

Horizon Pharma plc
Form 424B7
November 13, 2014
Table of Contents

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has become effective by rule of the Securities and Exchange Commission. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities, and neither we nor the selling shareholders are soliciting offers to buy these securities, in any state or other jurisdiction where the offer or sale is not permitted.

*Filed Pursuant to Rule 424(b)(7)
Registration No. 333-198852*

PRELIMINARY PROSPECTUS SUPPLEMENT

(To Prospectus dated September 19, 2014)

SUBJECT TO COMPLETION, DATED NOVEMBER 13, 2014

11,660,445 Shares

Ordinary Shares

Certain shareholders of Horizon Pharma plc are offering 11,660,445 ordinary shares. We will not receive any proceeds from the sales of ordinary shares in this offering.

Our ordinary shares are listed on The NASDAQ Global Market under the symbol HZNP . On November 12, 2014, the last reported sale price of our ordinary shares on The NASDAQ Global Market was \$13.10 per share.

Investing in our ordinary shares involves risks. See Risk Factors beginning on page S-6, and in the documents which are incorporated by reference in this prospectus supplement and the accompanying prospectus.

PRICE \$ A SHARE

	<i>Price to Public</i>	<i>Underwriting Discounts and Commissions</i>	<i>Proceeds to Selling Shareholders</i>
<i>Per Share</i>	\$	\$	\$
<i>Total</i>	\$	\$	\$

The selling shareholders have granted the underwriters the right to purchase up to an additional 1,749,066 ordinary shares at the public offering price less the underwriting discount. We will not receive any proceeds from the sales of ordinary shares in this offering.

The Securities and Exchange Commission and state securities regulators have not 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.

The underwriters expect to deliver the ordinary shares to purchasers on November , 2014.

*MORGAN STANLEY
COWEN AND COMPANY*

*CITIGROUP
JEFFERIES*

November , 2014

Table of Contents

TABLE OF CONTENTS

Prospectus Supplement

	Page
<u>About This Prospectus Supplement</u>	S-1
<u>Prospectus Supplement Summary</u>	S-3
<u>Risk Factors</u>	S-6
<u>Special Note Regarding Forward-Looking Statements</u>	S-51
<u>Use of Proceeds</u>	S-51
<u>Selling Shareholders</u>	S-52
<u>Material Tax Considerations</u>	S-54
<u>Underwriting</u>	S-63
<u>Legal Matters</u>	S-69
<u>Experts</u>	S-69
<u>Where You Can Find More Information</u>	S-69
Prospectus	

	Page
<u>About This Prospectus</u>	1
<u>About Horizon Pharma plc</u>	2
<u>Risk Factors</u>	4
<u>Special Note Regarding Forward-Looking Statements</u>	4
<u>Use of Proceeds</u>	5
<u>Selling Shareholders</u>	5
<u>Validity of Share Capital</u>	5
<u>Experts</u>	6
<u>Enforcement of Civil Liabilities Under United States Federal Securities Laws</u>	6
<u>Where You Can Find More Information</u>	6

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus form part of a registration statement on Form S-3 that Horizon Pharma plc filed with the Securities and Exchange Commission, or SEC, using the shelf registration process. Under this process, among other offerings that may occur from time to time under the registration statement, the selling shareholders named in this prospectus supplement under the caption Selling Shareholders are offering to sell our ordinary shares using this prospectus supplement and the accompanying prospectus.

This prospectus supplement describes the terms of the offering by the selling shareholders and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The accompanying prospectus, dated September 19, 2014, including the documents incorporated by reference, provides more general information. Generally, when we refer to this prospectus, we are referring to this prospectus supplement and the accompanying prospectus combined. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or in any document incorporated by reference that was filed with the SEC before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in this prospectus supplement or the accompanying prospectus or in any free writing prospectus that we have authorized for use in connection with this offering—the statement in the document having the later date modifies or supersedes the earlier statement. You should read this prospectus supplement and the accompanying prospectus, including the information incorporated by reference, and in any free writing prospectus that we have authorized for use in connection with this offering in their entirety before making an investment decision.

We, the selling shareholders and the underwriters have not authorized anyone to provide you with information other than the information contained in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering. This document may only be used where it is legal to sell these securities. You should not assume that the information contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus is accurate as of any date other than its respective date, regardless of when this prospectus supplement and the accompanying prospectus is delivered, or when any sale of our ordinary shares occurs. Our business, financial condition, results of operations and prospects may have changed since those dates.

This prospectus supplement, the accompanying prospectus and the information incorporated herein by reference include trademarks, service marks and trade names owned by us or others. 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.

On September 19, 2014, we and Horizon Pharma, Inc., or HPI, consummated a merger, or the Vidara Merger, contemplated by the transaction agreement and plan of merger that we entered into with HPI and certain other parties on March 18, 2014, as amended, or the merger agreement. In connection with the Vidara Merger, we were re-named Horizon Pharma plc and became the parent company of HPI, with HPI becoming our wholly-owned subsidiary. In the Vidara Merger, all outstanding shares of HPI's common stock were canceled and converted into the right to receive, on a one-for-one basis, our ordinary shares.

HPI was deemed to be the acquiring company for accounting purposes and the Vidara Merger is being accounted for as a reverse acquisition under the acquisition method of accounting for business combinations. As a result, the

historical financial statements of HPI became our historical financial statements. We are also

S-1

Table of Contents

considered to be the successor to HPI for certain purposes under both the Securities Act of 1933, as amended, or the Securities Act, and Securities Exchange Act of 1934, as amended, or the Exchange Act, and certain of HPI's historical reports filed under the Exchange Act are incorporated by reference in this prospectus. Prior to the Vidara Merger, we were known as Vidara Therapeutics International plc, or Vidara. The historical financial statements of Vidara for the years ended December 31, 2013 and 2012 and for the three months ended March 31, 2014, and pro forma financial information related to the Vidara Merger, are incorporated by reference in this prospectus from HPI's definitive proxy statement on Schedule 14A filed on August 7, 2014. The historical financial statements for Vidara for the three and six months ended June 30, 2014, and pro forma financial information related to the Vidara Merger for the six months ended and as of June 30, 2014 are incorporated by reference in this prospectus from Vidara's quarterly report on Form 10-Q filed on August 26, 2014 and our current report on Form 8-K filed on September 19, 2014, respectively. See

Where You Can Find More Information. A brief description of the historical business of Vidara prior to the Vidara Merger is included on page 3 of the accompanying prospectus. More information about the historical business of Vidara can be found in HPI's definitive proxy statement on Schedule 14A filed with the SEC on August 7, 2014.

References in this prospectus supplement to we, us and our refer to (i) upon and following the Vidara Merger, Horizon Pharma plc, a public limited company formed under the laws of Ireland, and its subsidiaries, including HPI, and (ii) prior to the Vidara Merger, Vidara Therapeutics International plc, a public limited company formed under the laws of Ireland, or Vidara, unless the context indicates otherwise.

Table of Contents

PROSPECTUS SUPPLEMENT SUMMARY

This summary may not contain all of the information that may be important to you. You should read this entire prospectus supplement and the accompanying prospectus, including the risks of investing in our ordinary shares incorporated by reference herein under the heading Risk Factors and under similar headings in the other documents that are incorporated by reference into this prospectus, as well as the financial statements and related notes, pro forma financial information, and other information incorporated by reference in this prospectus supplement and the accompanying prospectus, before making an investment decision.

Overview

We are a specialty biopharmaceutical company focused on improving patients' lives by identifying, developing, acquiring and commercializing differentiated products that address unmet medical needs. We market a portfolio of products in arthritis, inflammation and orphan diseases. Our U.S. marketed products are ACTIMMUNE® (interferon gamma-1b), DUEXIS® (ibuprofen/famotidine), RAYOS® (prednisone) delayed-release tablets and VIMOVO® (naproxen/esomeprazole). We developed DUEXIS and RAYOS/LODOTRA, acquired the U.S. rights to VIMOVO from AstraZeneca AB, or AstraZeneca, in November 2013 and acquired the U.S. rights to ACTIMMUNE as a result of the merger of the businesses of Horizon Pharma, Inc. and Vidara Therapeutics International plc in September 2014, or the Vidara Merger. We market our products in the United States through our field sales force of approximately 310 representatives. Our strategy is to develop, acquire or in-license additional innovative medicines or acquire companies, such as the recently-completed Vidara Merger.

On April 23, 2011, the U.S. Food and Drug Administration, or FDA, approved DUEXIS, a proprietary tablet formulation containing a fixed-dose combination of ibuprofen and famotidine in a single pill. DUEXIS is indicated for the relief of signs and symptoms of rheumatoid arthritis, or RA, osteoarthritis, or OA, and to decrease the risk of developing upper gastrointestinal ulcers in patients who are taking ibuprofen for these indications. We began detailing DUEXIS to physicians in December 2011. In June 2012, we licensed DUEXIS rights in Latin America to Grünenthal S.A., a private company focused on the promotion of pain products.

Our second approved product in the United States, RAYOS, known as LODOTRA outside the United States, is a proprietary delayed-release formulation of low-dose prednisone, first approved in Europe in March 2009, for the treatment of moderate to severe, active RA in adults, particularly when accompanied by morning stiffness. On July 26, 2012, the FDA approved RAYOS for the treatment of RA, polymyalgia rheumatica, or PMR, psoriatic arthritis, ankylosing spondylitis, or AS, asthma and chronic obstructive pulmonary disease and a number of other conditions. We are focusing our promotion of RAYOS in the United States on rheumatology indications, including RA and PMR. We began detailing RAYOS to a subset of U.S. rheumatologists in December 2012 and began the full launch in late January 2013 to the majority of U.S. rheumatologists and key primary care physicians. LODOTRA is currently marketed outside the United States by our distribution partner, Mundipharma International Corporation Limited, or Mundipharma.

On November 18, 2013, we entered into agreements with AstraZeneca pursuant to which we acquired from AstraZeneca and its affiliates certain intellectual property and other assets, and assumed from AstraZeneca and its affiliates certain liabilities, each with respect to VIMOVO, and obtained rights to develop other pharmaceutical products that contain gastroprotective agents in a single fixed combination oral solid dosage form with non-steroidal anti-inflammatory drugs, or NSAIDs, in the United States. VIMOVO (naproxen/esomeprazole magnesium) is a proprietary fixed-dose multi-layer delayed-release tablet combining an enteric-coated naproxen, an NSAID, core and an immediate-release esomeprazole, a proton pump inhibitor, layer surrounding the core. VIMOVO was originally developed by Pozen Inc., or Pozen, together with AstraZeneca pursuant to an exclusive global collaboration and

license agreement under which AstraZeneca and Pozen agreed to co-develop VIMOVO and AstraZeneca obtained exclusive rights to commercialize VIMOVO worldwide. On April 30, 2010, the FDA approved VIMOVO for the relief of the signs and symptoms of OA, RA, and AS and to decrease the risk of

S-3

Table of Contents

developing gastric ulcers in patients at risk of developing NSAID associated gastric ulcers. We announced the availability of Horizon-labeled VIMOVO on January 2, 2014, at which time we also began promotion with our primary care sales force.

As a result of the Vidara Merger, we began marketing ACTIMMUNE[®], a bioengineered form of interferon gamma-1b, a protein that acts as a biologic response modifier, in the United States. ACTIMMUNE is approved by the FDA for use in children and adults with chronic granulomatous disease, or CGD, and severe, malignant osteopetrosis, or SMO. ACTIMMUNE is indicated for reducing the frequency and severity of serious infections associated with CGD and for delaying time to disease progression in patients with SMO.

On October 17, 2014, we announced the acquisition of the U.S. rights to PENNSAID[®] (diclofenac sodium topical solution) 2% w/w, or PENNSAID 2%, from Nuvo Research Inc., or Nuvo. PENNSAID 2% is approved in the United States for the treatment of the pain of OA of the knee(s). As part of the acquisition, we entered into an eight-year exclusive supply agreement with Nuvo and we expect to begin selling PENNSAID 2% in early January 2015. We plan to expand our primary care sales force of 250 representatives by approximately 75 additional representatives and include PENNSAID 2% in our Prescriptions Made Easy , or PME, program.

Corporate Information

We are a public limited company formed under the laws of Ireland (registered number 507678) in December 2011. We were originally formed as a private limited liability company under the name Aravis Therapeutics International Limited and were subsequently re-named Vidara Therapeutics International Limited. In connection with the Vidara Merger, we were re-registered as a public limited company, Vidara Therapeutics International plc, became the parent company of and successor to HPI and were re-named Horizon Pharma plc. Our principal executive offices are located at Adelaide Chambers, Peter Street, Dublin 8, Ireland. Our telephone number is 011-353-1-649-8521. Our website address is www.horizonpharma.com. Information contained in, or accessible through, our website does not constitute a part of this prospectus supplement or the accompanying prospectus.

Table of Contents

The Offering

Ordinary shares offered by selling 11,660,445 shares
shareholders:

Option to purchase additional shares granted 1,749,066 shares
by the selling shareholders:

Ordinary shares outstanding before and immediately after this offering: 118,852,790 shares

Use of proceeds: The selling shareholders are selling all of the ordinary shares offered by this prospectus supplement. We will not receive any proceeds from the sale of shares by the selling shareholders.

Risk factors: Investing in our ordinary shares involves risks. See Risk Factors beginning on page S-6, and in the documents which are incorporated by reference in this prospectus supplement and the accompanying prospectus.

NASDAQ Global Market symbol: HZNP

Outstanding Shares

The number of ordinary shares outstanding before and immediately after this offering referenced above is as of October 31, 2014, and excludes, as of that date:

6,538,995 ordinary shares issuable upon the exercise of outstanding options, having a weighted average exercise price of \$8.47 per share;

1,497,631 ordinary shares issuable upon the settlement of restricted stock units;

7,825,821 ordinary shares issuable upon the exercise of outstanding warrants, having a weighted average exercise price of \$4.95 per share;

15,019,844 ordinary shares, all or a portion of which may be issued upon the conversion of our outstanding convertible senior notes;

10,201,769 ordinary shares reserved for future issuance under our 2014 Employee Share Purchase Plan;

15,111,575 ordinary shares reserved for future issuance under our 2014 Equity Incentive Plan; and

2,436,242 ordinary shares reserved for future issuance under our 2014 Non-Employee Equity Plan.

Unless otherwise indicated, all information contained in this prospectus supplement assumes no exercise by the underwriters of their option to purchase up to an additional 1,749,066 ordinary shares.

S-5

Table of Contents

RISK FACTORS

*Investing in our ordinary shares involves a high degree of risk. You should carefully review the risks and uncertainties described below and under the heading **Risk Factors** contained in our filings with the SEC that are incorporated by reference in this prospectus supplement and the accompanying prospectus, together with the other information in this prospectus supplement, the accompanying prospectus, the information and documents incorporated by reference herein, and in any free writing prospectus that we have authorized for use in connection with this offering. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations.*

Risks Related to Our Business and Industry

Our ability to generate revenues from our products is subject to attaining significant market acceptance among physicians, patients and healthcare payers.

DUEXIS[®], VIMOVO[®], ACTIMMUNE[®] and RAYOS[®]/LODOTRA[®], and other product or product candidates that we may develop, acquire, or in-license, such as PENNSAID 2% which we expect to begin commercializing in January 2015, may not attain market acceptance among physicians, patients, healthcare payers or the medical community. In the U.S. market, we began selling DUEXIS in December 2011. We began commercial sales of RAYOS, which was approved by the U.S. Food and Drug Administration, or FDA, in July 2012, to a subset of rheumatologists in the fourth quarter of 2012 with the full launch to the majority of U.S. rheumatologists and key primary care physicians in late January 2013. Outside the United States, LODOTRA has been sold in a limited number of countries and sales may not grow to expected levels, in part because we depend on our distribution partner, Mundipharma International Corporation Limited, or Mundipharma, for commercialization outside the United States. With respect to DUEXIS, we have only received marketing approval in the United Kingdom, or UK, thus far, and even if it is approved in other European countries, we do not expect the opportunity in Europe to be material to our business given the current state of the market in Europe for pain products and the revenue being generated by existing branded non-steroidal anti-inflammatory drugs, or NSAIDs, in Europe. There have been no sales of DUEXIS in the UK thus far. VIMOVO was launched in the U.S. market in the fourth quarter of 2010 by AstraZeneca AB, or AstraZeneca, under its license from Pozen Inc., or Pozen. Following our acquisition of the U.S. rights to VIMOVO in November 2013, we began selling VIMOVO in the first quarter of 2014. ACTIMMUNE was originally launched in the U.S. market in March 1991 by Genentech and in June 2012, Vidara Therapeutics International plc, or Vidara, acquired the intellectual property rights and certain assets related to the ACTIMMUNE product line. In September 2014, the businesses of Horizon Pharma, Inc. and Vidara were combined, and as a result we assumed the commercialization of ACTIMMUNE. In October 2014 we entered into an asset purchase agreement with Nuvo Research Inc. to acquire the U.S. rights to PENNSAID 2%, and we expect to begin commercializing PENNSAID 2% in the United States in January 2015. We believe that the degree of market acceptance and our ability to generate revenues from our products will depend on a number of factors, including:

timing of market introduction of our products as well as competitive drugs;

efficacy and safety of our products;

continued projected growth of the arthritis, pain and inflammation markets;

prevalence and severity of any side effects;

if and when we are able to obtain regulatory approvals for additional indications for our products;

acceptance by patients, primary care specialists and key specialists, including rheumatologists, orthopedic surgeons, pain specialists and specialists in pediatric immunology, allergy, infectious diseases and hematology/oncology;

availability of coverage and adequate reimbursement and pricing from government and other third-party payers;

S-6

Table of Contents

the performance of our distribution partners, over which we have limited control;

potential or perceived advantages or disadvantages of our products over alternative treatments, including cost of treatment and relative convenience and ease of administration;

strength of sales, marketing and distribution support;

the price of our products, both in absolute terms and relative to alternative treatments;

impact of past and future product price increases;

our ability to maintain a continuous supply of product for commercial sale;

the effect of current and future healthcare laws; and

product labeling or product insert requirements of the FDA or other regulatory authorities.

With respect to DUEXIS and VIMOVO, studies indicate that physicians do not commonly co-prescribe gastrointestinal, or GI, protective agents to high-risk patients taking NSAIDs. We believe this is due in part to a lack of awareness among physicians prescribing NSAIDs of the risk of NSAID-induced upper GI ulcers, in addition to the inconvenience of prescribing two separate medications and patient compliance issues associated with multiple prescriptions. If physicians remain unaware of, or do not otherwise believe in, the benefits of combining GI protective agents with NSAIDs, our market opportunity for DUEXIS and VIMOVO will be limited. Some physicians may also be reluctant to prescribe DUEXIS or VIMOVO due to the inability to vary the dose of ibuprofen and naproxen, respectively, or if they believe treatment with NSAIDs or GI protective agents other than those contained in DUEXIS and VIMOVO, including those of our competitors, would be more effective for their patients. With respect to each of DUEXIS, VIMOVO and RAYOS/LODOTRA, their higher cost compared to the generic or branded forms of their active ingredients alone may limit adoption by physicians, patients and healthcare payers. With respect to ACTIMMUNE, while it is the only FDA-approved treatment for chronic granulomatous disease, or CGD, and severe, malignant osteopetrosis, or SMO, they are very rare conditions and, as a result, our ability to grow ACTIMMUNE sales will depend on our ability to further penetrate this limited market. If DUEXIS, VIMOVO, ACTIMMUNE, RAYOS/LODOTRA, PENNSAID 2% or any other product that we may seek approval for, acquire or in-license fail to attain market acceptance, we may not be able to generate significant revenue to achieve or sustain profitability, which would have a material adverse effect on our business, results of operations, financial condition and prospects.

Our current business plan is highly dependent upon our ability to successfully execute on our sales and marketing strategy for the commercialization of DUEXIS, VIMOVO, ACTIMMUNE, RAYOS/LODOTRA and, beginning in January 2015, PENNSAID 2%. If we are unable to successfully execute on our sales and marketing strategy, we may not be able to generate significant product revenues or execute on our business plan.

Our strategy is to build a fully-integrated U.S.-focused biopharmaceutical company to successfully execute the commercialization of DUEXIS, VIMOVO, ACTIMMUNE, RAYOS and, beginning in January 2015, PENNSAID 2%

in the U.S. market. We may not be able to successfully commercialize DUEXIS, VIMOVO, ACTIMMUNE, RAYOS or PENNSAID 2% in the United States. Prior to our commercial launch of DUEXIS in the United States in December 2011, we did not have any experience commercializing pharmaceutical products on our own. LODOTRA was commercially launched in Europe by our exclusive distribution partners Merck Serono and Mundipharma. In order to commercialize any approved products, we must continue to build our sales, marketing, distribution, managerial and other non-technical capabilities. Although we have expanded our sales force to approximately 310 sales representatives in connection with our November 2013 acquisition of the U.S. rights to VIMOVO and our September 2014 acquisition of Vidara and we plan to further increase our sales force to approximately 385 sales representatives in connection with our recent acquisition of the U.S. rights to PENNSAID 2%, we currently have limited resources compared to some of our competitors, and the continued development of our own commercial organization to market these products and any additional products we may acquire or in-license will be expensive and time-consuming. We also cannot be certain that we will be able to continue to successfully develop this capability.

S-7

Table of Contents

As a result of the evolving role of various constituents in the prescription decision making process, we adjusted the profile of the sales representatives we hire from those with traditional pharmaceutical sales experience to those with successful business to business experience. For example, we have faced challenges due to pharmacists increasingly switching a patient's intended prescription from DUEXIS and VIMOVO to a generic or over the counter brand of their active ingredients. We have faced similar challenges for RAYOS with respect to generic brands and could face similar challenges with respect to PENNSAID 2% due to the availability of generic versions of PENNSAID 1.5%. While we believe the new profile of our representatives is better suited for this evolving environment, we cannot be certain that our representatives will be able to successfully protect DUEXIS, VIMOVO, RAYOS and PENNSAID 2% prescriptions or that we will be able to continue attracting and retaining sales representatives with our desired profile and skills. We will also have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain commercial personnel. To the extent we rely on additional third parties to commercialize any approved products, we may receive less revenues than if we commercialized these products ourselves. In addition, we may have little or no control over the sales efforts of any third parties involved in our commercialization efforts. In the event we are unable to successfully develop and maintain our own commercial organization or collaborate with a third-party sales and marketing organization, we would not be able to commercialize our product candidates and execute on our business plan.

Another key part of our commercial strategy is to drive prescriptions through our *Prescriptions-Made-Easy*, or PME, specialty pharmacy program. Through this program, physicians can have their patients' prescriptions for our products filled automatically, with the product shipped directly to the patient. Prescriptions that are filled through our PME program are therefore not subject to the efforts of traditional pharmacies to switch a physician's prescription of our products to a generic or over the counter brand. We expect that continued adoption of our PME program by physicians will be important to our ability to gain market share for our products as pressure from healthcare payors and pharmacy benefit managers, or PBMs, to use cheaper generic or over the counter brands instead of branded products increases. For example, two of the largest PBMs, which we estimate to currently control approximately 20% to 30% of prescriptions for DUEXIS and VIMOVO, are expected to place DUEXIS and VIMOVO on their exclusion lists beginning in 2015. Additional healthcare plans, including those that contract with these PBMs but use different formularies, may also choose to exclude our products from their formularies. To the extent we are unable to re-direct prescriptions currently filled through traditional pharmacies, including those associated with/controlled by these PBMs, to our PME program, we may experience a significant decline in DUEXIS and VIMOVO prescriptions as a result of formulary exclusions. Our ability to increase adoption of our PME program will depend on physician awareness and comfort with the program, and we have limited ability to influence whether physicians use our PME program to prescribe our products. If we are unable to increase adoption of our PME program for filling prescriptions of our products, our ability to maintain or increase prescriptions for our products will be impaired. In addition, we depend on a limited number of PME pharmacies to fulfill patient prescriptions under the PME program. The commercialization of our product and our operating results could be affected by any adverse events at any of those PME pharmacies.

If we are unable to successfully implement our commercial plans and drive adoption by patients and physicians of any approved products through our sales, marketing and commercialization efforts, or if our partners fail to successfully commercialize our products, then we will not be able to generate sustainable revenues from product sales which will have a material adverse effect on our business and prospects.

Our future prospects are highly dependent on the success of DUEXIS, VIMOVO, ACTIMMUNE, RAYOS/LODOTRA and, beginning in January 2015, PENNSAID 2%, and we may not be able to successfully commercialize these products. Failure to do so would adversely impact our financial condition and prospects.

Edgar Filing: Horizon Pharma plc - Form 424B7

A substantial majority of our resources are focused on the commercialization of DUEXIS, VIMOVO, ACTIMMUNE and RAYOS in the United States and we expect to begin commercialization of PENNSAID 2% in the United States in January 2015. Our ability to generate significant product revenues and to achieve commercial success in the near term will initially depend almost entirely on our ability to successfully commercialize these products in the United States. DUEXIS has been approved for marketing in the UK but is

S-8

Table of Contents

not yet approved in any other countries in Europe and therefore, unless we obtain regulatory approval in other countries, DUEXIS may not be commercialized to any significant extent outside of the United States. Even if DUEXIS is approved in other European countries, we do not expect the opportunity in Europe to be material to our business given the current state of the market in Europe for pain products and the revenue being generated by existing branded NSAIDs in Europe. Following our acquisition of the U.S. rights to VIMOVO in November 2013, our strategy has included bringing VIMOVO's pricing in-line with DUEXIS and thereby significantly increasing the value realized per prescription. We cannot guarantee that this strategy will continue to be effective generally, due to negative reactions to price increases or otherwise. Our initial strategy for RAYOS is to solely focus on the rheumatology indications approved for RAYOS where our Phase 3 clinical trial data supports our commercial plans. We initially launched RAYOS in the United States to a subset of rheumatologists in the fourth quarter of 2012, and the full launch to the majority of U.S. rheumatologists and key primary care physicians occurred in late January 2013. Although LODOTRA is approved for marketing in more than 35 countries outside the United States, to date it has only been marketed in a limited number of countries. While we anticipate that LODOTRA will be marketed in additional countries as our distribution partner, Mundipharma, formulates its reimbursement strategy, the ability to market LODOTRA in additional countries will depend on Mundipharma's ability to obtain reimbursement approvals in these countries. Our strategy with respect to ACTIMMUNE includes pricing increases, pursuing label expansion for additional indications, such as Friedreich's ataxia, or FA, and possible expansions of our sales force, but we cannot be certain that our pricing strategy will not result in downward pressure on sales or that we will be able to successfully complete clinical trials and obtain regulatory approvals in additional indications. Even if we obtain additional marketing and reimbursement approvals, our product revenues in Europe are entirely dependent upon the marketing efforts of our exclusive distribution partner, over which we have no control. Before we can market and sell these products in a particular jurisdiction, we need to obtain necessary regulatory approvals (from the FDA in the United States and from similar foreign regulatory agencies in other jurisdictions) and in some jurisdictions, reimbursement authorization. There are no guarantees that we or our commercialization partners will obtain any additional regulatory approvals for our products. Even if we or our commercialization partners obtain additional regulatory approvals, we may never generate significant revenues from any commercial sales of our products. If we fail to successfully commercialize DUEXIS, VIMOVO, ACTIMMUNE, RAYOS or PENNSAID 2%, we may be unable to generate sufficient revenues to sustain and grow our business, and our business, financial condition and results of operations will be adversely affected.

