.

Corporate Information

uniQure B.V. was incorporated on January 9, 2012 as a private company with limited liability (*besloten vennootschap met beperkte aansprakelijkheid*) under the laws of the Netherlands. Our business was founded in 1998 and was initially operated through our predecessor company, Amsterdam Molecular Therapeutics (AMT) Holding N.V., or AMT. In 2012, AMT undertook a corporate reorganization, pursuant to which uniQure B.V. acquired the entire business and assets of AMT and completed a share-for-share exchange with the shareholders of AMT. Effective February 10, 2014, in connection with our initial public offering we converted into a public company with limited liability (*naamloze vennootschap*) and changed our legal name from uniQure B.V. to uniQure N.V.

Our company is registered in the trade register of the Dutch Chamber of Commerce (*Kamer van Koophandel*) under number 54385229. Our headquarters are in Amsterdam, the Netherlands, and our registered office is located at Paasheuvelweg 25a, Amsterdam 1105 BP, the Netherlands and our telephone number is +31.20.240.6000.

Our website address is www.uniqure.com. The information contained in, and that can be accessed through, our website is not incorporated into and does not form a part of this prospectus supplement, the accompanying prospectus or any of the documents incorporated by reference herein or therein.

The Offering

Ordinary Shares Offered by Us	Ordinary shares having an aggregate offering price of up to $200,000,000.
Manner of Offering	"At-the-market" offering that may be made from time to time through our sales agent, SVB Leerink LLC. See "Plan of Distribution".

Use of Proceeds	We intend to use the net proceeds from this offering to fund the further development of our product candidates and for general corporate purposes, which may include capital expenditures, working capital and general and administrative expenses. We may also use a portion of the net proceeds to acquire or invest in businesses that are complementary to our own, although we have no current plans, commitments or agreements with respect to any acquisitions as of the date of this prospectus supplement. See "Use of Proceeds".
Risk Factors	Investing in our ordinary shares involves a high degree of risk. See the information contained in or incorporated by reference under the heading "Risk Factors" in this prospectus supplement, in the accompanying prospectus and in the documents incorporated by reference into this prospectus supplement and any free writing prospectus that we have authorized for use in connection with this offering.
Nasdaq Global Select Market Symbol	"QURE"

RISK FACTORS

Investing in our ordinary shares involves a high degree of risk. Our business, prospects, financial condition or operating results could be materially adversely affected by the risks identified below, as well as other risks not currently known to us or that we currently consider immaterial. The trading price of our ordinary shares could decline due to any of these risks, and you may lose all or part of your investment. Before deciding whether to invest in our ordinary shares, you should consider carefully the risk factors discussed below and those contained in the section entitled "Risk Factors" contained in our Annual Report on Form 10-K for the year ended December 31, 2020, as filed with the Securities and Exchange Commission, or SEC, which is incorporated herein by reference in its entirety, as well as any amendment or update to our risk factors reflected in subsequent filings with the SEC.

Risks Related to this Offering

Management will have broad discretion as to the use of the proceeds from this offering, and may not use the proceeds effectively.

We have not designated the amount of net proceeds from this offering to be used for any particular purpose. Our management will have broad discretion as to the application of the net proceeds from this offering and could use them for purposes other than those contemplated at the time of the offering or in a manner that does not effectively maximize the potential of our clinical development programs and pipeline. Our management's use of the net proceeds may not increase the market value of our ordinary shares.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional ordinary shares or other securities convertible into or exchangeable for our ordinary shares at prices that may not be the same as the prices per share in this offering. We may sell ordinary shares or other securities in any other offering at a price per share that is less than the prices per share paid by investors in this offering, and investors purchasing ordinary shares or other securities in the future could have rights superior to existing shareholders. The price per share at which we sell additional ordinary shares, or securities convertible or exchangeable into ordinary shares, in future transactions may be higher or lower than the prices per share paid by investors in this offering.

It is not possible to predict the aggregate proceeds resulting from sales made under the sales agreement.

Subject to certain limitations in the sales agreement and compliance with applicable law, we have the discretion to deliver a placement notice to SVB Leerink at any time throughout the term of the sales agreement. The number of ordinary shares that are sold through SVB Leerink after delivering a placement notice will fluctuate based on a number of factors, including the market price of the ordinary shares during the sales period, the limits we set with SVB Leerink in any applicable placement notice, and the demand for our ordinary shares during the sales period. Because the price per share of each ordinary share sold will fluctuate during the sales period, it is not currently possible to predict the aggregate proceeds to be raised in connection with those sales. We may also elect not to sell any ordinary shares pursuant to the sales agreement.

The ordinary shares offered hereby will be sold in "at the market" offerings, and investors who buy ordinary shares at different times will likely pay different prices.

Investors who purchase ordinary shares in this offering at different times will likely pay different prices, and so may experience different levels of dilution and different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices, and numbers of

ordinary shares sold in this offering. In addition, subject to the final determination by our board of directors, there is no minimum or maximum sales price for ordinary shares to be sold in this offering. Investors may experience a decline in the value of the ordinary shares they purchase in this offering as a result of sales made at prices lower than the prices they paid.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus, including the documents that we incorporate by reference herein and therein, contain "forward-looking statements" within the meaning of Section 27A of the Securities Act, and Section 21E of the Exchange Act. Forward-looking statements can be identified using terminology such as "believes," "expects," "anticipates," "plans," "may," "will," "projects," "continues," "estimates," "potential," "opportunity" and similar expressions. Similarly, statements that describe our future plans, strategies, intentions, expectations, objectives, goals or prospects are also forward-looking statements. Discussions containing these forward-looking statements may be found, among other places, in the "Business" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections incorporated by reference from our most recent Annual Report on Form 10-K and our Quarterly Reports on Form 10-Q for the quarterly periods ended subsequent to our filing of such Annual Report on Form 10-K, as well as any amendments thereto reflected in subsequent filings with the SEC. These forward-looking statements are based largely on our expectations and projections about future events and future trends affecting our business, and are subject to risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements. The risks and uncertainties include, among others, those noted in "Risk Factors" above and those included in the documents that we incorporate by reference herein.

In addition, past financial and/or operating performance is not necessarily a reliable indicator of future performance and you should not use our historical performance to anticipate results or future period trends. We can give no assurances that any of the events anticipated by the forward-looking statements will occur or, if any of them do, what impact they will have on our results of operations and financial condition. Except as required by law, we undertake no obligation to publicly revise our forward-looking statements to reflect events or circumstances that arise after the filing of this prospectus supplement or the filing of the accompanying prospectus or documents incorporated by reference herein and therein that include forward-looking statements.

USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds from the sale of the securities offered hereby. We intend to use the net proceeds from the sale of the securities offered hereby to fund the further development of our product candidates and for general corporate purposes, which may include capital expenditures, working capital and general and administrative expenses. We may also use a portion of the net proceeds to acquire or invest in businesses that are complementary to our own, although we have no current plans, commitments or agreements with respect to any acquisitions as of the date of this prospectus supplement.

MATERIAL U.S. FEDERAL AND DUTCH TAX CONSIDERATIONS

Material Dutch Tax Considerations

This summary solely addresses the principal Dutch tax consequences of the acquisition, ownership and disposal of our ordinary shares. It does not purport to describe all the tax considerations that may be relevant to a particular holder of our ordinary shares (a "Shareholder"). Shareholders are advised to consult their own tax counsel with respect to the tax consequences of acquiring, holding and/or disposing of our ordinary shares. Where in this summary English terms and expressions are used to refer to Dutch concepts, the meaning to be attributed to such terms and expressions shall be the meaning to be attributed to the equivalent Dutch concepts under Dutch tax law.

This summary does not address the tax consequences of:

- A Shareholder who is an individual, either resident or non-resident in the Netherlands, and who has a (deemed) substantial interest ((*fictief*) *aanmerkelijk belang*) in us within the meaning of the Dutch Income Tax Act 2001 (*Wet inkomstenbelasting 2001*). Generally, if a person holds an interest in us, such interest forms part of a (deemed) substantial interest in us, if any or more of the following circumstances is present:

  1. If a Shareholder, either alone or, together with such Shareholder's partner (a statutorily defined term) owns or is deemed to own, directly or indirectly, either a number of ordinary shares in us representing five percent or more of our total issued and outstanding capital (or the issued and outstanding capital of any class of our shares), or rights to acquire, directly or indirectly, shares, whether or not already issued, representing five percent or more of our total issued and outstanding capital (or the issued and outstanding capital of any class of our shares), or profit participating certificates (*winstbewijzen*), relating to five percent or more of our annual profit or to five percent of our liquidation proceeds.

  2. If the shares, profit participating certificates or rights to acquire shares in us are held or deemed to be held following the application of a non-recognition provision.

  3. If the partner of a Shareholder, or one of certain relatives of the Shareholder or of this partner has a substantial interest (as described under 1. and 2. above) in us.

- A Shareholder receiving income or realizing capital gains in their capacity as future, present or past employee (*werknemer*) or member of a management board (*bestuurder*), or supervisory director (*commissaris*); the income from which is taxable in the Netherlands.

- Pension funds, investment institutions (*fiscale beleggingsinstellingen*), exempt investment institutions (*vrijgestelde beleggingsinstellingen*) and other entities that are, in whole or in part, not subject to or exempt from corporate income tax in the Netherlands, as well as entities that are exempt from corporate income tax in their country of residence, such country of residence being another state of the European Union, Norway, Liechtenstein, Iceland or any other state with which the Netherlands have agreed to exchange information in line with international standards.

- A Shareholder who is an individual and who is a qualifying non-resident taxpayer within the meaning of article 7.8, paragraph 6, of the Dutch Income Tax Act 2001.

For purposes of Dutch personal income tax and Dutch corporate income tax, ordinary shares legally owned by a third party, such as a trustee, foundation or similar entity or arrangement, may under certain circumstances have to be allocated to the (deemed) settler, grantor or similar organizer (the "Settlor"), or, upon the death of the Settlor, such Settlor's beneficiaries in proportion to their entitlement to the estate of the Settlor of such trust or similar arrangement.

This summary is based on the tax laws and principles (unpublished case law not included) in the Netherlands as in effect on the date of this prospectus supplement, which are subject to changes that could prospectively or retroactively affect the stated tax consequences. Where in this summary the terms "the Netherlands" and "Dutch" are used, these refer solely to the European part of the Kingdom of the Netherlands.

Dividend Withholding Tax

General

We are generally required to withhold Dutch dividend withholding tax at a rate of 15% from dividends distributed by us; the dividend withholding tax is for account of the Shareholder. The concept dividends "distributed by us" as used in this section includes, but is not limited to:

- distributions of profits in cash or in kind, deemed and constructive distributions, and repayments of paid-in capital which are not recognized for Dutch dividend withholding tax purposes;
- liquidation proceeds, or proceeds from the repurchase or redemption of ordinary shares by us or one of our subsidiaries or other affiliated entities in excess of the average paid-in capital of those shares recognized for Dutch dividend withholding tax purposes;
- the par value of our ordinary shares issued to a Shareholder or an increase of the par value of our ordinary shares, to the extent that it does not appear that a contribution, recognized for Dutch dividend withholding tax purposes, has been made or will be made; and
- partial repayment of paid-in capital recognized for Dutch dividend withholding tax purposes, if and to the extent that there are net profits (*zuivere winst*), unless (a) the general meeting of shareholders has resolved in advance to make such repayment and (b) the par value of the ordinary shares concerned has been reduced by an equal amount by way of an amendment to our articles of association.

Remittance to the Dutch tax authorities

In general, we will be required to remit all amounts withheld as Dutch dividend withholding tax to the Dutch tax authorities. However, under certain circumstances, we are allowed to reduce the amount to be remitted to the Dutch tax authorities by the lesser of:

- 3% of the portion of the distribution paid by us that is subject to Dutch dividend withholding tax; and
- 3% of the dividends and profit distributions, before deduction of foreign withholding taxes, received by us from qualifying foreign subsidiaries in the current calendar year (up to the date of the distribution by us) and the two preceding calendar years, as far as such dividends and profit distributions have not yet been taken into account for purposes of establishing the above mentioned reduction.

Although this reduction reduces the amount of Dutch dividend withholding tax that we are required to remit to the Dutch tax authorities, it does not reduce the amount of tax that we are required to withhold on dividends distributed.

Residents of the Netherlands

A Shareholder which is resident or deemed resident in the Netherlands for Dutch tax purposes is generally entitled to a full credit of any Dutch dividend withholding tax against the Dutch (corporate) income tax liability of such Shareholder, and is generally entitled to a refund in the form of a negative assessment of Dutch (corporate) income tax, insofar such Dutch dividend withholding tax, together with

any other creditable domestic and/or foreign taxes, exceeds such Shareholder's aggregate Dutch income tax or Dutch corporate income tax liability.

If and to the extent that such a corporate Shareholder is eligible for the application of the participation exemption (*deelnemingsvrijstelling*) with respect to the ordinary shares and the participation (*deelneming*) forms part of the assets of the business enterprise of a Shareholder in the Netherlands, dividends distributed by us are in principle exempt from Dutch dividend withholding tax.

Pursuant to domestic anti-dividend stripping rules, no exemption from Dutch dividend withholding tax, credit against Dutch (corporate) income tax, refund or reduction of Dutch dividend withholding tax shall apply if the recipient of the dividend distributed by us is not considered to be the beneficial owner (*uiteindelijk gerechtigde*) as meant in these rules, of such dividends.

Non-residents of the Netherlands (including but not limited to U.S. Shareholders)

A non-resident Shareholder, which is resident in the non-European part of the Kingdom of the Netherlands or in a country that has concluded a tax treaty with the Netherlands, may be eligible for a full or partial relief or refund from Dutch dividend withholding tax, provided that (i) such relief or refund is timely and duly claimed, and (ii) the entitlement to such relief or refund is not restricted pursuant to a provision for the prevention of fraud or abuse included in such tax treaty.

In addition, pursuant to domestic law, a non-resident Shareholder that is not an individual, is entitled to an exemption from Dutch dividend withholding tax, provided that each of the following tests are satisfied:

1. the non-resident Shareholder is, according to the tax law of:

    a. a Member State of the European Union, or another state designated by a ministerial decree that is a party to the Agreement regarding the European Economic Area, resident there and it is not transparent for tax purposes according to the tax law of such state; or

    b. a state not being a Member State of the European Union or another state designated by a ministerial decree, that is a party to the Agreement regarding the European Economic Area (a "Third State") that has concluded a tax treaty with the Netherlands containing a provision for dividends, resident there and it is not transparent for tax purposes according to the tax law of such state; and

2. the non-resident Shareholder has an interest in us for which the participation exemption as referred to in article 13 Dutch Corporate Income Tax Act 1969 (*Wet op de vennootschapsbelasting* 1969, or CITA) or the participation credit under article 13aa CITA would apply if the Shareholder would be a resident in the Netherlands; and

3. the non-resident Shareholder is, according to a tax treaty concluded by its state of residence with another state, not considered resident in a Third State that has not concluded a tax treaty with the Netherlands containing a provision for dividends; and

4. the non-resident Shareholder does not carry out duties or activities comparable to an investment institution as described in article 6a or article 28 CITA respectively; and

5. the non-resident Shareholder does not hold the interest as mentioned under 2 here above with (one of) the main purpose(s) of the evasion of Dutch dividend withholding tax in the hands of another person and there is not an artificial arrangement or transaction or series thereof in place whereby: (i) an arrangement or transaction may consist of several steps or components; (ii) an arrangement or transaction or series thereof is regarded artificial to the extent it is not put in place for valid commercial reasons which reflect economic reality.

A non-resident Shareholder which is resident in a Member State of the European Union with which the Netherlands has concluded a tax treaty that provides for a reduction of Dutch tax on dividends based on the ownership of the number of voting rights, the test mentioned under 2 above is also satisfied if the non-resident Shareholder owns voting rights in us for which the participation exemption as referred to in article 13 CITA or a tax credit under article 13aa CITA would apply if the shareholder would be a resident in the Netherlands.

Pursuant to domestic anti-dividend stripping rules, no exemption from Dutch dividend withholding tax, refund or reduction of Dutch dividend withholding tax shall apply if the recipient of the dividend paid by us is not considered the beneficial owner (*uiteindelijk gerechtigde*) as meant in these rules, of such dividends. The Dutch tax authorities have taken the position that this beneficial ownership test can also be applied to deny relief from Dutch dividend withholding tax under tax treaties and the Tax Arrangement for the Kingdom (*Belastingregeling voor het Koninkrijk*).

A non-resident Shareholder which is subject to Dutch income tax or Dutch corporate income tax in respect of any benefits derived or deemed to be derived from our ordinary shares, including any capital gain realized on the disposal thereof, can generally credit the Dutch dividend withholding tax against its Dutch income tax or its Dutch corporate income tax liability, as applicable, and is generally entitled to a refund pursuant to a negative tax assessment if and to the extent the Dutch dividend withholding tax, together with any other creditable domestic and/or foreign taxes, exceeds its aggregate Dutch income tax or its aggregate Dutch corporate income tax liability, respectively.