We are solely dependent on Mundipharma to commercialize LODOTRA in Europe and certain Asian, Latin American, Middle Eastern, African and other countries. Failure of Mundipharma or any other third parties to successfully commercialize our products and product candidates in the applicable jurisdictions could have a material adverse effect on our business.

We rely on Mundipharma for commercialization of LODOTRA in various European countries and certain Asian, Latin American, Middle Eastern, African and other countries. We have limited contractual rights to force Mundipharma to invest significantly in commercialization of LODOTRA in its markets. In the event that Mundipharma or any other third party with any future commercialization rights to any of our products or product candidates fails to adequately commercialize those products or product candidates because it lacks adequate financial or other resources, decides to focus on other initiatives or otherwise, our ability to successfully commercialize our products or product candidates in the applicable jurisdictions would be limited, which would adversely affect our business, financial condition, results of operations and prospects. We have had disagreements with Mundipharma under our European agreements and may continue to have disagreements, which could harm commercialization of LODOTRA in Europe or result in the termination of our agreements with Mundipharma. We also rely on Mundipharma's ability to obtain regulatory approval for LODOTRA in certain Asian, Latin American, Middle Eastern, African and other countries. In addition, our agreements with Mundipharma may be terminated by either party in the event of a bankruptcy of the other party or upon an uncured material breach by the other party. If Mundipharma

terminated its agreements with us, we may not be able to secure an alternative distributor in the applicable territory on a timely basis or at all, in which case our ability to generate revenues from the sale of LODOTRA would be materially harmed.

S-9

Table of Contents

Our products are subject to extensive regulation, and we may not obtain additional regulatory approvals for our products.

The clinical development, manufacturing, labeling, packaging, storage, recordkeeping, advertising, promotion, export, marketing and distribution and other possible activities relating to our product candidates are, and any resulting drugs will be, subject to extensive regulation by the FDA and other regulatory agencies. Failure to comply with FDA and other applicable regulatory requirements may, either before or after product approval, subject us to administrative or judicially imposed sanctions.

To market any drugs outside of the United States, we and current or future collaborators must comply with numerous and varying regulatory and compliance related requirements of other countries. Approval procedures vary among countries and can involve additional product testing and additional administrative review periods, including obtaining reimbursement and pricing approval in select markets. The time required to obtain approval in other countries might differ from that required to obtain FDA approval. The regulatory approval process in other countries may include all of the risks associated with FDA approval as well as additional, presently unanticipated, risks. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others.

Applications for regulatory approval, including a marketing authorization application for marketing new drugs in Europe, must be supported by extensive clinical and preclinical data, as well as extensive information regarding chemistry, manufacturing and controls, or CMC, to demonstrate the safety and effectiveness of the applicable product candidate. The number and types of preclinical studies and clinical trials that will be required for regulatory approval varies depending on the product candidate, the disease or the condition that the product candidate is designed to target and the regulations applicable to any particular product candidate. Despite the time and expense associated with preclinical and clinical studies, failure can occur at any stage, and we could encounter problems that cause us to repeat or perform additional preclinical studies, CMC studies or clinical trials. Regulatory authorities could delay, limit or deny approval of a product candidate for many reasons, including because they:

may not deem a product candidate to be adequately safe and effective;

may not find the data from preclinical studies, CMC studies and clinical trials to be sufficient to support a claim of safety and efficacy;

may interpret data from preclinical studies, CMC studies and clinical trials significantly differently than we do;

may not approve the manufacturing processes or facilities associated with our product candidates;

may conclude that we have not sufficiently demonstrated long-term stability of the formulation for which we are seeking marketing approval;

may change approval policies (including with respect to our product candidates class of drugs) or adopt new regulations; or

may not accept a submission due to, among other reasons, the content or formatting of the submission.

Even if we believe that data collected from our preclinical studies, CMC studies and clinical trials of our product candidates are promising and that our information and procedures regarding CMC are sufficient, our data may not be sufficient to support marketing approval by regulatory authorities, or regulatory interpretation of these data and procedures may be unfavorable. Even if approved, product candidates may not be approved for all indications requested and such approval may be subject to limitations on the indicated uses for which the drug may be marketed, restricted distribution methods or other limitations. Our business and reputation may be harmed by any failure or significant delay in obtaining regulatory approval for the sale of any of our product candidates. We cannot predict when or whether regulatory approval will be obtained for any product candidate we develop.

S-10

Table of Contents

While we anticipate that LODOTRA will be marketed in additional countries as Mundipharma formulates its reimbursement strategy, the ability to market LODOTRA in additional countries will depend on Mundipharma's ability to obtain regulatory and reimbursement approvals in these countries. Similarly, our ability to market DUEXIS outside of the United States will depend on obtaining regulatory and reimbursement approval in any country where DUEXIS may be marketed. However, certain countries have a very difficult reimbursement environment and we may not obtain reimbursement approval in all countries where DUEXIS may be marketed, or we may obtain reimbursement approval at a level that would make marketing DUEXIS in certain countries not viable.

Our limited history of commercial operations makes evaluating our business and future prospects difficult, and may increase the risk of any investment in our ordinary shares.

Following our acquisition of Vidara in September 2014, we have four products approved in the United States, one product with broad approval for commercial sale in Europe, and another product approved only for commercial sale in the UK thus far. In addition we expect to begin commercializing PENNSAID 2% in the United States in January 2015 as a result of our recent acquisition of the U.S. rights to PENNSAID 2% from Nuvo. RAYOS/LODOTRA has been approved in the United States and over 30 other countries, including Australia, Korea, Israel and select countries within Europe. However, we have a limited history of marketing LODOTRA through our distribution partners, and LODOTRA is not yet marketed in all of the countries where it has been approved. DUEXIS was approved in the United States on April 23, 2011, and in March 2013 we announced we were granted marketing authorization for DUEXIS in the UK, and we have generated limited revenues for DUEXIS to date. We began the commercial sale of RAYOS in the United States in the fourth quarter of 2012, the commercial sale of VIMOVO in the United States in the first quarter of 2014 and the commercial sale of ACTIMMUNE as a combined company with Vidara in September 2014. We expect to begin commercializing PENNSAID 2% in the United States in January 2015. We face considerable risks and difficulties as a company with limited commercial operating history, particularly as a global consolidated entity with operating subsidiaries that also have limited operating histories. If we do not successfully address these risks, our business, prospects, operating results and financial condition will be materially and adversely harmed. Our limited commercial operating history, including our lack of any history commercializing PENNSAID 2%, and our limited history commercializing VIMOVO and, as a combined company, ACTIMMUNE, makes it particularly difficult for us to predict our future operating results and appropriately budget for our expenses. In the event that actual results differ from our estimates or we adjust our estimates in future periods, our operating results and financial position could be materially affected. For example, we may underestimate the resources we will require to successfully integrate our commercial organization with Vidara's or to commercialize VIMOVO, ACTIMMUNE and PENNSAID 2% within our organization or not realize the benefits we expect to derive from our recent acquisitions.

We only have U.S. rights to VIMOVO and PENNSAID 2% and have no control over the activities of AstraZeneca to commercialize VIMOVO outside of the United States or Nuvo or its licensees to commercialize PENNSAID 2% outside the United States, which could adversely impact commercialization of VIMOVO and PENNSAID 2% in the United States.

AstraZeneca has retained its existing rights to VIMOVO in territories outside of the United States, including the right to use the VIMOVO name and related trademark. Similarly, Nuvo has retained its rights to PENNSAID 2% in territories outside of the United States and has announced its intention to seek commercialization partners outside the United States. We have little or no control over AstraZeneca's activities with respect to VIMOVO outside of the United States or of Nuvo or its future commercial partners activities with respect to PENNSAID 2% outside of the United States, even though those activities could impact our ability to successfully commercialize VIMOVO and PENNSAID 2% in the United States. For example, AstraZeneca or its assignees or Nuvo or its assignees can make statements or use promotional materials with respect to VIMOVO or PENNSAID 2%, respectively, outside of the

United States that are inconsistent with our positioning of the products in the United States, and could sell VIMOVO or PENNSAID 2%, respectively, in foreign countries,

S-11

Table of Contents

including Canada, at prices that are dramatically lower than the prices we expect to charge in the United States. These activities and decisions, while occurring outside of the United States, could harm our commercialization strategy in the United States, in particular because AstraZeneca is continuing to market the product outside the United States under the same VIMOVO brand name that we are using in the United States. In addition, product recalls or safety issues with VIMOVO or PENNSAID 2% outside the United States, even if not related to the commercial product we sell in the United States, could result in serious damage to the brand in the United States and impair our ability to successfully market VIMOVO and PENNSAID 2%. We also rely on AstraZeneca and will rely on Nuvo or its assignees to provide us with timely and accurate safety information regarding the use of VIMOVO or PENNSAID 2%, respectively, outside of the United States, as we have or will have limited access to this information ourselves.

We rely on third parties to manufacture commercial supplies of all of our products, and we intend to rely on third parties to manufacture commercial supplies of any other approved products. The commercialization of any of our products could be stopped, delayed or made less profitable if those third parties fail to provide us with sufficient quantities of product or fail to do so at acceptable quality levels or prices or fail to maintain or achieve satisfactory regulatory compliance.

The facilities used by our third-party manufacturers to manufacture our products and product candidates must be approved by the applicable regulatory authorities. We do not control the manufacturing processes of third-party manufacturers and are currently completely dependent on our third-party manufacturing partners sanofi-aventis U.S. LLC, or sanofi-aventis U.S., operating through Valeant Pharmaceuticals International, Inc., or Valeant, its manufacturing partner located in Laval, Canada for production of DUEXIS, and Jagotec AG, or Jagotec, a wholly-owned subsidiary of SkyePharma PLC, located in Lyon, France, for production of RAYOS/LODOTRA. In August 2011, SkyePharma leased their entire pharmaceutical manufacturing business to Aenova France SAS, or Aenova. As such, Aenova is now a subcontractor for Jagotec for the manufacture of RAYOS/LODOTRA, with our consent. Sanofi Winthrop Industrie in France has been qualified as a backup manufacturer for DUEXIS. Bayer Pharma AG in Germany has been qualified as a backup manufacturer for RAYOS/LODOTRA. In December 2011, Valeant acquired Dermik, a dermatology unit of sanofi-aventis U.S., which includes the Laval, Canada site. Although, Valeant has taken over management and operations at the Laval, Canada facility, our manufacturing agreement remains with sanofi-aventis U.S. We purchase the primary active ingredients for DUEXIS from BASF Corporation in Bishop, Texas and Dr. Reddy's in India, and the primary active ingredient for RAYOS/LODOTRA from Tianjin Tianyao Pharmaceuticals Co., Ltd. in China and Sanofi Chimie in France. With respect to VIMOVO, we rely on AstraZeneca, including through its existing third party manufacturing arrangements, to supply finished VIMOVO product through 2014. After 2014, AstraZeneca will no longer be obligated to supply VIMOVO to us and we will need to rely on our own third-party manufacturing arrangements to ensure continued supply. In connection with our acquisition of the U.S. rights to VIMOVO, we have entered into a long-term master manufacturing services and product agreement with Patheon Pharmaceuticals Inc., or Patheon, for the supply of finished VIMOVO product. We have entered into long-term supply agreements with Divis Laboratories Limited and Minakem Holding SAS for the supply of the active pharmaceutical ingredients, or APIs, of VIMOVO. In addition, we are required to obtain AstraZeneca's consent prior to engaging any third-party manufacturers for esomeprazole, one of the APIs in VIMOVO, other than the third-party manufacturer(s) currently used by AstraZeneca or its affiliates or licensees. To the extent such manufacturers are unwilling or unable to manufacture esomeprazole for us on commercially-acceptable terms, we cannot guarantee that AstraZeneca would consent to our use of alternate sources of supply.

With respect to ACTIMMUNE, we rely on an exclusive supply agreement with Boehringer Ingelheim RCV GmbH & Co KG, or Boehringer Ingelheim, for manufacturing and supply. However, Boehringer Ingelheim also manufactures interferon gamma 1-b to supply its own commercial needs in its licensed territory, and this may lead to capacity allocation issues and supply constraints to us. Furthermore, we do not have a substitute supplier for ACTIMMUNE

and the process of identifying a substitute supplier and getting that supplier approved by the applicable regulatory authorities for manufacture and packaging of ACTIMMUNE can be a lengthy and costly process. ACTIMMUNE is manufactured by starting with cells from working cell bank samples which are derived

S-12

Table of Contents

from a master cell bank. We and Boehringer Ingelheim separately store multiple vials of the master cell bank. In the event of catastrophic loss at our or Boehringer Ingelheim's storage facility, it is possible that we could lose multiple cell banks and have the manufacturing capacity of ACTIMMUNE severely impacted by the need to substitute or replace the cell banks.

With respect to PENNSAID 2%, we rely on an exclusive supply agreement with Nuvo for manufacturing and supply. If Nuvo licenses its rights to PENNSAID 2% to commercialization partners outside of the United States, it is possible that Nuvo would also agree to manufacture and supply PENNSAID 2% for those partners. In that case, we would have no guarantee that fulfilling demand for PENNSAID 2% in territories outside the United States would impair Nuvo's ability to supply us with our requested quantities of PENNSAID 2% in the United States. In addition, while our supply agreement with Nuvo provides for the qualification of additional manufacturing sites for PENNSAID 2%, we and Nuvo may not be successful in finding alternative manufacturers to supply PENNSAID 2% or agreeing to commercially reasonable terms with alternate suppliers.

A key excipient used in PENNSAID as a penetration enhancer is dimethyl sulfoxide, or DMSO. Horizon and Nuvo rely on a sole proprietary form of DMSO for which we maintain a substantial safety stock. However, should something happen to this supply Horizon and Nuvo may not be able to qualify a second source.

If any of our third-party manufacturers cannot successfully manufacture material that conforms to our specifications and the applicable regulatory authorities' strict regulatory requirements, or pass regulatory inspection, they will not be able to secure or maintain regulatory approval for the manufacturing facilities. In addition, we have no control over the ability of third-party manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or any other applicable regulatory authorities do not approve these facilities for the manufacture of our products or if they withdraw any such approval in the future, or if our suppliers or third-party manufacturers decide they no longer want to supply our primary active ingredients or manufacture our products, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our products. To the extent any third-party manufacturers that we engage with respect to our products are different than those currently being used for commercial supply in the United States, the FDA will need to approve the facilities of those third-party manufacturers used in the manufacture of our products prior to our sale of any product using these facilities. If we cannot agree to terms with third-party manufacturers of VIMOVO APIs or the third party suppliers we engage do not have their facilities approved by the FDA with sufficient time to transition commercial supply of VIMOVO after 2014, we may experience supply shortages and our commercialization of VIMOVO would be substantially harmed.

Although we have entered into supply agreements for the manufacture of our products, our manufacturers may not perform as agreed or may terminate their agreements with us. Under our manufacturing and supply agreement with sanofi-aventis U.S., operating through Valeant, either we or sanofi-aventis U.S. may terminate the agreement upon an uncured breach by the other party or without cause upon two years prior written notice, so long as such notice is given after the third anniversary of the first commercial sale of DUEXIS. Under our master manufacturing services and product agreement with Patheon for finished VIMOVO product, either we or Patheon may terminate the agreement for uncured material breach by the other party or upon the other party's bankruptcy or insolvency, we may terminate the agreement if any regulatory authority takes any action or raises any objection that prevents us from commercializing the VIMOVO product and Patheon may terminate the agreement if we assign our rights or obligations under the agreement to a competitor of Patheon or to a party that, in the reasonable opinion of Patheon, is not a credit worthy substitute for us, or in certain other circumstances where we assign the agreement without Patheon's consent. Our manufacturing agreement with Boehringer Ingelheim has a term that runs until July 31, 2020, but the agreement may be terminated earlier by either us or Boehringer Ingelheim for an uncured material breach by the other party or upon the other party's bankruptcy or insolvency. Under our manufacturing and supply agreement

with Jagotec, either we or Jagotec may terminate the agreement in the event of an insolvency, liquidation or bankruptcy of the other party or upon an uncured breach by the other party. While we have the right to receive a continuing supply of RAYOS/LODOTRA from Jagotec for a period of 24 months after termination, we would need to move our manufacturing to our alternate supplier

S-13

Table of Contents

of RAYOS/LODOTRA, Bayer Pharma AG, in such an event and we would have to qualify a new back-up manufacturer. The initial term of our supply agreement with Nuvo for PENNSAID 2% is through December 31, 2022, but the agreement may be terminated earlier by either party for any uncured material breach by the other party of its obligations under the supply agreement or upon the bankruptcy or similar proceeding of the other party.

In addition, we do not have the capability to package any of our products for distribution. Consequently, we have entered into an agreement with Temmler Werke GmbH, or Temmler, for packaging of RAYOS/LODOTRA in certain European countries and in the United States, as well as any additional countries as may be agreed to by the parties. We intend to sell drug product finished and packaged by either Temmler or an alternate packager. At the end of 2012, Temmler was acquired by the Aenova Group. Valeant manufactures and supplies DUEXIS to us in final, packaged form for the United States as well as any additional countries as may be agreed to by the parties. During 2014, AstraZeneca is obligated to supply us VIMOVO in final, packaged form under a transition agreement and will work with us to transfer product packaging to Patheon. After 2014, we expect that Patheon will supply final, packaged VIMOVO product pursuant to the master manufacturing services and product agreement we executed in connection with our acquisition of the U.S. rights to VIMOVO. Boehringer Ingelheim supplies final, packaged ACTIMMUNE to us and Nuvo is obligated to supply final, packaged PENNSAID 2% to us, in each case under exclusive supply agreements.

The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, particularly in scaling up and validating initial production. These problems include difficulties with production costs and yields, quality control, including stability of the product, quality assurance testing, shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. Furthermore, if microbial, viral or other contaminations are discovered in the drug products or in the manufacturing facilities in which its products are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. We cannot assure you that issues relating to the manufacture of any of our products will not occur in the future. Additionally, our manufacturers may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. If our manufacturers were to encounter any of these difficulties, or otherwise fail to comply with their contractual obligations, our ability to commercialize our products in the United States or provide any product candidates to patients in clinical trials would be jeopardized. Any delay or interruption in our ability to meet commercial demand for our products will result in the loss of potential revenues and could adversely affect our ability to gain market acceptance for these products. In addition, any delay or interruption in the supply of clinical trial supplies could delay the completion of clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials completely.

Failures or difficulties faced at any level of our supply chain could materially adversely affect our business and delay or impede the development and commercialization of any of our products or product candidates and could have a material adverse effect on our business, results of operations, financial condition and prospects.

We have experienced recent growth and have expanded the size of our organization substantially in connection with our acquisition of the U.S. rights to VIMOVO in November 2013 and our acquisition of Vidara in September 2014, and we may experience difficulties in managing this growth as well as expected additional growth in connection with our acquisition of the U.S. rights to PENNSAID 2%.

As of December 31, 2010, we employed 41 full-time employees as a consolidated entity. In anticipation of the commercial launch of DUEXIS, we hired 80 sales representatives during the period from September 2011 through

Edgar Filing: Horizon Pharma plc - Form 424B7

October 2011. As of December 31, 2013 and September 30, 2014, we employed 304 and 463 full-time employees, respectively, as a consolidated entity. We plan to further increase the size of our sales force in connection with our recent acquisition of PENNSAID 2% to a total of approximately 385 representatives. We

S-14

Table of Contents

have also experienced, and may continue to experience, turnover of the sales representatives that we hired or will hire in connection with the commercialization of our products, requiring us to hire and train new sales representatives. Our management, personnel, systems and facilities currently in place may not be adequate to support this recent and anticipated growth, and we may not be able to retain or recruit qualified personnel in the future due to competition for personnel among pharmaceutical businesses.

As our commercialization plans and strategies develop, we will need to continue recruiting and training sales and marketing personnel and expect to need to expand the size of our employee base for managerial, operational, financial and other resources as a result of our recent acquisition of Vidara. Our ability to manage any future growth effectively may require us to do, among other things, the following:

continue to manage and expand the sales and marketing efforts for our existing products;

enhance our operational, financial and management controls, reporting systems and procedures;

expand our international resources;

successfully identify, recruit, hire, train, maintain, motivate and integrate additional employees;

establish and increase our access to commercial supplies of our products and product candidates;

expand our facilities and equipment; and

manage our internal development efforts effectively while complying with our contractual obligations to licensors, licensees, contractors, collaborators, distributors and other third parties.

In particular, the merger of the businesses of Horizon Pharma, Inc. and Vidara Therapeutic International plc is subject to numerous uncertainties and risks and will require significant efforts and expenditures. For example, we are transitioning Horizon Pharma, Inc. from a standalone public Delaware corporation to being part of a combined company organized in Ireland. This combination has resulted in many changes, including significant changes in the corporate business and legal entity structure, the integration of Vidara and its personnel with those of Horizon, and changes in systems. We are currently undertaking numerous complex transition activities, and we may encounter unexpected difficulties or incur unexpected costs, including:

difficulties in achieving growth prospects from combining the business of Vidara with that of Horizon;

difficulties in the integration of operations and systems;

difficulties in the assimilation of employees and corporate cultures;

challenges in preparing financial statements and reporting timely results at both a statutory level for multiple entities and jurisdictions and at a consolidated level for public reporting;

challenges in keeping existing customers and obtaining new customers; and

challenges in attracting and retaining key personnel.

If any of these factors impair our ability to integrate the operations of Horizon with those of Vidara successfully or on a timely basis, we may not be able to realize the business opportunities, growth prospects and anticipated tax synergies from combining the businesses. In addition, we may be required to spend additional time or money on integration that otherwise would be spent on the development and expansion of our business.

Our management may also have to divert a disproportionate amount of its attention away from day-to-day activities and towards managing these growth and integration activities. Our future financial performance and our ability to execute on our business plan will depend, in part, on our ability to effectively manage any future growth and our failure to effectively manage growth could have a material adverse effect on our business, results of operations, financial condition and prospects.

Table of Contents

If we are unable to effectively train and equip our sales force, our ability to successfully commercialize our products in the United States will be harmed.

As DUEXIS and RAYOS were not fully commercially launched in the United States until January 2012 and January 2013, respectively, and we did not begin commercializing VIMOVO in the United States until the first quarter of 2014, the members of our sales force have limited experience promoting the products. In addition, while the members of our sales force promoting ACTIMMUNE were previously promoting the product prior to the merger of the Horizon and Vidara businesses, we have not previously marketed ACTIMMUNE under Horizon's commercial organization. We expect to begin commercializing PENNSAID 2% in the United States in January 2015 and we currently have no experience marketing PENNSAID 2%. As a result, we are required to expend significant time and resources to train our sales force to be credible and persuasive in convincing physicians to prescribe and pharmacists to dispense our products. In addition, we must train our sales force to ensure that a consistent and appropriate message about our products is being delivered to our potential customers. Our sales representatives may also experience challenges promoting multiple products when they call on physicians and their office staff. This is particularly true with respect to DUEXIS, since VIMOVO is approved for similar indications and prescribed to similar patients, and prior to 2014 our sales representatives had previously been incentivized to increase DUEXIS market share at the expense of VIMOVO. We have also experienced, and may continue to experience, turnover of the sales representatives that we hired or will hire, requiring us to train new sales representatives. As a result of the managed care environment and pharmacies switching patients' prescriptions to a generic or over the counter brand, we have had to adjust the profile of the sales representatives we hire from the traditional pharmaceutical representative to a representative with business to business experience that is focused on the total office call in order to protect the prescription the physician has written and ensure the patient receives what their doctor ordered, which includes driving adoption of our PME program. If we are unable to effectively train our sales force and equip them with effective materials, including medical and sales literature to help them inform and educate potential customers about the benefits of our products and their proper administration and label indication, as well as our PME program, our efforts to successfully commercialize our products could be put in jeopardy, which could have a material adverse effect on our financial condition, share price and operations.

We face significant competition from other biotechnology and pharmaceutical companies, including those marketing generic products and our operating results will suffer if we fail to compete effectively.

The biotechnology and pharmaceutical industries are intensely competitive. We have competitors both in the United States and international markets, including major multinational pharmaceutical companies, biotechnology companies and universities and other research institutions. Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff, experienced marketing and manufacturing organizations and well-established sales forces. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors and we will have to find new ways to compete and may have to potentially merge with or acquire other businesses to stay competitive. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or in-licensing on an exclusive basis, products that are more effective and/or less costly than our products.

DUEXIS and VIMOVO face competition from Celebrex[®], marketed by Pfizer, and several other branded NSAIDs. DUEXIS and VIMOVO also face significant competition from the separate use of NSAIDs for pain relief and GI protective medications to reduce the risk of NSAID-induced upper GI ulcers. Both NSAIDs and GI protective medications are available in generic form and may be less expensive to use separately than DUEXIS or VIMOVO. PENNSAID 2% faces competition from generic versions of PENNSAID 1.5% and we expect that they will be priced significantly less than the price we intend to charge for PENNSAID 2% and Voltaren Gel, marketed by Endo

Pharmaceuticals, which is the market leader in the topical NSAID category. Legislation enacted in most states in the United States allows or, in some instances mandates, that a pharmacist dispense an available generic equivalent when filling a prescription for a branded product, in the absence of specific

S-16

Table of Contents

instructions from the prescribing physician. Because pharmacists often have economic and other incentives to prescribe lower-cost generics, if physicians prescribe DUEXIS, VIMOVO or PENNSAID 2%, those prescriptions may not result in sales. If we are unsuccessful in convincing physicians to complete prescriptions through our PME program or otherwise provide prescribing instructions prohibiting the substitution of generic ibuprofen and famotidine separately as a substitution for DUEXIS or generic naproxen and branded Nexium (esomeprazole) as a substitute for VIMOVO or generic PENNSAID 1.5% as a substitute for PENNSAID 2%, sales of DUEXIS, VIMOVO and PENNSAID 2% may suffer despite any success we may have in promoting DUEXIS, VIMOVO or PENNSAID 2% to physicians. In addition, other product candidates that contain ibuprofen and famotidine in combination or naproxen and esomeprazole in combination, while not currently known to us, may be developed and compete with DUEXIS or VIMOVO, respectively, in the future.

On February 15, 2012, we received a Paragraph IV Patent Certification from Par Pharmaceutical, Inc. advising that Par Pharmaceutical, Inc. had filed an Abbreviated New Drug Application, or ANDA, with the FDA for a generic version of DUEXIS, containing 800 mg of ibuprofen and 26.6 mg of famotidine. We subsequently filed patent infringement lawsuits against Par Pharmaceutical, Inc. and Par Pharmaceutical Companies, Inc., or collectively Par, relating to the ANDA and Par's intention to market a generic version of DUEXIS. On August 21, 2013, we entered into a settlement agreement, or the Par settlement agreement, and license agreement, or the Par license agreement, with Par relating to its patent infringement litigation. The Par settlement agreement provides for a full settlement and release by both us and Par of all claims that were or could have been asserted in the litigation and that arise out of the specific patent issues that were the subject of the litigation, including all resulting damages or other remedies.

Under the Par license agreement, we granted Par a non-exclusive license (that is only royalty-bearing in some circumstances), or the License, to manufacture and commercialize Par's generic version of DUEXIS in the United States after the generic entry date and to take steps necessary to develop inventory of, and obtain regulatory approval for, but not commercialize, Par's generic version of DUEXIS prior to the generic entry date. The License covers all patents owned or controlled by us during the term of the Par license agreement that would, absent the License, be infringed by the manufacture, use, sale, offer for sale, or importation of Par's generic version of DUEXIS in the United States. Unless terminated sooner pursuant to the terms of the Par license agreement, the License will continue until the last to expire of the licensed patents and/or applicable periods of regulatory exclusivity.

Under the Par license agreement, the generic entry date is January 1, 2023; however, Par may be able to enter the market earlier in certain circumstances. Such events relate to the resolution of potential future third party DUEXIS patent litigation, the entry of other third party generic versions of DUEXIS or certain specific changes in DUEXIS market conditions. Only in the event that Par enters the DUEXIS market due to the specified changes in DUEXIS market conditions will the License become royalty-bearing, with the royalty obligations ceasing upon the occurrence of one of the other events that would have allowed Par to enter the DUEXIS market.

Under the Par license agreement, we also agreed not to sue or assert any claim against Par for infringement of any patent or patent application owned or controlled by us during the term of the Par license agreement based on the manufacture, use, sale, offer for sale, or importation of Par's generic version of DUEXIS in the United States.

The Par license agreement may be terminated by us if Par commits a material breach of the agreement that is not cured or curable within 30 days after we provide notice of the breach. We may also terminate the Par license agreement immediately if Par or any of its affiliates initiate certain challenges to the validity or enforceability of any of the licensed patents or their foreign equivalents. In addition, the Par license agreement will terminate automatically upon termination of the Par settlement agreement.

Edgar Filing: Horizon Pharma plc - Form 424B7

On July 15, 2013, we received a Paragraph IV Patent Certification from Watson Laboratories, Inc. Florida, known as Actavis Laboratories FL, Inc., or Watson, advising that Watson had filed an ANDA with the FDA for a generic version of RAYOS, containing up to 5 mg of prednisone. Watson has not advised us as to the timing or

S-17

Table of Contents

status of the FDA's review of its filing. On August 26, 2013, we, together with Jagotec, filed suit in the United States District Court for the District of New Jersey against Watson, Actavis Pharma, Inc., Andrx Corp., and Actavis, Inc., or collectively WLF, seeking an injunction to prevent the approval of the ANDA. The lawsuit alleges that WLF has infringed U.S. Patent Nos. 6,488,960, 6,677,326, 8,168,218, 8,309,124 and 8,394,407 by filing an ANDA seeking approval from the FDA to market generic versions of RAYOS containing 1 mg, 2 mg and 5 mg of prednisone prior to the expiration of the patents. The subject patents are listed in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. The commencement of the patent infringement lawsuit stays, or bars, FDA approval of WLF's ANDA for 30 months or until an earlier district court decision that the subject patents are not infringed or are invalid. We, together with Jagotec have granted WLF a covenant not to sue with respect to US Patent Nos. 6,677,326 and 8,168,218, respectively, and accordingly these patents have been dismissed from the lawsuit. The Markman claim construction hearing took place on October 16, 2014 and on November 10, 2014, the court issued a claims construction order adopting our construction of both of the patent claim terms at issue in the hearing. The court has not yet set a trial date for the WLF action.

On September 12, 2013, we received a Paragraph IV Patent Certification from Par Pharmaceutical, Inc. advising that Par Pharmaceutical, Inc. had filed an ANDA with the FDA for a generic version of RAYOS containing up to 5 mg of prednisone. On October 22, 2013, we, together with Jagotec, filed suit in the United States District Court for the District of New Jersey against Par seeking an injunction to prevent the approval of the ANDA. The lawsuit alleged that Par had infringed U.S. Patent Nos. 6,488,960, 6,677,326, 8,168,218, 8,309,124 and 8,394,407 by filing an ANDA seeking approval from the FDA to market generic versions of RAYOS prior to the expiration of the patents. The subject patents are listed in the FDA's Orange Book. On November 20, 2013, we were notified by counsel for Par that Par Pharmaceutical, Inc. had elected to withdraw its ANDA with the FDA for a generic version of RAYOS containing 2 mg and 5 mg of prednisone. On December 5, 2013, we entered into a Stipulation of Dismissal with Par Pharmaceutical, Inc. whereby Par Pharmaceutical, Inc. agreed to withdraw its application to market a generic version of RAYOS.

Currently, patent litigation is pending in the District of New Jersey against four generic companies intending to market VIMOVO before the expiration of patents listed in the Orange Book. These cases are in the District of New Jersey and have been consolidated for discovery purposes. They are collectively known as the VIMOVO cases, and involve the following sets of defendants: (i) Dr. Reddy's Laboratories Inc. and Dr. Reddy's Laboratories Ltd., or collectively, Dr. Reddy's; (ii) Lupin Ltd. and Lupin Pharmaceuticals Inc., or collectively, Lupin; (iii) Mylan Pharmaceuticals Inc., Mylan Laboratories Limited, and Mylan Inc., or collectively, Mylan; and (iv) Watson Laboratories, Inc. Florida, known as Actavis Laboratories FL, Inc. and Actavis Pharma, Inc., or collectively, Actavis. Patent litigation in the District of New Jersey against a fifth generic company, Anchen Pharmaceuticals Inc., or Anchen, was dismissed after Anchen recertified under Paragraph III. We understand that Dr. Reddy's has entered into a settlement with AstraZeneca with respect to patent rights directed to Nexium for the commercialization of VIMOVO, and that according to the settlement agreement, Dr. Reddy's is now able to commercialize VIMOVO under AstraZeneca's Nexium patent rights. The settlement agreement, however, has no effect on the Pozen VIMOVO patents, which are still the subject of patent litigations. As part of our acquisition of the U.S. rights to VIMOVO, we have taken over and are responsible for the patent litigations that include the Pozen patents licensed to us under the Pozen license agreement.

The VIMOVO cases were filed on April 21, 2011, July 25, 2011, October 28, 2011, January 4, 2013, May 10, 2013, June 28, 2013 and October 23, 2013 and collectively include allegations of infringement of U.S. Patent Nos. 6,926,907 and 8,557,285. We understand the cases arise from Paragraph IV Notice Letters providing notice of the filing of an ANDA with the FDA seeking regulatory approval to market a generic version of VIMOVO before the expiration of the patents-in-suit. We understand the Dr. Reddy's notice letters were dated March 11, 2011 and November 20, 2012; the Lupin notice letters were dated June 10, 2011 and March 12, 2014; the Mylan notice letter

Edgar Filing: Horizon Pharma plc - Form 424B7

was dated May 16, 2013; and the Actavis notice letters were dated March 29, 2013 and November 5, 2013; and the Anchen notice letter was dated September 16, 2011. The court has issued a claims construction order and has set a pretrial schedule but has not yet set a trial date.

S-18

Table of Contents

If we are unsuccessful in any of the on-going patent litigations, we will likely face generic competition with respect to VIMOVO and/or RAYOS and our sales of VIMOVO and/or RAYOS will be substantially harmed.

ACTIMMUNE is the only drug currently approved by the FDA specifically for the treatment for CGD and SMO. While there are additional or alternative approaches used to treat patients with CGD and SMO, there are currently no products on the market that compete directly with ACTIMMUNE. The current clinical standard of care to treat CGD patients in the United States is the use of concomitant triple prophylactic therapy comprising ACTIMMUNE, an oral antibiotic agent and an oral antifungal agent. However, the FDA-approved labeling for ACTIMMUNE does not discuss this triple prophylactic therapy, and physicians may choose to prescribe one or both of the other modalities in the absence of ACTIMMUNE. Because of the immediate and life-threatening nature of SMO, the preferred treatment option for SMO is often to have the patient undergo a bone marrow transplant which, if successful, will likely obviate the need for further use of ACTIMMUNE in that patient. We are aware of a number of research programs investigating the potential of gene therapy as a possible cure for CGD. Additionally, other companies may be pursuing the development of products and treatments that target the same diseases and conditions which ACTIMMUNE is currently approved to treat. As a result, it is possible that our competitors may develop new drugs that manage CGD or SMO more effectively, cost less or possibly even cure CGD or SMO. In addition, U.S. healthcare legislation passed in March 2010 authorized the FDA to approve biological products, known as biosimilars, that are similar to or interchangeable with previously approved biological products, like ACTIMMUNE, based upon potentially abbreviated data packages. Biosimilars are likely to be sold at substantially lower prices than branded products because the biosimilar manufacturer would not have to recoup the research and development and marketing costs associated with the branded product. The development and commercialization of any competing drugs or the discovery of any new alternative treatment for CGD or SMO could have a material adverse effect on sales of ACTIMMUNE and its profitability.

The availability and price of our competitors' products could limit the demand, and the price we are able to charge, for our products. We will not successfully execute on our business objectives if the market acceptance of our products is inhibited by price competition, if physicians are reluctant to switch from existing products to our products, or if physicians switch to other new products or choose to reserve our products for use in limited patient populations.

In addition, established pharmaceutical companies may invest heavily to accelerate discovery and development of novel compounds or to in-license and develop novel compounds that could make our products obsolete. Our ability to compete successfully with these companies and other potential competitors will depend largely on our ability to leverage our experience in clinical, regulatory and commercial development to:

develop, acquire or in-license medicines that are superior to other products in the market;

attract qualified clinical, regulatory, and sales and marketing personnel;

obtain patent and/or other proprietary protection for our products and technologies;

obtain required regulatory approvals; and

successfully collaborate with pharmaceutical companies in the discovery, development and commercialization of new product candidates.

In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to be approved and overcome price competition and to be commercially successful. Accordingly, our competitors may succeed in obtaining patent protection, obtaining FDA approval or discovering, developing and commercializing medicines before we do, which would have a material adverse impact on our business. The inability to compete with existing products or subsequently introduced products would have a material adverse impact on our business, financial condition and prospects.

S-19

Table of Contents

Our business operations may subject us to numerous commercial disputes, claims and/or lawsuits.

Operating in the pharmaceutical industry, particularly the commercialization of pharmaceutical products, involves numerous commercial relationships, complex contractual arrangements, uncertain intellectual property rights, potential product liability and other aspects that create heightened risks of disputes, claims and lawsuits. In particular, we may face claims related to the safety of our products, intellectual property matters, employment matters, tax matters, commercial disputes, competition, sales and marketing practices, environmental matters, personal injury, insurance coverage and acquisition or divestiture-related matters. Any commercial dispute, claim or lawsuit may divert our management's attention away from our business, we may incur significant expenses in addressing or defending any commercial dispute, claim or lawsuit, and we may be required to pay damage awards or settlements or become subject to equitable remedies that could adversely affect our operations and financial results.

We are currently in litigation with multiple generic drug manufacturers regarding intellectual property infringement. For example, we are currently involved in Hatch Waxman litigation with generic drug manufacturers related to RAYOS and VIMOVO. Litigation related to these disputes may be costly and time-consuming and could materially and adversely impact our financial position and results of operations if resolved against us.

Similarly, from time to time we are involved in disputes with distributors, PBMs and licensing partners regarding their and our rights and performance of obligations under contractual arrangements. For example, we previously entered into a rebate agreement with a PBM, pursuant to which we were required to pay certain rebates on certain of our products that were reimbursed by health plans contracting with the PBM with respect to their formularies. Earlier this year, we sent a notice alerting the PBM of certain material breaches by the PBM under the agreement and indicating that the agreement would automatically terminate if the material breaches were not cured within 30 days. Among other things, the breaches by the PBM involved repeated invoices that included claims for rebates which were not eligible for payment under the agreement. Following the 30-day period, during which the PBM did not take action to cure the breaches or formally respond to the notice, we sent another notice informing the PBM that the agreement was terminated as of the end of the 30-day period in accordance with its terms and we ceased paying further rebates under the agreement. On November 6, 2014, we received a letter from the PBM asserting that the breaches we alleged in our termination notice were not material breaches and therefore the agreement was not terminated and remains in effect. In addition, the PBM claimed that we owe \$38.5 million in past price protection and utilization rebates related to VIMOVO and DUEXIS, in addition to further rebates on sales of VIMOVO and DUEXIS continuing after the date we believe the agreement was terminated. The substantial majority of these rebate claims relate to price protection rebates on VIMOVO which we believe are precluded under the agreement, particularly because VIMOVO was not covered under the agreement until after we had established an initial price for VIMOVO under a Horizon-owned National Drug Code, or NDC. Based upon the terms of the agreement and the PBM's actions, we believe that the PBM's claims in its November 6, 2014 letter are without merit and we intend to vigorously defend against them. However, we cannot predict the outcome of this dispute, including whether it will result in litigation. If we are unsuccessful in defending against the PBM's claims, and in light of the significant number of health plans that contract with the PBM, we could be forced to make substantial payments to the PBM for past and/or future rebates, at least through 2014. While the stated term of the agreement was through 2015, even if the PBM successfully argued that we did not validly terminate the contract due to material breach, we do not expect that we would owe further rebates in 2015 based on certain actions of the PBM. We cannot guarantee, however, that the PBM would not attempt to make arguments to the contrary. We also believe that we may have claims for damages that we could assert against the PBM. In any event, resolving the dispute with the PBM or being subject to related litigation may be costly and time-consuming and could materially and adversely impact our financial position and results of operations if resolved against us.

Table of Contents

A variety of risks associated with operating our business and marketing our products internationally could materially adversely affect our business.

In addition to our U.S. operations, we have operations in Ireland, Switzerland and Germany. Moreover, LODOTRA is currently being marketed in a limited number of countries outside the United States, and Mundipharma is in the process of obtaining pricing and reimbursement approval for, and preparing to market, LODOTRA in other European countries, as well as in certain Asian, Latin American, Middle Eastern and African countries. Also, Grünenthal S.A. is in the registration process for the commercialization of DUEXIS in Latin America. We face risks associated with our international operations, including possible unfavorable regulatory, pricing and reimbursement, political, tax and labor conditions, which could harm our business. We are subject to numerous risks associated with international business activities, including:

compliance with differing or unexpected regulatory requirements for our products;

compliance with Irish laws and the maintenance of our Irish tax residency with respect to our overall corporate structure and administrative operations, including the need to generally hold meetings of our board of directors and make decisions in Ireland, which may make certain corporate actions more cumbersome, costly and time-consuming;

compliance with Swiss laws with respect to our Horizon Pharma AG subsidiary, including laws requiring maintenance of cash in the subsidiary to avoid overindebtedness, which requires Horizon Pharma AG to maintain assets in excess of its liabilities;

difficulties in staffing and managing foreign operations;

in certain circumstances, including with respect to the commercialization of LODOTRA in Europe and certain Asian, Latin American, Middle Eastern and African countries, and commercialization of DUEXIS in Latin America, increased dependence on the commercialization efforts and regulatory compliance of our distributors or strategic partners;

compliance with German laws with respect to our Horizon Pharma GmbH subsidiary through which Horizon Pharma AG conducts most of its European operations;

foreign government taxes, regulations and permit requirements;

United States and foreign government tariffs, trade restrictions, price and exchange controls and other regulatory requirements;

anti-corruption laws, including the Foreign Corrupt Practices Act;

economic weakness, including inflation, natural disasters, war, events of terrorism or political instability in particular foreign countries;

fluctuations in currency exchange rates, which could result in increased operating expenses and reduced revenues, and other obligations related to doing business in another country;

compliance with tax, employment, immigration and labor laws, regulations and restrictions for employees living or traveling abroad;

workforce uncertainty in countries where labor unrest is more common than in the United States;

production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;

changes in diplomatic and trade relationships; and

challenges in enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States.

Table of Contents

These and other risks associated with our international operations may materially adversely affect our business, financial condition and results of operations.

If we fail to develop, acquire or in-license other product candidates or products, our business and prospects would be limited.

A key element of our strategy is to develop, acquire or in-license and commercialize a portfolio of other product candidates in addition to DUEXIS, VIMOVO, ACTIMMUNE, RAYOS/LODOTRA and PENNSAID 2%. Because we do not have proprietary drug discovery technology, the success of this strategy depends in large part upon the combination of our regulatory, development and commercial capabilities and expertise and our ability to identify, select and acquire or in-license clinically enabled product candidates for the treatment of pain-related diseases, or for therapeutic indications that complement or augment our current targets, or that otherwise fit into our development or strategic plans on terms that are acceptable to us. Identifying, selecting and acquiring, licensing promising product candidates requires substantial technical, financial and human resources expertise. Efforts to do so may not result in the actual acquisition or license of a particular product candidate, potentially resulting in a diversion of our management's time and the expenditure of our resources with no resulting benefit. If we are unable to identify, select and acquire or license suitable product candidates from third parties on terms acceptable to us, our business and prospects will be limited.

Moreover, any product candidate we identify, select and acquire or license may require additional, time-consuming development or regulatory efforts prior to commercial sale, including preclinical studies if applicable, and extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to the risk of failure that is inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and/or effective for approval by regulatory authorities. In addition, we cannot assure you that any such products that are approved will be manufactured or produced economically, successfully commercialized or widely accepted in the marketplace or be more effective or desired than other commercially available alternatives.

In addition, if we fail to successfully commercialize and further develop our products, there is a greater likelihood that we will fail to successfully develop a pipeline of other product candidates to follow our existing products, and our business and prospects would therefore be harmed.

Our November 2013 acquisition of the U.S. rights to VIMOVO, the September 2014 merger with Vidara and our October 2014 acquisition of the U.S. rights to PENNSAID 2%, and any other strategic transactions that we may pursue in the future could have a variety of negative consequences, and we may not realize the benefits of such transactions or attempts to engage in such transactions.

We acquired the U.S. rights to VIMOVO in November 2013, merged the businesses of Horizon Pharma, Inc. and Vidara in September 2014 and acquired the U.S. rights to PENNSAID 2% in October 2014, and from time to time, we may seek to engage in additional strategic transactions with third parties, such as acquisitions of companies or divisions of companies, asset purchases or in-licensing of product candidates or technologies that we believe will complement or augment our existing business. We may also consider a variety of other business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and other investments. Any such transaction may require us to incur non-recurring and other charges, increase our near and long-term expenditures, pose significant integration challenges, create additional tax, legal, accounting and operational complexities in our business, require additional expertise, result in dilution to our existing shareholders and disrupt our management and business, which could harm our operations and financial results. For example, in connection with our acquisition of the U.S. rights to VIMOVO, we assumed primary responsibility for the existing

patent infringement litigation with respect to VIMOVO, and have also agreed to reimburse certain legal expenses of Pozen with respect to its continued involvement in such litigation, and we expect that this will result in substantial on-going expenses and potential distractions to our management team. Because VIMOVO is approved for similar indications and prescribed to similar patients compared to

S-22

Table of Contents

DUEXIS, we may also experience lower prescriptions of DUEXIS as we seek to commercialize VIMOVO, particularly from the approximately 30% of physicians that currently prescribe both products. Moreover, we face significant competition in seeking appropriate strategic partners and transactions, and the negotiation process for any strategic transaction can be time-consuming and complex. In addition, we may not be successful in our efforts to engage in certain strategic transactions because our financial resources and research and development pipeline may be insufficient, our product candidates and programs may be deemed to be at too early of a stage of development for collaborative effort and/or third parties may not view our product candidates and programs as having the requisite potential. We may not be able to expand our business or realize our strategic goals if we do not have sufficient funding or cannot borrow or raise additional capital. There is no assurance that following our acquisition of the U.S. rights to VIMOVO, the merger with Vidara, our acquisition of the U.S. rights to PENNSAID 2% or any other strategic transaction, we will achieve the anticipated revenues, net income or tax benefits that we believe to justify such transaction. Any failures or delays in entering into strategic transactions could also delay or negatively impact the development and commercialization of our product candidates and reduce their competitiveness even if they reach the market. In addition, any failures or delays in entering into strategic transactions anticipated by analysts or the investment community could result in a decline in our share price.

We may not be able to successfully maintain our low tax rates, which could adversely affect our business and financial condition, results of operations and growth prospects.

We are incorporated in Ireland and maintain subsidiaries in multiple jurisdictions, including the United States, Switzerland, Luxemburg and Bermuda. Vidara was able to achieve a low average tax rate through the performance of certain functions and ownership of certain assets in tax-efficient jurisdictions, including Ireland and Bermuda, together with intra-group service and transfer pricing agreements, each on an arm's length basis. We are continuing a substantially similar structure and arrangements. Taxing authorities, such as the U.S. Internal Revenue Service, or IRS, actively audit and otherwise challenge these types of arrangements, and have done so in the pharmaceutical industry. We expect that these challenges will continue as a result of the recent increase in scrutiny and political attention on corporate tax structures. The IRS may challenge our structure and transfer pricing arrangements through an audit or lawsuit. Responding to or defending such a challenge could be expensive and consume time and other resources, and divert management's time and focus from operating our business. We cannot predict whether taxing authorities will conduct an audit or file a lawsuit challenging this structure, the cost involved in responding to any such audit or lawsuit, or the outcome. If we are unsuccessful, we may be required to pay taxes for prior periods, interest, fines or penalties, and may be obligated to pay increased taxes in the future, any of which could require us to reduce our operating expenses, decrease efforts in support of our products or seek to raise additional funds, all of which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

The IRS may not agree with our conclusion that we should be treated as a foreign corporation for U.S. federal income tax purposes following the combination of the businesses of Horizon Pharma, Inc. and Vidara Therapeutics International plc.

Although Horizon Pharma plc is incorporated in Ireland, the IRS, may assert that we should be treated as a U.S. corporation (and, therefore, a U.S. tax resident) for U.S. federal income tax purposes pursuant to Section 7874 of the Internal Revenue Code of 1986, as amended, or the Code. A corporation is generally considered a tax resident in the jurisdiction of its organization or incorporation for U.S. federal income tax purposes. Because Horizon Pharma plc, the parent company of our organization, is an Irish incorporated entity, it would generally be classified as a foreign corporation (and, therefore, a non-U.S. tax resident) under these rules. Section 7874 provides an exception pursuant to which a foreign incorporated entity may, in certain circumstances, be treated as a U.S. corporation for U.S. federal income tax purposes.

Edgar Filing: Horizon Pharma plc - Form 424B7

Under Section 7874, and as a result of the fact that the former shareholders of Horizon owned (within the meaning of Section 7874) less than 80% (by both vote and value) of the combined entity's stock immediately

S-23

Table of Contents

after the merger we believe we qualify as a foreign corporation for U.S. federal income tax purposes following the merger. However, there can be no assurance that there will not exist in the future a subsequent change in the facts or in law which might cause us to be treated as a domestic corporation for U.S. federal income tax purposes, including with retroactive effect.

Further, there can be no assurance that the IRS will agree with the position that the ownership test was satisfied. There is limited guidance regarding the application of Section 7874 of the Code, including with respect to the provisions regarding the application of the ownership test. If we were unable to be treated as a foreign corporation for U.S. federal income tax purposes, one of our significant strategic reasons for completing the Vidara merger would be nullified and we may not be able to recoup the significant investment in completing the transaction.

Future changes to U.S. and non-U.S. tax laws could materially adversely affect us.

Under current law, we expect to be treated as a foreign corporation for U.S. federal income tax purposes following the Vidara merger. However, changes to the rules in Section 7874 of the Code or regulations promulgated thereunder or other guidance issued by the Treasury or the IRS could adversely affect our status as a foreign corporation for U.S. federal income tax purposes, and any such changes could have prospective or retroactive application to us or our shareholders. On May 20, 2014 Senator Carl Levin and Representative Sander M. Levin introduced The Stop Corporate Inversions Act of 2014 (the bill) in the Senate and House of Representatives, respectively. In its current form, the bill would treat us as a U.S. Corporation as a result of the former shareholders of Horizon Pharma, Inc. owning 50% or more of the combined entity's stock immediately following the Vidara merger. If enacted, the bill would apply to taxable years ending after May 8, 2014 and does not contain an exception for transactions subject to a binding commitment on that date.

In addition, the U.S. Congress, the Organization for Economic Co-operation and Development, and other Government agencies in jurisdictions where we and our affiliates do business have had an extended focus on issues related to the taxation of multinational corporations and there are several current legislative proposals that, if enacted, would substantially change the U.S. federal income tax system as it relates to the taxation of multinational corporations. One example is in the area of base erosion and profit shifting, where payments are made between affiliates from a jurisdiction with high tax rates to a jurisdiction with lower tax rates. As a result, the tax laws in the United States and other countries in which we and our affiliates do business could change on a prospective or retroactive basis, and any such changes could materially and adversely affect us.

If we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our management, sales and marketing and scientific and medical personnel, including our Chairman, President and Chief Executive Officer, Timothy P. Walbert; our Executive Vice President and Chief Business Officer, Robert F. Carey; our Executive Vice President and Chief Financial Officer, Paul W. Hoelscher; our Executive Vice President, Development, Manufacturing and Regulatory Affairs and Chief Medical Officer, Jeffrey W. Sherman, M.D., and other members of our executive committee. In order to retain valuable employees at our company, in addition to salary and cash incentives, we provide incentive stock options that vest over time. The value to employees of stock options that vest over time will be significantly affected by movements in our share price that are beyond our control, and may at any time be insufficient to counteract more lucrative offers from other companies.

Despite our efforts to retain valuable employees, members of our management, sales and marketing, regulatory affairs, clinical affairs, medical affairs and development teams may terminate their employment with us on short notice. Although we have written employment arrangements with all of our employees, these

S-24

Table of Contents

employment arrangements generally provide for at-will employment, which means that our employees can leave our employment at any time, with or without notice. The loss of the services of any of our executive officers or other key employees and our inability to find suitable replacements could potentially harm our business, financial condition and prospects. We do not maintain key man insurance policies on the lives of these individuals or the lives of any of our other employees. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level, and senior managers as well as junior, mid-level, and senior sales and marketing and scientific and medical personnel.

Many of the other biotechnology and pharmaceutical companies with whom we compete for qualified personnel have greater financial and other resources, different risk profiles and longer histories in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high quality candidates than that which we have to offer. If we are unable to continue to attract and retain high quality personnel, the rate and success at which we can develop and commercialize products and product candidates will be limited.