Taxes on Income and Capital Gains

Residents of the Netherlands

Individuals

A Shareholder, who is an individual resident or deemed to be resident in the Netherlands for Dutch income tax purposes will be subject to Dutch personal income tax at the progressive rates (up to a maximum rate of 49.50% (2021)) under the Dutch Income Tax Act 2001 on the income derived from the ordinary shares and gains realized on the disposal thereof if:

- such Shareholder derives any benefits from the ordinary shares, which are attributable to an enterprise of such Shareholder, whether as an entrepreneur or pursuant to a co-entitlement to the net worth (*medegerechtigd tot het vermogen*) of an enterprise other than as a shareholder or an entrepreneur; or

- such income or gain is taxable in the hands of such Shareholder as benefits from miscellaneous activities (*resultaat uit overige werkzaamheden*), including but not limited to activities with respect to the ordinary shares that are beyond the scope of regular active portfolio management activities (*normaal, actief vermogensbeheer*).

If neither of the two abovementioned conditions apply, the individual Shareholder will be taxed under the regime for savings and investments (*inkomen uit sparen en beleggen*). Irrespective of the actual income and capital gains realized, the annual taxable benefit of all the assets and allowable liabilities of a Shareholder who is taxed under this regime, including the ordinary shares, is set at a deemed return on the fair market value of the assets reduced by the allowable liabilities on January 1 of each year.

Depending on the aggregate amount of the fair market value of the assets reduced by the allowable liabilities, the deemed return ranges from 1.898% up to 5.69% (2021). This deemed return is subject to income tax at a flat rate of 31%. Taxation only occurs if and to the extent the fair market value of the assets reduced by the allowable liabilities exceeds a threshold (*heffingvrij vermogen*) of €50,000 (2021). The deemed return will be adjusted annually based on historic market yields.

Corporate entities

Generally, a Shareholder that is a corporation, another entity with a capital divided into shares, a cooperative (association), or another legal entity that has an enterprise to which the ordinary shares are attributable, that is resident or deemed to be resident in the Netherlands for Dutch corporate income tax purposes will be subject to Dutch corporate income tax, levied at a rate of 25% (15% over profits up to €245,000) over income derived from the ordinary shares and gains realized upon the acquisition, redemption and disposal of ordinary shares (rates and brackets for 2021).

If and to the extent that such Shareholder is eligible for the application of the participation exemption with respect to income derived from the ordinary shares, any gains and losses (with the exception of liquidation losses under strict conditions) realized on the ordinary shares are exempt from Dutch corporate income tax.

Non-residents of the Netherlands (including but not limited to U.S. Shareholders)

Individuals

A Shareholder, who is an individual not resident or deemed to be resident in the Netherlands for Dutch income tax purposes will not be subject to any Dutch taxes on income or capital gains in respect of dividends distributed by us or in respect of any gain realized on the disposal or deemed disposal of ordinary shares (other than dividend withholding tax as described above), except if:

- such holder has an enterprise or an interest in an enterprise that is, in whole or in part, carried on through a permanent establishment or a permanent representative in the Netherlands and to which enterprise or part of an enterprise, as the case may be, the ordinary shares are attributable; or

- such income or gain is taxable in the hands of such Shareholder as benefits from miscellaneous activities in the Netherlands, including but not limited to activities with respect to the ordinary shares that are beyond the scope of regular active portfolio management activities.

If one of the two abovementioned conditions apply, the income or gains in respect of dividends distributed by us or in respect of any capital gain realized on the disposal or deemed disposal of ordinary shares will in general be subject to Dutch personal income tax at the progressive rates up to 49.50% (2021).

Corporate entities

A Shareholder, that is not an individual, and is not resident or deemed to be resident in the Netherlands for Dutch corporate income tax purposes, will not be subject to any Dutch taxes on income or capital gains in respect of dividends distributed by us, or in respect of any gain realized, on the disposal or deemed disposal of ordinary shares (other than dividend withholding tax as described above), except if:

1. such Shareholder has an enterprise or an interest in an enterprise that is, in whole or in part, carried on through a permanent establishment or a permanent representative in the Netherlands, to which the ordinary shares are attributable; or

2. such Shareholder has a substantial interest or a deemed substantial interest in us, which interest is held with (one of) the main purpose(s) of the evasion of income tax in the hands of another person and there is an artificial arrangement or transaction or series thereof whereby: (i) an arrangement or transaction may consist of several steps or components; (ii) an arrangement or transaction or series thereof is regarded artificial to the extent it is not put in place for valid commercial reasons which reflect economic reality; or

3. such Shareholder is an entity resident of Aruba, Curaçao or Saint Martin with a permanent establishment or permanent representative in Bonaire, Saint Eustatius or Saba to which such income or gain is attributable, and the permanent establishment or permanent representative would be deemed to be resident of the Netherlands for Dutch corporate income tax purposes (i) had the permanent establishment been a corporate entity (*lichaam*), or (ii) had the activities of the permanent representative been conducted by a corporate entity, respectively.

A Shareholder as mentioned under 1 here above is not subject to Dutch corporate income tax for income and capital gains derived, if the ordinary shares are attributable to the permanent establishment in the Netherlands and the participation exemption as referred to in article 13 CITA applies to those ordinary shares.

If one of the abovementioned conditions applies, income derived from the ordinary shares and gains realized on ordinary shares will, in general, be subject to Dutch corporate income tax levied at a rate of 25% (15% over profits up to €245,000) (rates and brackets for 2021).

Gift or Inheritance Taxes

No Dutch gift or Dutch inheritance tax is due in respect of any gift, in form or in substance, of the ordinary shares by, or inheritance of the shares on the death of a Shareholder except if:

- at the time of the gift or death of the Shareholder, the Shareholder is resident, or deemed to be resident, in the Netherlands for purposes of Dutch gift tax or Dutch inheritance tax, as applicable; or

- in the case of a gift of ordinary shares by an individual who at the date of the gift was neither resident nor deemed to be resident in the Netherlands (i) such individual dies within 180 days after the date of the gift, while being resident or deemed to be resident in the Netherlands; or (ii) the gift of ordinary shares is made under a condition precedent (*opschortende voorwaarde*) and the Shareholder is resident, or is deemed to be resident in the Netherlands at the time the condition is fulfilled.

For purposes of the above, a gift of ordinary shares made under a condition precedent is deemed to be made at the time the condition precedent is satisfied.

For purposes of Dutch gift or Dutch inheritance taxes, an individual not holding the Dutch nationality will be deemed to be resident in the Netherlands, inter alia, if such individual has been resident in the Netherlands at any time during the ten years preceding the date of the gift or such individual's death. Additionally, for purposes of Dutch gift tax, an individual not holding the Dutch nationality will be deemed to be resident in the Netherlands if such individual has been resident in the Netherlands at any time during the twelve months preceding the date of the gift. Applicable tax treaties may override deemed residency in the Netherlands.

Value Added Tax

No Dutch value added tax will arise in respect of payments in consideration for the issue, acquisition, ownership and disposal of ordinary shares, other than value added taxes on fees payable in respect of services not exempt from Dutch value added tax.

Other Taxes and Duties

No Dutch registration tax, capital tax, custom duty, transfer tax, stamp duty or any other similar tax or duty will be payable in the Netherlands in respect of or in connection with the subscription, issue, placement, allotment, delivery or transfer of the ordinary shares.

Residence

A Shareholder will not become resident, or deemed resident in the Netherlands for Dutch tax purposes by reason only of holding the ordinary shares.

Material U.S. Federal Income Tax Considerations

The following general summary of the material U.S. federal income tax considerations applicable to the acquisition, ownership and disposition of our ordinary shares is based upon current law and does not purport to be a comprehensive discussion of all the tax considerations that may be relevant to our ordinary shares.

This summary is based on current provisions of the Internal Revenue Code of 1986, as amended (the "Code"), existing, final, temporary and proposed U.S. Treasury Regulations, administrative rulings and judicial decisions, in each case as available on the date of this annual report. All of the foregoing are subject to change, which change could apply retroactively and could affect the tax consequences described below.

This section summarizes the material U.S. federal income tax considerations to U.S. holders, as defined below, of ordinary shares.

This summary addresses only the U.S. federal income tax considerations for U.S. holders that acquire the ordinary shares at their original issuance and hold the ordinary shares as capital assets (generally, property held for investment). This summary does not address all U.S. federal income tax matters that may be relevant to a particular U.S. holder. **Each prospective investor should consult a professional tax advisor with respect to the tax consequences of the acquisition, ownership or disposition of the ordinary shares**. This summary does not address tax considerations applicable to a holder of ordinary shares that may be subject to special tax rules including, without limitation, the following:

- certain financial institutions;
- insurance companies;
- dealers or traders in securities, currencies, or notional principal contracts;
- tax-exempt entities and retirement plans;
- regulated investment companies;
- persons that hold the ordinary shares as part of a hedge, straddle, conversion, constructive sale or similar transaction involving more than one position;
- persons that hold the ordinary shares through partnerships, S corporations, or certain other pass-through entities;
- holders (whether individuals, corporations or partnerships) that are treated as expatriates for some or all U.S. federal income tax purposes;
- dealers in stock, securities or currencies, brokers;
- real estate investment trusts;
- holders that own (or are deemed to own) 10% or more of our voting shares; and
- holders that have a "functional currency" other than the U.S. dollar..

Further, this summary does not address alternative minimum tax considerations or the considerations applicable to the holders of equity interests in entities that own our ordinary shares. In

addition, this discussion does not consider the U.S. tax consequences to holders of ordinary shares that are not "U.S. holders" (as defined below).

For the purposes of this summary, a "U.S. holder" is a beneficial owner of ordinary shares that is (or is treated as), for U.S. federal income tax purposes:

- an individual who is either a citizen or resident of the United States;
- a corporation created or organized in or under the laws of the United States or any state of the United States or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust, if a court within the United States is able to exercise primary supervision over its administration and one or more U.S. persons have the authority to control all of the substantial decisions of such trust or the trust has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a U.S. person.

If a partnership holds ordinary shares, the tax treatment of a partner therein will generally depend upon the status of the partner and upon the activities of the partnership. A holder of ordinary shares that is treated as a partnership for U.S. federal income tax purposes should consult its own tax adviser regarding the U.S. federal income tax considerations applicable to it and its partners of the purchase, ownership and disposition of our ordinary shares.

We will not seek a ruling from the U.S. Internal Revenue Service, or IRS, with regard to the U.S. federal income tax treatment of an investment in our ordinary shares, and we cannot provide assurance that the IRS will agree with the conclusions set forth below.

Distributions

Subject to the discussion under "*Passive foreign investment company considerations*" below, the gross amount of any distribution (including any amounts withheld in respect of Dutch withholding tax) actually or constructively received by a U.S. holder with respect to ordinary shares will be taxable to the U.S. holder as a dividend to the extent of our current and accumulated earnings and profits as determined under U.S. federal income tax principles. Distributions in excess of earnings and profits will be non-taxable to the U.S. holder to the extent of, and will be applied against and reduce, the U.S. holder's adjusted tax basis in the ordinary shares. Distributions in excess of earnings and profits and such adjusted tax basis will generally be taxable to the U.S. holder as capital gain from the sale or exchange of property. However, since we do not calculate our earnings and profits under U.S. federal income tax principles, it is expected that any distribution will be reported as a dividend, even if that distribution would otherwise be treated as a non-taxable return of capital or as capital gain under the rules described above. A dividend paid in non-U.S. currency must be included in a U.S. holder's income as a U.S. dollar amount based on the exchange rate in effect on the date such dividend is actually or constructively received, regardless of whether the dividend is in fact converted into U.S. dollars. If the dividend is converted to U.S. dollars on the date of receipt, a U.S. holder generally will not recognize a foreign currency gain or loss. If the non-U.S. currency is converted into U.S. dollars on a later date, however, the U.S. Holder must include in income any gain or loss resulting from any exchange rate fluctuations. Such gain or loss will generally be ordinary income or loss and will be from sources within the United States for foreign tax credit limitation purposes. U.S. Holders should consult their own tax advisors regarding the tax consequences to them if our company pays dividends in non-U.S. currency. The amount of any distribution of property other than cash will be the fair market value of that property on the date of distribution. The U.S. holder will not be eligible for any dividends-received deduction in respect of the dividend otherwise allowable to corporations.

Under the Code and subject to the discussion below regarding the "Medicare tax," qualified dividends received by non-corporate U.S. holders (*i.e.*, individuals and certain trusts and estates) are subject to a maximum income tax rate of 20%. This reduced income tax rate is applicable to dividends paid by "qualified foreign corporations" to such non-corporate U.S. holders that meet the applicable requirements, including a minimum holding period (generally, at least 61 days during the 121-day period beginning 60 days before the ex-dividend date). We expect to be considered a qualified foreign corporation under the Code. Accordingly, dividends paid by us to non-corporate U.S. holders with respect to shares that meet the minimum holding period and other requirements are expected to be treated as "qualified dividend income." However, dividends paid by us will not qualify for the 20% maximum U.S. federal income tax rate if we are treated, for the tax year in which the dividends are paid or the preceding tax year, as a "passive foreign investment company" for U.S. federal income tax purposes, as discussed below.

Dividends received by a U.S. holder with respect to ordinary shares generally will be treated as foreign source income for the purposes of calculating that holder's foreign tax credit limitation. Subject to applicable conditions and limitations, and subject to the discussion in the next paragraph, any Dutch income tax withheld on dividends may be deducted from taxable income or credited against a U.S. holder's U.S. federal income tax liability. The limitation on foreign taxes eligible for the U.S. foreign tax credit is calculated separately with respect to specific classes of income. For this purpose, dividends distributed by us generally will constitute "passive category income" (but, in the case of some U.S. holders, may constitute "general category income").

Upon making a distribution to shareholders, we may be permitted to retain a portion of the amounts withheld as Dutch dividend withholding tax. See "—Taxation in the Netherlands—Dividend Withholding Tax—General." The amount of Dutch withholding tax that we may retain reduces the amount of dividend withholding tax that we are required to pay to the Dutch tax authorities but does not reduce the amount of tax we are required to withhold from dividends paid to U.S. holders. In these circumstances, it is likely that the portion of dividend withholding tax that we are not required to pay to the Dutch tax authorities with respect to dividends distributed to U.S. holders would not qualify as a creditable tax for U.S. foreign tax credit purposes.

Sale or Other Disposition of Ordinary Shares

A U.S. holder will generally recognize gain or loss for U.S. federal income tax purposes upon the sale or exchange of ordinary shares in an amount equal to the difference between the U.S. dollar value of the amount realized from such sale or exchange and the U.S. holder's tax basis for those ordinary shares. Subject to the discussion under "*Passive foreign investment company considerations*" below, this gain or loss will generally be a capital gain or loss and will generally be treated as from sources within the United States. Such capital gain or loss will be treated as long-term capital gain or loss if the U.S. holder has held the ordinary shares for more than one year at the time of the sale or exchange. Long-term capital gains of non-corporate holders may be eligible for a preferential tax rate; the deductibility of capital losses is subject to limitations. A U.S. holder that receives non-U.S. currency on the disposition of our ordinary shares will realize an amount equal to the U.S. dollar value of the foreign currency received on the date of disposition (or in the case of cash basis and electing accrual basis taxpayers, the settlement date) whether or not converted into U.S. dollars at that time. Very generally, the U.S. holder will recognize currency gain or loss if the U.S. dollar value of the currency received on the settlement date differs from the amount realized with respect to the ordinary shares. Any currency gain or loss on the settlement date or on any subsequent disposition of the foreign currency generally will be U.S. source ordinary income or loss.

Medicare Tax

A "United States person," within the meaning of the Code, that is an individual, an estate or a nonexempt trust is generally subject to a 3.8% surtax on the lesser of (i) the United States person's "net investment income" for the year and (ii) the excess of the United States person's "modified adjusted gross income" for that year over a threshold (which, in the case of an individual, will be between $125,000 and $250,000, depending on the individual's U.S. tax filing status). A U.S. holder's net investment income generally will include, among other things, dividends on, and gains from the sale or other taxable disposition of, our ordinary shares, unless (with certain exceptions) those dividends or gains are derived in the ordinary course of a trade or business. Net investment income may be reduced by deductions properly allocable thereto; however, the U.S. foreign tax credit may not be available to reduce the surtax.

Passive foreign investment company considerations. A corporation organized outside the United States generally will be classified as a passive foreign investment company, or PFIC, for U.S. federal income tax purposes in any taxable year in which either: (i) at least 75% of its gross income is passive income, or (ii) on average at least 50% of the gross value of its assets is attributable to assets that produce passive income or are held for the production of passive income. In arriving at this calculation, a pro rata portion of the income and assets of each corporation in which we own, directly or indirectly, at least a 25% interest, as determined by the value of such corporation, must be taken into account. Passive income for this purpose generally includes dividends, interest, royalties, rents and gains from commodities and securities transactions.

We believe that we were a PFIC for the 2020 taxable year. As of the date of this prospectus supplement we do not expect to be a PFIC for the 2021 taxable year. Based on our estimated gross income, the average value of our gross assets, and the nature of the active businesses conducted by our "25% or greater" owned subsidiaries, we do not expect that we will be classified as a PFIC in the 2021 taxable year. Our status as a PFIC for any taxable year will depend on our assets and activities in each year, and because this is a factual determination made annually after the end of each taxable year, there can be no assurance that we will not be considered a PFIC for the current taxable year or any future taxable year. The market value of our assets may be determined in large part by reference to the market price of our ordinary shares, which is likely to fluctuate and may fluctuate considerably given that market prices of technology companies have been especially volatile. In addition, the composition of our income and assets will be affected by how, and how quickly, we spend our cash.

If we are a PFIC for any taxable year during which a U.S. holder held ordinary shares, under the "default PFIC regime" (i.e., in the absence of one of the elections described below) gain recognized by the U.S. holder on a sale or other disposition (including a pledge) of the ordinary shares would be allocated ratably over the U.S. holder's holding period for the ordinary shares. The amounts allocated to the taxable year of the sale or other disposition and to any year before we became a PFIC would be taxed as ordinary income. The amount allocated to each other taxable year would be subject to tax at the highest rate in effect for individuals or corporations, as appropriate, for that taxable year, and an interest charge would be imposed on the resulting tax liability for that taxable year. Similar rules would apply to the extent any distribution in respect of ordinary shares exceeds 125% of the average of the annual distributions on ordinary shares received by a U.S. holder during the preceding three years or the holder's holding period, whichever is shorter. It should be noted that, until such time as we make a distribution, there are no tax consequences under the default PFIC regime to U.S. holders. However, if we ever did make a distribution it would in all likelihood be an excess distribution (because we would not have previously made any distributions to holders of ordinary shares). At that point, and for all subsequent distributions, the rules described above would apply to U.S. holders. U.S. holders should also be aware that a foreign company that becomes a PFIC while a U.S. shareholder owns stock in the company remains a PFIC with respect to that shareholder for as long as the shareholder holds the stock (even if the company is at some point no longer classified as a PFIC), unless the shareholder had

made an appropriate election or a purging election. Accordingly, even though our PFIC status may have no immediate impact on a U.S. holder's U.S. tax liability (if we do not make any distributions or if we do not have any net earnings or capital gains), the U.S. holder's future tax liability as a shareholder in our company may be affected by elections that the U.S. holder makes (or is unable to make) today. For this reason, it is important for U.S. holders to consult their own tax advisors about the consequences of PFIC status.

In the event we are treated as a PFIC, the tax consequences under the default PFIC regime described above could be avoided by either a "mark- to-market" or "qualified electing fund" election. As long as our ordinary shares are regularly traded on the Nasdaq Global Select Market or another "qualified exchange," a U.S. holder making a mark-to-market election generally would not be subject to the PFIC rules discussed above, except with respect to any portion of the holder's holding period for our ordinary shares that precedes the effective date of the election. Instead, the electing holder would include in ordinary income, for each taxable year in which we were a PFIC, an amount equal to any excess of: (a) the fair market value of the ordinary shares as of the close of such taxable year over (b) the electing holder's adjusted tax basis in such ordinary shares. In addition, an electing holder would be allowed a deduction in an amount equal to the lesser of (y) the excess, if any, of (i) the electing holder's adjusted tax basis in the ordinary shares over (ii) the fair market value of such ordinary shares as of the close of such taxable year or (z) the excess, if any, of (i) the amount included in ordinary income because of the election for prior taxable years over (ii) the amount allowed as a deduction because of the election for prior taxable years. The election would cause adjustments in the electing holder's tax basis in the ordinary shares to reflect the amount included in gross income or allowed as a deduction because of the election. In addition, upon a sale or other taxable disposition of ordinary shares, an electing holder would recognize ordinary income or loss (not to exceed the excess, if any, of (1) the amount included in ordinary income because of the election for prior taxable years over (2) the amount allowed as a deduction because of the election for prior taxable years).

Alternatively, a U.S. holder making a valid and timely "QEF election" generally would not be subject to the default PFIC regime discussed above. Instead, for each PFIC year to which such an election applied, the electing holder would be subject to U.S. federal income tax on the electing holder's pro rata share of our net capital gain and ordinary earnings, regardless of whether such amounts were actually distributed to the electing holder. However, because we do not intend to prepare or provide the information that would permit the making of a valid QEF election, that election will not be available to U.S. holders.

If we were considered a PFIC for the current taxable year or any future taxable year, a U.S. holder would be required to file annual information returns for such year, whether or not the U.S. holder disposed of any ordinary shares or received any distributions in respect of ordinary shares during such year.

Backup Withholding and Information Reporting.

U.S. holders generally will be subject to information reporting requirements with respect to dividends on ordinary shares and on the proceeds from the sale, exchange or disposition of ordinary shares that are paid within the United States or through U.S.-related financial intermediaries, unless the U.S. holder is an "exempt recipient." In addition, U.S. holders may be subject to backup withholding (currently at a 24% rate) on such payments, unless the U.S. holder provides a taxpayer identification number and a duly executed IRS Form W-9 (or applicable successor form) or otherwise establishes an exemption. Backup withholding is not an additional tax, and the amount of any backup withholding will be allowed as a credit against a U.S. holder's U.S. federal income tax liability and may entitle such holder to a refund, provided that the required information is timely furnished to the IRS.

PLAN OF DISTRIBUTION

We have entered into the sales agreement with SVB Leerink LLC, or SVB Leerink, under which we may issue and sell from time to time our ordinary shares having an aggregate offering price of up to $200,000,000 through SVB Leerink as our sales agent. Sales of our ordinary shares, if any, will be made at market prices by any method that is deemed to be an "at-the-market offering" as defined in Rule 415 under the Securities Act, including sales made directly on The Nasdaq Global Select Market or any other trading market for our ordinary shares. If authorized by us in writing, SVB Leerink may purchase our ordinary shares as principal.

SVB Leerink will offer our ordinary shares subject to the terms and conditions of the sales agreement on a daily basis or as otherwise agreed upon by us and SVB Leerink. We will designate the maximum amount of ordinary shares to be sold through SVB Leerink on a daily basis or otherwise determine such maximum amount together with SVB Leerink. Subject to the terms and conditions of the sales agreement, SVB Leerink will use its commercially reasonable efforts to sell on our behalf all of the ordinary shares requested to be sold by us. We may instruct SVB Leerink not to sell ordinary shares if the sales cannot be effected at or above the price designated by us in any such instruction. SVB Leerink or we may suspend the offering of our ordinary shares being made through SVB Leerink under the sales agreement upon proper notice to the other party. SVB Leerink and we each have the right, by giving written notice as specified in the sales agreement, to terminate the sales agreement in each party's sole discretion at any time.

The aggregate compensation payable to SVB Leerink as sales agent equals 3% of the gross sales price of the ordinary shares sold through them pursuant to the sales agreement. We have also agreed to reimburse SVB Leerink for up to $50,000 of the actual outside legal expenses incurred by SVB Leerink and up to $10,000 of filing fees and associated legal expenses of SVB Leerink's outside counsel for filings with the Financial Industry Regulatory Authority Corporate Financing Department in connection with the transactions contemplated by the sales agreement. We estimate that the total expenses in connection with the transactions contemplated by the sales agreement payable by us, excluding commissions payable to SVB Leerink under the sales agreement, will be approximately $300,000.

The remaining sales proceeds, after deducting any expenses payable by us and any transaction fees imposed by any governmental, regulatory, or self-regulatory organization in connection with the sales, will equal our net proceeds for the sale of such ordinary shares.

SVB Leerink will provide written confirmation to us following the close of trading on The Nasdaq Global Select Market on each day in which ordinary shares are sold through them as sales agent under the sales agreement. Each confirmation will include the number of ordinary shares sold through SVB Leerink as sales agent on that day, the volume weighted average price of the ordinary shares sold, the percentage of the daily trading volume and the net proceeds to us.

Settlement for sales of ordinary shares will occur, unless the parties agree otherwise, on the second business day that is also a trading day following the date on which any sales were made in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

In connection with the sales of our ordinary shares on our behalf, SVB Leerink may be deemed to be an "underwriter" within the meaning of the Securities Act, and the compensation paid to SVB Leerink may be deemed to be underwriting commissions or discounts. We have agreed in the sales agreement to provide indemnification and contribution to SVB Leerink against certain liabilities, including liabilities under the Securities Act. As sales agent, SVB Leerink will not engage in any transaction that stabilizes our ordinary shares.

The sales agreement has been included as an exhibit to a Current Report on Form 8-K that we filed with the Securities and Exchange Commission in connection with this offering and is incorporated into this prospectus supplement by reference.

Our ordinary shares are listed on The Nasdaq Global Select Market and trade under the symbol "QURE." The transfer agent of our ordinary shares is Computershare Trust Company, N.A.

SVB Leerink and/or its affiliates have provided, and may in the future provide, various investment banking and other financial services for us for which services they have received, and may in the future receive, customary fees.

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area (each a "Relevant Member State"), no offering or sale of ordinary shares which are the subject of the offering and placement contemplated by this prospectus supplement, the accompanying prospectus and the sales agreement (the "Shares") to the public in that Relevant Member State may be made, except that an offer to the public in that Relevant Member State of any Shares may be made 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) per Relevant Member State; or

(c) in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of Shares shall require uniQure or any other person to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

The offer and sale of Shares shall not be made in the Netherlands, unless in reliance on Article 1(4) of the Prospectus Regulation and provided (a) such offer and sale is made exclusively to legal entities which are qualified investors (as defined under the Prospectus Regulation); or (b) a standard exemption logo and exemption wording are disclosed.

For the purposes of this provision, the expression an "offer to the public" in relation to any Shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offering and any Shares to be offered so as to enable an investor to decide to purchase or subscribe for any Shares and the expression "Prospectus Regulation" means Regulation (EU) 2017/1129 (as amended) and includes any relevant delegated regulations.

LEGAL MATTERS

Legal matters with respect to U.S. federal and New York law in connection with this offering will be passed upon for us by Morgan, Lewis & Bockius UK LLP, London, England. Certain legal matters with respect to Dutch law in connection with the validity of the ordinary shares being offered by this prospectus supplement and other legal matters will be passed upon for us by Rutgers Posch Visée Endedijk N.V., Amsterdam, the Netherlands. Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts, is U.S. counsel and NautaDutilh N.V., Amsterdam, the Netherlands is Dutch counsel for SVB Leerink in connection with this offering.

EXPERTS

The consolidated financial statements of uniQure N.V. as of December 31, 2020 and 2019, and for the years then ended, and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2020 have been incorporated by reference herein and in the registration statement in reliance upon the report of KPMG Accountants N.V., independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing. The audit report covering the December 31, 2020 financial statements refers to a change in the method of accounting for leases as of January 1, 2019 due to the adoption of ASC 842, Leases.

The financial statements for the year ended December 31, 2018 incorporated in this prospectus supplement by reference to the Annual Report on Form 10 K for the year ended December 31, 2020 have been so incorporated in reliance on the report of PricewaterhouseCoopers Accountants N.V., an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We are subject to the reporting requirements of the Exchange Act and file annual, quarterly and current reports, proxy statements and other information with the SEC. SEC filings are available at the SEC's website at http://www.sec.gov.

This prospectus supplement is only part of a registration statement on Form S-3 that we have filed with the SEC under the Securities Act, and therefore omits certain information contained in the registration statement. We have also filed exhibits and schedules with the registration statement that are excluded from this prospectus supplement, and you should refer to the applicable exhibit or schedule for a complete description of any statement referring to any contract or other document.

We also maintain a website at www.uniqure.com, through which you can access our SEC filings. The information set forth on our website is not part of this prospectus supplement.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" the information we file with it, which means that we can disclose important information to you by referring you to those documents. Information incorporated by reference is part of this prospectus supplement and the accompanying prospectus. Later information filed with the SEC will update and supersede this information. The SEC's Internet site can be found at http://www.sec.gov.

We incorporate by reference the documents listed below and any future filings made with the SEC under Sections 13(a), 13 (c), 14 or 15(d) of the Exchange Act after the date of this prospectus supplement until the termination of the offering of the ordinary shares covered by this prospectus supplement (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items):

- our Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on March 1, 2021; and
- the description of our ordinary shares contained in our registration statement on Form 8-A as filed with the SEC on January 31, 2014, as updated or amended in any amendment or report filed for such purpose.

We undertake to provide without charge to each person (including any beneficial owner) who receives a copy of this prospectus supplement and the accompanying prospectus, upon written or oral request, a copy of all of the preceding documents that are incorporated by reference (other than exhibits, unless the exhibits are specifically incorporated by reference into these documents). You may request a copy of these filings, at no cost, by writing or telephoning us at the following address or telephone number: 113 Harwell Avenue, Lexington, MA 02421, telephone number +1.339.970.7000.

In accordance with Rule 412 of the Securities Act, any statement contained in a document incorporated by reference herein shall be deemed modified or superseded to the extent that a statement contained herein or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein modifies or supersedes such statement.

Table of Contents

PROSPECTUS

Ordinary Shares offered by uniQure N.V.
Warrants
Rights
Debt Securities
Purchase Contracts
Units
Ordinary Shares by Selling Shareholders

From time to time, we may offer, issue and sell any combination of the securities described in this prospectus in one or more offerings, or a selling shareholder or shareholders may offer ordinary shares for sale under this prospectus. We may also offer securities as may be issuable upon conversion, redemption, repurchase, exchange or exercise of any securities registered hereunder, including any applicable antidilution provisions.

This prospectus provides a general description of the securities we may offer. Each time we or a selling shareholder offer securities, we will provide specific terms of the securities offered in a supplement to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference, before you invest in any of the securities being offered.

This prospectus may not be used to consummate a sale of any securities unless accompanied by a prospectus supplement.

Our ordinary shares are listed on The Nasdaq Global Select Market under the symbol "QURE." On February 26, 2021, the last reported sales price of our ordinary shares was $36.70 per share. The applicable prospectus supplement will contain information, where applicable, as to any other listing on The Nasdaq Global Select Market or any securities market or other exchange of the securities, if any, covered by the prospectus supplement.

We or a selling shareholder will sell these securities directly to investors, through agents designated from time to time or to or through underwriters or dealers, on a continuous or delayed basis. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus. If any agents or underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such agents or underwriters and any applicable fees, commissions, discounts or option to purchase additional securities will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" contained in the applicable prospectus supplement and any related free writing prospectus, 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 March 1, 2021

TABLE OF CONTENTS

ABOUT THIS PROSPECTUS

This prospectus is part of an automatic shelf registration statement that we filed with the Securities and Exchange Commission, or SEC, as a "well-known seasoned issuer" as defined in Rule 405 under the Securities Act of 1933, as amended, or the Securities Act. Under this shelf registration process, we may sell any combination of the securities described in this prospectus and our selling shareholders may sell their ordinary shares in one or more offerings. This prospectus provides you with a general description of the securities we may offer.

Each time we sell securities under this prospectus, we will provide a prospectus supplement that will contain specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in any documents that we have incorporated by reference into this prospectus. You should read this prospectus, any applicable prospectus supplement and any related free writing prospectus, together with the information incorporated herein by reference as described under the heading "Incorporation of Certain Information By Reference," before investing in any of the securities offered.

This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.

Neither we, nor any agent, underwriter or dealer has authorized any person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus, any applicable prospectus supplement or any related free writing prospectus prepared by or on behalf of us or to which we have referred you. This prospectus, any applicable supplement to this prospectus or any related free writing prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor does this prospectus, any applicable supplement to this prospectus or any related free writing prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

You should not assume that the information contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus, any applicable prospectus supplement or any related free writing prospectus is delivered, or securities are sold, on a later date.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the heading "Where You Can Find More Information."

Unless otherwise mentioned or unless the context indicates otherwise, as used in this prospectus, the terms "uniQure," the "Company," "we," "us" and "our" refer to uniQure N.V., a public company with limited liability (*naamloze vennootschap*) under the laws of the Netherlands, together with its subsidiaries.

This prospectus and the information incorporated herein and therein by reference include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus are the property of their respective owners.

SUMMARY

This summary highlights selected information from this prospectus and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus, the applicable prospectus supplement and any related free writing prospectus, including the risks of investing in our securities discussed under the heading "Risk Factors" contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus. You should also carefully read the information incorporated by reference into this prospectus, including our consolidated financial statements, and the exhibits to the registration statement of which this prospectus is a part.

Company Overview

General

We are a leader in the field of gene therapy, seeking to develop single treatments with potentially curative results for patients suffering from genetic and other devastating diseases. We are advancing a focused pipeline of innovative gene therapies, including product candidates for the treatment of hemophilia B, which we intend to license to CSL Behring pursuant to the CSL Behring Agreement described below, and Huntington's disease. We believe our validated technology platform and manufacturing capabilities provide us distinct competitive advantages, including the potential to reduce development risk, cost, and time to market. We produce our Adeno-associated virus, or AAV,-based gene therapies in our own facilities with a proprietary, commercial-scale, current good manufacturing practices, or cGMP,-compliant, manufacturing process. We believe our Lexington, Massachusetts-based facility is one of the world's most versatile gene therapy manufacturing facilities.

Key events

CSL Behring commercialization and license agreement

On June 24, 2020, uniQure biopharma B.V., a wholly-owned subsidiary of uniQure N.V., entered into a commercialization and license agreement, or the CSL Behring Agreement, with CSL Behring LLC, or CSL Behring, pursuant to which CSL Behring will receive exclusive global rights to etranacogene dezaparvovec, our investigational gene therapy for patients with hemophilia B which we refer to herein as Product.

Under the terms of the CSL Behring Agreement, we will receive a $450.0 million upfront cash payment upon the closing of the transactions contemplated by the CSL Behring Agreement and we will be eligible to receive up to $1.6 billion in additional payments based on the achievement of regulatory and commercial milestones. The CSL Behring agreement also provides that we will be eligible to receive tiered double-digit royalties in a range of up to a low-twenties percent of net sales of the Product based on sales thresholds.