We are, with respect to DUEXIS, VIMOVO, ACTIMMUNE and RAYOS, and will be, with respect to PENNSAID 2% and any other product candidate for which we obtain FDA approval or acquire or in-license, subject to ongoing FDA obligations and continued regulatory review, which may result in significant additional expense. Additionally, any other product candidate, if approved by the FDA, could be subject to labeling and other restrictions and market withdrawal, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

Any regulatory approvals that we obtain for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials and surveillance to monitor the safety and efficacy of the product candidate. In addition, if the FDA approves a product candidate, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with current good manufacturing practices, or cGMPs, good clinical practices, or GCPs, international conference on harmonization regulations, or ICH regulations, and good laboratory practices, or GLPs, which are regulations and guidelines enforced by the FDA for all of our products in clinical development, for any clinical trials that we conduct post-approval. In connection with our November 2013 acquisition of the U.S. rights to VIMOVO, we assumed responsibility for completing an ongoing Pediatric Research Equity Act post-marketing requirement study in children 12 years to 16 years and 11 months of age with Juvenile RA for which the FDA recently granted an extension with a final report due date of December 2015. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory product recalls;

fines, Warning Letters or holds on clinical trials;

refusal by the FDA to approve pending applications or supplements to approved applications filed by us or our strategic partners, or suspension or revocation of product license approvals;

product seizure or detention, or refusal to permit the import or export of products; and

injunctions, the imposition of civil or criminal penalties, or exclusions.

If we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would have a material adverse effect on our business, results of operations, financial condition and prospects.

S-25

Table of Contents

Coverage and reimbursement may not be available, or reimbursement may be available at only limited levels, for our products, which could make it difficult for us to sell our products profitably or to successfully execute planned product price increases.

Market acceptance and sales of our products will depend in large part on global coverage and reimbursement policies and may be affected by future healthcare reform measures, both in the United States and other key international markets. Successful commercialization of our products will depend in part on the availability of governmental and third-party payer reimbursement for the cost of our products. Government health administration authorities, private health insurers and other organizations generally provide reimbursement for healthcare. In particular, in the United States, private health insurers and other third-party payers often provide reimbursement for products and services based on the level at which the government (through the Medicare or Medicaid programs) provides reimbursement for such treatments. In the United States, the European Union and other significant or potentially significant markets for our products and product candidates, government authorities and third-party payers are increasingly attempting to limit or regulate the price of medical products and services, particularly for new and innovative products and therapies, which has resulted in lower average selling prices. Further, the increased emphasis on managed healthcare in the United States and on country and regional pricing and reimbursement controls in the European Union will put additional pressure on product pricing, reimbursement and usage, which may adversely affect our product sales and results of operations. These pressures can arise from rules and practices of managed care groups, judicial decisions and governmental laws and regulations related to Medicare, Medicaid and healthcare reform, pharmaceutical reimbursement policies and pricing in general. These pressures may create negative reactions to any product price increases, or limit the amount by which we may be able to increase our product prices, which may adversely affect our product sales and results of operations. Even though we have contracts with PBMs, that does not guarantee that they will perform in accordance with the contracts, nor does it preclude them from taking adverse actions against us, which could materially adversely affect our operating results. For example, we were recently informed that two significant PBMs would be placing DUEXIS and VIMOVO on their exclusion lists beginning in 2015, which will result in a loss of reimbursement for patients whose healthcare plans have adopted these PBM lists. Additional healthcare plan formularies may also exclude our products from reimbursement due to the actions of these PBMs, future price increases we may implement, our use of co-pay programs, or other reasons. If our strategies to mitigate formulary exclusions are not effective, these events may reduce the likelihood that physicians prescribe our products and increase the likelihood that prescriptions for our products are not filled.

Outside of the United States, the success of our products, including LODOTRA and, if widely approved, DUEXIS, will depend largely on obtaining and maintaining government coverage, because in many countries patients are unlikely to use prescription drugs that are not covered by their government healthcare programs. To date, LODOTRA is approved in over 35 countries outside the United States, and reimbursement for LODOTRA has been obtained in Germany, Italy, Sweden and Switzerland. Mundipharma is seeking coverage for LODOTRA in a number of countries and currently sells LODOTRA without coverage in a limited number of countries. Negotiating coverage and reimbursement with governmental authorities can delay commercialization by 12 months or more. Coverage and reimbursement policies may adversely affect our ability to sell our products on a profitable basis. In many international markets, governments control the prices of prescription pharmaceuticals, including through the implementation of reference pricing, price cuts, rebates, revenue-related taxes and profit control, and we expect prices of prescription pharmaceuticals to decline over the life of the product or as volumes increase. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceutical products, which we believe has impacted the reimbursement rates and timing to launch for LODOTRA to date, and we expect these discounts to continue as countries attempt to manage healthcare expenditures, especially in light of current economic conditions. For example, legislation was recently enacted in Germany that will increase the rebate on prescription pharmaceuticals and likely lower the revenues from the sale of LODOTRA in Germany that we would otherwise receive. As a result of these pricing practices, it may become difficult to achieve profitability or expected rates of

growth in revenue or results of operations. Any shortfalls in revenue could adversely affect our business, financial condition and results of operations.

S-26

Table of Contents

In light of such policies and the uncertainty surrounding proposed regulations and changes in the coverage and reimbursement policies of governments and third-party payers, we cannot be sure that coverage and reimbursement will be available for DUEXIS or LODOTRA in any additional markets or for any other product candidates that we may develop. Also, we cannot be sure that reimbursement amounts will not reduce the demand for, or the price of, our products. If coverage and reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our products.

We expect to experience pricing pressures in connection with the sale of our products, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative proposals. There may be additional pressure by payers and healthcare providers to use generic drugs that contain the active ingredients found in DUEXIS, VIMOVO, RAYOS/LODOTRA and PENNSAID 2% or any other product candidates that we may develop, acquire or in-license. If we fail to successfully secure and maintain coverage and adequate reimbursement for our products or are significantly delayed in doing so, we will have difficulty achieving market acceptance of our products and expected revenue and profitability which would have a material adverse effect on our business, results of operations, financial condition and prospects. We may also experience pressure from payers concerning certain promotional approaches that we may implement such as co-pay programs whereby we assist patients to achieve an acceptable co-pay for our product, which may be contrary to payers' financial interests. If we are unsuccessful with our co-pay initiatives, we would be at a competitive disadvantage in terms of pricing versus preferred branded and generic competitors.

We are subject to federal, state and foreign healthcare laws and regulations and implementation or changes to such healthcare laws and regulations could adversely affect our business and results of operations.

The United States and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals to regulate and to change the healthcare system in ways that could affect our ability to sell our products profitably. In the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

If we are found to be in violation of any of these laws or any other federal or state regulations, we may be subject to civil and/or criminal penalties, damages, fines, exclusion from federal health care programs and the restructuring of our operations. Any of these could have a material adverse effect on our business and financial results. Since many of these laws have not been fully interpreted by the courts, there is an increased risk that we may be found in violation of one or more of their provisions. Any action against us for violation of these laws, even if we ultimately are successful in our defense, will cause us to incur significant legal expenses and divert our management's attention away from the operation of our business.

We expect that the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, the PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we may receive for any approved product. An expansion in the government's role in the U.S. healthcare industry may cause general downward pressure on the prices of prescription drug products, lower reimbursements for providers using our products, reduce product utilization and adversely affect our business and results of operations. It is unclear whether and to what extent, if at all, other anticipated developments resulting from the federal healthcare reform legislation, such as an increase in the number of people with health insurance and an increased focus on preventive medicine, may provide us additional revenue to offset the annual excise tax (on certain drug product sales) enacted under the PPACA, subject to limited exceptions. It is possible that the tax burden, if we are not excepted, would

adversely affect our financial performance, which in turn could cause the price of our share to decline. Any reduction in reimbursement from government programs may result in a similar reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to

S-27

Table of Contents

generate revenue, attain profitability, or commercialize our current products and/or those for which we may receive regulatory approval in the future.

We are subject, directly or indirectly, to federal and state healthcare fraud and abuse and false claims laws and regulations. Prosecutions under such laws have increased in recent years and we may become subject to such litigation. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

In the United States, we are subject directly, or indirectly through our customers, to various state and federal fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act, federal and state privacy and security laws, sunshine laws, government price reporting laws, and other fraud laws, as described in greater detail in the Government Regulation Section of this report. These laws may impact, among other things, our proposed sales, marketing and educational programs, as well as other possible relationships with customers, payers, and patients.

Compliance with these laws, including the development of a comprehensive compliance program, is difficult, costly and time consuming and companies that do not comply with these state laws face civil penalties. Even if we structure our programs with the intent of compliance with such laws, there can be no certainty that we would not need to defend our business activities against enforcement or litigation, in light of the fact that there is significant enforcement interest in pharmaceutical companies in the United States, and some of the applicable laws are quite broad in scope with very narrow exceptions.

We are unable to predict whether we could be subject to actions under any of these or other fraud and abuse laws, or the impact of such actions. If we are found to be in violation of any of the laws described above and other applicable state and federal fraud and abuse laws, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from government healthcare reimbursement programs and the curtailment or restructuring of our operations, all of which could have a material adverse effect on our business and results of operations.

Our products or any other product candidate that we develop may cause undesirable side effects or have other properties that could delay or prevent regulatory approval or commercialization, result in product re-labeling or withdrawal from the market or have a significant impact on customer demand.

Undesirable side effects caused by any product candidate that we develop could result in the denial of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications, or cause us to evaluate the future of our development programs. In our two Phase 3 clinical trials with DUEXIS, the most commonly reported treatment-emergent adverse events were nausea, dyspepsia, diarrhea, constipation and upper respiratory tract infection. In Phase 3 endoscopic registration clinical trials with VIMOVO, the most commonly reported treatment-emergent adverse events were erosive gastritis, dyspepsia, gastritis, diarrhea, gastric ulcer, upper abdominal pain, nausea and upper respiratory tract infection. The most common side effects observed in pivotal trials for ACTIMMUNE were flu-like or constitutional symptoms such as fever, headache, chills, myalgia and fatigue. The most commonly reported treatment-emergent adverse events in the Phase 3 clinical trials with RAYOS/LODOTRA included flare in RA-related symptoms, abdominal pain, nasopharyngitis, headache, flushing, upper respiratory tract infection, back pain and weight gain. The most common adverse events reported in a Phase 2 clinical trial of PENNSAID 2% were application site reactions, such as dryness, exfoliation, erythema, pruritus, pain, induration, rash and scabbing.

In addition, the FDA or other regulatory authorities may require, or we may undertake, additional clinical trials to support the safety profile of our product candidates.

Table of Contents

In addition, if we or others identify undesirable side effects caused by our products or any other product candidate that we may develop that receives marketing approval, or if there is a perception that the product is associated with undesirable side effects:

regulatory authorities may require the addition of labeling statements, such as a black box warning or a contraindication;

regulatory authorities may withdraw their approval of the product or place restrictions on the way it is prescribed; and

we may be required to change the way the product is administered, conduct additional clinical trials or change the labeling of the product or implement a risk evaluation and mitigation strategy.

If any of these events occurred with respect to our products, our ability to generate significant revenues from the sale of these products would be significantly harmed.

We rely on third parties to conduct our preclinical and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines or if they experience regulatory compliance issues, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

We have agreements with third-party contract research organizations, or CROs, to conduct our clinical programs, including those required for post-marketing commitments. We may also have the need to enter into other such agreements in the future if we were to develop other product candidates or conduct clinical trials in additional indications for our existing products. We rely heavily on these parties for the execution of our clinical studies, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol. We and our CROs are required to comply with current GCP or ICH regulations. The FDA enforces these GCP or ICH regulations through periodic inspections of trial sponsors, principal investigators and trial sites. If we or our CROs fail to comply with applicable GCP or ICH regulations, the data generated in our clinical trials may be deemed unreliable and our submission of marketing applications may be delayed or the FDA may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our clinical trials comply or complied with GCP or ICH regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations, and may require a large number of test subjects. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of our CROs violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs on commercially reasonable terms, or at all. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our products and product candidates. As a result, our results of operations and the commercial prospects for our products and product candidates would be harmed, our costs could increase and

our ability to generate revenues could be delayed.

Switching or adding additional CROs can involve substantial cost and require extensive management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter

S-29

Table of Contents

similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition or prospects.

In addition, pursuant to a March 2011 letter agreement and in connection with our waiver of certain milestone payments, Mundipharma initiated a separate Phase 3 clinical trial for LODOTRA for the potential treatment of polymyalgia rheumatica, or PMR. We had limited control over the timing and implementation of the planned clinical trial and in February 2014, Mundipharma informed us that they had terminated the clinical trial primarily due to recruitment difficulties based on the inclusion criteria and as a result of the cessation of production of the comparator product Decortin® 1mg.

We also, as part of the April 23, 2011 FDA approval of DUEXIS, had a commitment under the Pediatric Research Equity Act, or PREA, to conduct an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients. We were notified by FDA on October 2, 2014 that we had either met or they had released us from all of the requirements under such assessment and we are in the process of winding down the remaining open study.

In addition, in connection with our November 2013 acquisition of the U.S. rights to VIMOVO, we assumed responsibility for completing an ongoing PREA post-marketing requirement study in children 12 years to 16 years and 11 months of age with Juvenile Idiopathic Arthritis for which the FDA recently granted an extension with a final report due date of December 2015. Although we are committed to carrying out these commitments, there are challenges in conducting studies in pediatric patients including availability of study sites, patients, and obtaining parental informed consent.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results.

Clinical testing is expensive and can take many years to complete, and its outcome is uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of potential product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical testing.

To the extent that we are required to conduct additional clinical development of DUEXIS, VIMOVO, ACTIMMUNE, RAYOS/LODOTRA or PENNSAID 2% or we conduct clinical development of earlier stage product candidates or for additional indications for ACTIMMUNE or RAYOS/LODOTRA, we may experience delays in these clinical trials. We do not know whether any additional clinical trials will be initiated in the future, begin on time, need to be redesigned, enroll patients on time or be completed on schedule, if at all. Clinical trials can be delayed for a variety of reasons, including delays related to:

obtaining regulatory approval to commence a trial;

reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;

obtaining institutional review board or ethics committee approval at each site;

recruiting suitable patients to participate in a trial;

having patients complete a trial or return for post-treatment follow-up;

clinical sites dropping out of a trial;

adding new sites; or

manufacturing sufficient quantities of product candidates for use in clinical trials.

S-30

Table of Contents

Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. Furthermore, we expect to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our future clinical trials and while we intend to have agreements governing their committed activities, we will have limited influence over their actual performance.

We could encounter delays if prescribing physicians encounter unresolved ethical issues associated with enrolling patients in clinical trials of our product candidates in lieu of prescribing existing treatments that have established safety and efficacy profiles. Further, a clinical trial may be suspended or terminated by us, our collaborators, the FDA or other regulatory authorities due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we experience delays in the completion of, or if we terminate, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may harm our business, financial condition, results of operations and prospects significantly. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

Business interruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or man-made disasters or business interruptions. While we carry insurance for certain of these events and have implemented disaster management plans and contingencies, the occurrence of any of these business interruptions could seriously harm our business and financial condition and increase our costs and expenses. Following the closing of our acquisition of Vidara, we conduct or plan to conduct significant management operations at both our global headquarters located in Dublin, Ireland and our U.S. headquarters located in Deerfield, Illinois. If our Dublin or Deerfield offices were affected by a natural or man-made disaster or other business interruption, our ability to manage our domestic and foreign operations could be impaired, which could materially and adversely affect our results of operations and financial condition. We currently rely, and intend to rely in the future, on third-party manufacturers and suppliers to produce our products. Our ability to obtain commercial supplies of our products could be disrupted and our results of operations and financial condition could be materially and adversely affected if the operations of these suppliers were affected by a man-made or natural disaster or other business interruption. The ultimate impact of such events on us, our significant suppliers and our general infrastructure is unknown.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our products.

We face an inherent risk of product liability as a result of the commercial sales of our products and the clinical testing of our product candidates. For example, we may be sued if any of our products or product candidates allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such

product liability claims may include allegations of defects in manufacturing, defects

S-31

Table of Contents

in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

decreased demand for our products or product candidates that we may develop;

injury to our reputation;

withdrawal of clinical trial participants;

initiation of investigations by regulators;

costs to defend the related litigation;

a diversion of management's time and our resources;

substantial monetary awards to trial participants or patients;

product recalls, withdrawals or labeling, marketing or promotional restrictions;

loss of revenue;

exhaustion of any available insurance and our capital resources;

the inability to commercialize our products or product candidates; and

a decline in our share price.

Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. We currently carry product liability insurance covering our clinical studies and commercial product sales in the amount of \$20 million in the aggregate. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. If we determine that it is prudent to increase our product liability coverage due to

the on-going commercialization of DUEXIS, VIMOVO, ACTIMMUNE and RAYOS in the United States, the planned commercialization of PENNSAID 2% in the United States, and/or the potential commercial launches of DUEXIS and LODOTRA in additional markets, we may be unable to obtain such increased coverage on acceptable terms or at all. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

Our business involves the use of hazardous materials, and we and our third-party manufacturers must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our third-party manufacturers' activities involve the controlled storage, use and disposal of hazardous materials owned by us, including the components of our product candidates and other hazardous compounds. We and our manufacturers are subject to federal, state and local as well as foreign laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental contamination or injury from these materials. In the event of an accident, state, federal or foreign authorities may curtail the use of these materials and interrupt our business operations. We do not currently maintain hazardous materials insurance coverage. If we are subject to any liability as a result of our third-party manufacturers' activities involving hazardous materials, our business and financial condition may be adversely affected. In the

Table of Contents

future we may seek to establish longer term third-party manufacturing arrangements, pursuant to which we would seek to obtain contractual indemnification protection from such third-party manufacturers potentially limiting this liability exposure.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations, provide accurate information to the FDA, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Business Conduct and Ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

Risks Related to Our Financial Position and Capital Requirements

We have incurred significant operating losses since our inception and anticipate that we will continue to incur losses for the foreseeable future.

We have a limited operating history and even less history operating as a combined organization following the Vidara merger. We have financed our operations primarily through equity and debt financings and the issuance of convertible notes and have incurred significant operating losses since our inception. We had net losses of \$232.0 million for the nine months ended September 30, 2014 and \$149.0 million, \$87.8 million and \$113.3 million for the years ended December 31, 2013, 2012 and 2011, respectively. As of September 30, 2014, we had an accumulated deficit of \$692.9 million. We do not know whether or when we will become profitable. Our prior losses, combined with possible future losses, have had and will continue to have an adverse effect on our shareholders' deficit and working capital. Our losses have resulted principally from costs incurred in our development activities for our products and product candidates, commercialization activities related to our product launches and costs associated with derivative liability accounting. We anticipate that we will continue to incur operating losses until such time as the revenues we generate from the sale of our products are sufficient to cover our operating expenses.

We have limited product revenues and other sources of revenues. We may never achieve or sustain profitability, which would depress the market price of our ordinary shares and could cause our investors to lose all or a part of their investment.

Our ability to become profitable depends upon our ability to generate revenues from sales of our products. DUEXIS was approved by the FDA on April 23, 2011, and we began generating revenues from sales of DUEXIS in late 2011 following the commercial launch in the United States. LODOTRA is approved for marketing in over 35 countries outside the United States, and to date we have generated only limited revenues from sales of LODOTRA. RAYOS

was approved by the FDA on July 26, 2012, and we began marketing it in the United States through our full field sales force in late January 2013. Following our November 2013 acquisition of the U.S. rights to VIMOVO, we began commercialization efforts in the United States in the first quarter of 2014.

S-33

Table of Contents

ACTIMMUNE was originally launched in the U.S. market in March 1991 by Genentech and in June 2012, Vidara acquired the intellectual property rights and certain assets related to the ACTIMMUNE product line. In September 2014, the businesses of Horizon Pharma, Inc. and Vidara were combined, and as a result we assumed the commercialization of ACTIMMUNE. In October 2014 we acquired the U.S. rights to PENNSAID 2% and expect to begin commercializing PENNSAID 2% in the United States in January 2015. We may never be able to successfully commercialize DUEXIS, VIMOVO, ACTIMMUNE, RAYOS or PENNSAID 2% or develop or commercialize other products in the United States, which we believe represents our most significant commercial opportunity. Our ability to generate future revenues depends heavily on our success in:

commercializing our existing products and any other product candidates for which we obtain approval; and

FDA approvals for additional indications for ACTIMMUNE; and

securing additional foreign regulatory approvals for LODOTRA and DUEXIS; and

developing, acquiring or in-licensing and commercializing a portfolio of other product candidates in addition to DUEXIS, VIMOVO, ACTIMMUNE, RAYOS/LODOTRA and PENNSAID 2%.

Even if we do generate additional product sales, we may never achieve or sustain profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the market price of our ordinary shares and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations.

We may need to obtain additional financing to successfully commercialize or further develop our existing products, or to develop, acquire or in-license other products.

Our operations have consumed substantial amounts of cash since inception. We expect to continue to spend substantial amounts to:

commercialize our existing products in the United States, including due to the substantial expansion of our sales force we completed in connection with our November 2013 acquisition of the U.S. rights to VIMOVO and the planned additional expansion of our sales force in connection with our acquisition of the U.S. rights to PENNSAID 2%;

complete the regulatory approval process, and any future required clinical development related thereto, for our products;

potentially acquire or in-license additional complementary products or products that augment our current product portfolio; and

conduct clinical trials with respect to ACTIMMUNE for other potential indications beyond GCD or SMO. While we believe that our existing cash and cash equivalents at September 30, 2014 of \$248.8 million, together with interest thereon, and borrowings available under our credit facilities will be sufficient to fund our operations to the point of generating positive cash flow based on our current expectations of continued revenue growth, we may need to raise additional funds if we choose to expand our commercialization or development efforts more rapidly than we presently anticipate, if we develop, acquire or in-license additional products or acquire companies, or if our revenues do not meet expectations.

We cannot be certain that additional funding will be available on acceptable terms, or at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our products or product candidates or one or more of our other research and development initiatives. We also could be required to:

seek collaborators for one or more of our current or future product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available; or

S-34

Table of Contents

relinquish or license on unfavorable terms our rights to technologies or product candidates that we otherwise would seek to develop or commercialize ourselves.

On June 17, 2014, we entered into a credit agreement with a group of lenders to provide us with \$300.0 million in financing through a five-year senior secured credit facility, or the Senior Secured Credit Facility. Funding of the Senior Secured Credit Facility occurred coincident with the closing of the merger with Vidara. While the credit agreement provides for an uncommitted accordion facility from which we may potentially finance future acquisitions, funding under the accordion facility is subject to the satisfaction of certain financial and other conditions that we may not be able to meet at the times we may desire to fund an acquisition opportunity. If we are otherwise unable to secure financing to support future acquisitions, our ability to execute on a key aspect of our overall growth strategy would be impaired.

Our Swiss subsidiary, Horizon Pharma AG, is subject to Swiss laws regarding overindebtedness that require Horizon Pharma AG to maintain assets in excess of its liabilities. As of September 30, 2014, Horizon Pharma AG was not overindebted. However, Horizon Pharma AG has previously been overindebted, including at December 31, 2013. We will continue to monitor and review Horizon Pharma AG's financial position and, as necessary, will address any overindebtedness, which could require us to have cash at Horizon Pharma AG in excess of its near term operating needs and could affect our ability to have sufficient cash at our other subsidiaries to meet their near term operating needs.

Any of the above events could significantly harm our business, financial condition and prospects and cause the price of our ordinary shares to decline.

Raising additional capital may cause dilution to our existing shareholders, restrict our operations or require us to relinquish intellectual property rights to our product candidates.

We may seek additional capital through a combination of private and public equity offerings, debt financings, receivables or royalty financings, strategic partnerships and alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our existing shareholders will be diluted, and the terms may include liquidation or other preferences that adversely affect the rights of our shareholders. Debt, receivables and royalty financings may be coupled with an equity component, such as warrants to purchase shares, which could also result in dilution of our existing shareholders' ownership. The incurrence of additional indebtedness would result in increased fixed payment obligations and could also result in certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. For example, our borrowings under the Senior Secured Credit Facility subject us to significant fixed payment obligations in the future as we become obligated to repay the debt, and the Senior Secured Credit Facility contains affirmative and negative covenants that restrict our ability to incur additional indebtedness, grant liens, make investments, engage in mergers or dispositions, prepay other indebtedness and issue dividends or other distributions. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our product candidates, or grant licenses on terms that are not favorable to us.

We generally have broad discretion in the use of our cash and may not use it effectively.

Our management has broad discretion in the application of our cash, and investors will be relying on the judgment of our management regarding the use of our cash. Our management may not apply our cash in ways that ultimately increase the value of any investment in our securities. We expect to use our existing cash to fund U.S. commercialization activities for DUEXIS, VIMOVO, ACTIMMUNE, RAYOS and, beginning in January 2015,

PENNSAID 2%, to potentially fund additional regulatory approvals of DUEXIS, ACTIMMUNE and RAYOS/LODOTRA, to potentially fund development life cycle management or manufacturing activities of ACTIMMUNE, RAYOS/LODOTRA and PENNSAID 2% for other indications and for working capital, capital

S-35

Table of Contents

expenditures and general corporate purposes. We may also invest our cash in short-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our shareholders. If we do not invest or apply our cash in ways that enhance shareholder value, we may fail to achieve expected financial results, which could cause the price of our ordinary shares to decline.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

Under Section 382 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an ownership change (generally defined as a greater than 50% change (by value) in its equity ownership over a three year period), the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be limited. In September 2012, the sale of common stock and warrants to purchase ordinary shares in a public equity offering by Horizon Pharma, Inc. triggered an ownership change limitation and, as a result, we will be subject to annual limits on our ability to utilize net operating loss carryforwards of Horizon Pharma, Inc. We estimate that these annual limits will be a cumulative carryforward of \$49.9 million in 2014, and at a minimum, \$22.0 million for each of 2015 and 2016 assuming only the carryforward limitation. The net operating loss carryforward limitation is cumulative such that any use of the carryforwards below the limitation in one year will result in a corresponding increase in the limitation for the subsequent tax year.

Following certain acquisitions of a U.S. corporation by a foreign corporation, Section 7874 of the Code limits the ability of the acquired U.S. corporation and its U.S. affiliates to utilize U.S. tax attributes such as net operating losses to offset U.S. taxable income resulting from certain transactions. Based on the limited guidance available, we expect this limitation is applicable following the Vidara merger. As a result, it is not currently expected that Horizon Pharma, Inc. or our other U.S. affiliates will be able to utilize their U.S. tax attributes to offset their U.S. taxable income, if any, resulting from certain taxable transactions following the Vidara merger. Notwithstanding this limitation, we expect that Horizon Pharma, Inc. will be able to fully utilize its U.S. net operating losses prior to their expiration. As a result of this limitation, however, it may take Horizon Pharma, Inc. longer to use its net operating losses. Moreover, contrary to these expectations, it is possible that the limitation under Section 7874 of the Code on the utilization of U.S. tax attributes could prevent Horizon Pharma, Inc. from fully utilizing its U.S. tax attributes prior to their expiration if Horizon Pharma, Inc. does not generate taxable income consistent with its expectations.