Pursuant to the CSL Behring Agreement, we will be responsible for the completion of our Phase III HOPE-B pivotal trial of etranacogene dezaparvovec, or the HOPE-B trial, manufacturing process validation, and the manufacturing supply of the Product until such time that these capabilities may be transferred to CSL Behring or its designated contract manufacturing organization. Concurrently with the execution of the CSL Behring Agreement, we and CSL Behring entered into a development and commercial supply agreement, pursuant to which, among other things, we will supply the Product to CSL Behring at an agreed-upon price. Clinical development and regulatory activities performed by us pursuant to the CSL Behring Agreement will be reimbursed by CSL Behring. CSL Behring will be responsible for global regulatory submissions and commercialization requirements for the Product.

Other than under the CSL Behring Agreement, neither we nor CSL Behring may perform any clinical trials, with the exception of trials required to extend the label or gain marketing authorization outside the United States or the European Union, for any gene therapy product, (including deoxyribonucleic acid, or DNA, and ribonucleic acid, or RNA) gene-editing product, or any other product comprising an AAV vector to conduct nucleotide transfer (including DNA and RNA) for the treatment, prevention, or cure of hemophilia B for a period commencing on June 24, 2020 and continuing for a period of four years following the first commercial sale of the Product in the United States, and neither we nor CSL Behring may commercialize such a product for a period commencing as of June 24, 2020 and continuing for a period of seven years following the first commercial sale of the Product in the United States. This exclusivity commitment would not bind any party that acquirers us and that owns or controls such a product so long as certain precautions are followed to ensure that CSL Behring's confidential information and our proprietary technology related to the Product are not used or accessed by personnel of such acquirer who are developing or commercializing such competing product.

Unless earlier terminated as described below, the CSL Behring Agreement will continue on a country-by-country basis until expiration of the royalty term in a country. The royalty term expires in a country on the later of (a) 15 years after the first commercial sale of the Product in such country, (b) expiration of regulatory exclusivity for the Product in such country and (c) expiration of all valid claims of specific licensed patents covering the Product in such country. Either we or CSL Behring may terminate the CSL Behring Agreement for the other party's material breach if such breach is not cured within a specified cure period. In addition, if CSL Behring fails to commercialize the Product in any of a group of major countries for an extended period of time following the first regulatory approval of the Product in any of such group of countries (other than due to certain specified reasons) and such failure has not been cured within a specified cure period, then we may terminate the CSL Behring Agreement. CSL Behring may also terminate the CSL Behring Agreement for convenience.

The effectiveness of the transactions contemplated by the CSL Behring Agreement is contingent on completion of review under antitrust laws in the United States, Australia, and the United Kingdom, and certain provisions of the CSL Behring Agreement will not become effective until after we receive all such regulatory approvals.

On November 11, 2020, the Australian Competition and Consumer Commission, or the ACCC, determined, pursuant to section 50 of the Competition and Consumer Act 2010 of Australia, that it will not intervene in the CSL Behring Agreement. Thus, the ACCC has completed its review of the CSL Behring Agreement, and the transactions contemplated by the CSL Behring Agreement may close from the perspective of the Australian competition authority.

On November 24, 2020, the Competition and Markets Authority in the United Kingdom, or the CMA, adopted a decision not to refer the CSL Behring Agreement for proceedings under section 33 of the Enterprise Act 2002 of the United Kingdom. The decision was made public by the CMA on January 6, 2021. Thus, the CMA has completed its review of the CSL Behring Agreement, and the transactions contemplated by the CSL Behring Agreement may close from the perspective of the United Kingdom competition authority.

On December 3, 2020, we and CSL Behring filed a premerger notification and report form under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, or the HSR Act. On January 4, 2021, the United States Federal Trade Commission, or the FTC, issued to us a request for additional information and documentary material, or a Second Request, under the HSR Act. The FTC similarly issued a Second Request to CSL Behring also with respect to the antitrust review of the CSL Behring Agreement. The effect of the Second Request is to extend the waiting period imposed under the HSR Act until 30 days after all parties to the CSL Behring Agreement have substantially complied with the requests unless the waiting period is terminated earlier by the FTC or voluntarily extended by the

parties. We do not believe that the FTC will determine that the consummation of the transaction contemplated by the CSL Behring Agreement will result in a violation of the HSR Act. However, there can be no assurance as to the outcome of the Second Request.

Closing of the transaction contemplated by the CSL Behring Agreement is expected to materially impact our profitability and cash flows. Receipt of the $450.0 million payment due on closing would extend the funding of our operations into the second half of 2024 (assuming a full repayment of funds borrowed from Hercules Capital Inc., or Hercules, under our term loan facility by 2023). However, we expect to continue to incur losses and to generate negative cash flows beyond the fiscal year in which we would close the transaction.

Hemophilia B program—Etranacogene dezaparvovec (AMT-061)

Etranacogene dezaparvovec is our lead gene therapy candidate and includes an AAV serotype 5, which we collectively refer to as AAV-5, vector incorporating the functional human Factor IX, or FIX, Padua variant. We are currently conducting a pivotal study in patients with severe and moderately-severe hemophilia B.

In August 2018, we initiated a Phase IIb dose-confirmation study of etranacogene dezaparvovec and in September 2018, we completed the dosing for that study. In February, May, July, and December 2019, and in December 2020, we presented updated data from the Phase IIb dose-confirmation study of etranacogene dezaparvovec. The most recent data that we announced from the Phase IIb study of etranacogene dezaparvovec show that all three patients experienced increasing and sustained FIX levels after a one-time administration of etranacogene dezaparvovec. Mean FIX activity was 44.2% of normal two years after administration, exceeding threshold FIX levels generally considered sufficient to significantly reduce the risk of bleeding events. The first patient achieved FIX activity of 44.7% of normal, the second patient was 51.6% of normal and the third patient was 36.3% of normal. The second and third patients had previously screen-failed and were excluded from another gene therapy study due to pre-existing neutralizing antibodies to a different AAV vector. At two years after dosing, two of the three participants remain free from bleeds and use of FIX replacement therapy. A single bleed has been reported in one participant, who has used a total of two FIX infusions (excluding surgery). All patients have remained free of prophylaxis in the two years since receiving etranacogene dezaparvovec.

In June 2018, we initiated the six-month lead-in period of our HOPE-B trial. The HOPE-B trial is a multinational, multi-center, open-label, single-arm study to evaluate the safety and efficacy of etranacogene dezaparvovec. After the six-month lead-in period, patients received a single intravenous administration of etranacogene dezaparvovec. Patients enrolled in the HOPE-B trial were tested for the presence of pre-existing neutralizing antibodies to AAV-5 but not excluded from the trial based on their titers.

The primary endpoints of the study are based on the FIX activity level achieved following the administration of etranacogene dezaparvovec after 26 weeks and 52 weeks after dosing as well as annualized bleed rates during the 52 weeks after dosing.

In March 2020, we completed dosing of the 54 patients in the HOPE-B trial. The targeted number of patients to be dosed per the clinical trial protocol was 50. As set forth below, we have implemented and continue to implement various measures to allow us to closely monitor the trial within the guidance provided by the U.S. Food and Drug Administration, or the FDA, regarding the impact of the COVID-19 coronavirus pandemic to minimize any risk or disruption in patient follow-up visits.

In December 2020, we announced top-line data from the HOPE-B trial. The 26-week follow-up date from the trial showed that FIX activity in the 54 patients increased after dosing from £ 2% to a mean of 37.2% at 26 weeks, meeting a first primary endpoint of the HOPE-B trial. No correlation

between pre-existing neutralizing antibodies and FIX activity was found in patients with neutralizing antibody titers up to 678.2, a range expected to include more than 95% of the general population; one patient with a neutralizing antibody titer of 3,212.3 did not show an increase in FIX activity. Less than 1% of the general population is expected to have neutralizing antibody titers of greater than 3,000.

During the 26-week period after dosing, 15 patients (28%) reported a total of 21 bleeding events, representing a reduction of 83% compared to the 123 bleeding events reported by 38 patients (70%) during the observational lead-in phase of the trial. Total bleeds include any bleeding event reported after the treatment of etranacogene dezaparvovec, including spontaneous, traumatic, and those associated with unrelated medical procedures, whether or not FIX treatment was required. Of the total bleeding events reported during the 26-week period after dosing, only three were classified as spontaneous bleeds requiring treatment, representing a reduction of 92% compared to the 37 such bleeding events reported during the observational lead-in phase. Mean annualized usage of FIX replacement therapy, a secondary endpoint in the clinical trial, declined by 96% during the 26-week period after dosing compared to the observational lead-in phase. Etranacogene dezaparvovec was generally well-tolerated. As of the November 2020 cut-off date, most adverse events were classified as mild (81.5%). The most common events included transaminase elevation treated with steroids per protocol (9 patients; 17%), infusion-related reactions (7 patients; 13%), headache (7 patients; 13%) and influenza-like symptoms (7 patients; 13%). Liver enzyme elevations resolved with a tapering course of corticosteroids and FIX activity remained in the mild range in the steroid treated patients. No relationship between safety and neutralizing antibody titers was observed. Based on interactions with the FDA and the European Medicines Agency, or the EMA, we plan to incorporate FIX activity and bleeding rates at 52 weeks as additional co-primary endpoints in the study.

On December 21, 2020, our clinical trials of etranacogene dezaparvovec, including our HOPE-B trial, were placed on clinical hold by the FDA. The clinical hold was initiated following the submission of a safety report in mid-December 2020 relating to a possibly related serious adverse event associated with a preliminary diagnosis of hepatocellular carcinoma, or HCC, a form of liver cancer, in one patient in the HOPE-B trial that was treated with etranacogene dezaparvovec in October 2019. The patient has multiple risk factors associated with HCC, including a twenty-five-year history of hepatitis C, hepatitis B virus, evidence of non-alcoholic fatty liver disease and advanced age. Chronic infections with hepatitis B and C have been associated with approximately 80% of HCC cases.

The liver lesion was detected during a routine abdominal ultrasound conducted as part of the required study assessments in patients at one-year post dosing. A surgical resection of the lesion has occurred, and an analysis of the tissue samples was initiated in early 2021. On February 19, 2021, we reported initial results from this analysis to the FDA in accordance with pharmacovigilance requirements. We are gathering final data from these molecular analyses and will be preparing a detailed response to the FDA's clinical hold questions regarding this event. Currently, we do not have adequate data to determine a possible causal relationship, especially in the context of the other known risk factors. We currently do not anticipate any impact on our regulatory submission timelines, including the filing of a BLA.

No other cases of HCC have been reported in our clinical trials conducted in more than 67 patients in hemophilia B, with some patients dosed more than 5 years ago.

Etranacogene dezaparvovec has been granted Breakthrough Therapy Designation by the FDA and access to the current priority medicines ("PRIME") initiative by the EMA.

Huntington's disease program (AMT-130)

AMT-130 is our novel gene therapy candidate for the treatment of Huntington's disease. AMT-130 utilizes our proprietary, gene-silencing miQURE platform and incorporates an AAV vector carrying an miRNA specifically designed to silence the huntingtin gene and the potentially highly toxic exon 1

protein fragment. AMT-130 has received orphan drug and Fast Track designations from the FDA and Orphan Medicinal Product Designation from the EMA.

In June 2020, we announced the completion of the first two patient procedures in the Phase I/II clinical trial of AMT-130 for the treatment of Huntington's disease. These procedures occurred after a postponement that resulted from the COVID-19 pandemic and the associated states of emergency declarations in the United States. The Phase I/II protocol is a randomized, imitation surgery-controlled, double-blinded study conducted at three surgical sites, and multiple referring, non-surgical sites in the U.S. The primary objective of the study is to evaluate the safety, tolerability, and efficacy of AMT-130 at two doses.

On September 25, 2020, we announced that the independent Data Safety Monitoring Board, or the DSMB, overseeing the Phase I/II clinical trial of AMT-130 for the treatment of Huntington's disease had met and reviewed 90-day safety data from the first two patients enrolled in the trial. No significant safety concerns were noted to prevent further dosing.

On October 13, 2020, we announced the completion of the third and fourth patient procedures in the Phase I/II clinical trial.

On February 8, 2020, we announced that the DSMB had met and reviewed the six-month safety data from the first two enrolled patients and the 90-day safety data from the next two enrolled patients in the study. No significant safety concerns were noted to prevent further dosing, and the final six patients in the first cohort are now cleared for enrollment.

BMS collaboration

We and Bristol-Myers Squibb, or BMS, entered into a collaboration and license agreement in May 2015, or the BMS CLA. BMS had initially designated four Collaboration Targets in 2015 and in accordance with the terms of the BMS CLA could have designated a fifth to tenth Collaboration Target.

In February 2019, BMS requested a one-year extension of the initial research term. In April 2019, following an assessment of the progress of this collaboration and our expanding proprietary programs, we notified BMS that we did not intend to agree to an extension of the initial research term. Accordingly, the initial four-year research term under the collaboration terminated on May 21, 2019.

On December 1, 2020, we and BMS amended the BMS CLA, or the amended BMS CLA. Following the amendment BMS is no longer entitled to designate a fifth to tenth Collaboration Target and as such we are no longer entitled to receive an aggregate $16.5 million in target designation payments for research, development, and regulatory milestone payments related to the fifth and tenth Collaboration Targets. For a period of one-year from the effective date of the amended BMS CLA, BMS may replace up to two of the four active Collaboration Targets with two new targets in the field of cardiovascular disease. We continue to be entitled to receive up to $217.0 million for each of the four Collaboration Targets if defined milestones are achieved, as well as royalties on net sales associated with any Collaboration Target. On December 17, 2020, BMS designated one of the four Collaboration Targets as a candidate to advance into IND-enabling studies entitling us to receive a $4.4 million research milestone payment. We recorded the $4.4 million as License Revenue in the twelve months period ended December 31, 2020.

The amended BMS CLA does not extend the initial research term. BMS may place purchase orders to provide limited services primarily related to analytical and development efforts in respect of the four Collaboration Targets. BMS may request such services for a period not to exceed the earlier of (i) the completion of all activities under a Research Plan and (ii) either (A) three years after the last replacement target has been designated by BMS during the one-year replacement period following the

amended BMS CLA effective date or (B) three years if no replacement targets are designated during this one-year period and BMS continues to reimburse us for these services.

For as long as any of the four Collaboration Targets are being advanced, BMS may place a purchase order to be supplied with research, clinical and commercial supplies. Subject to the terms of the amended BMS CLA, BMS has the right to terminate the research, clinical and commercial supply relationships, and has certain remedies for failures of supply, up to and including technology transfer for any such failure that otherwise cannot be reasonably resolved. Both we and BMS may agree to a technology transfer of manufacturing capabilities pursuant to the terms of the amended BMS CLA.

We have agreed to certain restrictions on our ability to work independently of the collaboration, either directly or indirectly through any affiliate or third party, on certain programs that would be competitive with a Collaboration Target. We have agreed to indication exclusivity for the current four Collaboration Targets. BMS may add or change the exclusive indications in the process of replacing Collaboration Targets as described above. We can opt out of the indication exclusivity by giving up certain economic rights under the amended BMS CLA for each such indication that is affected by us opting out. If we opt out of an exclusive indication, we could pursue other targets for such indication other than a Collaboration Target.

The amended BMS CLA also terminated two warrants to increase BMS ownership in the Company up to 19.9% through purchasing a specific number of our ordinary shares following the designation of a seventh, and a tenth Collaboration Target, respectively. We and BMS agreed that upon the consummation of a change of control transaction of uniQure that occurs prior to the earlier of (i) December 1, 2026 and (ii) BMS' delivery of a target cessation notice for all four Collaboration Targets, uniQure (or its third party acquirer) shall pay to BMS a one-time, non-refundable, non-creditable cash payment of $70.0 million, provided that (x) if $70.0 million is greater than five percent of the net proceeds (as contractually defined) from such change of control transaction, the payment shall be an amount equal to five percent of such net proceeds, and (y) if $70.0 million is less than one percent of such net proceeds, the change of control payment shall be an amount equal to one percent of such net proceeds. We have not consummated any change of control transaction as of December 31, 2020 that would obligate us to make a payment to BMS.

The amended BMS CLA did not change any of the provisions of the Investor Agreement with BMS that we entered into in 2015. We have granted BMS certain registration rights that allow BMS to require us to register our securities beneficially held by BMS under the U.S. Securities Exchange Act of 1934, as amended, or the Exchange Act. BMS may make up to two such demands for us to register the shares, provided that we may deny such demand if (i) the market value of the shares to be registered is less than $10.0 million (provided however, if BMS holds less than $10.0 million worth of our shares, we must comply with their demand for registration), (ii) we certify to BMS that we plan to effect a registration within 120 days of their demand or we are engaged in a transaction that would be required to be disclosed in a registration statement and that is not reasonably practicable to be disclosed at that time, or (iii) we have already effected one registration statement within the twelve months preceding BMS's demand for registration. In addition, independent of their demand registration rights, upon the occurrence of certain events, we must also provide BMS the opportunity to include their ordinary shares in any registration statement that we effect.

We also continue to grant BMS certain information rights under the Investor Agreement, although these requirements may be satisfied by our public filings required by U.S. securities laws.

BMS also continues to be subject to a lock up pursuant to the Investor Agreement for as long as BMS holds more than 4.9% of our ordinary shares (as of December 31, 2020 BMS holds 5.3%). Without our prior consent, BMS may not sell or dispose any of its current ordinary shares.

The Investor Agreement also continues to require BMS to vote all of our ordinary shares it beneficially holds in favor of all items on the agenda for the relevant general meeting of shareholders of our company as proposed on behalf of our company, unless, in the context of a change of control or similar transaction, BMS has itself made an offer to our company or our board in connection with the transaction that is the subject of the vote, in which case it is free to vote its shares at its discretion. This voting provision will terminate upon the later of the date on which BMS no longer beneficially owns at least 4.9% of our outstanding ordinary shares, the closing of a transaction that provides BMS exclusive and absolute discretion to vote our shares it beneficially holds, or the termination of the amended BMS CLA for breach by us.

Term loan facility

As of December 31, 2020, a $35.0 million term loan was outstanding in accordance with the Second Amended and Restated Loan and Security Agreement, or the 2018 Amended Facility, between us and Hercules.

On January 29, 2021 we and Hercules entered into amendments to the 2018 Amended Facility, or the 2021 Amended Facility. Pursuant to the 2021 Amended Facility, Hercules agreed to make additional term loans in the maximum aggregate amount of $100.0 million, or the 2021 Term Loan, increasing the aggregate principal amount of the term loan facility from $35.0 million to up to $135.0 million. On January 29, 2021 we drew down $35.0 million of the 2021 Term Loan. We may draw down the remaining $65.0 million under the 2021 Term Loan in a series of one or more advances of not less than $20.0 million each until December 15, 2021. Advances under the 2021 Term Loan bear interest at a rate equal to the greater of (i) 8.25% or (ii) 8.25% plus the prime rate, less 3.25% per annum. The principal balance and all accrued but unpaid interest on advances under the 2021 Term Loan is due on June 1, 2023, which such date may be extended by us by up to two twelve-month periods. Advances under the 2021 Term Loan may not be prepaid until six-months after the Closing Date, following which we may prepay all such advances without charge.

In addition to the 2021 Term Loan, the amendment also extends the interest only payment period of the previously funded $35.0 million term loan from January 1, 2022 to June l, 2023.

Corporate Information

uniQure B.V. was incorporated on January 9, 2012 as a private company with limited liability (*besloten vennootschap met beperkte aansprakelijkheid*) under the laws of the Netherlands. Our business was founded in 1998 and was initially operated through our predecessor company, Amsterdam Molecular Therapeutics (AMT) Holding N.V., or AMT. In 2012, AMT undertook a corporate reorganization, pursuant to which uniQure B.V. acquired the entire business and assets of AMT and completed a share-for-share exchange with the shareholders of AMT. Effective February 10, 2014, in connection with our initial public offering we converted into a public company with limited liability (*naamloze vennootschap*) and changed our legal name from uniQure B.V. to uniQure N.V.

Our company is registered with the trade register of the Dutch Chamber of Commerce (*handelsregister van de Kamer van Koophandel*) under number 54385229. Our corporate seat is in Amsterdam, the Netherlands, and our registered office is located at Paasheuvelweg 25a, Amsterdam 1105 BP, the Netherlands, and our telephone number is +31.20.240.6000.

Our website address is www.uniqure.com. The information contained in, or that can be accessed through, our website is not part of this prospectus.

The Securities We May Offer

We may offer debt securities, warrants, rights, purchase contracts, units, or ordinary shares from time to time. We may also offer securities of the types listed above that are convertible or exchangeable into one or more of the other securities so listed, from time to time in one or more offerings under this prospectus, together with any applicable prospectus supplement and any related free writing prospectus, at prices and on terms to be determined by market conditions at the time of the relevant offering. This prospectus provides you with a general description of the securities we may offer.

The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a part.

Selling Shareholders

Information about selling shareholders, including their identities and the number of ordinary shares to be registered on their behalf, will be set forth in a prospectus supplement, in a post-effective amendment or in filings we make with the SEC under the Exchange Act, that are incorporated by reference into this prospectus. Such selling shareholders may include existing shareholders, our executive officers and our directors.

Selling shareholders shall not sell any ordinary shares pursuant to this prospectus until we have identified such selling shareholders in a subsequent prospectus supplement. However, the selling shareholders may sell or transfer all or a portion of their ordinary shares pursuant to any available exemption from the registration requirements of the Securities Act.

This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.

We may sell the securities directly to investors or through underwriters, dealers or agents. We, and our underwriters or agents, reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities through underwriters or agents, we will include in the applicable prospectus supplement:

- the names of those underwriters or agents;
- applicable fees, discounts and commissions to be paid to them;
- details regarding option to purchase additional securities, if any; and
- the estimated net proceeds to us.

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully review the risks and uncertainties described under the heading "Risk Factors" contained in any applicable prospectus supplement and any related free writing prospectus, and under similar headings in our Annual Report on Form 10-K for the year ended December 31, 2020, as updated by our annual, quarterly and other reports and documents that are incorporated by reference into this prospectus, before deciding whether to purchase any of the securities being registered pursuant to the registration statement of which this prospectus is a part. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities, and the occurrence of any of these risks might cause you to lose all or part of your investment. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations. Please also read carefully the section below titled "Special Note Regarding Forward-Looking Statements."

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, each prospectus supplement and the information incorporated by reference in this prospectus and each prospectus supplement contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, which we refer to as the Securities Act, and Section 21E of the Exchange Act, that involve a number of risks and uncertainties. Although our forward-looking statements reflect the good faith judgment of our management, these statements can only be based on facts and factors currently known by us. Consequently, these forward-looking statements are inherently subject to risks and uncertainties, and actual results and outcomes may differ materially from results and outcomes discussed in the forward-looking statements.

Forward-looking statements can be identified by the use of forward-looking words such as "believes," "expects," "anticipates," "plans," "may," "will," "projects," "continues," "estimates," "potential," "opportunity" and similar expressions.. These statements include but are not limited to statements under the captions "Business," "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and in other sections included in any applicable prospectus supplement or incorporated by reference from our Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, as applicable, as well as our other filings with the SEC. You should be aware that the occurrence of any of the events discussed under the heading "Risk Factors" in any applicable prospectus supplement and any documents incorporated by reference herein or therein could substantially harm our business, operating results and financial condition and that if any of these events occurs, it could adversely affect the value of an investment in our securities.

The cautionary statements made in this prospectus are intended to be applicable to all related forward-looking statements wherever they may appear in this prospectus or in any prospectus supplement or any documents incorporated by reference herein or therein. We urge you not to place undue reliance on these forward-looking statements, which speak only as of the date they are made. Except as required by law, we assume no obligation to update our forward-looking statements, even if new information becomes available in the future.

USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds from the sale of the securities offered hereby. Except as described in any prospectus supplement or any related free writing prospectus that we may authorize to be provided to you, we currently intend to use the net proceeds from the sale of the securities offered hereby for general corporate purposes, which may include capital expenditures, debt repayment, working capital and general and administrative expenses. We may also use a portion of the net proceeds to acquire or invest in businesses that are complementary to our own,

although we have no current plans, commitments or agreements with respect to any acquisitions as of the date of this prospectus. We will set forth in the applicable prospectus supplement or free writing prospectus our intended use for the net proceeds received from the sale of any securities sold pursuant to the prospectus supplement or free writing prospectus. Pending these uses, we intend to invest the net proceeds in short-term obligations of the U.S. government and its agencies.

We will not receive any proceeds from the sale of ordinary shares in a secondary offering by any selling shareholders. The selling shareholders will pay any underwriting or broker discounts and commissions and expenses incurred by the selling shareholders for brokerage, accounting, tax, or legal services or any other expenses incurred by the selling shareholders in disposing of the ordinary shares in a secondary offering. We will bear all other costs, fees, and expenses incurred in effecting the registration of the securities covered by this prospectus, including, without limitation, all registration and filing fees and fees and expenses of our counsel and our accountants.

DESCRIPTION OF ORDINARY SHARES

The description below of our ordinary shares and provisions of our articles of association are summaries and are qualified by reference to our articles of association and the applicable provisions of Dutch law.

The following description of the general terms and provisions of our ordinary shares is a summary only and therefore is not complete and is subject to, and qualified in its entirety by reference to, the terms and provisions of our articles of association. Our articles of association have been filed with the SEC as an exhibit to the registration statement of which this prospectus forms a part and you should read our articles of association for provisions that may be important to you.

Authorized Ordinary Shares

Our articles of association provide an authorized share capital of 60,000,000 ordinary shares, each with a nominal value per share of €0.05. As of February 25, 2021, we had 44,993,987 ordinary shares issued and outstanding. We do not have any preferred shares authorized or issued and outstanding.

Form of Ordinary Shares

We issue our ordinary shares in registered book-entry form and such shares are not certificated.

Issuance of Ordinary Shares

We may issue ordinary shares subject to the maximum prescribed by our authorized share capital contained in our articles of association. Our board has the power to issue ordinary shares if and only to the extent that the general meeting of shareholders has designated to the board such authority. Currently our articles of association provide for an authorized share capital which amounts to €3,000,000 and is divided into one class of shares, being 60,000,000 ordinary shares, each with a nominal value of €0.05 per share. A designation of authority to the board to issue ordinary shares remains effective for the period specified by the general meeting of shareholders and may be granted up to a maximum of five years from the date of designation. The general meeting of shareholders may renew this designation annually.

Without this designation, only the general meeting of shareholders has the power to authorize the issuance of ordinary shares upon the proposal of the board. Currently, our board is authorized to issue ordinary shares until December 17, 2021 under the restrictions specified in our articles of association and the designation.

In connection with the issuance of ordinary shares, at least the nominal value must be paid for such shares. No obligation other than to pay up the nominal amount of and any premium agreed upon

an ordinary share may be imposed upon a shareholder against the shareholder's will, by amendment of the articles of association or otherwise. Subject to Dutch law, payment for ordinary shares must be in cash to the extent no other contribution has been agreed and may be made in the currency approved by us.

Any increase in the number of authorized ordinary shares and the introduction of different classes of shares would require the approval of an amendment to our articles of association in order to effect such increase or introduction. Such amendment would need to be made by a proposal of the board and adoption by the shareholders at a general meeting of shareholders by a majority vote.

Nasdaq Global Market Listing

Our ordinary shares are listed on The Nasdaq Global Select Market under the symbol "QURE."

Comparison of Dutch corporate law and our Articles of Association and Delaware corporate law

The following comparison between Dutch corporate law, which applies to us, and Delaware corporate law, the law under which many publicly listed companies in the United States are incorporated, discusses additional matters not otherwise described in this prospectus. This summary is subject to Dutch law, including Book 2 of the Dutch Civil Code and Delaware corporation law, including the Delaware General Corporation Law.

Corporate governance

Duties of directors

The Netherlands. We have a one-tier board structure consisting of our executive director and non-executive directors. Under the one-tier board structure, both the executive and non-executive directors will be collectively responsible for the management performed by the one-tier board and for the general policy and strategy of a company. The executive directors are responsible for the day-to-day management of a company. The non-executive directors are responsible for supervising the conduct of, and providing advice to, the executive directors and for providing supervision with respect to the company's general state of affairs. Each executive director and non-executive director has a duty to act in the corporate interest of the company. Under Dutch law, the corporate interest extends to the interests of all corporate stakeholders, such as shareholders, creditors, employees, customers and suppliers. The duty to act in the corporate interest of the company also applies in the event of a proposed sale or split-up of a company, whereby the circumstances generally dictate how such duty is to be applied. Any resolution of the board regarding a significant change in the identity or character of a company requires shareholders' approval.

Delaware. The board of directors bears the ultimate responsibility for managing the business and affairs of a corporation. In discharging this function, directors of a Delaware corporation owe fiduciary duties of care and loyalty to the corporation and to its stockholders. Delaware courts have decided that the directors of a Delaware corporation are required to exercise informed business judgment in the performance of their duties. Informed business judgment means that the directors have informed themselves of all material information reasonably available to them. Delaware courts have also imposed a heightened standard of conduct upon directors of a Delaware corporation who take any action designed to defeat a threatened change in control of the corporation. In addition, under Delaware law, when the board of directors of a Delaware corporation approves the sale or break-up of a corporation, the board of directors may, in certain circumstances, have a duty to obtain the highest value reasonably available to the stockholders.

Director terms

The Netherlands. Under Dutch law, executive directors of a listed company are generally appointed for a term of a maximum of four years and reappointed for a term of a maximum of four years at a time. Non-executive directors of a listed company are generally appointed for a term of a maximum of four years and reappointed once for another term of a maximum of four years. Non-executive directors of a listed company may subsequently be reappointed for a term of a maximum of two years, which reappointment may be extended by at most two years. Our executive and non-executive directors are, in principle, appointed by the general meeting of shareholders upon the binding nomination of the non-executive directors.

The general meeting of shareholders is entitled at all times to suspend or dismiss a director. The general meeting of shareholders may only adopt a resolution to suspend or dismiss such director by at least a two-thirds majority of the votes cast, if such majority represents more than half of the issued share capital of the company.

Delaware. The Delaware General Corporation Law generally provides for a one-year term for directors, but permits directorships to be divided into up to three classes with up to three-year terms, with the years for each class expiring in different years, if permitted by a company's certificate of incorporation, an initial bylaw or a bylaw adopted by the stockholders. A director elected to serve a term on such a classified board may not be removed by stockholders without cause. There is no limit in the number of terms a director may serve.

Director vacancies

The Netherlands. Under Dutch law, directors are appointed by the general meeting of shareholders. Under our articles of association, directors are, in principle, appointed by the general meeting of shareholders upon the binding nomination by the non-executive directors. However, the general meeting of shareholders may at all times overrule such binding nomination by a resolution adopted by at least a two-thirds majority of the votes cast, provided such majority represents more than half of the issued share capital of our company. If the general meeting of shareholders overrules the binding nomination, the non-executive directors must make a new nomination.

Delaware. The Delaware General Corporation Law provides that vacancies and newly created directorships may be filled by a majority of the directors then in office (even though less than a quorum) unless (1) otherwise provided in the certificate of incorporation or bylaws of the corporation or (2) the certificate of incorporation directs that a particular class of stock is to elect such director, in which case any other directors elected by such class, or a sole remaining director elected by such class, will fill such vacancy.

Conflict-of-interest transactions

The Netherlands. Pursuant to Dutch law and our articles of association, directors may not take part in any discussion or decision-making that involves a subject or transaction in relation to which they have a personal direct or indirect conflict of interest with us. Our articles of association provide that if as a result thereof, the board is unable to act the resolution will be adopted by the general meeting of shareholders.

Delaware. The Delaware General Corporation Law generally permits transactions involving a Delaware corporation and an interested director of that corporation if:

- the material facts as to the director's relationship or interest are disclosed and a majority of disinterested directors consent;

- the material facts are disclosed as to the director's relationship or interest and a majority of shares entitled to vote thereon consent; or

- the transaction is fair to the corporation at the time it is authorized by the board of directors, a committee of the board of directors or the stockholders.

Shareholder rights

Voting rights

The Netherlands. In accordance with Dutch law and our articles of association, each issued ordinary share confers the right to cast one vote at the general meeting of shareholders. Each holder of ordinary shares may cast as many votes as it holds ordinary shares. Ordinary shares that are held by us or our direct or indirect subsidiaries do not confer the right to vote. Dutch law does not permit cumulative voting for the election of executive directors and non-executive directors.

For each general meeting of shareholders, a record date will be applied with respect to ordinary shares in order to establish which shareholders are entitled to attend and vote at a specific general meeting of shareholders. Such record date is set by the board. The record date and the manner in which shareholders can register and exercise their rights will be set out in the convocation notice of the meeting.

Delaware. Under the Delaware General Corporation Law, each stockholder is entitled to one vote per share of stock, unless the certificate of incorporation provides otherwise. In addition, the certificate of incorporation may provide for cumulative voting at all elections of directors of the corporation, or at elections held under specified circumstances. Either the certificate of incorporation or the bylaws may specify the number of shares and/or the amount of other securities that must be represented at a meeting in order to constitute a quorum, but in no event will a quorum consist of less than one third of the shares entitled to vote at a meeting.

Stockholders as of the record date for the meeting are entitled to vote at the meeting, and the board of directors may fix a record date that is no more than 60 nor less than ten days before the date of the meeting, and if no record date is set then the record date is the close of business on the day next preceding the day on which notice is given, or if notice is waived then the record date is the close of business on the day next preceding the day on which the meeting is held. The determination of the stockholders of record entitled to notice or to vote at a meeting of stockholders shall apply to any adjournment of the meeting, but the board of directors may fix a new record date for the adjourned meeting.

Shareholder proposals

The Netherlands. Pursuant to our articles of association, extraordinary general meetings of shareholders will be convened by the board or by those who are authorized by law or pursuant to our articles of association to do so. Pursuant to Dutch law, one or more shareholders representing at least one-tenth of the issued share capital of the company may request the Dutch court in preliminary relief proceedings to order that they be authorized by the court to convene a general meeting of shareholders. The court shall disallow the request if it does not appear that the applicants have previously requested the board to convene a general meeting of shareholders and the board has taken the necessary steps so that the general meeting of shareholders could be held within six weeks after the request.

The agenda for a general meeting of shareholders must include such items requested by one or more shareholders representing at least 3% of the issued share capital of a company or such lower percentage as the articles of association may provide. Our articles of association do not state such lower percentage.

Delaware. Delaware law does not specifically grant stockholders the right to bring business before an annual or special meeting. However, if a Delaware corporation is subject to the SEC's proxy rules, a stockholder who owns at least $2,000 in market value, or 1% of the corporation's securities entitled to vote, may propose a matter for a vote at an annual or special meeting in accordance with those rules.