Any limitation on our ability to use our net operating loss carryforwards will likely increase the taxes we would otherwise pay in future years if we were not subject to such limitations.

Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and share price.

As widely reported, global credit and financial markets have experienced extreme disruptions in the past several years, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates, and uncertainty about economic stability. While there has been some recent improvement in some of these financial metrics, there can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment and continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate again, or do not improve, it may make any necessary debt or equity financing more difficult to complete, more costly, and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and share price and could require us to delay or abandon commercialization or development plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive these difficult economic times, which could directly affect our ability to attain our

operating goals on schedule and on budget.

S-36

Table of Contents

At September 30, 2014, we had \$248.8 million of cash and cash equivalents consisting of cash and money market funds. While we are not aware of any downgrades, material losses, or other significant deterioration in the fair value of our cash equivalents or marketable securities since September 30, 2014, no assurance can be given that further deterioration in conditions of the global credit and financial markets would not negatively impact our current portfolio of cash equivalents or marketable securities or our ability to meet our financing objectives. Further dislocations in the credit market may adversely impact the value and/or liquidity of marketable securities owned by us.

Changes in accounting rules or policies may affect our financial position and results of operations.

U.S. generally accepted accounting principles and related implementation guidelines and interpretations can be highly complex and involve subjective judgments. Changes in these rules or their interpretation, the adoption of new guidance or the application of existing guidance to changes in our business could significantly affect our financial position and results of operations. In addition, our operation as an Irish company with multiple subsidiaries in different jurisdictions adds additional complexity to the application of U.S. generally accepted accounting principles and this complexity will be exacerbated further if we complete additional strategic transactions. Changes in the application of existing rules or guidance applicable to us or our wholly-owned subsidiaries could significantly affect our consolidated financial position and results of operations.

Servicing our debt requires a significant amount of cash, and we may not have sufficient cash flow from our business to pay our substantial debt.

In November 2013, Horizon Pharma, Inc. issued \$150.0 million aggregate principal amount of 5.00% Convertible Senior Notes due 2018, or the Convertible Senior Notes, to investors pursuant to note purchase agreements with such investors, and we subsequently guaranteed this debt at our parent entity. As of October 31, 2014, \$80.6 million of principal amount of the Convertible Senior Notes remained outstanding. We also substantially increased our overall indebtedness to finance the Vidara merger. On June 17, 2014, we entered into the Senior Secured Credit Facility and borrowed \$300.0 million, which is due after a five-year period. Our ability to make scheduled payments of the principal of, to pay interest on or to refinance our indebtedness, including the Convertible Senior Notes and our borrowings under the Senior Secured Credit Facility, depends on our future performance, which is subject to economic, financial, competitive and other factors beyond our control. Our business may not continue to generate cash flow from operations in the future sufficient to service our debt and make necessary capital expenditures. If we are unable to generate such cash flow, we may be required to adopt one or more alternatives, such as selling assets, restructuring debt or obtaining additional equity capital on terms that may be onerous or highly dilutive. Our ability to refinance our indebtedness will depend on the capital markets and our financial condition at such time. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations.

Covenants imposed by the Senior Secured Credit Facility restrict our business and operations in many ways and if we do not effectively manage our covenants, our financial conditions and results of operations could be adversely affected.

The Senior Secured Credit Facility provides for (i) a committed five-year \$300 million term loan facility, the proceeds of which were used primarily to effect the Vidara merger and pay fees and expenses in connection therewith and are being used in part for general corporate purposes; (ii) an uncommitted accordion facility subject to the satisfaction of certain financial and other conditions; and (iii) one or more uncommitted refinancing loan facilities with respect to loans under the Senior Secured Credit Facility. The Senior Secured Credit Facility imposes various covenants that limit our ability and/or our restricted subsidiaries' ability to, among other things:

incur or assume liens or additional debt or provide guarantees in respect of obligations of other persons;

issue redeemable preferred shares;

S-37

Table of Contents

pay dividends or distributions or redeem or repurchase capital stock;

prepay, redeem or repurchase certain debt;

make loans, investments, acquisitions (including acquisitions of exclusive licenses) and capital expenditures;

enter into agreements that restrict distributions from our subsidiaries;

sell assets and capital stock of our subsidiaries;

enter into certain transactions with affiliates; and

consolidate or merge with or into, or sell substantially all of our assets to, another person.

The covenants imposed by the Senior Secured Credit Facility and our obligations to service our outstanding debt:

limit our ability to borrow additional funds for working capital, capital expenditures, acquisitions or other general business purposes;

limit our ability to use our cash flow or obtain additional financing for future working capital, capital expenditures, acquisitions or other general business purposes;

may require us to use a substantial portion of our cash flow from operations to make debt service payments;

limit our flexibility to plan for, or react to, changes in our business and industry;

place us at a competitive disadvantage compared to our less leveraged competitors; and

increase our vulnerability to the impact of adverse economic and industry conditions.

If we are unable to successfully manage the limitations and decreased flexibility on our business due to our significant debt obligations, we may not be able to capitalize on strategic opportunities or grow our business to the extent we would be able to without these limitations.

Our failure to comply with any of the covenants could result in a default under the credit agreement, which could permit the administrative agent to, or permit the required lenders to cause the administrative agent to, declare all or part of any outstanding loans to be immediately due and payable or to exercise any remedies provided to the

administrative agent, including proceeding against the collateral granted to secure our obligations under the Senior Secured Credit Facility. An event of default under the Senior Secured Credit Facility could also lead to an event of default under the terms of our Convertible Senior Notes. Any such event of default or any exercise of rights and remedies by our creditors could seriously harm our business.

If intangible assets that we have recorded in connection with the Vidara merger become impaired, we could have to take significant charges against earnings.

In connection with the accounting for the Vidara merger, we have recorded a significant amount of intangible assets. Under U.S. GAAP, we must assess, at least annually and potentially more frequently, whether the value of goodwill and other indefinite-lived intangible assets has been impaired. Amortizing intangible assets will be assessed for impairment in the event of an impairment indicator. Any reduction or impairment of the value of goodwill or other intangible assets will result in a charge against earnings, which could materially adversely affect our results of operations and shareholders' equity in future periods.

Table of Contents

Risks Related to Our Intellectual Property

If we are unable to obtain or protect intellectual property rights related to our products and product candidates, we may not be able to compete effectively in our market.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our products and product candidates. The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in-license may fail to result in issued patents with claims that cover the products in the United States or in other foreign countries. If this were to occur, early generic competition could be expected against DUEXIS, VIMOVO, ACTIMMUNE, RAYOS/LODOTRA, PENNSAID 2% and other product candidates in development. There is no assurance that the potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing based on a pending patent application. In particular, because the APIs in DUEXIS, VIMOVO and RAYOS/LODOTRA have been on the market as separate products for many years, it is possible that these products have previously been used off-label in such a manner that such prior usage would affect the validity of our patents or our ability to obtain patents based on our patent applications.

Even if patents do successfully issue, third parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed or invalidated.

On February 15, 2012, we received a Paragraph IV Patent Certification from Par Pharmaceutical, Inc. advising that Par Pharmaceutical, Inc. had filed an ANDA with the FDA for a generic version of DUEXIS, containing 800 mg of ibuprofen and 26.6 mg of famotidine. In March 2012, we filed a patent infringement lawsuit in the United States District Court for the District of Delaware against Par for filing an ANDA against DUEXIS and seeking an injunction to prevent the approval of Par's ANDA and/or prevent Par from selling a generic version of DUEXIS. In January 2013, we filed a second suit against Par in the United States District Court for the District of Delaware claiming patent infringement of additional patents that have been issued for DUEXIS and seeking an injunction to prevent the approval of Par's ANDA and/or prevent Par from selling a generic version of DUEXIS.

On August 21, 2013, we entered into the Par settlement agreement and Par license agreement with Par relating to its patent infringement litigation. The Par settlement agreement provides for a full settlement and release by both us and Par of all claims that were or could have been asserted in the litigation and that arise out of the specific patent issues that were the subject of the litigation, including all resulting damages or other remedies.

Under the Par license agreement, we granted Par a non-exclusive license (that is only royalty-bearing in some circumstances) to manufacture and commercialize Par's generic version of DUEXIS in the United States after the generic entry date and to take steps necessary to develop inventory of, and obtain regulatory approval for, but not commercialize, Par's generic version of DUEXIS prior to the generic entry date or the License. The License covers all patents owned or controlled by us during the term of the Par license agreement that would, absent the License, be infringed by the manufacture, use, sale, offer for sale, or importation of Par's generic version of DUEXIS in the United States. Unless terminated sooner pursuant to the terms of the Par license agreement, the License will continue until the last to expire of the licensed patents and/or applicable periods of regulatory exclusivity.

Under the Par license agreement, the generic entry date is January 1, 2023; however, Par may be able to enter the market earlier in certain circumstances. Such events relate to the resolution of potential future third party DUEXIS patent litigation, the entry of other third party generic versions of DUEXIS or certain specific changes in DUEXIS market conditions. Only in the event that Par enters the DUEXIS market due to the specified changes in DUEXIS

market conditions will the License become royalty-bearing, with the royalty obligations ceasing upon the occurrence of one of the other events that would have allowed Par to enter the DUEXIS market.

S-39

Table of Contents

Under the Par license agreement, we also agreed not to sue or assert any claim against Par for infringement of any patent or patent application owned or controlled by us during the term of the Par license agreement based on the manufacture, use, sale, offer for sale, or importation of Par's generic version of DUEXIS in the United States.

The Par license agreement may be terminated by us if Par commits a material breach of the agreement that is not cured or curable within 30 days after we provide notice of the breach. We may also terminate the Par license agreement immediately if Par or any of its affiliates initiate certain challenges to the validity or enforceability of any of the licensed patents or their foreign equivalents. In addition, the Par license agreement will terminate automatically upon termination of the Par settlement agreement.

On July 15, 2013, we received a Paragraph IV Patent Certification from Watson advising that Watson had filed an ANDA with the FDA for a generic version of RAYOS, containing up to 5 mg of prednisone. Watson has not advised us as to the timing or status of the FDA's review of its filing. On August 26, 2013, we, together with Jagotec, filed suit in the United States District Court for the District of New Jersey against WLF seeking an injunction to prevent the approval of the ANDA. The lawsuit alleges that WLF has infringed U.S. Patent Nos. 6,488,960, 6,677,326, 8,168,218, 8,309,124, and 8,394,407 by filing an ANDA seeking approval from the FDA to market generic versions of RAYOS containing 1 mg, 2 mg, and 5 mg of prednisone prior to the expiration of the patents. The subject patents are listed in the FDA's Orange Book. The commencement of the patent infringement lawsuit stays, or bars, FDA approval of WLF's ANDA for 30 months or until an earlier district court decision that the subject patents are not infringed or are invalid. We, together with Jagotec have granted WLF a covenant not to sue with respect to US Patent Nos. 6,677,326 and 8,168,218, respectively, and accordingly these patents have been dismissed from the lawsuit. The Markman claim construction hearing took place on October 16, 2014 and on November 10, 2014, the court issued a claims construction order adopting our construction of both of the patent claim terms at issue in the hearing. The court has not yet set a trial date for the WLF action.

On September 12, 2013, we received a Paragraph IV Patent Certification from Par Pharmaceutical, Inc. advising that Par Pharmaceutical, Inc. had filed an ANDA with the FDA for a generic version of RAYOS, containing up to 5 mg of prednisone. On October 22, 2013, we, together with Jagotec, filed suit in the United States District Court for the District of New Jersey against Par seeking an injunction to prevent the approval of the ANDA. The lawsuit alleged that Par had infringed U.S. Patent Nos. 6,488,960, 6,677,326, 8,168,218, 8,309,124 and 8,394,407 by filing an ANDA seeking approval from the FDA to market generic versions of RAYOS prior to the expiration of the patents. The subject patents are listed in the FDA's Orange Book. On November 20, 2013, we were notified by counsel for Par that Par Pharmaceutical, Inc. had elected to withdraw its ANDA with the FDA for a generic version of RAYOS containing 2 mg and 5 mg of prednisone. On December 5, 2013, we entered into a Stipulation of Dismissal with Par Pharmaceutical, Inc. whereby Par Pharmaceutical, Inc. agreed to withdraw its application to market a generic version of RAYOS.

Currently, patent litigation is pending in the District of New Jersey against four generic companies intending to market VIMOVO before the expiration of patents listed in the Orange Book. These cases are in the District of New Jersey and have been consolidated for discovery purposes. They are collectively known as the VIMOVO cases, and involve the following sets of defendants: (i) Dr. Reddy's; (ii) Lupin; (iii) Mylan; and (iv) Actavis. Patent litigation in the District of New Jersey against a fifth generic company, Anchen, was dismissed after Anchen recertified under Paragraph III. We understand that Dr. Reddy's has entered into a settlement with AstraZeneca with respect to patent rights directed to Nexium for the commercialization of VIMOVO, and that according to the settlement agreement, Dr. Reddy's is now able to commercialize VIMOVO under AstraZeneca's Nexium patent rights. The settlement agreement, however, has no effect on the Pozen VIMOVO patents, which are still the subject of patent litigations. As part of our acquisition of the U.S. rights to VIMOVO, we have taken over and are responsible for the patent litigations that include the Pozen patents licensed to us under the Pozen license agreement.

Table of Contents

The VIMOVO cases were filed on April 21, 2011, July 25, 2011, October 28, 2011, January 4, 2013, May 10, 2013, June 28, 2013 and October 23, 2013 and collectively include allegations of infringement of U.S. Patent Nos. 6,926,907 and 8,557,285. We understand the cases arise from Paragraph IV Notice Letters providing notice of the filing of an ANDA with the FDA seeking regulatory approval to market a generic version of VIMOVO before the expiration of the patents-in-suit. We understand the Dr. Reddy's notice letters were dated March 11, 2011 and November 20, 2012; the Lupin notice letter were dated June 10, 2011 and March 12, 2014; the Mylan notice letter was dated May 16, 2013; the Actavis notice letters were dated March 29, 2013 and November 5, 2013; and the Anchen notice letter was dated September 16, 2011. The court has issued a claims construction order and has set a pretrial schedule but has not yet set a trial date.

We intend to vigorously defend our intellectual property rights relating to DUEXIS, VIMOVO, ACTIMMUNE and RAYOS, but we cannot predict the outcome of the WLF matter related to RAYOS or the DRL cases, the Mylan cases, or the Watson cases related to VIMOVO. Any adverse outcome in these matters or any new generic challenges that may arise could result in one or more generic versions of DUEXIS, VIMOVO, ACTIMMUNE and/or RAYOS being launched before the expiration of the listed patents, which could adversely affect our ability to successfully execute our business strategy to increase sales of DUEXIS, VIMOVO, ACTIMMUNE and/or RAYOS and would negatively impact our financial condition and results of operations, including causing a significant decrease in our revenues and cash flows.

Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. If the patent applications we hold with respect to DUEXIS, VIMOVO, ACTIMMUNE, RAYOS/LODOTRA or PENNSAID 2% fail to issue or if their breadth or strength of protection is threatened, it could dissuade companies from collaborating with us to develop them and threaten our ability to commercialize our products. We cannot offer any assurances about which, if any, patents will issue or whether any issued patents will be found not invalid and not unenforceable or will go unthreatened by third parties. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we were the first to file any patent application related to our products or any other product candidates. Furthermore, if third parties have filed such patent applications, an interference proceeding in the United States can be provoked by a third party or instituted by us to determine who was the first to invent any of the subject matter covered by the patent claims of our applications.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable, processes for which patents are difficult to enforce and any other elements of our drug discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. Although we expect all of our employees to assign their inventions to us, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed or that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques.

Our ability to obtain patents is highly uncertain because, to date, some legal principles remain unresolved, there has not been a consistent policy regarding the breadth or interpretation of claims allowed in patents in the United States and the specific content of patents and patent applications that are necessary to support and interpret patent claims is highly uncertain due to the complex nature of the relevant legal, scientific and factual issues. Changes in either patent laws or interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property or narrow the scope of our patent protection. For example, on September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a

number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The United States Patent and Trademark Office, or U.S. PTO, has developed new and untested regulations and procedures to

S-41

Table of Contents

govern the full implementation of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective in March 2013. The Leahy-Smith Act has also introduced procedures making it easier for third-parties to challenge issued patents, as well as to intervene in the prosecution of patent applications. Finally, the Leahy-Smith Act contains new statutory provisions that still require the U.S. PTO to issue new regulations for their implementation and it may take the courts years to interpret the provisions of the new statute. Accordingly, it is too early to tell what, if any, impact the Leahy-Smith Act will have on the operation of our business and the protection and enforcement of our intellectual property. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. In addition, the Patient Protection and Affordable Care Act allows applicants seeking approval of biosimilar or interchangeable versions of biological products such as ACTIMMUNE to initiate a process for challenging some or all of the patents covering the innovator biological product used as the reference product. This process is complicated and could result in the limitation or loss of certain patent rights. An inability to obtain, enforce and defend patents covering our proprietary technologies would materially and adversely affect our business prospects and financial condition.

Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States and Canada. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. For example, if the issuance to us, in a given country, of a patent covering an invention is not followed by the issuance, in other countries, of patents covering the same invention, or if any judicial interpretation of the validity, enforceability, or scope of the claims in, or the written description or enablement in, a patent issued in one country is not similar to the interpretation given to the corresponding patent issued in another country, our ability to protect our intellectual property in those countries may be limited. Changes in either patent laws or in interpretations of patent laws in the United States and other countries may materially diminish the value of our intellectual property or narrow the scope of our patent protection. If we are unable to prevent material disclosure of the non-patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

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

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions and inter party reexamination proceedings before the U.S. PTO. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we and our collaborators are developing product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our products and/or any other product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications, which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of

competent jurisdiction to cover the manufacturing process of any of our product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire. Similarly, if any third-party patent were held by

S-42

Table of Contents

a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy, the holders of any such patent may be able to block our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize one or more of our product candidates, which could harm our business significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our products, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties.

If we fail to comply with our obligations in the agreements under which we license rights to technology from third parties, we could lose license rights that are important to our business.

We are a party to a number of technology licenses that are important to our business and expect to enter into additional licenses in the future. For example, we hold an exclusive license to SkyePharma AG's proprietary technology and know-how covering the delayed release of corticosteroids relating to RAYOS/LODOTRA. If we fail to comply with our obligations under our agreement with SkyePharma or our other license agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to market products covered by the license, including RAYOS/LODOTRA.

In connection with our November 2013 acquisition of the U.S. rights to VIMOVO, we (i) received the benefit of a covenant not to sue under AstraZeneca's patent portfolio with respect to Nexium (which shall automatically become a license under such patent portfolio if and when AstraZeneca reacquires control of such patent portfolio from Merck Sharp & Dohme Corp. and certain of its affiliates), (ii) were assigned AstraZeneca's amended and restated collaboration and license agreement for the United States with Pozen under which AstraZeneca has in-licensed exclusive rights under certain of Pozen's patents with respect to VIMOVO, and (iii) acquired AstraZeneca's co-ownership rights with Pozen with respect to certain joint patents covering VIMOVO, all for the commercialization of VIMOVO in the United States. If we fail to comply with our obligations under our agreements with AstraZeneca or if we fail to comply with our obligations under our agreements with Pozen as we take over AstraZeneca's agreements with Pozen, our rights to commercialize VIMOVO in the United States may be adversely affected or terminated by AstraZeneca or Pozen.

We also license rights to patents, know-how and trademarks for ACTIMMUNE from Genentech, under an agreement that remains in effect for so long as we continue to commercialize and sell ACTIMMUNE. However, Genentech may terminate the agreement upon our material default, if not cured within a specified period of time. Genentech may also terminate the agreement in the event of our bankruptcy or insolvency. Upon such a termination of the agreement, all intellectual property rights conveyed to us under the agreement, including the rights to the ACTIMMUNE trademark,

revert to Genentech. If we fail to comply with our obligations under this agreement, we could lose the ability to market and distribute ACTIMMUNE, which would have a material adverse effect on our business, financial condition or results of operations.

S-43

Table of Contents

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our collaborators or licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our ordinary shares.

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

Periodic maintenance fees on any issued patent are due to be paid to the U.S. PTO and foreign patent agencies in several stages over the lifetime of the patent. The U.S. PTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors that control the prosecution and maintenance of our licensed patents fail to maintain the patents and patent applications covering our product candidates, our competitors might be able to enter the market, which would have a material adverse effect on our business.

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

We employ individuals who were previously employed at other biotechnology or pharmaceutical companies. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of our employees former employers or other third parties. We may also be

subject to claims that former employers or other third parties have an ownership interest in our patents. Litigation may be necessary to defend against these claims. There is no

S-44

Table of Contents

guarantee of success in defending these claims, and if we are successful, litigation could result in substantial cost and be a distraction to our management and other employees.

Risks Related to Ownership of our Ordinary Shares

We do not know whether an active, liquid and orderly trading market will develop for our ordinary shares or what the market price of our ordinary shares will be and as a result it may be difficult for you to sell your ordinary shares.

Although our ordinary shares are listed on The NASDAQ Global Market, an active trading market for our shares may never fully develop or be sustained even if it does. Further, an inactive market may impair our ability to raise capital by selling our ordinary shares and may impair our ability to enter into strategic partnerships or acquire companies or products by using our ordinary shares as consideration.

The market price of our ordinary shares historically has been volatile and is likely to be highly volatile, and you could lose all or part of your investment.

The trading price of our ordinary shares has been highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, including limited trading volume. In addition to the factors discussed in this Risk Factors section and elsewhere in this report, these factors include:

our failure to successfully execute our commercialization strategy with respect to our approved products, particularly our commercialization of our products in the United States;

disputes or other developments relating to intellectual property and other proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our products and product candidates;

unanticipated serious safety concerns related to the use of our products;

adverse regulatory decisions;

changes in laws or regulations applicable to our business, products or product candidates, including but not limited to clinical trial requirements for approvals or tax laws;

inability to comply with our debt covenants and to make payments as they become due;

inability to obtain adequate commercial supply for any approved product or inability to do so at acceptable prices;

developments concerning our commercial partners, including but not limited to those with our sources of manufacturing supply;

our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial;

adverse results or delays in clinical trials;

our failure to successfully develop, acquire, and/or in-license additional product candidates or obtain approvals for additional indications for our existing product candidates;

introduction of new products or services offered by us or our competitors;

our inability to effectively manage our growth;

overall performance of the equity markets and general political and economic conditions;

failure to meet or exceed revenue and financial projections we may provide to the public;

actual or anticipated variations in quarterly operating results;

Table of Contents

failure to meet or exceed the estimates and projections of the investment community;

publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;

our inability to successfully enter new markets;

the termination of a collaboration or the inability to establish additional collaborations;

announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;

our inability to maintain an adequate rate of growth;

ineffectiveness of our internal controls or our inability to otherwise comply with financial reporting requirements;

adverse U.S. and foreign tax exposure;

additions or departures of key management, commercial or regulatory personnel;

issuances of debt or equity securities;

significant lawsuits, including patent or shareholder litigation;

changes in the market valuations of similar companies;

sales of our ordinary shares by us or our shareholders in the future;

trading volume of our ordinary shares;

effects of natural or man-made catastrophic events or other business interruptions; and

other events or factors, many of which are beyond our control.

In addition, the stock market in general, and The NASDAQ Global Market and the stocks of biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may adversely affect the market price of our ordinary shares, regardless of our actual operating performance.

We do not intend to pay dividends on our ordinary shares so any returns will be limited to the value of our shares.

We have never declared or paid any cash dividends on our ordinary shares. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future, including due to limitations imposed by the Senior Secured Credit Facility. Any return to shareholders will therefore be limited to the increase, if any, of our share price.

Our officers, directors and funds affiliated with our directors own a significant percentage of our stock and will be able to influence matters subject to stockholder approval.

Our officers, directors and funds affiliated with our directors held in the aggregate approximately 8% of our outstanding voting ordinary shares as of September 30, 2014. Therefore, these shareholders have the ability to influence us through this ownership position, including through matters requiring stockholder approval. For example, these shareholders may be able to influence the elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction, such as the proposed merger with Vidara. This may discourage unsolicited acquisition proposals or offers for our ordinary shares that our shareholders may feel are in their best interest.

Table of Contents

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

As a public company, we have incurred and will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. In particular, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, as well as rules subsequently implemented by the SEC and the NASDAQ Stock Market, Inc., or NASDAQ, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. These rules and regulations have substantially increased our legal and financial compliance costs and have made some activities more time-consuming and costly. These effects will be exacerbated by our recent transition to an Irish company and the integration of Vidara's business and operations into the historical business and operating structure of Horizon Pharma, Inc. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations. The increased costs will continue to decrease our net income or increase our net loss, and may require us to reduce costs in other areas of our business or increase the prices of our products or services. For example, these rules and regulations make it more difficult and more expensive for us to obtain and maintain director and officer liability insurance. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers. If we fail to comply with the continued listing requirements of NASDAQ, our ordinary shares could be delisted from The NASDAQ Global Market, which would adversely affect the liquidity of our ordinary shares and our ability to obtain future financing.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. In particular, we are required to perform annual system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act, or Section 404. Our independent registered public accounting firm is also required to deliver a report on the effectiveness of our internal control over financial reporting. Our testing, or the testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses. Our compliance with Section 404 requires that we incur substantial accounting expense and expend significant management efforts, particularly because of our Irish parent company structure and international operations. In particular, prior to the Vidara merger, Vidara and its affiliate entities were not subject to the requirements of the Sarbanes-Oxley Act. We intend to take appropriate measures to establish or implement an internal control environment at the former Vidara entities aimed at successfully adopting the requirements of Section 404 of the Sarbanes-Oxley Act of 2002. However, it is possible that we may experience delays in implementing or be unable to implement the required internal controls over financial reporting and other disclosure controls and procedures. We currently do not have an internal audit group, and we may need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge, as well as retain and work with consultants with such knowledge. Moreover, if we are not able to comply with the requirements of Section 404 or if we or our independent registered public accounting firm identify deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses, the market price of our ordinary shares could decline and we could be subject to sanctions or investigations by NASDAQ, the SEC or other regulatory authorities, which would require additional financial and management resources.

New laws and regulations as well as changes to existing laws and regulations affecting public companies, including the provisions of the Sarbanes-Oxley Act and rules adopted by the SEC and by NASDAQ, would likely result in increased costs to us as we respond to their requirements.

S-47

Table of Contents

Sales of a substantial number of our ordinary shares in the public market could cause our share price to decline.

If our existing shareholders sell, or indicate an intention to sell, substantial amounts of our ordinary shares in the public market, the trading price of our ordinary shares could decline. In addition, our ordinary shares that are either subject to outstanding options or reserved for future issuance under our employee benefit plans are or may become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and Rule 144 and Rule 701 under the Securities Act. If these additional ordinary shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our ordinary shares could decline.