Action by written consent

The Netherlands. Under Dutch law, the articles of association of a company may provide that shareholders' resolutions may be adopted in writing without holding a general meeting of shareholders, provided that the resolution is adopted unanimously by all shareholders that are entitled to vote. For a listed company, this method of adopting resolutions is not feasible.

Delaware. Although permitted by Delaware law, publicly listed companies do not typically permit stockholders of a corporation to take action by written consent.

Appraisal rights

The Netherlands. The concept of appraisal rights does not exist under Dutch law. However, pursuant to Dutch law a shareholder who for its own account contributes at least 95% of our issued share capital may initiate proceedings against our minority shareholders jointly for the transfer of their ordinary shares to it. The proceedings are held before the Enterprise Chamber of the Amsterdam Court of Appeal (*Ondernemingskamer van het gerechtshof Amsterdam*). The Enterprise Chamber may grant the claim for squeeze-out in relation to all minority shareholders and will determine the price to be paid for the ordinary shares, if necessary after appointment of one or three experts who will offer an opinion to the Enterprise Chamber on the value to be paid for the ordinary shares of the minority shareholders.

Furthermore, Dutch law provides that, to the extent the acquiring company in a cross-border merger is organized under the laws of another European Union, or European Economic Area member state, a shareholder of a Dutch disappearing company who has voted against the cross-border merger may file a claim with the Dutch company for compensation. The compensation is to be determined by one or more independent experts.

Delaware. The Delaware General Corporation Law provides for stockholder appraisal rights, or the right to demand payment in cash of the judicially determined fair value of the stockholder's shares, in connection with certain mergers and consolidations.

Shareholder suits

The Netherlands. In the event a third party is liable to a Dutch company, only a company itself can initiate a civil action against that third party. An individual shareholder does not have the right to initiate an action on behalf of a company. This individual shareholder may, in its own name, have an individual right to initiate an action against such third party in the event that the cause for the liability of that third party also constitutes a tortious act directly against that individual shareholder. The Dutch Civil Code provides for the possibility (for shareholders) to initiate such action collectively. A collective action can be instituted against a defendant by a foundation or association whose objective it is to protect the rights of a group of persons having similar interests. A collective action relating to an event prior to November 15, 2016 cannot result in an order for payment of monetary damages but may only result in a declaratory judgment (*verklaring voor recht*) regarding liability. In order to obtain montetary damages, the foundation or association and the defendant may reach—often on the basis of such declaratory judgment—a collective settlement agreement. A Dutch court may declare the collective settlement agreement binding upon the members of the class with an opt-out right for an individual injured party. An individual injured party may also itself—outside the collective action—reach an individual settlement agreement (and have it declared binding by the Dutch court) or institute an

action for monetary damages. Since January 1, 2020, a collective action relating to an event on or after November 15, 2016 can, however, also result in an order for payment of monetary damages. As a general rule, a court decision granting or dismissing the collective action is binding on all members of the class who reside in the Netherlands and did not use their right to opt out of the collective action (earlier on in the collective action, as soon as the class was defined and the scope of the collective action was determined by the Dutch court) as well as to members of the class residing abroad who joined the collective action by opting in.

Delaware. Under the Delaware General Corporation Law, a stockholder may bring a derivative action on behalf of the corporation to enforce the rights of the corporation. An individual also may commence a class action suit on behalf of himself and other similarly situated stockholders where the requirements for maintaining a class action under Delaware law have been met. A person may institute and maintain such a suit only if that person was a stockholder at the time of the transaction which is the subject of the suit. In addition, under Delaware case law, the plaintiff normally must be a stockholder at the time of the transaction that is the subject of the suit and throughout the duration of the derivative suit. Delaware law also requires that the derivative plaintiff make a demand on the directors of the corporation to assert the corporate claim before the suit may be prosecuted by the derivative plaintiff in court, unless such a demand would be futile.

Repurchase of shares

The Netherlands. Under Dutch law, a company such as ours may not subscribe for newly issued shares in its own share capital. Such company may, however, subject to certain restrictions under Dutch law and its articles of association, acquire shares in its own share capital. We may acquire fully paid-up ordinary shares in our own share capital at any time for no valuable consideration. Furthermore, subject to certain provisions of Dutch law and our articles of association, we may repurchase fully paid-up ordinary shares in our own share capital if (1) such repurchase would not cause our shareholders' equity to fall below an amount equal to the sum of the paid-up and called-up part of the issued share capital and the reserves we are required to maintain pursuant to applicable law or our articles of association and (2) we would not as a result of such repurchase hold more than 50% of our own issued share capital.

Other than ordinary shares acquired for no valuable consideration, ordinary shares may only be acquired following a resolution of our board, acting pursuant to an authorization for the repurchase of ordinary shares granted by the general meeting of shareholders. An authorization by the general meeting of shareholders for the repurchase of ordinary shares can be granted for a maximum period of 18 months. Such authorization must specify the number of ordinary shares that may be acquired, the manner in which these ordinary shares may be acquired and the price range within which the shares may be acquired. Our board has been authorized, for a period of 18 months to be calculated from the date of the annual general meeting of shareholders held on June 17, 2020, to cause the repurchase of ordinary shares by us of up to 10% of our issued share capital, for a price per share between the nominal value of the ordinary shares and an amount of 110% of the highest price of the ordinary shares officially quoted on any of the official stock markets we are listed on during any of the 30 banking days preceding the date the repurchase is effected or proposed.

No authorization of the general meeting of shareholders is required if fully paid-up ordinary shares are acquired by us with the intention of transferring such ordinary shares to our employees under an applicable employee stock purchase plan, provided such ordinary shares are officially quoted on any of the official stock markets.

Delaware. Under the Delaware General Corporation Law, a corporation may purchase or redeem its own shares unless the capital of the corporation is impaired or the purchase or redemption would cause an impairment of the capital of the corporation. A Delaware corporation may, however, purchase or redeem out of capital any of its preferred shares or, if no preferred shares are outstanding, any of its own shares if such shares will be retired upon acquisition and the capital of the corporation will be reduced in accordance with specified limitations.

Anti-takeover provisions

The Netherlands. Under Dutch law, various protective measures are possible and permissible within the boundaries set by Dutch statutory law and Dutch case law. We have adopted several provisions that may have the effect of making a takeover of our company more difficult or less attractive, including:

- the staggered three-year terms of our directors, as a result of which only approximately one-third of our directors will be subject to election in any one year;
- a provision that our directors may only be removed by the general meeting of shareholders by a two-thirds majority of votes cast representing more than half of our issued share capital; and
- requirements that certain matters, including an amendment of our articles of association, may only be brought to our shareholders for a vote upon a proposal by our board.

Delaware. In addition to other aspects of Delaware law governing fiduciary duties of directors during a potential takeover, the Delaware General Corporation Law also contains a business combination statute that protects Delaware companies from hostile takeovers and from actions following the takeover by prohibiting some transactions once an acquirer has gained a significant holding in the corporation.

- Section 203 of the Delaware General Corporation Law prohibits "business combinations," including mergers, sales and leases of assets, issuances of securities and similar transactions by a corporation or a subsidiary with an interested stockholder that beneficially owns 15% or more of a corporation's voting stock, within three years after the person becomes an interested stockholder, unless: the transaction that will cause the person to become an interested stockholder is approved by the board of directors of the target prior to the transactions;
- after the completion of the transaction in which the person becomes an interested stockholder, the interested stockholder holds at least 85% of the voting stock of the corporation not including shares owned by persons who are directors and representatives of interested stockholders and shares owned by specified employee benefit plans; or
- after the person becomes an interested stockholder, the business combination is approved by the board of directors of the corporation and holders of at least 66.67% of the outstanding voting stock, excluding shares held by the interested stockholder.

A Delaware corporation may elect not to be governed by Section 203 by a provision contained in the original certificate of incorporation of the corporation or an amendment to the original certificate of incorporation or to the bylaws of the company, which amendment must be approved by a majority of the shares entitled to vote and may not be further amended by the board of directors of the corporation. Such an amendment is not effective until twelve months following its adoption.

Inspection of books and records

The Netherlands. Our board provides the shareholders, at the general meeting of shareholders, with all information that the shareholders require for the exercise of their powers, unless doing so would be contrary to an overriding interest of ours. Our board must give reason for electing not to provide such information on the basis of an overriding interest.

Delaware. Under the Delaware General Corporation Law, any stockholder may inspect certain of the corporation's books and records, for any proper purpose, during the corporation's usual hours of business.

Removal of directors

The Netherlands. Under our articles of association, the general meeting of shareholders is at all times entitled to suspend or dismiss a director. The general meeting of shareholders may only adopt a resolution to suspend or dismiss such a director by at least a two-thirds majority of the votes cast, provided such majority represents more than half of the issued share capital of our company.

Delaware. Under the Delaware General Corporation Law, any director or the entire board of directors may be removed, with or without cause, by the holders of a majority of the shares then entitled to vote at an election of directors, except (1) unless the certificate of incorporation provides otherwise, in the case of a corporation whose board is classified, stockholders may effect such removal only for cause, or (2) in the case of a corporation having cumulative voting, if less than the entire board is to be removed, no director may be removed without cause if the votes cast against his removal would be sufficient to elect him if then cumulatively voted at an election of the entire board of directors, or, if there are classes of directors, at an election of the class of directors of which he is a part.

Preemptive rights

The Netherlands. Under Dutch law, in the event of an issuance of ordinary shares, each shareholder will have a pro rata preemptive right in proportion to the aggregate nominal value of the ordinary shares held by such shareholder (with the exception of ordinary shares to be issued to employees or ordinary shares issued against a contribution other than in cash). Under our articles of association, the preemptive rights in respect of newly issued ordinary shares may be restricted or excluded by a resolution of the general meeting of shareholders upon proposal of our board. The general meeting of shareholders may designate our board to restrict or exclude the preemptive rights in respect of newly issued ordinary shares. Such designation can be granted for a period not exceeding five years. A resolution of the general meeting of shareholders to restrict or exclude the preemptive rights or to designate the board as the authorized body to do so requires a two-thirds majority of the votes cast, if less than one half of our issued share capital is represented at the meeting. The same applies to the granting of rights to subscribe for our ordinary shares but does not apply to the issuance of our ordinary shares pursuant to the exercise of a previously acquired right to subscribe for our ordinary shares.

At our annual general meeting of shareholders held on June 17, 2020, the general meeting of shareholders resolved to authorize our board for a period of 18 months with effect from the date of the meeting to restrict or exclude preemptive rights accruing to shareholders in connection with the issue of ordinary shares or rights to subscribe for ordinary shares.

Delaware. Under the Delaware General Corporation Law, stockholders have no preemptive rights to subscribe for additional issues of stock or to any security convertible into such stock unless, and to the extent that, such rights are expressly provided for in the certificate of incorporation.

Dividends

The Netherlands. Dutch law provides that dividends may be distributed after adoption of the annual accounts by the general meeting of shareholders from which it appears that such dividend distribution is allowed. Moreover, dividends may be distributed only to the extent that the shareholders' equity exceeds the amount of the paid-up and called-up part of the issued share capital of the company and the reserves that must be maintained under applicable law or the articles of association. Interim dividends may be declared as provided in the articles of association and may be distributed only to the extent that the shareholders' equity exceeds the amount of the paid-up and called-up part of the issued share capital of the company and the reserves that must be maintained under applicable law or the articles of association, as apparent from an interim statement of assets and liabilities.

Under our articles of association, any amount of profit may be carried to a reserve as our board determines. After reservation by our board of any profit, the remaining profit will be at the disposal of the shareholders. Our corporate policy is to only make a distribution of dividends to our shareholders after the adoption of our annual accounts demonstrating that such distribution is legally permitted. However, our board is permitted to declare interim dividends without the approval of the general meeting of shareholders.

Dividends will be made payable not later than thirty days after the date they were declared unless the body declaring the dividend determines a different date. Claims to dividends not made within five years and one day from the date that such dividends became payable will lapse and any such amounts will be considered to have been forfeited to us (*verjaring*).

Delaware. Under the Delaware General Corporation Law, a Delaware corporation may pay dividends out of its surplus (the excess of net assets over capital), or in case there is no surplus, out of its net profits for the fiscal year in which the dividend is declared and/or the preceding fiscal year (provided that the amount of the capital of the corporation is not less than the aggregate amount of the capital represented by the issued and outstanding stock of all classes having a preference upon the distribution of assets). In determining the amount of surplus of a Delaware corporation, the assets of the corporation, including stock of subsidiaries owned by the corporation, must be valued at their fair market value as determined by the board of directors, without regard to their historical book value. Dividends may be paid in the form of shares, property or cash.

Shareholder vote on certain reorganizations

The Netherlands. Under Dutch law, the general meeting of shareholders must approve resolutions of the board relating to a significant change in the identity or the character of the company or the business of the company, which includes:

- a transfer of the business or virtually the entire business to a third party;
- the entry into or termination of a long-term cooperation of the company or a subsidiary with another legal entity or company or as a fully liable partner in a limited partnership or general partnership, if such cooperation or termination is of a far-reaching significance for the company; and
- the acquisition or divestment by the company or a subsidiary of a participating interest in the capital of a company having a value of at least one third of the amount of its assets according to its balance sheet and explanatory notes or, if the company prepares a consolidated balance sheet, according to its consolidated balance sheet and explanatory notes, according to the last adopted annual accounts of the company.

Delaware. Under the Delaware General Corporation Law, the vote of a majority of the outstanding shares of capital stock entitled to vote thereon generally is necessary to approve a merger or consolidation or the sale of all or substantially all of the assets of a corporation. The Delaware General Corporation Law permits a corporation to include in its certificate of incorporation a provision requiring for any corporate action the vote of a larger portion of the stock or of any class or series of stock than would otherwise be required.

Under the Delaware General Corporation Law, no vote of the stockholders of a surviving corporation to a merger is needed, however, unless required by the certificate of incorporation, if (1) the agreement of merger does not amend in any respect the certificate of incorporation of the surviving corporation, (2) the shares of stock of the surviving corporation are not changed in the merger and (3) the number of shares of common stock of the surviving corporation into which any other shares, securities or obligations to be issued in the merger may be converted does not exceed 20% of the surviving corporation's common stock outstanding immediately prior to the effective date of

the merger. In addition, stockholders may not be entitled to vote in certain mergers with other corporations that own 90% or more of the outstanding shares of each class of stock of such corporation, but the stockholders will be entitled to appraisal rights.

Remuneration of directors

The Netherlands. Under Dutch law and our articles of association, we must adopt a remuneration policy for our board. Such remuneration policy shall be adopted by the general meeting of shareholders upon the proposal of our non-executive directors. The remuneration of our executive directors will be determined by our non-executive directors with due observance of our remuneration policy; the remuneration of our non-executive directors will be determined by our board with due observance of our remuneration policy.

Delaware. Under the Delaware General Corporation Law, the stockholders do not generally have the right to approve the compensation policy for directors or the senior management of the corporation, although certain aspects of executive compensation may be subject to binding or advisory stockholder votes due to the provisions of U.S. federal securities and tax law, as well as stock exchange requirements.

Transfer Agent and Registrar

Computershare Trust Company, N.A. serves as transfer agent and registrar for our ordinary shares.

DESCRIPTION OF DEBT SECURITIES

In this section, references to "holders" mean those who own debt securities registered in their own names on the books that uniQure N.V. or the indenture trustee maintains for this purpose, and not those who own beneficial interests in debt securities registered in street name or in debt securities issued in book-entry form through one or more depositaries. Owners of beneficial interests in the debt securities should read the section below entitled "Book-Entry Procedures and Settlement."

General

The debt securities offered by this prospectus will be either senior or subordinated debt. Senior debt securities or subordinated debt securities may be convertible or exchangeable into our ordinary shares or other securities as described under "—Convertible or Exchangeable Securities" below. We will issue senior debt under a senior debt indenture, we will issue subordinated debt under a subordinated debt indenture and we will issue convertible debt securities under a convertible debt indenture. We sometimes refer to the senior debt indenture, the subordinated debt indenture and the convertible debt indenture individually as an indenture and collectively as the indentures. The indentures will be between us and a trustee. The terms of the indenture governing the convertible debt securities will be substantially similar to the terms of the indenture governing the senior debt securities described below, except that the indenture governing the convertible debt securities will include provisions with respect to the conversion of such convertible debt securities, omit certain provisions described under "—Defeasance" below, prohibit any modification to the terms of convertibility without the consent of the holders and permit any holder to institute action to enforce such terms of convertibility. The indentures are exhibits to the registration statement of which this prospectus forms a part. You can obtain copies of the indentures by following the directions outlined in "Where You Can Find Additional Information" or by contacting the indenture trustee.

The following briefly summarizes the material provisions of the indentures and the debt securities, other than pricing and related terms which will be disclosed for a particular series of debt securities in a prospectus supplement. You should read the more detailed provisions of the applicable indenture, including the defined terms, for provisions that may be important to you. You should also read the

particular terms of a series of debt securities, which will be described in more detail in a prospectus supplement. Wherever particular sections or defined terms of the applicable indenture are referred to, such sections or defined terms are incorporated into this prospectus by reference, and the statement in this prospectus is qualified by that reference.

The indentures provide that our debt securities may be issued in one or more series, with different terms, in each case as we authorize from time to time. We also have the right to reopen a previous issue of a series of debt securities by issuing additional debt securities of such series.

Information in the Prospectus Supplement

The prospectus supplement for any offered series of debt securities will describe the following terms, as applicable:

- the title or designation of the offered debt securities;
- whether the debt is senior or subordinated;
- whether there is any collateral securing the debt securities;
- whether the debt securities are convertible or exchangeable into other securities;
- the aggregate principal amount offered and the authorized denominations;
- the initial public offering price;
- the maturity date or dates;
- any sinking fund or other provision for payment of the debt securities prior to their stated maturity;
- whether the debt securities are fixed rate debt securities or floating rate debt securities or original issue discount debt securities;
- if the debt securities are fixed rate debt securities, the yearly rate at which the debt securities will bear interest, if any;
- if the debt securities are floating rate debt securities, the method of calculating the interest rate;
- if the debt securities are original issue discount debt securities, their yield to maturity;
- the date or dates from which any interest will accrue, or how such date or dates will be determined, and the interest payment dates and any related record dates;
- if other than in U.S. Dollars, the currency or currency unit in which payment will be made;
- any provisions for the payment of additional amounts for taxes;
- the denominations in which the currency or currency unit of the securities will be issuable if other than denominations of $1,000 and integral multiples thereof;
- the terms and conditions on which the debt securities may be redeemed at the option of the Company;
- any obligation of the Company to redeem, purchase or repay the debt securities at the option of a holder upon the happening of any event and the terms and conditions of redemption, purchase or repayment;
- the names and duties of any co-indenture trustees, depositaries, authenticating agents, calculation agents, paying agents, transfer agents or registrars for the debt securities;

- any material provisions of the applicable indenture described in this prospectus that do not apply to the debt securities;
- the ranking of the specific series of debt securities relative to other outstanding indebtedness;
- if the debt securities are subordinated, the aggregate amount of outstanding indebtedness, as of a recent date, that is senior to the subordinated securities, and any limitation on the issuance of additional senior indebtedness;
- the place where we will pay principal and interest;
- additional provisions, if any, relating to the defeasance of the debt securities;
- any United States federal income tax consequences, if material;
- the dates on which premium, if any, will be paid;
- our right, if any, to defer payment of interest and the maximum length of this deferral period;
- any listing of the debt securities on a securities exchange; and
- any other specific terms of the debt securities.

We will issue the debt securities only in registered form. As currently anticipated, debt securities of a series will trade in book-entry form, and global notes will be issued in physical (paper) form, as described below under "Book-Entry Procedures and Settlement."

Senior Debt

We will issue senior debt securities under the senior debt indenture. These senior debt securities will rank on an equal basis with all our other unsecured debt except subordinated debt.

Subordinated Debt

We will issue subordinated debt securities under the subordinated debt indenture. Subordinated debt will rank subordinate and junior in right of payment, to the extent set forth in the subordinated debt indenture, to all our senior debt (both secured and unsecured).

In general, the holders of all senior debt are first entitled to receive payment of the full amount unpaid on senior debt before the holders of any of the subordinated debt securities are entitled to receive a payment on account of the principal or interest on the indebtedness evidenced by the subordinated debt securities in certain events.

If we default in the payment of any principal of, or premium, if any, or interest on any senior debt when it becomes due and payable after any applicable grace period, then, unless and until the default is cured or waived or ceases to exist, we cannot make a payment on account of or redeem or otherwise acquire the subordinated debt securities.

If there is any insolvency, bankruptcy, liquidation or other similar proceeding relating to us or our property, then all senior debt must be paid in full before any payment may be made to any holders of subordinated debt securities.

Furthermore, if we default in the payment of the principal of and accrued interest on any subordinated debt securities that is declared due and payable upon an event of default under the subordinated debt indenture, holders of all our senior debt will first be entitled to receive payment in full in cash before holders of such subordinated debt can receive any payments.

Senior debt means:

- the principal, premium, if any, interest and any other amounts owing in respect of indebtedness of the Company and/or of our subsidiaries that may guarantee our debt for money borrowed and indebtedness evidenced by securities, notes, debentures, bonds or other similar instruments issued by us, including the senior debt securities and letters of credit;
- all capitalized lease obligations;
- all hedging obligations;
- all obligations representing the deferred purchase price of property; and
- all deferrals, renewals, extensions and refundings of obligations of the type referred to above;

but senior debt does not include:

- subordinated debt securities; and
- any indebtedness that by its terms is subordinated to, or ranks on an equal basis with, our subordinated debt securities.

Convertible Debt

We will issue convertible debt securities under the convertible debt indenture. Convertible debt securities will be convertible into ordinary shares on the terms set forth in the convertible debt indenture. The convertible debt indenture will provide that the conversion price is subject to customary anti-dilution adjustments in connection with stock dividends, stock splits, stock combinations, reclassifications and other similar events.

Covenants

Amalgamation and Sale of Assets. We may not, in a single transaction or a series of related transactions:

- consolidate, amalgamate or merge with or into any other person; or
- directly or indirectly, transfer, sell, lease or otherwise dispose of all or substantially all of our assets,

unless, in either such case:

- in a transaction in which we do not survive or in which we sell, lease or otherwise dispose of all or substantially all of our assets, the successor entity to us expressly assumes, by a supplemental indenture executed and delivered to the indenture trustee in a form reasonably satisfactory to the indenture trustee, all of our obligations under the indenture;
- immediately before and after giving effect to the transaction, no default on the debt securities exists; and
- an officer's certificate and an opinion of counsel setting forth certain statements are delivered to the indenture trustee.

Other Covenants. In addition, any offered series of debt securities may have additional covenants which will be described in the prospectus supplement, limiting or restricting, among other things:

- our ability to incur indebtedness;
- our ability to pay dividends, to repurchase or redeem our capital stock;
- our ability to create dividend and other payment restrictions affecting our subsidiaries;

- mergers and consolidations by us;
- sales of assets by us;
- our ability to enter into transactions with affiliates;
- our ability to incur liens; and
- our ability to enter into sale and leaseback transactions.

Modification of the Indentures

Under the indentures, we and the indenture trustee may amend the indentures, without the consent of any holder of the debt securities to:

- cure ambiguities, defects or inconsistencies;
- comply with the covenants described under "—Amalgamation and Sale of Assets";
- add to our covenants for the benefit of the holders of all or any series of debt securities (and if such covenants are to be for the benefit of less than all series of debt securities, stating that such covenants are expressly being included for the benefit of such series) or to surrender any rights or power conferred upon us;
- add any additional events of default for the benefit of the holders of all or a series of debt securities;
- establish the form or terms of debt securities of any series;
- provide for uncertificated debt securities in addition to or in place of certificated debt securities;
- secure the debt securities of one or more series;
- evidence the succession of another person to the Company and the assumption of the covenants in the indentures and in the debt securities by such successor; or any co-issuer of the debt securities;
- add or change any provision of the indentures to permit the issuance of the debt securities in bearer form, registrable or not registrable as to principal, with or without interest coupons;
- appoint a successor indenture trustee;
- add to, change or eliminate any provision of the indentures so long as such addition, change or elimination does not affect the rights of the holders; or
- conform any provision of the indentures to the description of securities contained in this prospectus or any similar provision in any prospectus supplement relating to an offer of a series of debt securities under the indentures.

We and the indenture trustee may, with the consent of the holders of at least a majority in aggregate principal amount of the debt securities of a series, modify the applicable indenture or the rights of the holders of the securities of such series. However, no such modification may, without the consent of each holder of an affected debt security:

- extend the fixed maturity of any such debt securities;
- reduce the rate or change the time of payment of interest on such debt securities;
- reduce the principal amount of such securities or the premium, if any, on such debt securities;
- change or waive the redemption provisions of such debt securities;

- change any obligation of ours to maintain an office or agency;
- reduce the amount of the principal payable on acceleration of any debt securities issued originally at a discount;
- adversely affect in any material respect the ranking on such debt securities;
- adversely affect in any material respect the right, if any, to convert such debt securities;
- adversely affect any right of repayment or repurchase at the option of the holder;
- reduce or postpone any sinking fund or similar provision;
- change the currency or currency unit in which any such debt securities are payable or the right of selection thereof;
- impair the right to sue for the enforcement of any payment on such debt securities;
- reduce the percentage of debt securities of a series whose holders need to consent to the modification or a waiver; or
- with respect to subordinated debt securities, modify or change any provisions of the indenture or the related definitions affecting the subordination or ranking of any debt securities, in a manner which adversely affects the holders.

Defaults

Each indenture provides that events of default regarding any series of debt securities will be:

- our failure to pay required interest on any debt security of such series for 30 days;
- our failure to pay principal or premium, if any, on any debt security of such series when due;
- our failure to make any deposit of any sinking fund payment when due on debt securities of such series;
- our failure to perform for 30 days after notice any other covenant in the relevant indenture other than a covenant included in the relevant indenture solely for the benefit of a series of debt securities other than the series at issue;
- a breach by us of the covenant with respect to amalgamation and sale of assets;
- our failure to pay beyond any applicable grace period, or the acceleration of, indebtedness in excess of $35,000,000; and
- certain events of bankruptcy or insolvency, whether voluntary or not.

If an event of default regarding debt securities of any series issued under the indentures should occur and be continuing, either the indenture trustee or the holders of 25% in the principal amount of outstanding debt securities of such series may declare each debt security of that series due and payable. If an event of default regarding debt securities results from certain events of bankruptcy, insolvency or reorganization with respect to us, such amount with respect to the debt securities will be due and payable immediately without any declaration or other act on the part of the holders of outstanding debt securities or the indenture trustee. We are required to file annually with the indenture trustee a statement of an officer as to the fulfillment by us of our obligations under the indenture during the preceding year.

No event of default regarding one series of debt securities issued under an indenture is necessarily an event of default regarding any other series of debt securities.

Holders of a majority in principal amount of the outstanding debt securities of any series will be entitled to control certain actions of the indenture trustee under an indenture and to waive past defaults regarding such series. The indenture trustee generally cannot be required by any of the holders of debt securities to take any action, unless one or more of such holders shall have provided to the indenture trustee satisfactory security or indemnity.

If an event of default occurs and is continuing regarding a series of debt securities, the indenture trustee may use any sums that it holds under the relevant indenture for its own reasonable compensation and expenses incurred prior to paying the holders of debt securities of such series.

Before any holder of any series of debt securities may institute action for any remedy, the holders of not less than 25% in principal amount of the debt securities of that series outstanding must request the indenture trustee to take action. Holders must also offer and give satisfactory security and indemnity against liabilities incurred by the indenture trustee for taking such action, and the indenture trustee must have failed to institute any proceeding within 60 days after receiving such request and offer of indemnity. These limitations do not apply, however, to a suit by a holder of any series of debt securities to enforce payment of principal, interest or premium.

Defeasance

After we have deposited with the indenture trustee cash or government securities, in trust for the benefit of the holders, sufficient to pay the principal of, premium, if any, and interest on the debt securities of such series when due, and satisfied certain other conditions, including receipt of an opinion of counsel that holders will not recognize taxable gain or loss for U.S. Federal income tax purposes, we may elect to have our obligations discharged with respect to the outstanding debt securities of any series ("defeasance and discharge"). Defeasance and discharge means that we will be deemed to have paid and discharged the entire indebtedness represented by the outstanding debt securities of such series under the applicable indenture, except for:

- the rights of holders of the debt securities to receive principal, interest and any premium when due;
- our obligations with respect to the debt securities concerning issuing temporary debt securities, registration of transfer of debt securities, mutilated, destroyed, lost or stolen debt securities and the maintenance of an office or agency for payment for security payments held in trust;
- the rights, powers, trusts, duties and immunities of the indenture trustee; and
- the defeasance provisions of the indenture.

Alternatively, we may elect to have our obligations released with respect to certain covenants in the applicable indenture ("covenant defeasance"). Any omission to comply with these obligations will not constitute a default or an event of default with respect to the debt securities of any series. In the event covenant defeasance occurs, certain events, not including non-payment, bankruptcy and insolvency events, described under "Events of Default" will no longer constitute an event of default for that series.

Governing Law

Unless otherwise stated in the prospectus supplement, the debt securities and the indentures will be governed by New York law.

Payment and Paying Agents

Distributions on the debt securities other than those represented by global notes will be made in the designated currency against surrender of the debt securities at the corporate trust office of the

indenture trustee. Payment will be made to the registered holder at the close of business on the record date for such payment. Interest payments will be made at the principal corporate trust office of the indenture trustee, or by a check mailed to the holder at his or her registered address. Payments in any other manner will be specified in the prospectus supplement applicable to the particular series of debt securities.

Transfer and Exchange

Debt securities may be presented for exchange, and debt securities other than a global security may be presented for registration of transfer, at the corporate trust office of the indenture trustee. Holders will not have to pay any service charge for any registration of transfer or exchange of debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with such registration of transfer or exchange of debt securities.

DESCRIPTION OF WARRANTS

We may issue warrants to purchase our debt or equity securities or securities of third parties or other rights, including rights to receive payment in cash or securities based on the value, rate or price of one or more specified commodities, currencies, securities or indices, or any combination of the foregoing. Warrants may be issued independently or together with any other securities and may be attached to, or separate from, such securities. A series of warrants may be issued under a separate warrant indenture between us and a warrant agent. The terms of any warrants to be issued and a description of the material provisions of any applicable warrant indenture will be set forth in the applicable prospectus supplement.

The applicable prospectus supplement will describe the following terms of any warrants in respect of which this prospectus is being delivered:

- the title of such warrants;
- the aggregate number of such warrants;
- the price or prices at which such warrants will be issued;
- the currency or currencies, in which the price of such warrants will be payable;
- the securities or other rights, including rights to receive payment in cash or securities based on the value, rate or price of one or more specified commodities, currencies, securities or indices, or any combination of the foregoing, purchasable upon exercise of such warrants;
- the price at which and the currency or currencies, in which the securities or other rights purchasable upon exercise of such warrants may be purchased;
- the date on which the right to exercise such warrants shall commence and the date on which such right shall expire;
- if applicable, the minimum or maximum amount of such warrants which may be exercised at any one time;
- if applicable, the designation and terms of the securities with which such warrants are issued and the number of such warrants issued with each such security;
- if applicable, the date on and after which such warrants and the related securities will be separately transferable;
- information with respect to book-entry procedures, if any;
- if applicable, a discussion of any material United States Federal income tax considerations; and

- any other terms of such warrants, including terms, procedures and limitations relating to the exchange and exercise of such warrants.

DESCRIPTION OF RIGHTS

We may issue rights to purchase our securities. These rights may be issued independently or together with any other security offered by this prospectus and may or may not be transferable by the person receiving the rights in the rights offering. In connection with any rights offering, we may enter into a standby underwriting agreement with one or more underwriters pursuant to which the underwriter will purchase any securities that remain unsubscribed for upon completion of the rights offering.

The applicable prospectus supplement relating to any rights will describe the terms of the offered rights, including, where applicable, the following:

- the exercise price for the rights;
- the number of rights issued to each securityholder;
- the extent to which the rights are transferable;
- any other terms of the rights, including terms, procedures and limitations relating to the exchange and exercise of the rights;
- the date on which the right to exercise the rights will commence and the date on which the right will expire;
- the amount of rights outstanding;
- the extent to which the rights include an over-subscription privilege with respect to unsubscribed securities; and
- the material terms of any standby underwriting arrangement entered into by us in connection with the rights offering.

DESCRIPTION OF PURCHASE CONTRACTS

We may issue purchase contracts, including contracts obligating holders to purchase from us, and us to sell to the holders, a specified number of our ordinary shares at a future date or dates. The price per ordinary share and the number of ordinary shares may be fixed at the time the purchase contracts are issued or may be determined by reference to a specific formula set forth in the purchase contracts. The purchase contracts may require us to make periodic payments to holders or vice versa, and these payments may be unsecured or prefunded on some basis. The purchase contracts may require holders to secure their obligations under those contracts in a specified manner. The applicable prospectus supplement will describe the terms of the purchase contracts, including if applicable, any collateral arrangements.

DESCRIPTION OF UNITS

We may issue units consisting of one or more debt securities, purchase contracts, warrants, rights, ordinary shares or any combination of such securities. The applicable prospectus supplement will describe:

- the terms of the units and of the securities comprising the units, including whether and under what circumstances the securities comprising the units may be traded separately;
- a description of the terms of any unit agreement governing the units; and

- a description of the provisions for the payment, settlement, transfer or exchange or the units.

CONVERTIBLE OR EXCHANGEABLE SECURITIES

We may issue securities of the types described in this prospectus that are convertible or exchangeable into other securities described herein. The terms of such convertible or exchangeable securities will be set forth in a prospectus supplement.

SELLING SHAREHOLDERS

This prospectus also relates to the possible resale by certain of our shareholders, who we refer to in the prospectus as the "selling shareholders," of ordinary shares. The ordinary shares to be sold by the selling shareholders pursuant to this prospectus were or will be issued by us to the selling shareholders in transactions exempt from the registration provisions of the Securities Act pursuant to the exemption set forth in Section 4(2) thereof relative to sales by an issuer not involving any public offering or in reliance on Regulation S under the Securities Act regarding sales by an issuer in offshore transactions.