Certain holders of our ordinary shares are entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. For example, we are subject to a registration rights agreement with certain holders of our ordinary shares prior to the Vidara merger, including certain of the selling shareholders. Pursuant to this agreement, we filed and are required to maintain a registration statement covering the resale of our ordinary shares held by these shareholders and in certain circumstances, these holders can require us to participate in an underwritten public offering of their ordinary shares, such as this offering. Any sales of securities by these shareholders or a public announcement of such sales could have a material adverse effect on the trading price of our ordinary shares.

Future sales and issuances of our ordinary shares, securities convertible into our ordinary shares or rights to purchase ordinary shares or convertible securities could result in additional dilution of the percentage ownership of our shareholders and could cause our share price to decline.

Additional capital may be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our shareholders may experience substantial dilution. We may sell ordinary shares, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell ordinary shares, convertible securities or other equity securities in subsequent transactions, our existing shareholders may be materially diluted. New investors in such subsequent transactions could gain rights, preferences and privileges senior to those of holders of our ordinary shares. We also maintain equity incentive plans, including our 2014 Equity Incentive Plan, 2014 Non-Employee Equity Plan and 2014 Employee Share Purchase Plan, and intend to grant additional ordinary share awards under these and future plans, which will result in additional dilution to existing shareholders.

Irish law differs from the laws in effect in the United States and may afford less protection to holders of our securities.

It may not be possible to enforce court judgments obtained in the United States against us in Ireland based on the civil liability provisions of the U.S. federal or state securities laws. In addition, there is some uncertainty as to whether the courts of Ireland would recognize or enforce judgments of U.S. courts obtained against us or our directors or officers based on the civil liabilities provisions of the U.S. federal or state securities laws or hear actions against us or those persons based on those laws. We have been advised that the United States currently does not have a treaty with Ireland providing for the reciprocal recognition and enforcement of judgments in civil and commercial matters. Therefore, a final judgment for the payment of money rendered by any U.S. federal or state court based on civil liability, whether or not based solely on U.S. federal or state securities laws, would not automatically be enforceable in Ireland.

As an Irish company, we are governed by the Irish Companies Acts, which differs in some material respects from laws generally applicable to U.S. corporations and shareholders, including, among others, differences relating to interested director and officer transactions and shareholder lawsuits. Likewise, the duties of directors and officers of an Irish company generally are owed to the company only. Shareholders of Irish companies generally do not have a personal

right of action against directors or officers of the company and may exercise

S-48

Table of Contents

such rights of action on behalf of the company only in limited circumstances. Accordingly, holders of our securities may have more difficulty protecting their interests than would holders of securities of a corporation incorporated in a jurisdiction of the United States.

Provisions of our articles of association could delay or prevent a takeover of us by a third party.

Our articles of association could delay, defer or prevent a third party from acquiring us, despite the possible benefit to our shareholders, or otherwise adversely affect the price of our ordinary shares. For example, our articles of association:

permit our board of directors to issue one or more series of preferred shares with rights and preferences designated by our board;

impose advance notice requirements for shareholder proposals and nominations of directors to be considered at shareholder meetings;

stagger the terms of our board of directors into three classes; and

require the approval of a supermajority of the voting power of the shares of our share capital entitled to vote generally in the election of directors for shareholders to amend or repeal our articles of association.

These provisions may discourage potential takeover attempts, discourage bids for our ordinary shares at a premium over the market price or adversely affect the market price of, and the voting and other rights of the holders of, our ordinary shares. These provisions could also discourage proxy contests and make it more difficult for you and other shareholders to elect directors other than the candidates nominated by our board.

A transfer of our ordinary shares may be subject to Irish stamp duty.

In certain circumstances, the transfer of shares in an Irish incorporated company will be subject to Irish stamp duty, which is a legal obligation of the buyer. This duty is currently charged at the rate of 1.0% of the price paid or the market value of the shares acquired, if higher. Because our ordinary shares are traded on a recognized stock exchange in the United States, an exemption of this stamp duty is available to transfers by shareholders who hold our ordinary shares beneficially through brokers which in turn hold those shares through the Depositary Trust Company, or DTC, to holders who also hold through DTC. However, a transfer by a record holder who holds our ordinary shares directly in his, her or its own name could be subject to this stamp duty. We, in our absolute discretion and insofar as the Companies Acts or any other applicable law permit, may, or may provide that a subsidiary of ours will, pay Irish stamp duty arising on a transfer of our ordinary shares on behalf of the transferee of such ordinary shares. If stamp duty resulting from the transfer of our ordinary shares which would otherwise be payable by the transferee is paid by us or any of our subsidiaries on behalf of the transferee, then in those circumstances, we will, on our behalf or on behalf of our subsidiary (as the case may be), be entitled to (i) seek reimbursement of the stamp duty from the transferee, (ii) set-off the stamp duty against any dividends payable to the transferee of those ordinary shares and (iii) claim a first and permanent lien on the ordinary shares on which stamp duty has been paid by us or our subsidiary for the amount of stamp duty paid. Our lien shall extend to all dividends paid on those ordinary shares.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.

The trading market for our ordinary shares will depend in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who cover us downgrade our shares or publish inaccurate or unfavorable research about our business, our share price would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our ordinary shares could decrease, which might cause our share price and trading volume to decline.

Table of Contents

We may become involved in securities class action litigation that could divert management's attention and harm our business and could subject us to significant liabilities.

The stock markets have from time to time experienced significant price and volume fluctuations that have affected the market prices for the equity securities of pharmaceutical companies. These broad market fluctuations may cause the market price of our ordinary shares to decline. In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and biopharmaceutical companies have experienced significant stock price volatility in recent years. We may become involved in this type of litigation in the future. Even if we are successful in defending against any such claims, litigation could result in substantial costs and may be a distraction to management, and may result in unfavorable results that could adversely impact our financial condition and prospects.

S-50

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein contain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. These statements are based on our current expectations, assumptions, estimates and projections about our business and our industry, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the future results, levels of activity, performance or achievements expressed or implied by the forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

Sales, growth prospects and commercialization plans related to DUEXIS[®], VIMOVO[®], RAYOS[®], ACTIMMUNE[®], PENNSAID[®] 2% and any future products;

Our business strategy and plans to develop, acquire or in-license additional innovative medicines or acquire companies;

availability of coverage and adequate reimbursement and pricing from government and other third-party payers for our products;

the expected synergies and other benefits, including tax, financial and strategic benefits, of the Vidara Merger to us and our shareholders;

our ability to protect our intellectual property and defend our patents; and

the sufficiency of our cash resources and our expectations regarding our future cash flow, expenses, revenues, financial results and capital requirements.

In some cases, you can identify forward-looking statements by terms such as anticipates, expects, intends, predicts, believes, seeks, estimates, could, would, will, may, can, continue, potential, should, plan, and similar expressions intended to identify forward-looking statements. While we believe that we have a reasonable basis for each forward-looking statement, we caution you that these statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance, time frames or achievements to be materially different from the information expressed or implied by these forward-looking statements. We discuss many of these risks, uncertainties and other factors in greater detail under the heading Risk Factors contained in our quarterly report on Form 10-Q filed with the SEC on November 6, 2014, and incorporated by reference in this prospectus supplement and the accompanying prospectus, as well as in the other information in this prospectus supplement, the accompanying prospectus and the information and documents incorporated by reference herein. Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements. Also, these forward-looking statements represent our estimates and assumptions only as of the date such forward-looking statements are made. You should read carefully this prospectus supplement, the accompanying prospectus and the information incorporated herein and therein by reference as described under the heading Where You Can Find More Information in this prospectus supplement and with the understanding that our

actual future results may be materially different from what we expect. We hereby qualify all of our forward-looking statements by these cautionary statements.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

USE OF PROCEEDS

The selling shareholders are offering all of the ordinary shares offered by this prospectus supplement and will receive all of the net proceeds from this offering. For more information about the selling shareholders, see **Selling Shareholders** in this prospectus supplement.

S-51

Table of Contents

We will not receive any of the proceeds from this offering. We have agreed to pay all expenses incurred with respect to the registration of the ordinary shares, our own expenses incurred in this offering, and certain legal expenses of the selling shareholders up to \$50,000. The selling shareholders will pay all other fees and expenses that they incur in connection with this offering, including all underwriting discounts and commissions.

SELLING SHAREHOLDERS

The following table sets forth (i) the selling shareholders, (ii) the number and percentage of our ordinary shares that each of the selling shareholders beneficially owned as of October 31, 2014, (iii) the number of ordinary shares proposed to be sold in this offering by each of the selling shareholders, (iv) the number of ordinary shares subject to the underwriters' option to purchase additional shares and (v) the number and percentage of our ordinary shares that will be beneficially owned by each of the selling shareholders following this offering.

Beneficial ownership is determined in accordance with the rules of the SEC and includes voting or investment power with respect to our ordinary shares. Generally, a person beneficially owns ordinary shares if the person has or shares with others the right to vote those ordinary shares or to dispose of them, or if the person has the right to acquire voting or disposition rights within 60 days. The percentages in the table below are based on 118,852,790 ordinary shares outstanding as of October 31, 2014. Except as otherwise indicated in the footnotes to the table or in cases where community property laws apply, we believe that each person identified in the table possesses sole voting and investment power over all ordinary shares beneficially owned by such person.

The number of shares beneficially owned by each selling shareholder in the table below and the footnotes thereto is based upon information provided to us by the selling shareholders, and we have not independently verified this information.

Selling Shareholder	Beneficial Ownership		Ordinary Shares Offered Hereby	Number of Ordinary Shares subject to the Option to Purchase Additional Shares	Beneficial Ownership After the Sale of the Ordinary Shares		Beneficial Ownership After the Sale of the Ordinary Shares (If the Option to Purchase Additional Shares is Exercised in Full)	
	Number	%			Number	%	Number	%
Balaji Venkataraman ⁽¹⁾	16,586,317	14.0	6,086,957	913,043	10,499,360	8.8	9,586,317	8.1
Essex Woodlands Health Ventures Fund VII, L.P. ⁽²⁾	5,755,196	4.8	3,000,000	450,000	2,755,196	2.3	2,305,196	1.9
Virinder Nohria ⁽³⁾	2,214,836	1.9	1,739,130	260,870	475,706	*	214,836	*
Mohun Patrick Nohria 2013 Gift Trust ⁽⁴⁾	784,512	*	682,184	102,328	102,328	*	0	0
Timothy P. Walbert ⁽⁵⁾	844,952	*	130,435	19,565	714,517	*	694,952	*
Jeffrey W. Sherman, M.D., FACP ⁽⁶⁾	324,483	*	21,739	3,260	302,744	*	299,484	*

* Less than 1%

- (1) Includes 6,152,720 ordinary shares held by Mayura Trust A. Mayura One LLC is the trustee of the Mayura Trust A. The managing members of Mayura One LLC are Balaji Venkataraman, Christopher Graham and Christopher Manning. The beneficiaries of Mayura Trust A are Mr. Venkataraman and his descendants. Mr. Graham and Mr. Manning disclaim beneficial ownership of any ordinary shares held by Mayura Trust A. Also includes 10,433,597 ordinary shares held by Altiva Capital, LLC of which Mr. Venkataraman is the sole managing member. 78% of Altiva Capital, LLC is owned by Mayura Trust A and the remaining 22% is owned by family trusts of which Mr. Venkataraman's wife and children are the beneficiaries and he and his wife are each trustees. The 6,086,957 ordinary shares offered, and the 913,043 ordinary shares subject to the option to purchase additional shares, are being sold by Altiva Capital, LLC. Excludes 784,512 ordinary

S-52

Table of Contents

- shares held by the Mohun Patrick Nohria 2013 Gift Trust (referred to in note 4 below), of which Mr. Venkataraman is a trustee, as Mr. Venkataraman disclaims beneficial ownership of such ordinary shares. Mr. Venkataraman is one of the managing members and the Executive Chairman, and beneficially owns 57.5% of the outstanding voting membership interests, of Vidara Therapeutics Holdings LLC, or Vidara Holdings, which, prior to the Vidara Merger was our sole shareholder. Prior to the Vidara Merger, Mr. Venkataraman served as (i) a member of the board of directors of our company and certain of our affiliates, including, Hamilton Merger Sub, Inc., Hamilton Holdings (USA), Inc., Aravis Limited, Vidara Therapeutics Research Limited and AGI Therapeutics Limited and (ii) the Secretary, Treasurer and Executive Chairman of our subsidiary, Vidara Therapeutics Inc. The address for Mr. Venkataraman is 13185 Owens Way, Alpharetta, GA 30004.
- (2) Includes (i) 5,064,827 ordinary shares and (ii) 690,369 ordinary shares issuable upon exercise of warrants. James L. Currie, Jeff Himawan, Martin Sutter, Immanuel Thangaraj and Petri Vainio share voting and investment power over the shares held by Essex Woodlands Health Ventures Fund VII, L.P. and each disclaim beneficial ownership of such shares except to the extent of any pecuniary interest therein. Dr. Himawan currently serves as a member of our board of directors and is a managing director of Essex Woodlands Health Ventures Fund VII, L.P. The address for Essex Woodlands Health Ventures Fund VII, L.P. is 335 Bryant St., 3rd Floor, Palo Alto, CA 94301.
 - (3) Virinder Nohria currently serves as a member of our board of directors. Prior to the Vidara Merger, Dr. Nohria served as our Chief Executive Officer and as a member of our board of directors. Dr. Nohria is also a managing member of Vidara Holdings.
 - (4) The trustees of the Mohun Patrick Nohria 2013 Gift Trust, or Nohria Trust, are Balaji Venkataraman and Aashish Nohria, each of whom has the power to vote and dispose of these ordinary shares and disclaims beneficial ownership of these ordinary shares except to the extent of any pecuniary interest therein. The beneficiary of the Nohria Trust is Mohun Patrick Nohria, who is the son of Virinder Nohria, one of our directors. The address for this trust is 13185 Owens Way, Alpharetta, GA 30004.
 - (5) Includes (i) 164,060 shares, (ii) 33,210 restricted stock units that are expected to fully vest within 60 days of October 31, 2014 and (iii) 647,682 shares that Mr. Walbert has the right to acquire from us within 60 days of October 31, 2014 pursuant to the exercise of stock options. Mr. Walbert serves as our chairman of our board of directors and as our President and Chief Executive Officer.
 - (6) Includes (i) 99,298 shares, (ii) 8,208 restricted stock units that are expected to fully vest within 60 days of October 31, 2014 and (iii) 216,977 shares that Dr. Sherman has the right to acquire from us within 60 days of October 31, 2014 pursuant to the exercise of stock options. Dr. Sherman serves as our Executive Vice President, Research and Development and Chief Medical Officer.

Additional Relationships and Transactions with Certain Selling Shareholders

Virinder Nohria, M.D., Ph.D. Amendment to Employment Agreement and Consulting Agreement

We have entered into an amendment to the employment agreement with Dr. Nohria, one of our directors. Per the amendment to the employment agreement, Dr. Nohria's employment with Vidara has been terminated, and Dr. Nohria received a \$484,000 lump sum payment that was contingent on his execution of a general release of claims. We have also entered into a consulting agreement with Dr. Nohria. Per the consulting agreement, Dr. Nohria has been hired as a consultant by us for a term of one year, and will be paid \$10,000 per month of service as a consultant.

Financings

In March 2012, HPI closed a private placement with a select group of institutional and accredited investors, or the PIPE financing. Upon the closing of the PIPE financing, HPI received gross proceeds of approximately \$50.8 million resulting from the sale of 14,033,829 units at a price of \$3.62125 per unit. Each unit consisted of one share of our common stock and a warrant to purchase 0.25 shares of our common stock at an exercise price of \$4.308 per share. Essex Woodlands Health Ventures Fund VII, L.P. purchased 2,761,477 shares of HPI's common stock and warrants to

purchase 690,369 shares of HPI s common stock for approximately \$10.0 million in the PIPE financing.

S-53

Table of Contents

MATERIAL TAX CONSIDERATIONS

The information presented under the caption "U.S. Federal Income Tax Consequences to U.S. Holders" below is a discussion of the material U.S. federal income tax consequences to U.S. Holders (as defined below) of investing in ordinary shares. The information presented under the caption "Irish Tax Consequences" is a discussion of the material Irish tax consequences of investing in ordinary shares.

You should consult your tax adviser regarding the applicable tax consequences to you of investing in our ordinary shares under the laws of the United States (federal, state and local), Ireland and any other applicable foreign jurisdiction.

U.S. Federal Income Tax Consequences to U.S. Holders

The following are the material U.S. federal income tax consequences to U.S. Holders (as defined below) of owning and disposing of ordinary shares acquired in this offering. This discussion does not address any aspects of U.S. taxation other than U.S. federal income taxation, does not address any U.S. state, local or non-U.S. tax considerations, and does not purport to be a comprehensive description of all tax considerations that may be relevant to a particular person's decision to acquire ordinary shares. This discussion applies only to U.S. Holders that hold their ordinary shares as capital assets for U.S. federal income tax purposes. In addition, it does not describe all of the tax consequences that may be relevant in light of a U.S. Holder's particular circumstances including alternative minimum, gift, estate and Medicare contribution tax consequences, and does not address the tax consequences applicable to U.S. Holders subject to special rules, such as:

a holder of ordinary shares who actually or constructively owns or is deemed to own 10% or more of the total combined voting power of all classes of our shares entitled to vote;

a U.S. Holder who is also resident or ordinarily resident in Ireland for Irish tax purposes or who is otherwise subject to Irish income tax or capital gains tax with respect to our ordinary shares;

a bank or other financial institution;

an insurance company;

a dealer or trader in securities who uses a mark-to-market method of tax accounting;

a person holding ordinary shares as part of a hedging transaction, straddle, wash sale, conversion transaction or integrated transaction or a person entering into a constructive sale with respect to ordinary shares;

a U.S. Holder whose functional currency for U.S. federal income tax purposes is not the U.S. dollar;

an entity classified as a partnership or other pass-through entity for U.S. federal income tax purposes, including persons that will hold our ordinary shares through such an entity;

a tax-exempt entity, including an individual retirement account or Roth IRA or retirement plan;

a U.S. expatriate;

a real estate investment trust;

a regulated investment company;

a person who acquired our ordinary shares pursuant to the exercise of an employee stock option or otherwise as compensation;

a person holding our ordinary shares in connection with a trade or business conducted outside of the United States; or

a U.S. Holder who holds ordinary shares through a financial account at a foreign financial institution that does not meet the requirements for avoiding future withholding with respect to certain payments under Sections 1471 through 1474 of the Internal Revenue Code of 1986, as amended, or the Code.

Table of Contents

If an entity that is classified as a partnership for U.S. federal income tax purposes holds ordinary shares, the U.S. federal income tax treatment of a partner will generally depend on the status of the partner and the activities of the partnership. Partnerships holding ordinary shares and partners in such partnerships should consult their tax advisers as to the particular U.S. federal income tax consequences of owning and disposing of ordinary shares.

This discussion is based on the Code, administrative pronouncements, judicial decisions and final, temporary and proposed U.S. Treasury regulations all as of the date hereof, any of which is subject to change, possibly with retroactive effect, and to differing interpretations, all of which could affect the tax considerations described below. There can be no assurances that the Internal Revenue Service, or IRS, will not take a position concerning the tax consequences of the acquisition, ownership and disposition of the ordinary shares or that such a position would not be sustained.

A U.S. Holder is a holder who is a beneficial owner of ordinary shares and for U.S. federal income tax purposes is:

an individual citizen or individual resident of the United States;

a corporation, or other entity taxable as a corporation, created or organized in or under the laws of the United States or any political subdivision thereof; 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 ability to control all of the substantial decisions of such trust or has a valid election in effect to be treated as a United States person; or

an estate the income of which is subject to U.S. federal income taxation regardless of its source.

U.S. Holders should consult their tax advisers concerning the U.S. federal, state, local and foreign tax consequences of owning and disposing of ordinary shares in their particular circumstances.

Subject to the discussion below under **Passive Foreign Investment Company Rules**, this discussion assumes that we are a foreign corporation that is not, and will not become, a passive foreign investment company, or PFIC, as described below.

Taxation of Distributions

Although we do not currently plan to pay dividends, any future distributions paid on ordinary shares will be treated as taxable dividends to a U.S. Holder to the extent of such U.S. Holder's pro rata share of our current and/or accumulated earnings and profits (as determined under U.S. federal income tax principles). To the extent that a distribution paid to a U.S. Holder with respect to our ordinary shares exceeds such U.S. Holder's pro rata share of our current and accumulated earnings and profits, it will be treated as a non-taxable return of capital to the extent of the U.S. Holder's basis in the ordinary shares (determined on a share-by-share basis), will reduce (but not below zero) such basis, and thereafter will be treated as a capital gain. Please see **Sale or Other Disposition of Ordinary Shares**. We may not maintain calculations of our earnings and profits under U.S. federal income tax principles. If this is the case, distributions, if any, generally will be reported to U.S. Holders as dividends. The amount of any dividend income paid in euros will be the U.S. dollar amount calculated by reference to the exchange rate in effect on the date of receipt,

regardless of whether the payment is in fact converted into U.S. dollars. If the dividend is converted into U.S. dollars on the date of receipt, a U.S. Holder should not be required to recognize foreign currency gain or loss in respect of the dividend income. A U.S. Holder may have foreign currency gain or loss if the dividend is converted into U.S. dollars after the date of receipt.

Dividends received by a non-corporate U.S. Holder are eligible to be taxed at reduced rates, up to a maximum of 20%, if we are a qualified foreign corporation and certain other applicable requirements, including holding period requirements, are met. The reduced rate applicable to dividends paid to non-corporate U.S. Holders is not available for dividends paid by a PFIC (described below) or in certain other situations,

S-55

Table of Contents

including if we are not a qualified foreign corporation. A non-United States corporation (other than a corporation that is classified as a PFIC for the taxable year in which the dividend is paid or the preceding taxable year) generally will be considered to be a qualified foreign corporation (a) if it is eligible for the benefits of a comprehensive tax treaty with the United States which the Secretary of Treasury of the United States determines is satisfactory for purposes of this provision and which includes an exchange of information provision, or (b) with respect to any dividend it pays on shares of stock which are readily tradable on an established securities market in the United States. The ordinary shares are listed on The NASDAQ Global Market, which is an established securities market in the United States, and we expect the ordinary shares to be readily tradable on The NASDAQ Global Market. However, there can be no assurance that the ordinary shares will be considered readily tradable on an established securities market in the United States in later years. The Company, which is incorporated under the laws of Ireland, believes that it qualifies as a resident of Ireland for purposes of, and is eligible for the benefits of, the Convention between the Government of the United States of America and the Government of Ireland for the Avoidance of Double Taxation and the Prevention of Fiscal Evasion with Respect to Taxes on Income and Capital Gains, signed on July 28, 1997, or the U.S.-Ireland Tax Treaty, although there can be no assurance in this regard. Further, the IRS has determined that the U.S.-Ireland Tax Treaty is satisfactory for purposes of the qualified dividend rules and that it includes an exchange-of-information program. Therefore, subject to the discussion under *Passive Foreign Investment Company Rules*, below, such dividends will generally be *qualified dividend income* in the hands of individual U.S. holders, provided that the holding period requirement and certain other requirements are met. Dividends received by a corporate U.S. Holder will not be eligible for the dividends-received deduction generally available to U.S. corporate shareholders under the Code for dividends received from certain U.S. and non-U.S. corporations.

For foreign tax credit limitation purposes, distributions paid on the ordinary shares that are treated as dividends will be treated as income from sources outside the United States and will generally constitute passive category income.

Sale or Other Disposition of Ordinary Shares

For U.S. federal income tax purposes, gain or loss recognized on the sale or other disposition of ordinary shares generally will be capital gain or loss, and will be long-term capital gain or loss if the U.S. Holder held the shares for more than one year. The amount of the gain or loss will equal the difference between the U.S. Holder's adjusted tax basis in the ordinary shares disposed of and the amount realized on the disposition, in each case as determined in U.S. dollars. Long-term capital gains recognized by non-corporate U.S. Holders are taxable at reduced rates up to a maximum rate of 20%. There are limitations on the deductibility of capital losses. For a cash basis taxpayer, units of foreign currency paid or received are translated into U.S. dollars at the spot rate on the settlement date of the purchase or sale. In that case, no foreign currency exchange gain or loss will result from currency fluctuations between the trade date and the settlement date of such a purchase or sale. An accrual basis taxpayer, however, may elect the same treatment required of cash basis taxpayers with respect to purchases and sales of the ordinary shares that are traded on an established securities market, provided the election is applied consistently from year to year. Such election may not be changed without the consent of the IRS. For an accrual basis taxpayer who does not make such election, units of foreign currency paid or received are translated into U.S. dollars at the spot rate on the trade date of the purchase or sale. Such an accrual basis taxpayer may recognize exchange gain or loss based on currency fluctuations between the trade date and settlement date. Any gain or loss will generally be U.S.-source gain or loss for foreign tax credit limitation purposes.

Passive Foreign Investment Company Rules

In general, a corporation organized outside the United States will be a PFIC 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 value of its assets is attributable to assets that produce passive income or are held for the production of passive income. Passive income for this

purpose generally includes, among other things, dividends, interest, royalties, rents, and gains from commodities transactions and from the sale or exchange of property that gives rise to passive income.

S-56

Table of Contents

Assets that produce or are held for the production of passive income include cash, even if held as working capital or raised in a public offering, marketable securities and other assets that may produce passive income. The average value of a corporation's assets for this purpose, in the case of a corporation whose shares are publicly traded for the taxable year, generally is the average of their fair market value at the end of each quarter. In determining whether a non-U.S. corporation is a PFIC, a proportionate share of the income and assets of each corporation in which it owns, directly or indirectly, at least a 25% interest (by value) is taken into account.

Based on our application of the test described above to the projected composition of our income and the projected composition and estimated values of our assets, we do not believe that we will be a PFIC in 2014 or subsequent years. Nevertheless, because the calculation of the value of our assets may be based in part on the value of our ordinary shares, which is likely to fluctuate after the offering, it is difficult to predict for any tax year whether we may be a PFIC. Therefore, there can be no assurance that we will not be a PFIC in 2014 or any subsequent taxable year or that the IRS will agree with our conclusion regarding our PFIC status for any taxable year.

If we are a PFIC in any taxable year during which a U.S. Holder owns ordinary shares, such U.S. Holder could be liable for additional taxes and interest charges upon certain distributions by us and on any gain recognized on a sale, exchange or other disposition, including a pledge, of ordinary shares, whether or not we continue to be a PFIC. We do not currently intend to provide the information necessary for U.S. holders to make qualified electing fund elections if we were treated as a PFIC for any taxable year. In addition, certain annual tax reporting would be required. You should consult your tax advisor concerning the tax consequences to you if we are a PFIC and certain tax elections you may wish to make to mitigate any adverse tax consequences that might arise in the event we are a PFIC.

Information Reporting and Backup Withholding

Payments of dividends and sales proceeds that are made within the United States or through certain U.S.-related financial intermediaries generally are subject to information reporting, and may be subject to backup withholding, unless (i) the U.S. Holder is a corporation or other exempt recipient or (ii) in the case of backup withholding, the U.S. Holder provides a correct taxpayer identification number and certifies that it is not subject to backup withholding.