No selling shareholder will sell any ordinary shares pursuant to this prospectus until we have identified such selling shareholder and the ordinary shares being offered for resale by such selling shareholder in a prospectus supplement. The prospectus supplement for any offering by the selling shareholders of ordinary shares will include the following information:

- the name of each participating selling shareholder;
- the nature of any position, office, or other material relationship which each selling shareholder has had within the past three years with us or any of our predecessors or affiliates;
- the number of ordinary shares held by each selling shareholder prior to the offering;
- the number of ordinary shares to be offered for each selling shareholder's account; and
- the number, and, if applicable, the percentage of ordinary shares held by each of the selling shareholders before and after completion of the sale of the maximum number of ordinary shares that may be offered by such selling shareholder under such prospectus supplements.

Alternatively, we may provide this information in a post-effective amendment to the registration statement of which this prospectus forms a part or in a periodic or current report that we file pursuant to Section 13 or 15(d) of the Exchange Act and that is incorporated by reference into this prospectus. See "Incorporation of Certain Documents by Reference" for more information.

We do not know when or in what amounts the selling shareholders may offer ordinary shares for sale of which selling shareholders will participate in any such offering. However, the selling shareholders may sell or transfer all or a portion of their ordinary shares pursuant to any available exemption from the registration requirements of the Securities Act.

FORM, EXCHANGE AND TRANSFER

We will issue only in registered form; no securities will be issued in bearer form. We will issue each security in book-entry form only, unless otherwise specified in the applicable prospectus supplement. Securities 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 securities represented by the global security. Those who own beneficial interests in a global security 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. Only the depositary will be entitled to transfer or

exchange a security in global form, since it will be the sole holder of the security. These book-entry securities are described below under "Book-Entry Procedures and Settlement."

If any securities are issued in non-global form or cease to be book-entry securities (in the circumstances described in the next section), the following will apply to them:

- The securities will be issued in fully registered form in denominations stated in the prospectus supplement. You may exchange securities for securities of the same series in smaller denominations or combined into fewer securities of the same series of larger denominations, as long as the total amount is not changed.

- You may exchange, transfer, present for payment or exercise securities at the office of the relevant indenture trustee or agent indicated in the prospectus supplement. You may also replace lost, stolen, destroyed or mutilated securities at that office. We may appoint another entity to perform these functions or we may perform them ourselves.

- You will not be required to pay a service charge to transfer or exchange your securities, but you may be required to pay 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 your proof of legal ownership. The transfer agent may also require an indemnity before replacing any securities.

- If we have the right to redeem, accelerate or settle any securities before their maturity or expiration, and we exercise that right as to less than all those securities, we may block the transfer or exchange of those securities 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 security selected for early settlement, except that we will continue to permit transfers and exchanges of the unsettled portion of any security being partially settled.

- If fewer than all of the securities represented by a certificate that are payable or exercisable in part are presented for payment or exercise, a new certificate will be issued for the remaining amount of securities.

BOOK-ENTRY PROCEDURES AND SETTLEMENT

Most offered securities will be book-entry (global) securities. Upon issuance, all book-entry securities will be represented by one or more fully registered global securities, without coupons. Each global security will be deposited with, or on behalf of, The Depository Trust & Clearing Corporation, or DTC, a securities depositary, and will be registered in the name of Cede & Co. or another nominee of DTC. DTC, Cede & Co., or such nominee, will thus be the only registered holder of these securities. Except as set forth below, the registered global securities may be transferred, in whole but not in part, only to Cede & Co., another nominee of DTC or to a successor of DTC or its nominee.

Purchasers of securities may only hold interests in the global securities through DTC if they are participants in the DTC system. Individual certificates in respect of the securities will not be issued in exchange for the registered global securities, except in very limited circumstances. Purchasers may also hold interests through a securities intermediary—banks, brokerage houses and other institutions that maintain securities accounts for customers—that has an account with DTC or its nominee. DTC will maintain accounts showing the security holdings of its participants, and these participants will in turn maintain accounts showing the security holdings of their customers. Some of these customers may themselves be securities intermediaries holding securities for their customers. Thus, each beneficial owner of a book-entry security will hold that security indirectly through a hierarchy of intermediaries, with DTC at the top and the beneficial owner's own securities intermediary at the bottom.

The securities of each beneficial owner of a book-entry security will be evidenced solely by entries on the books of the beneficial owner's securities intermediary. The actual purchaser of the securities will generally not be entitled to have the securities represented by the global securities registered in its name and will not be considered the owner under the declaration. In most cases, a beneficial owner will also not be able to obtain a paper certificate evidencing the holder's ownership of securities. The book-entry system for holding securities eliminates the need for physical movement of certificates and is the system through which most publicly traded common stock (or in our case, ordinary shares) is held in the United States. However, the laws of some jurisdictions require some purchasers of securities to take physical delivery of their securities in definitive form. These laws may impair the ability to transfer book-entry securities.

Title to book-entry interests in the securities will pass by book-entry registration of the transfer within the records of DTC in accordance with its procedures.

If DTC notifies us that it is unwilling or unable to continue as a clearing system in connection with the registered global securities or ceases to be a clearing agency registered under the Exchange Act, and a successor clearing system is not appointed by us within 90 days after receiving that notice from DTC or upon becoming aware that DTC is no longer so registered, we will issue or cause to be issued individual certificates in registered form on registration of transfer of, or in exchange for, book-entry interests in the securities represented by registered global securities upon delivery of those registered global securities for cancellation. We may also permit beneficial owners of book-entry securities represented by a global security to exchange their beneficial interests for definitive (paper) securities if, in our sole discretion, we decide to allow some or all book-entry securities to be exchangeable for definitive securities in registered form.

Unless we indicate otherwise, any global security that is exchangeable will be exchangeable in whole for definitive securities in registered form, with the same terms and of an equal aggregate principal amount. Definitive securities will be registered in the name or names of the person or persons specified by DTC in a written instruction to the registrar of the securities. DTC may base its written instruction upon directions that it receives from its participants.

In this prospectus, for book-entry securities, references to actions taken by security holders will mean actions taken by DTC upon instructions from its participants, and references to payments and notices of redemption to security holders will mean payments and notices of redemption to DTC as the registered holder of the securities for distribution to participants in accordance with DTC's procedures.

Initial settlement for the securities offered on a global basis through DTC will be made in immediately available funds. Secondary market trading between DTC's participants will occur in the ordinary way in accordance with DTC's rules and will be settled in immediately available funds using DTC's Same-Day Funds Settlement System.

Although DTC has agreed to the foregoing procedures in order to facilitate transfers of interests in the securities among participants thereof, it is under no obligation to perform or continue to perform the foregoing procedures and these procedures may be changed or discontinued at any time.

DTC is a limited purpose trust company organized under the laws of the State of New York, a member of the Federal Reserve System, a clearing corporation within the meaning of the New York Uniform Commercial Code and a clearing agency registered under section 17A of the Securities Exchange Act of 1934. The rules applicable to DTC and its participants are on file with the SEC.

We will not have any responsibility or liability for any aspect of the records relating to, or payments made on account of, beneficial ownership interest in the book-entry securities or for maintaining, supervising or reviewing any records relating to the beneficial ownership interests.

PLAN OF DISTRIBUTION

We or the selling shareholder may offer the offered securities in one or more of the following ways from time to time:

- to or through underwriters or dealers;
- by ourselves directly;
- through agents; or
- through a combination of any of these methods of sale.

In compliance with the guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum commission or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate principal amount of securities offered pursuant to this prospectus. We anticipate, however, that the maximum commission or discount to be received in any particular offering of securities will be significantly less than this amount.

The prospectus supplement relating to a particular offering of securities will set forth the terms of such offering, including:

- the type of securities to be offered;
- the name or names of any underwriters, dealers or agents and the amounts of securities underwritten or purchased by each of them;
- the purchase price of the offered securities and the proceeds to us from such sale;
- any underwriting discounts and commissions or agency fees and other items constituting underwriters' or agents' compensation, which in the aggregate will not exceed 8% of the gross proceeds of the offering;
- the initial public offering price;
- any discounts or concessions to be allowed or reallowed or paid to dealers; and
- any securities exchanges on which such offered securities may be listed.

Any initial public offering prices, discounts or concessions allowed or reallowed or paid to dealers may be changed from time to time.

The distribution of the offered securities may be effected from time to time in one or more transactions at a fixed price or prices, which may be changed, at market prices prevailing at the time of sale, at prices related to such prevailing market prices or at negotiated prices.

If underwriters are used in an offering of offered securities, such offered securities will be acquired by the underwriters for their own account and may be resold from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. The securities may be either offered to the public through underwriting syndicates represented by one or more managing underwriters or by one or more underwriters without a syndicate. Unless otherwise set forth in the prospectus supplement, the underwriters will not be obligated to purchase offered securities unless specified conditions are satisfied, and if the underwriters do purchase any offered securities, they will purchase all offered securities.

In connection with underwritten offerings of the offered securities and in accordance with applicable law and industry practice, underwriters may over-allot or effect transactions that stabilize, maintain or otherwise affect the market price of the offered securities at levels above those that might otherwise prevail in the open market, including by entering stabilizing bids, effecting syndicate covering transactions or imposing penalty bids, each of which is described below.

- A stabilizing bid means the placing of any bid, or the effecting of any purchase, for the purpose of pegging, fixing or maintaining the price of a security.

- A syndicate covering transaction means the placing of any bid on behalf of the underwriting syndicate or the effecting of any purchase to reduce a short position created in connection with the offering.

- A penalty bid means an arrangement that permits the managing underwriter to reclaim a selling concession from a syndicate member in connection with the offering when offered securities originally sold by the syndicate member are purchased in syndicate covering transactions.

These transactions may be effected on an exchange or automated quotation system, if the securities are listed on that exchange or admitted for trading on that automated quotation system, or in the over-the-counter market or otherwise.

If a dealer is utilized in the sales of offered securities, we or the selling shareholder will sell such offered securities to the dealer as principal. The dealer may then resell such offered securities to the public at varying prices to be determined by such dealer at the time of resale. Any such dealer may be deemed to be an underwriter, as such term is defined in the Securities Act, of the offered securities so offered and sold. The name of the dealer and the terms of the transaction will be set forth in the related prospectus supplement.

We or the selling shareholder 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 indicates, in connection with those derivatives, such third parties (or their affiliates) may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, such persons 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 securities, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of securities. Such persons will be underwriters and, if not identified in this prospectus, will be identified in the applicable prospectus supplement (or a post-effective amendment).

Sales to or through one or more underwriters or agents in at-the-market offerings will be made pursuant to the terms of a distribution agreement with the underwriters or agents. Such underwriters or agents may act on an agency basis or on a principal basis. During the term of any such agreement, ordinary shares may be sold on a daily basis on any stock exchange, market or trading facility on which the ordinary shares are traded, in privately negotiated transactions or otherwise as agreed with the underwriters or agents. The distribution agreement will provide that any ordinary share sold will be sold at negotiated prices or at prices related to the then prevailing market prices for our ordinary shares. Therefore, exact figures regarding proceeds that will be raised or commissions to be paid cannot be determined at this time and will be described in a prospectus supplement. Pursuant to the terms of the distribution agreement, we may also agree to sell, and the relevant underwriters or agents may agree to solicit offers to purchase, blocks of our ordinary shares or other securities. The terms of each such distribution agreement will be described in a prospectus supplement.

We may sell our ordinary shares pursuant to dividend reinvestment, share purchase plans and similar plans in which our shareholders as well as other investors may participate. Purchasers of ordinary shares under such plans may, upon resales, be deemed to be underwriters. These ordinary shares may be resold in market transactions (including coverage of short positions), in privately negotiated transactions or otherwise. Ordinary shares sold under any such plans may be issued at a discount to the market price of the ordinary shares. The difference between the price owners who may be deemed to be underwriters pay us for our ordinary shares acquired under any such plan, after deduction of the applicable discount from the market price, and the price at which such shares are

resold, may be deemed to constitute underwriting commissions or fees received by these owners in connection with such transactions.

We may also issue our ordinary shares to officers, directors, employees, consultants, agents or other persons pursuant to awards made under our equity incentive plans. Such ordinary shares may be resold by our officers and directors under this prospectus as indicated in a prospectus supplement.

We or the selling shareholder may loan ordinary shares to underwriters, agents and others, pursuant to share lending agreements, which may be offered for sale in transactions, including block sales, on any securities exchange, market or trading facility.

We or the selling shareholder may loan or pledge securities to a financial institution or other third party that in turn may sell the securities using this prospectus. Such financial institution or third party may transfer its short position to investors in our securities or in connection with a simultaneous offering of other securities offered by this prospectus.

Offered securities may be sold directly by us or the selling shareholder to one or more institutional purchasers, or through agents designated by us from time to time, at a fixed price or prices, which may be changed, or at varying prices determined at the time of sale. Any such agent may be deemed to be an underwriter as that term is defined in the Securities Act. Any agent involved in the offer or sale of the offered securities in respect of which this prospectus is delivered will be named, and any commissions payable by us to such agent will be set forth, in the prospectus supplement relating to that offering. Unless otherwise indicated in such prospectus supplement, any such agent will be acting on a best efforts basis for the period of its appointment.

If so indicated in the applicable prospectus supplement, we or the selling shareholder(s) will authorize agents, underwriters or dealers to solicit offers from certain types of institutions to purchase offered securities from us at the public offering price set forth in such prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. Such contracts will be subject only to those conditions set forth in the prospectus supplement and the prospectus supplement will set forth the commission payable for solicitation of such contracts.

In addition, ordinary shares may be issued in exchange for debt securities.

Each series of offered securities, other than the ordinary shares which are listed on the Nasdaq Global Select Market, will be a new issue of securities and will have no established trading market. Any underwriters to whom offered securities are sold for public offering and sale may make a market in such offered securities, but such underwriters will not be obligated to do so and may discontinue any market making at any time without notice. The offered securities may or may not be listed on a national securities exchange. No assurance can be given that there will be a market for the offered securities.

One or more firms, referred to as "remarketing firms," may also offer or sell the securities, if the prospectus supplement so indicates, in connection with a remarketing arrangement upon their purchase. Remarketing firms will act as principals for their own accounts or as agents for us. These remarketing firms will offer or sell the securities in accordance with a redemption or repayment pursuant to the terms of the securities. The prospectus supplement will identify any remarketing firm and the terms of its agreement, if any, with us and will describe the remarketing firm's compensation. Remarketing firms may be deemed to be underwriters in connection with the securities they remarket. Remarketing firms may be entitled under agreements that may be entered 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.

Underwriters, dealers, agents and remarketing firms may be entitled, under agreements with us, to indemnification by us against certain civil liabilities, including liabilities under the Securities Act

relating to material misstatements and omissions, or to contribution with respect to payments which the underwriters, dealers or agents may be required to make in respect thereof. Underwriters, dealers, agents and remarketing firms may be customers of, engage in transactions with, or perform services for, us and our affiliates in the ordinary course of business.

LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, certain legal matters in connection with the offering and the validity of the securities offered by this prospectus, and any supplement thereto, will be passed upon for us by Morgan, Lewis & Bockius UK LLP. Certain legal matters with respect to Dutch law in connection with the validity of the ordinary shares being offered by this prospectus and other legal matters will be passed upon for us by Rutgers Posch Visée Endedijk N.V., Amsterdam, the Netherlands. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The consolidated financial statements of uniQure N.V. as of December 31, 2020 and 2019, and for the years then ended, and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2020 have been incorporated by reference herein and in the registration statement in reliance upon the report of KPMG Accountants N.V., independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing. The audit report covering the December 31, 2020 financial statements refers to a change in the method of accounting for leases as of January 1, 2019 due to the adoption of ASC 842, Leases.

The financial statements for the year ended December 31, 2018 incorporated in this prospectus by reference to the Annual Report on Form 10 K for the year ended December 31, 2020 have been so incorporated in reliance on the report of PricewaterhouseCoopers Accountants N.V., an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may obtain information on the operation of the Public Reference Room by calling the SEC at (800) SEC-0330. The SEC maintains a website that contains reports, proxy statements and other information regarding issuers that file electronically with the SEC, including us. The address of the SEC website is www.sec.gov.

We maintain a website at www.uniqure.com. Information contained in or accessible through our website does not constitute a part of this prospectus.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The documents incorporated by reference into this prospectus contain important information that you should read about us. The information incorporated by reference is considered to be a part of this prospectus, and information in documents that we file later with the SEC will automatically update and supersede information contained in documents filed earlier with the SEC or contained in this prospectus.

The following documents are incorporated by reference into this document:

- our Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on March 1, 2021; and
- the description of our ordinary shares contained in our registration statement on Form 8-A as filed with the SEC on January 31, 2014, as updated or amended in any amendment or report filed for such purpose

We also incorporate by reference into this prospectus all documents (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (i) after the date of the initial filing of the registration statement of which this prospectus forms a part, or (ii) after the date of this prospectus but prior to the termination of the offering. These documents include periodic reports, such as Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as well as proxy statements. Information in these documents updates and supplements the information provided in this prospectus. Any statements in these documents will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, without charge upon written or oral request, a copy of any or all of the documents that are incorporated by reference into this prospectus but not delivered with the prospectus, including exhibits which are specifically incorporated by reference into such documents. You should direct any requests for documents by writing us at 113 Hartwell Avenue, Lexington, MA 02421, or telephoning us at +1.339.970.7000.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference into this document will be deemed to be modified or superseded for purposes of the document to the extent that a statement contained in this document or any other subsequently filed document that is deemed to be incorporated by reference into this document modifies or supersedes the statement.

Up to $200,000,000

Ordinary Shares

PROSPECTUS SUPPLEMENT

SVB Leerink

March 1, 2021