The amount of any backup withholding from a payment to a U.S. Holder will be allowed as a credit against the U.S. Holder's U.S. federal income tax liability and may entitle it to a refund, provided that the required information is timely furnished to the IRS.

Reporting Obligations for Specified Foreign Financial Assets

U.S. Holders who are individuals are required to report on Form 8938 specified foreign financial assets that they own if the aggregate value of those assets exceeds certain threshold amounts. Specified foreign financial assets may include stock of a foreign issuer such as our ordinary shares if not held through a financial account maintained at a U.S. financial institution, as defined in the applicable rules. Individual U.S. Holders should consult their own tax advisors as to the possible application of this reporting obligation under their particular circumstances.

Irish Tax Consequences

The following is a general summary of the material Irish tax considerations applicable to certain investors who are the beneficial owners of our ordinary shares. It is based on existing Irish law and practices in effect on the date of this prospectus supplement and correspondence with the Irish Revenue Commissioners. Legislative, administrative or judicial changes may modify the tax consequences described below.

Edgar Filing: Horizon Pharma plc - Form 424B7

The statements do not constitute tax advice and are intended only as a general guide. Furthermore, this information applies only to ordinary shares held as capital assets and does not apply to all categories of

S-57

Table of Contents

shareholders, such as dealers in securities, trustees, insurance companies, collective investment schemes and shareholders who have, or who are deemed to have, acquired their ordinary shares by virtue of an office or employment. This summary is not exhaustive and you should consult your own tax advisers as to the tax consequences in Ireland, or other relevant jurisdictions, of the acquisition, ownership and disposition of our ordinary shares.

Withholding Tax on Dividends

Although we do not currently plan to pay dividends, distributions made by us would generally be subject to Irish dividend withholding tax, or DWT, at the standard rate of income tax (currently 20%), unless one of the exemptions described below applies, which we believe should be the case for the majority of our shareholders. For DWT purposes, a dividend includes any distribution made by us to our shareholders, including cash dividends, non-cash dividends and additional stock or units taken in lieu of a cash dividend. Where applicable, we are responsible for withholding DWT at source and forwarding the relevant payment to the Irish Revenue Commissioners.

Certain shareholders (both individual and corporate) are entitled to an exemption from DWT. In particular, a non-Irish resident shareholder is not subject to DWT on dividends received from us if such shareholder is:

an individual shareholder resident for tax purposes in a relevant territory, and the individual is neither resident nor ordinarily resident in Ireland. Relevant territory for the purposes of DWT is defined to include all EU member states and all of those countries with which Ireland has signed a double tax treaty, which countries include: Albania; Armenia; Australia; Austria; Bahrain; Belarus; Belgium; Bosnia & Herzegovina; Botswana; Bulgaria; Canada; Chile; China; Croatia; Cyprus; Czech Republic; Denmark; Egypt; Estonia; Finland; France; Georgia; Germany; Greece; Hong Kong; Hungary; Iceland; India; Israel; Italy; Japan; Korea; Kuwait; Latvia; Lithuania; Luxembourg; Macedonia; Malaysia; Malta; Mexico; Moldova; Montenegro; Morocco; The Netherlands; New Zealand; Norway; Pakistan; Panama; Poland; Portugal; Qatar; Romania; Russia; Saudi Arabia; Serbia; Singapore; Slovak Republic; Slovenia; South Africa; Spain; Sweden; Switzerland; Thailand; Turkey; United Arab Emirates; Ukraine; United Kingdom; the United States; Uzbekistan; Vietnam; and Zambia;

a corporate shareholder that is not resident for tax purposes in Ireland and which is ultimately controlled, directly or indirectly, by persons resident in a relevant territory ;

a corporate shareholder resident for tax purposes in a relevant territory provided that such corporate shareholder is not under the control, whether directly or indirectly, of a person or persons who is or are resident in Ireland;

a corporate shareholder that is not resident for tax purposes in Ireland and whose principal class of shares (or those of its 75% parent) is substantially and regularly traded on a stock exchange in Ireland, on a recognized stock exchange in a relevant territory or on such other stock exchange approved by the Irish Minister for Finance; or

a corporate shareholder that is not resident for tax purposes in Ireland and is wholly-owned, directly or indirectly, by two or more companies where the principal class of shares of each of such companies is substantially and regularly traded on a stock exchange in Ireland, on a recognized stock exchange in a relevant territory or on such other stock exchange approved by the Irish Minister for Finance, and provided that, in all cases noted above but subject to the matters described below, the shareholder has provided the appropriate Irish DWT form to his or her broker (in the case of ordinary shares held through the Depositary Trust Company, or DTC), or to our transfer agent (in the case of ordinary shares held directly i.e. outside of DTC), at least seven business days before the record date for the first dividend payment to which they are entitled.

S-58

Table of Contents

Should we decide to pay a dividend, we will enter into an agreement with an institution which will be recognized by the Irish Revenue Commissioners as a qualifying intermediary prior to paying any dividends or making any distributions. This will satisfy one of the Irish requirements for dividends to be paid free of DWT to certain shareholders who hold their ordinary shares through DTC, as described below. The agreement will generally provide for certain arrangements relating to cash distributions in respect of those ordinary shares that are held through DTC. The agreement will also provide that the qualifying intermediary will distribute or otherwise make available to Cede & Co., as nominee for DTC, any cash dividend or other cash distribution to be made to holders of the deposited securities, after we deliver or cause to be delivered to the qualifying intermediary the cash to be distributed.

We will rely on information received directly or indirectly from brokers and our transfer agent in determining where shareholders reside, whether they have provided the required U.S. forms and whether they have provided the required Irish DWT forms, as described below. Shareholders who are required to file Irish DWT forms in order to receive their dividends free of DWT should note that such forms are valid for five years and new forms must be filed before the expiration of that period in order to continue to enable them to receive dividends without DWT.

In most cases, individual shareholders resident in a relevant territory should complete a non-resident Form V2A and corporate (company) shareholders resident in a relevant territory should complete a non-resident Form V2B. Where a shareholder is neither an individual nor a company but is resident in a relevant territory, it should complete a non-resident Form V2C. Please contact your broker or your tax adviser if you have any questions regarding Irish dividend withholding tax.

Shares Held by U.S. Resident Shareholders

Dividends on our ordinary shares that are owned by residents of the United States and held beneficially through DTC will not be subject to DWT provided that the address of the beneficial owner of the ordinary shares in the records of the broker is in the United States. We strongly recommend that such shareholders ensure that their information has been properly recorded by their brokers (so that such brokers can further transmit the relevant information to our qualifying intermediary) by filing a Form W-9 with their broker.

Dividends on our ordinary shares that are owned by residents of the United States and held directly will not be subject to DWT provided that the shareholder has completed the appropriate Irish DWT form and this form remains valid. Such shareholders must provide the appropriate Irish DWT form to our transfer agent at least seven business days before the record date for the first dividend payment to which they are entitled.

If any shareholder who is resident in the United States receives a dividend subject to DWT, he or she should generally be able to make an application for a refund from the Irish Revenue Commissioners on the prescribed form.

While the United States/Ireland Double Tax Treaty contains provisions regarding withholding, due to the wide scope of the exemptions from DWT available under Irish domestic law, it would generally be unnecessary for a United States resident shareholder to have to rely on the treaty provisions.

Shares Held by Residents of Relevant Territories Other than the United States

Dividends on our ordinary shares that are owned by residents of relevant territories other than the United States will not be subject to DWT provided that the shareholder has completed the appropriate Irish DWT form and this form remains valid. Such shareholders must provide the appropriate Irish DWT form to his or her broker (in the case of ordinary shares held through DTC), or to our transfer agent (in the case of ordinary shares held directly), at least seven business days before the record date for the first dividend payment to which they are entitled.

If any shareholder resident in a relevant territory receives a dividend subject to DWT, he or she should generally be able to make an application for a refund from the Irish Revenue Commissioners on the prescribed form.

S-59

Table of Contents

Shares Held by Residents of Ireland

Most shareholders who are resident or ordinarily resident in Ireland (other than Irish resident companies) will be subject to DWT in respect of dividend payments on their ordinary shares.

Shareholders that are residents of Ireland but are entitled to receive dividends without DWT must provide the appropriate Irish DWT form to his or her broker (in the case of ordinary shares held through DTC), or to our transfer agent (in the case of ordinary shares held directly), at least seven business days before the record date for the first dividend payment to which they are entitled.

Shareholders who are resident or ordinarily resident in Ireland or are otherwise subject to Irish tax should consult their own tax advisers.

Shares Held by Other Persons

Shareholders who do not reside in relevant territories or in Ireland should be subject to DWT, but there are a number of other exemptions that could apply on a case-by-case basis. Dividends paid to such shareholders will be paid subject to DWT unless the relevant shareholder has provided the appropriate Irish DWT form to his or her broker (in the case of ordinary shares held through DTC), or to our transfer agent (in the case of ordinary shares held directly), at least seven business days before the record date for the first dividend payment to which they are entitled.

If any shareholder who is not a resident of a relevant territory or Ireland but is exempt from withholding receives a dividend subject to DWT, he or she may make an application for a refund from the Irish Revenue Commissioners on the prescribed form.

Income Tax on Dividends Paid on Ordinary Shares

Shareholders who are neither resident nor ordinarily resident in Ireland and who are entitled to an exemption from DWT generally have no additional liability to Irish income tax or to the universal social charge on a dividend from us unless a shareholder holds his or her ordinary shares in connection with a trade or business carried on by such shareholder in Ireland through a branch or agency in Ireland.

Shareholders who are neither resident nor ordinarily resident in Ireland and who are not entitled to an exemption from DWT generally have no additional liability to Irish income tax or to the universal social charge on a dividend from us. The DWT deducted by us discharges the liability to Irish income tax and to the universal social charge. This however is not the case where a shareholder holds his or her ordinary shares in connection with a trade or business carried on by such shareholder in Ireland through a branch or agency in Ireland.

Shareholders who are resident or ordinarily resident in Ireland may be subject to Irish tax and/or levies on dividends received from us. Such shareholders should consult their own tax advisers.

Irish Tax on Capital Gains

Shareholders who are neither resident nor ordinarily resident in Ireland and who do not hold their shares in connection with a trade or business carried on by such shareholders in Ireland through a branch or agency should not be within the charge to Irish tax on capital gains on a disposal of our ordinary shares.

Edgar Filing: Horizon Pharma plc - Form 424B7

Shareholders who are resident or ordinarily resident in Ireland or shareholders that hold their shares in connection with a trade or business carried on by such shareholders in Ireland through a branch or agency may be subject to Irish tax on capital gains on a disposal of our ordinary shares. Such shareholders should consult their own tax advisers.

S-60

Table of Contents

Capital Acquisitions Tax

Irish capital acquisitions tax, or CAT, is comprised principally of gift tax and inheritance tax. CAT could apply to a gift or inheritance of our ordinary shares irrespective of the place of residence, ordinary residence or domicile of the parties. This is because an interest in our ordinary shares may be regarded as property situated in Ireland as our share register must be held in Ireland. The person who receives the gift or inheritance has primary liability for CAT.

CAT is levied at a rate of 33% above certain tax-free thresholds. The appropriate tax-free threshold is dependent upon (i) the relationship between the donor and the donee and (ii) the aggregation of the values of previous gifts and inheritances received by the donee from persons within the same category of relationship for CAT purposes. Gifts and inheritances passing between spouses are exempt from CAT.

Shareholders should consult their own tax advisers as to whether CAT is creditable or deductible in computing any domestic tax liabilities.

Stamp Duty

Irish stamp duty may be payable in respect of transfers of our ordinary shares (currently at the rate of 1% of the price paid or the market value of the shares acquired, if greater).

Shares held through DTC

A transfer of our ordinary shares from a seller who holds those shares through DTC, to a buyer who holds the acquired ordinary shares through DTC will not be subject to Irish stamp duty.

Shares held outside of DTC or transferred into or out of DTC

A transfer of our ordinary shares (i) by a seller who holds those shares outside of DTC to any buyer, or (ii) by a seller who holds those shares through DTC to a buyer who holds the acquired ordinary shares outside of DTC, may be subject to Irish stamp duty. The person accountable for payment of stamp duty is the buyer or, in the case of a transfer by way of a gift or for less than market value, all parties to the transfer.

A shareholder who holds ordinary shares outside of DTC may transfer those shares into DTC without giving rise to Irish stamp duty provided that the shareholder would be the beneficial owner of the related book-entry interest in those shares recorded in the systems of DTC (and in exactly the same proportions) as a result of the transfer and at the time of the transfer into DTC there is no sale of those book-entry interests to a third party being contemplated by the shareholder. Similarly, a shareholder who holds ordinary shares through DTC may transfer those shares out of DTC without giving rise to Irish stamp duty provided that the shareholder would be the beneficial owner of the ordinary shares (and in exactly the same proportions) as a result of the transfer, and at the time of the transfer out of DTC there is no sale of those shares to a third party being contemplated by the shareholder. In order for the share registrar to be satisfied as to the application of this Irish stamp duty treatment where relevant, the shareholder must confirm to us that the shareholder would be the beneficial owner of the related book-entry interest in those ordinary shares recorded in the systems of DTC (and in exactly the same proportions) (or vice-versa) as a result of the transfer and there is no agreement for the sale of the related book-entry interest or the ordinary shares or an interest in the ordinary shares, as the case may be, by the shareholder to a third party being contemplated.

In order for DTC, Cede & Co. and National Securities Clearing Corporation, or NSCC, which provides clearing services for securities that are eligible for the depository and book-entry transfer services provided by DTC and

registered in the name of Cede & Co., which entities are referred to collectively as the DTC Parties, to agree to provide services with respect to our ordinary shares, we concluded with the Revenue Commissioners of

S-61

Table of Contents

Ireland a composition agreement under which we have assumed any obligation of paying the liability for any Irish stamp duty or similar Irish transfer or documentary tax with respect to our ordinary shares, on transfers to which any of the DTC Parties is a party or which may be processed through the services of any of the DTC Parties, and the DTC Parties have received confirmation from the Revenue Commissioners of Ireland that while such composition agreement remains in force, the DTC Parties shall not be liable for any Irish stamp duty with respect to our ordinary shares. In addition, to assure the DTC Parties that they will not be liable for any Irish stamp duty or similar Irish transfer or documentary tax with respect to our ordinary shares under any circumstances (including as a result of a change in applicable law), and to make other provisions with respect to our ordinary shares required by the DTC Parties, we and Computershare Trust Company, NA., a U.S. national banking association acting as our transfer agent, or Computershare, entered into a Special Eligibility Agreement for Securities, dated as of September 19, 2014, with DTC, Cede & Co. and NSCC, or the DTC Eligibility Agreement. The DTC Eligibility Agreement provides for certain indemnities of the DTC Parties by us and Computershare (as to which we have agreed to indemnify Computershare) and also provides that DTC may impose a global lock on our ordinary shares or otherwise limit transactions in the shares, or cause the shares to be withdrawn, and NSCC may, in its sole discretion, exclude our ordinary shares from its Continuous Net Settlement service or any other service, and any of the DTC Parties may take other restrictive measures with respect to our ordinary shares as it may deem necessary and appropriate, without any liability on the part of any the DTC Parties except in the case of gross negligence or willfull misconduct on the part of any of the DTC Parties, (i) at any time that it may appear to any of the DTC Parties, in its sole discretion acting in good faith, that to continue to hold or process transactions in our ordinary shares will give rise to any Irish stamp duty or similar Irish transfer or documentary tax liability with respect to our ordinary shares on the part of any of the DTC Parties or (ii) otherwise as the DTC's rules or the NSCC's rules provide.

Payment of Stamp Duty

Our official share register must be maintained in Ireland. Registration in this share register is determinative of shareholding. Only shareholders will be entitled to receive dividends, if any when declared.

A written instrument of transfer is required under Irish law in order for a transfer of the legal ownership of ordinary shares to be registered on our official share register. Such instruments of transfer may be subject to Irish stamp duty, which must be paid prior to the official share register being updated.

A holder of ordinary shares who holds ordinary shares through DTC will not be the legal owner of such ordinary shares (instead, the depository (for example, Cede & Co., as nominee for DTC) will be the holder of record of such ordinary shares). Accordingly, a transfer of ordinary shares from a person who holds such ordinary shares through DTC to a person who also holds such ordinary shares through DTC will not be registered in our official share register, i.e., the depository will remain the record holder of such ordinary shares.

Our memorandum and articles of association delegate to each director, our secretary or an assistant secretary the authority to execute an instrument of transfer on behalf of a transferring party, which such person may do if for any reason such instrument is required and has not already been lodged with us.

To the extent that stamp duty is due but has not been paid, we, in our absolute discretion and insofar as the Companies Acts or any other applicable law permit, may, or may provide that a subsidiary of ours will, pay Irish stamp duty arising on a transfer of ordinary shares on behalf of the transferee of such ordinary shares. If stamp duty resulting from the transfer of ordinary shares which would otherwise be payable by the transferee is paid by us or any subsidiary of ours on behalf of the transferee, then in those circumstances, we will, on our behalf or on behalf of our subsidiary (as the case may be), be entitled to (i) seek reimbursement of the stamp duty from the transferee, (ii) set-off the stamp duty against any dividends payable to the transferee of those ordinary shares and (iii) to claim a first and permanent

lien on the ordinary shares on which stamp duty has been paid by us or our subsidiary for the amount of stamp duty paid. Our lien shall extend to all dividends paid on those ordinary shares.

S-62

Table of Contents**UNDERWRITERS**

Under the terms and subject to the conditions in an underwriting agreement dated the date of this prospectus supplement, the underwriters named below, for whom Morgan Stanley & Co. LLC, Citigroup Global Markets Inc., Cowen and Company, LLC and Jefferies LLC are acting as representatives, have severally agreed to purchase, and the selling shareholders have agreed to sell to them, severally, the number of shares indicated below:

Name	Number of Shares
Morgan Stanley & Co. LLC	
Citigroup Global Markets Inc.	
Cowen and Company, LLC	
Jefferies LLC	
Total:	11,660,445

The underwriters and the representatives are collectively referred to as the underwriters and the representatives, respectively. The underwriters are offering the ordinary shares subject to their acceptance of the shares from the selling shareholders and subject to prior sale. The underwriting agreement provides that the obligations of the several underwriters to pay for and accept delivery of the ordinary shares offered by this prospectus supplement are subject to the approval of certain legal matters by their counsel and to certain other conditions. The underwriters are obligated to take and pay for all of the ordinary shares offered by this prospectus supplement if any such shares are taken. However, the underwriters are not required to take or pay for the shares covered by the underwriters' option to purchase additional shares described below.

The underwriters initially propose to offer part of the ordinary shares directly to the public at the offering price listed on the cover page of this prospectus supplement and part to certain dealers at a price that represents a concession not in excess of \$ _____ a share under the public offering price. After the initial offering of the ordinary shares, the offering price and other selling terms may from time to time be varied by the representatives. Sales of shares made outside of the United States may be made by affiliates of the underwriters.

The selling shareholders have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus supplement, to purchase up to 1,749,066 additional ordinary shares at the public offering price listed on the cover page of this prospectus supplement, less underwriting discounts and commissions. To the extent the option is exercised, each underwriter will become obligated, subject to certain conditions, to purchase about the same percentage of the additional ordinary shares as the number listed next to the underwriter's name in the preceding table bears to the total number of ordinary shares listed next to the names of all underwriters in the preceding table.

The following table shows the per share and total public offering price, underwriting discounts and commissions, and proceeds before expenses to the selling shareholders. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase up to 1,749,066 additional shares of common stock.

Per Share	No Exercise	Total Full Exercise
------------------	--------------------	----------------------------

Edgar Filing: Horizon Pharma plc - Form 424B7

Public offering price	\$	\$	\$
Underwriting discounts and commissions to be paid by the selling shareholders	\$	\$	\$
Proceeds, before expenses, to the selling shareholders	\$	\$	\$

The estimated offering expenses payable by us are approximately \$1,000,000. Certain of the selling shareholders will bear the fees and expenses of their counsel of approximately \$40,000.

S-63

Table of Contents

Our ordinary shares are listed on The NASDAQ Global Market under the trading symbol HZNP .

We, all of our directors and officers, and certain of our existing shareholders have agreed that, without the prior written consent of the representatives on behalf of the underwriters, we and they will not, during the period ending 90 days after the date of this prospectus supplement (the restricted period) and subject to specified exceptions:

offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, any ordinary shares or any securities convertible into or exercisable or exchangeable for ordinary shares; or

enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the ordinary shares,

whether any such transaction described above is to be settled by delivery of common stock or such other securities, in cash or otherwise. In addition, we have agreed that, without the prior written consent of the representatives on behalf of the underwriters, we will not, during the restricted period, file any registration statement with the SEC relating to the offering of any ordinary shares or any security convertible into or exercisable or exchangeable for ordinary shares (other than on Form S-8 with respect to our equity incentive plans described in this prospectus supplement), and such other person have agreed that they will not, during the restricted period, make any demand for, or exercise any right with respect to, the registration of, any ordinary shares or any security convertible into or exercisable or exchangeable for ordinary shares.

The restrictions described in the immediately preceding paragraph are subject to customary exceptions, including the following:

the issuance by us of ordinary shares upon the exercise of an option or warrant or the conversion of a security outstanding on the date of the underwriting agreement of which the underwriters have been advised in writing, including our 5.00% Convertible Senior Notes due 2018; and

the entry into any agreement to issue or issuance during the 90-day restricted period of a number of ordinary shares not greater than 15% of the total number of ordinary shares outstanding on the date of this prospectus supplement in connection with any strategic transaction; provided, that each recipient of ordinary shares issued shall execute a substantially similar lock-up agreement.

The restricted period described in the preceding paragraphs will be extended if:

during the last 17 days of the 90-day restricted period we issue an earnings release or material news event relating to us occurs, or

prior to the expiration of the 90-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the restricted period or provide notification to Morgan Stanley & Co. LLC of any earnings release or material news or material event that may give rise to an extension of the initial 90-day restricted period,

in which case the restrictions described in the preceding paragraph will continue to apply until the expiration of the 18-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event.

The representatives, in their sole discretion, may release the ordinary shares and other securities subject to the lock-up agreements described above in whole or in part at any time.

In order to facilitate the offering of the ordinary shares, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the ordinary shares. Specifically, the underwriters may sell

S-64

Table of Contents

more shares than they are obligated to purchase under the underwriting agreement, creating a short position. A short sale is covered if the short position is no greater than the number of shares available for purchase by the underwriters under the option to purchase additional shares. The underwriters can close out a covered short sale by exercising the option or purchasing shares in the open market. In determining the source of shares to close out a covered short sale, the underwriters will consider, among other things, the open market price of shares compared to the price available under the option. The underwriters may also sell shares in excess of the option, creating a naked short position. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in this offering. As an additional means of facilitating this offering, the underwriters may bid for, and purchase, ordinary shares in the open market to stabilize the price of the ordinary shares. These activities may raise or maintain the market price of the ordinary shares above independent market levels or prevent or retard a decline in the market price of the ordinary shares. The underwriters are not required to engage in these activities and may end any of these activities at any time.

In addition, in connection with this offering certain of the underwriters (and selling group members) may engage in passive market making transactions in our ordinary shares on The NASDAQ Global Market prior to the pricing and completion of this offering. Passive market making consists of displaying bids on The NASDAQ Global Market no higher than the bid prices of independent market makers and making purchases at prices no higher than these independent bids and effected in response to order flow. Net purchases by a passive market maker on each day are generally limited to a specified percentage of the passive market maker's average daily trading volume in the ordinary shares during a specified period and must be discontinued when such limit is reached. Passive market making may cause the price of our ordinary shares to be higher than the price that otherwise would exist in the open market in the absence of these transactions. If passive market making is commenced, it may be discontinued at any time.

We, the selling shareholders and the underwriters have agreed to indemnify each other against certain liabilities, including liabilities under the Securities Act.

A prospectus in electronic format may be made available on websites maintained by one or more underwriters, or selling group members, if any, participating in this offering. The representatives may agree to allocate a number of ordinary shares to underwriters for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters that may make Internet distributions on the same basis as other allocations.

Other Relationships

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Certain of the underwriters and their respective affiliates have, from time to time, performed, and may in the future perform, various financial advisory and investment banking services for us, for which they received or will receive customary fees and expenses.

In addition, in the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investment and securities activities may involve our securities and instruments. The underwriters and their respective affiliates may also make investment recommendations or publish or express independent research views in respect of such securities

or instruments and may at any time hold, or recommend to clients that they acquire, long or short positions in such securities and instruments.

S-65

Table of Contents

Selling Restrictions

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State) an offer to the public of any of our ordinary shares may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of any of our ordinary shares may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

- (a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- (b) to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives for any such offer; or
- (c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares of our common stock shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an offer to the public in relation to any of our ordinary shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any of our ordinary shares to be offered so as to enable an investor to decide to purchase any of our ordinary shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State, and the expression 2010 PD Amending Directive means Directive 2010/73/EU.

United Kingdom

Each underwriter has represented and agreed that:

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

France

Neither this prospectus supplement nor any other offering material relating to the shares described in this prospectus supplement has been submitted to the clearance procedures of the Autorité des Marchés Financiers or of the competent authority of another member state of the European Economic Area and notified to the Autorité des Marchés Financiers. The shares have not been offered or sold and will not be offered or sold, directly or indirectly, to the public in France. Neither this prospectus supplement nor any other offering material relating to the shares has been or will be:

- (a) released, issued, distributed or caused to be released, issued or distributed to the public in France; or

S-66

Table of Contents

(b) used in connection with any offer for subscription or sale of the shares to the public in France. Such offers, sales and distributions will be made in France only:

- (a) to qualified investors (*investisseurs qualifiés*) and/or to a restricted circle of investors (*cercle restreint d'investisseurs*), in each case investing for their own account, all as defined in, and in accordance with articles L.411-2, D.411-1, D.411-2, D.734-1, D.744-1, D.754-1 and D.764-1 of the French *Code monétaire et financier*;
- (b) to investment services providers authorized to engage in portfolio management on behalf of third parties; or
- (c) in a transaction that, in accordance with article L.411-2-II-1°-or-2°-or 3° of the French *Code monétaire et financier* and article 211-2 of the General Regulations (*Règlement Général*) of the *Autorité des Marchés Financiers*, does not constitute a public offer (*appel public à l'épargne*).

The shares may be resold directly or indirectly, only in compliance with articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French *Code monétaire et financier*.

Hong Kong

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

Japan

The shares offered in this prospectus supplement have not been and will not be registered under the Financial Instruments and Exchange Law of Japan. The shares have not been offered or sold and will not be offered or sold, directly or indirectly, in Japan or to or for the account of any resident of Japan (including any corporation or other entity organized under the laws of Japan), except (i) pursuant to an exemption from the registration requirements of the Financial Instruments and Exchange Law and (ii) in compliance with any other applicable requirements of Japanese law.

Singapore

This prospectus supplement has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be

offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to compliance with conditions set forth in the SFA.

S-67

Table of Contents

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- (a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:
 - (a) to an institutional investor (for corporations, under Section 274 of the SFA) or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than S\$200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions specified in Section 275 of the SFA;
 - (b) where no consideration is or will be given for the transfer; or
 - (c) where the transfer is by operation of law.

Australia

No prospectus or other disclosure document (as defined in the Corporations Act 2001 (Cth) of Australia, or the Corporations Act) in relation to the common stock has been or will be lodged with the Australian Securities & Investments Commission, or the ASIC. This document has not been lodged with ASIC and is only directed to certain categories of exempt persons. Accordingly, if you receive this document in Australia:

- (a) you confirm and warrant that you are either:
 - (i) a sophisticated investor under section 708(8)(a) or (b) of the Corporations Act;
 - (ii) a sophisticated investor under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to us which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made;
 - (iii) a person associated with the company under section 708(12) of the Corporations Act; or

(iv) a professional investor within the meaning of section 708(11)(a) or (b) of the Corporations Act, and to the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor, associated person or professional investor under the Corporations Act any offer made to you under this document is void and incapable of acceptance; and

(b) you warrant and agree that you will not offer any of the ordinary shares for resale in Australia within 12 months of that common stock being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

S-68

Table of Contents

LEGAL MATTERS

McCann FitzGerald Solicitors, Dublin, Ireland will pass upon the validity of the ordinary shares offered by this prospectus supplement. Certain legal matters in connection with this offering relating to U.S. law will be passed upon for us by Cooley LLP, San Diego, California. Certain legal matters in connection with this offering relating to U.S. law will be passed upon for Essex Woodlands Health Ventures Fund VII, L.P., one of the selling shareholders, by Perkins Coie LLP, Chicago, Illinois. Certain legal matters in connection with this offering relating to U.S. law will be passed upon for the remaining selling shareholders by Mayer Brown LLP, New York, New York. Certain legal matters are being passed upon for the underwriters by Goodwin Procter LLP, New York, New York.

EXPERTS

The financial statements and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Report on Internal Control over Financial Reporting) incorporated in this prospectus by reference to the Annual Report on Form 10-K of HPI for the year ended December 31, 2013 have been so incorporated in reliance on the report (which contains an explanatory paragraph relating to HPI's ability to continue as a going concern as described in Note 1 to the financial statements) of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

The combined financial statements of Vidara Therapeutics International Limited and subsidiaries and Vidara Therapeutics, Inc. as of December 31, 2013 and December 31, 2012, and for the years then ended, have been incorporated by reference into this prospectus in reliance upon the report of Habif, Arogeti & Wynne LLP, an independent registered public accounting firm, and upon the authority of said firm as experts in accounting and auditing.

Ernst & Young LLP, independent registered public accounting firm, has audited the statements of revenues and direct expenses and related notes thereto of the ACTIMMUNE® Product Line of InterMune, Inc. for the year ended December 31, 2011 and for the period from January 1, 2012 through June 18, 2012, which are incorporated by reference in this prospectus. These financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

The statement of assets acquired of the VIMOVO Product Line of AstraZeneca LP as of December 31, 2012, and the related statement of net revenues and direct expenses for the year then ended, have been incorporated by reference in this prospectus in reliance upon the report of KPMG LLP, independent auditors, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference room. The SEC also maintains an Internet site that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC, including us. The SEC's Internet site can be found at <http://www.sec.gov>.

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 another document that we or HPI have filed with the SEC. You should read the information incorporated by reference because it is an important part of this prospectus

Table of Contents

supplement. Information in this prospectus supplement supersedes information incorporated by reference that we or HPI filed with the SEC prior to the date of this prospectus supplement. We incorporate by reference the following information or documents that we and HPI have filed with the SEC:

HPI's Annual Report on Form 10-K for the fiscal year ended December 31, 2013, filed with the SEC on March 13, 2014;

the information specifically incorporated by reference into HPI's Annual Report on Form 10-K for the fiscal year ended December 31, 2013 from HPI's definitive proxy statement on Schedule 14A, filed with the SEC on May 20, 2014;

HPI's Quarterly Reports on Form 10-Q for the quarters ended March 31, 2014 and June 30, 2014 filed with the SEC on May 9, 2014 and August 7, 2014, respectively;

HPI's Current Reports on Form 8-K (other than information furnished rather than filed) filed with the SEC on January 16, 2014, February 6, 2014, March 4, 2014, March 19, 2014, March 20, 2014, April 17, 2014, May 9, 2014, June 18, 2014, June 19, 2014, July 2, 2014, July 28, 2014, August 7, 2014 and September 18, 2014;

Vidara's Quarterly Report on Form 10-Q for the quarter ended June 30, 2014 filed with the SEC on August 26, 2014;

the following information from HPI's definitive proxy statement on Schedule 14A filed with the SEC on August 7, 2014:

the information under the sections entitled Selected Historical Financial Data of Vidara and The ACTIMMUNE Business of InterMune, Management's Discussion and Analysis of Financial Condition and Results of Operations of Vidara, Unaudited Pro Forma Combined Financial Information, The Business of Vidara, Management and Other Information of New Horizon, Executive Compensation, and Certain Relationships and Related Party Transactions;

the audited combined financial statements of Vidara Therapeutics International Limited and subsidiaries and Vidara Therapeutics, Inc., including the combined balance sheets as of December 31, 2013 and 2012, and the related audited combined statements of operations, changes in shareholders equity and cash flows for each of the years in the two-year period ended December 31, 2013, and the notes related thereto, and the report of Habif, Arogeti & Wynne, independent registered public accounting firm, included on pages F-1 to F-23;

Edgar Filing: Horizon Pharma plc - Form 424B7

the unaudited interim combined financial statements of Vidara Therapeutics International Limited and subsidiaries and Vidara Therapeutics, Inc., including the unaudited interim combined balance sheets as of March 31, 2014 and the unaudited interim combined statements of operations and cash flows for the three months ended March 31, 2014 and 2013 and the notes related thereto, including on pages F-24 to F-30; and

the audited statements of revenues and direct expenses of the ACTIMMUNE Product Line of InterMune, Inc. for the year ended December 31, 2011 and the period from January 1, 2012 to June 18, 2012 and the report of Ernst & Young LLP, an independent registered public accounting firm, included on pages F-31 to F-36;

our Current Reports on Form 8-K (other than information furnished rather than filed) filed with the SEC on September 19, 2014, September 22, 2014, September 24, 2014, September 26, 2014, October 14, 2014, October 17, 2014, October 24, 2014, October 28, 2014, November 5, 2014, November 10, 2014 and November 13, 2014; and

our Quarterly Report on Form 10-Q for the quarter ended September 30, 2014 filed with the SEC on November 6, 2014.

S-70

Table of Contents

Any information in any of the foregoing documents will automatically be deemed to be modified or superseded to the extent that information in this prospectus or in a later filed document that is incorporated or deemed to be incorporated herein by reference modifies or replaces such information.

We also incorporate by reference any future filings (other than portions of such filings that are furnished and not filed and exhibits to such filings that are related to such portions) made with the SEC by us pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act until the termination of the offering of all of the securities covered by this prospectus supplement. Information in such future filings updates and supplements the information provided in this prospectus supplement. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document that we or HPI 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 furnish without charge to each person, including any beneficial owner, to whom a prospectus is delivered, upon written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents. Any such request may be made by writing or telephoning us at the following address or phone number:

Horizon Pharma plc

Attn: Investor Relations

c/o Horizon Pharma Holdings USA, Inc.

520 Lake Cook Road, Suite 520

Deerfield, IL 60015

Telephone: +1 (224) 383-3000

S-71

Table of Contents

PROSPECTUS

Ordinary Shares

From time to time, we or selling shareholders may offer and sell our ordinary shares in amounts, at prices and on terms described in one or more supplements to this prospectus.

This prospectus describes some of the general terms that may apply to an offering of our ordinary shares. The specific terms and any other information relating to a specific offering, including the names of any selling shareholders, will be set forth in a post-effective amendment to the registration statement of which this prospectus is a part or in a supplement to this prospectus, or may be set forth in one or more documents incorporated by reference in this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with a specific offering. You should read this prospectus, the applicable prospectus supplement and any free writing prospectuses we have authorized for use in connection with a specific offering, as well as any documents incorporated by reference in this prospectus and the applicable prospectus supplement, carefully before you invest.

We and any selling shareholders may offer and sell our ordinary shares to or through one or more underwriters, dealers and agents, or directly to purchasers, on a continuous or delayed basis. The supplements to this prospectus will provide the specific terms of the plan of distribution. The net proceeds we expect to receive from sales of our ordinary shares will be set forth in the applicable prospectus supplement.

We are considered the successor to Horizon Pharma, Inc., or HPI, for certain purposes under both the Securities Act of 1933, as amended, or the Securities Act, and Securities Exchange Act of 1934, as amended, or the Exchange Act. As the result of a merger involving us and HPI, all outstanding shares of the common stock, par value \$0.0001 per share, of HPI were canceled and converted into the right to receive our ordinary shares on a one-for-one basis.

Our ordinary shares are listed on The NASDAQ Global Market under the symbol HZNP. On September 19, 2014, the last reported sale price of our ordinary shares on The NASDAQ Global Market was \$12.70.

Investing in our ordinary shares involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading Risk Factors on page 4, and under similar headings in any prospectus supplement and in any free writing prospectus we have authorized for use in connection with a specific offering, and 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 September 19, 2014.

Table of Contents

TABLE OF CONTENTS

	Page
<u>About This Prospectus</u>	1
<u>About Horizon Pharma plc</u>	2
<u>Risk Factors</u>	4
<u>Special Note Regarding Forward-Looking Statements</u>	4
<u>Use of Proceeds</u>	5
<u>Selling Shareholders</u>	5
<u>Validity of Share Capital</u>	5
<u>Experts</u>	6
<u>Enforcement of Civil Liabilities Under United States Federal Securities Laws</u>	6
<u>Where You Can Find More Information</u>	6

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or SEC, using the shelf registration process. By using a shelf registration statement, we and any selling shareholders may offer and sell our ordinary shares from time to time in one or more offerings. No limit exists on the aggregate number of ordinary shares that we and any selling shareholders may sell pursuant to the registration statement.

We have not authorized anyone to provide you with information other than the information contained in, or incorporated by reference into, this prospectus and the applicable prospectus supplement, along with the information contained in any free writing prospectuses we have authorized for use in connection with a specific offering. This document may only be used where it is legal to sell these securities. You should not assume that the information contained in this prospectus, in any applicable prospectus supplement or in any free writing prospectuses we have authorized for use in connection with a specific offering is accurate as of any date other than its respective date, regardless of when this prospectus, any prospectus supplement or any free writing prospectus we have authorized for use in connection with a specific offering is delivered, or when any sale of our ordinary shares occurs. If there is any inconsistency between the information in this prospectus and a prospectus supplement, you should rely on the information in the prospectus supplement.

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

We urge you to read carefully this prospectus, the applicable prospectus supplement and any free writing prospectuses we have authorized for use in connection with a specific offering, together with the information incorporated herein by reference as described under the heading **Where You Can Find More Information**, before deciding whether to invest in any of our ordinary shares being offered.

We are a public limited company formed under the laws of Ireland that was formerly named Vidara Therapeutics International plc. On September 19, 2014, we and HPI consummated the merger contemplated by the transaction agreement and plan of merger that we entered into with HPI and certain other parties on March 18, 2014, as amended. In connection with the merger, we were re-named Horizon Pharma plc and became the parent company of HPI, with HPI becoming our wholly-owned subsidiary. In the merger, all outstanding shares of HPI's common stock were canceled and converted into the right to receive, on a one-for-one basis, our ordinary shares. We are considered the successor to HPI for certain purposes under both the Securities Act of 1933, as amended, and Securities Exchange Act of 1934, as amended, including for purposes of our eligibility to file this registration statement on Form S-3. Unless the context otherwise requires, references in this prospectus to we, us and our refer to (i) upon and following the merger, Horizon Pharma plc and its subsidiaries, including HPI, and (ii) prior to the merger, Vidara Therapeutics International plc, a public limited company formed under the laws of Ireland, or Vidara, unless the context indicates otherwise.

This prospectus may not be used to consummate a sale of our ordinary shares unless accompanied by a prospectus supplement.

Table of Contents

ABOUT HORIZON PHARMA PLC

Overview

We are a specialty biopharmaceutical company focused on improving patients' lives by identifying, developing, acquiring and commercializing differentiated products that address unmet medical needs. We market a portfolio of products in arthritis, pain, inflammation and orphan diseases. Our U.S. marketed products are ACTIMMUNE® (interferon gamma-1b), DUEXIS® (ibuprofen/famotidine), RAYOS® (prednisone) delayed-release tablets and VIMOVO® (naproxen/esomeprazole). We market our products in the United States through our field sales force of approximately 315 representatives.

Recent Developments

On September 19, 2014, we and HPI consummated the merger contemplated by the transaction agreement and plan of merger that we entered into with HPI and certain other parties on March 18, 2014, as amended. In connection with the merger, we were re-named Horizon Pharma plc and became the parent company of HPI, with HPI becoming our wholly-owned subsidiary. In the merger, all outstanding shares of HPI's common stock were canceled and converted into the right to receive, on a one-for-one basis, our ordinary shares. Immediately after giving effect to the issuance of our ordinary shares to the former HPI stockholders in the merger, approximately 106,130,396 of our ordinary shares were outstanding, of which approximately 70.5% were held by the former HPI stockholders. The remaining 29.5% of our ordinary shares outstanding immediately after giving effect to the merger were held by Vidara Therapeutics Holdings LLC, the sole shareholder of our company prior to the merger, which acquired our ordinary shares prior to the merger. Our ordinary shares trade on the same exchange, The NASDAQ Global Market, and under the trading symbol, HZNP, that the shares of HPI common stock traded on and under prior to the merger.

HPI is deemed to be the acquiring company for accounting purposes and the transaction is being accounted for as a reverse acquisition under the acquisition method of accounting for business combinations. As a result, the historical financial statements of HPI became our historical financial statements. We are also considered to be the successor to HPI for certain purposes under both the Securities Act and the Exchange Act, and certain of HPI's historical reports filed under the Exchange Act are incorporated by reference in this prospectus. Prior to the merger, we were known as Vidara Therapeutics International plc, or Vidara. The historical financial statements for Vidara for the years ended December 31, 2013 and 2012 and for the three months ended March 31, 2014, and pro forma financial information related to the merger, are incorporated by reference in this prospectus from HPI's definitive proxy statement on Schedule 14A filed on August 7, 2014. The historical financial statements for Vidara for the three and six months ended June 30, 2014, and pro forma financial information related to the merger as of June 30, 2014 are incorporated by reference in this prospectus from Vidara's quarterly report on Form 10-Q filed on August 26, 2014 and our current report on Form 8-K filed on September 19, 2014, respectively. See [Where You Can Find More Information](#). A brief description of the historical business of Vidara prior to the merger is also set forth below. More information about the historical business of Vidara can be found in HPI's definitive proxy statement on Schedule 14A filed with the Securities and Exchange Commission on August 7, 2014.

Historical Business of HPI

HPI's specialty pharmaceutical business focused on developing, acquiring and in-licensing innovative medicines and acquiring companies to target unmet therapeutic needs in arthritis, pain and inflammatory diseases by executing a targeted commercial approach among specific target physicians such as primary care physicians, orthopedic surgeons and rheumatologists, while taking advantage of its commercial strengths and the infrastructure it had put in place. HPI's marketed products, which continue to be marketed by the combined company, are DUEXIS®, VIMOVO® and

RAYOS[®]/LODOTRA[®]. HPI developed DUEXIS[®] and RAYOS[®]/LODOTRA[®] and acquired the U.S. rights to VIMOVO[®] from AstraZeneca AB, or AstraZeneca, in November 2013.

Table of Contents

On April 23, 2011, the U.S. Food and Drug Administration, or FDA, approved DUEXIS[®], a proprietary tablet formulation containing a fixed-dose combination of ibuprofen and famotidine in a single pill. DUEXIS[®] is indicated for the relief of signs and symptoms of rheumatoid arthritis, or RA, osteoarthritis, or OA, and to decrease the risk of developing upper gastrointestinal, or GI, ulcers in patients who are taking ibuprofen for these indications. In June 2012, HPI licensed DUEXIS[®] rights in Latin America to Grünenthal S.A., or Grünenthal, a private company focused on the promotion of pain products.

HPI's second approved product in the United States, RAYOS[®], known as LODOTRA[®] outside the United States, is a proprietary delayed-release formulation of low-dose prednisone approved originally in Europe for the treatment of moderate to severe, active RA in adults, particularly when accompanied by morning stiffness. On July 26, 2012, the FDA approved RAYOS[®] for the treatment of RA, polymyalgia rheumatica, or PMR, psoriatic arthritis, or PsA, ankylosing spondylitis, or AS, asthma and chronic obstructive pulmonary disease, or COPD, and a number of other conditions. LODOTRA[®] is currently marketed outside the United States by HPI's distribution partner, Mundipharma International Corporation Limited, or Mundipharma.

On November 18, 2013, HPI entered into agreements with AstraZeneca pursuant to which it acquired from AstraZeneca and its affiliates certain intellectual property and other assets, and assumed from AstraZeneca and its affiliates certain liabilities, each with respect to VIMOVO[®], and obtained rights to develop other pharmaceutical products that contain gastroprotective agents in a single fixed combination oral solid dosage form with NSAIDs in the United States. VIMOVO[®] (naproxen/esomeprazole magnesium) is a proprietary fixed-dose multi-layer delayed-release tablet combining an enteric-coated naproxen, an NSAID, core and an immediate-release esomeprazole, a proton pump inhibitor, or PPI, layer surrounding the core. On April 30, 2010, the FDA approved VIMOVO[®] for the relief of the signs and symptoms of OA, RA and AS and to decrease the risk of developing gastric ulcers in patients at risk of developing NSAID associated gastric ulcers. HPI announced the availability of Horizon-labeled VIMOVO[®] on January 2, 2014 and began selling VIMOVO[®] in early February 2014.

More information about the historical business of HPI can be found in HPI's annual and quarterly reports that are incorporated by reference in this prospectus. See [Where You Can Find More Information](#).

Historical Business of Vidara

Overview

Vidara's biopharmaceutical business focused on the treatment of patients with serious, difficult-to-treat inherited disorders and rare diseases. Vidara's only commercial product and source of revenue, which continues to be marketed by the combined company, is ACTIMMUNE[®] (interferon gamma-1b), an injectable biologic drug prescribed for the management of two rare disorders:

Chronic granulomatous disease (CGD): CGD is a life-threatening congenital disorder of leukocyte cell function caused by defects in the enzyme complex responsible for phagocyte superoxide generation. CGD causes patients, primarily children, to be vulnerable to severe, recurrent bacterial and fungal infections resulting in frequent and prolonged hospitalizations and commonly death.

Severe, malignant osteopetrosis (SMO): SMO is a life-threatening, congenital disorder that primarily affects children. This disease is caused by defects in one or more genes involved in the formation, development, and

function of osteoclast cells and by deficient phagocyte oxidative metabolism. SMO results in increased susceptibility to infections and bone overgrowth that can lead to blindness and/or deafness. Currently, ACTIMMUNE® is the only drug approved by the FDA for the treatment for CGD and SMO in the United States. Vidara marketed and distributed ACTIMMUNE® only in the United States and it has not sought regulatory approval to market and sell ACTIMMUNE® in any other markets. Due to the rare and serious

Table of Contents

nature of these diseases, Vidara established a specialty sales force that focuses on marketing to a limited number of healthcare practitioners who specialize in fields such as pediatric immunology, allergy, infectious diseases and hematology/oncology to help them understand the potential benefits of ACTIMMUNE® for their patients with CGD and SMO.

More information about the historical business of Vidara can be found in HPI's definitive proxy statement on Schedule 14A filed with the Securities and Exchange Commission on August 7, 2014.

Corporate Information

We are a public limited company formed under the laws of Ireland (registered number 507678) in December 2011. We were originally formed as a private limited liability company under the name Aravis Therapeutics International Limited and were subsequently re-named Vidara Therapeutics International Limited. In connection with the merger, we were re-registered as a public limited company, Vidara Therapeutics International plc, became the parent company of and successor to HPI and were re-named Horizon Pharma plc. Our principal executive offices are located at Adelaide Chambers, Peter Street, Dublin 8, Ireland. Our telephone number is 011-353-1-649-8521. Our website address is www.horizonpharma.com. Information contained in, or accessible through, our website does not constitute a part of this prospectus or any prospectus supplement.

RISK FACTORS

Investing in our ordinary shares involves a high degree of risk. You should carefully consider the risk factors identified in the applicable prospectus supplement and in any free writing prospectuses we have authorized for use in connection with a specific offering, as well as under the section entitled "Risk Factors" contained in HPI's quarterly report on Form 10-Q and definitive proxy statement on Schedule 14A, each filed with the Securities and Exchange Commission on August 7, 2014, and incorporated by reference in this prospectus, as the same may be amended, supplemented or superseded from time to time by other reports we file with the SEC after the date of this prospectus, in addition to the other information contained in this prospectus, any applicable prospectus supplement, the documents incorporated by reference herein or therein, and in any free writing prospectuses we have authorized for use in connection with a specific offering, before deciding whether to purchase any of our ordinary shares. 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 ordinary shares, and you may lose all or part of your investment.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference herein contain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. These statements are based on our current expectations, assumptions, estimates and projections about our business and our industry, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the future results, levels of activity, performance or achievements expressed or implied by the forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

the expected synergies and other benefits, including tax, financial and strategic benefits, of the merger to us and our shareholders;

sales of DUEXIS[®], VIMOVO[®], RAYOS[®], ACTIMMUNE[®] and any future products;

availability of coverage and adequate reimbursement and pricing from government and other third-party payers for our products;

our ability to obtain adequate clinical and commercial supplies of our products from current and new single source suppliers and manufacturers;

Table of Contents

our ability to protect our intellectual property and defend our patents; and

the sufficiency of our cash resources and our expectations regarding our future cash flow, expenses, revenues, financial results and capital requirements.

In some cases, you can identify forward-looking statements by terms such as anticipates, expects, intends, plans, predicts, believes, seeks, estimates, could, would, will, may, can, continue, potential, should, terms and similar expressions intended to identify forward-looking statements. While we believe that we have a reasonable basis for each forward-looking statement, we caution you that these statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance, time frames or achievements to be materially different from the information expressed or implied by these forward-looking statements. We discuss many of these risks, uncertainties and other factors in greater detail under the heading Risk Factors contained in the applicable prospectus supplement, in any free writing prospectuses we have authorized for use in connection with a specific offering, in HPI's quarterly report on Form 10-Q and definitive proxy statement on Schedule 14A, each filed with the Securities and Exchange Commission on August 7, 2014, and incorporated by reference in this prospectus, and under similar headings in our future reports that we file with the SEC and that are incorporated by reference in this prospectus. Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements. Also, these forward-looking statements represent our estimates and assumptions only as of the date such forward-looking statements are made. You should read carefully this prospectus, the applicable prospectus supplement and any free writing prospectuses we have authorized for use in connection with a specific offering, together with the information incorporated herein by reference as described under the heading Where You Can Find More Information and with the understanding that our actual future results may be materially different from what we expect. We hereby qualify all of our forward-looking statements by these cautionary statements.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

USE OF PROCEEDS

Except as described in the applicable prospectus supplement or in any free writing prospectuses that we may authorize for use in connection with a specific offering, we currently intend to use the net proceeds from our sale of our ordinary shares for general corporate purposes. We may also use a portion of the net proceeds to acquire or invest in businesses, products and product candidates that are complementary to our own or that we consider strategic. Pending these uses, we expect to invest the net proceeds in investment-grade, interest-bearing securities. We will not receive any of the proceeds from sales of our ordinary shares by selling shareholders, if any, pursuant to this prospectus.

SELLING SHAREHOLDERS

If the registration statement of which this prospectus is a part is used by any selling shareholder for the resale of any ordinary shares registered thereunder, information about such selling shareholder, its beneficial ownership of our securities and its relationship with us will be set forth in a post-effective amendment to the registration statement, in a supplement to this prospectus, or in one or more documents incorporated by reference in this prospectus or the applicable prospectus supplement.

VALIDITY OF SHARE CAPITAL

Unless otherwise stated in the applicable prospectus supplement, the validity of the ordinary shares being offered hereby will be passed upon by A&L Goodbody, Dublin, Ireland.

Table of Contents

EXPERTS

The financial statements and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Report on Internal Control over Financial Reporting) incorporated in this prospectus and registration statement by reference to the Annual Report on Form 10-K of Horizon Pharma, Inc. for the year ended December 31, 2013 have been so incorporated in reliance on the report (which contains an explanatory paragraph relating to the Company's ability to continue as a going concern as described in Note 1 to the financial statements) of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

The combined financial statements of Vidara Therapeutics International Limited and subsidiaries and Vidara Therapeutics, Inc. as of December 31, 2013 and December 31, 2012, and for the years then ended, have been incorporated by reference into this prospectus and in the registration statement in reliance upon the report of Habif, Arogeti & Wynne LLP, an independent registered public accounting firm, and upon the authority of said firm as experts in accounting and auditing.

Ernst & Young LLP, independent registered public accounting firm, has audited the statements of revenues and direct expenses and related notes thereto of the ACTIMMUNE® Product Line of InterMune, Inc. for the year ended December 31, 2011 and for the period from January 1, 2012 through June 18, 2012, which are incorporated by reference in this prospectus and elsewhere in the registration statement. These financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

The statement of assets acquired of the VIMOVO Product Line of AstraZeneca LP as of December 31, 2012, and the related statement of net revenues and direct expenses for the year then ended, have been incorporated by reference herein and in the registration statement in reliance upon the report of KPMG LLP, independent auditors, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

ENFORCEMENT OF CIVIL LIABILITIES UNDER UNITED STATES FEDERAL SECURITIES LAWS

We are a public limited company formed under the laws of Ireland, and certain of our officers and directors are or may in the future be residents outside the United States. All or a substantial portion of our assets or the assets of such non-resident persons may be located outside of the United States. As a result, it may not be possible to effect service of process within the United States upon such persons or us, or to enforce against such persons or us in U.S. courts judgments obtained in such courts predicated upon the civil liability provisions of the federal securities laws of the United States. There is no treaty between Ireland and the United States providing for the reciprocal enforcement of foreign judgments. We have been advised by counsel that there is doubt as to the enforceability in Ireland, in original actions or in actions for enforcement of judgments of U.S. courts, of liabilities predicated solely upon the securities laws of the United States. Consequently, it may be difficult for investors to enforce against us, our directors or our officers in Ireland judgments obtained in the United States which are predicated upon the civil liability provisions of the federal securities laws of the United States.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference room. The SEC also maintains an Internet site that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC, including us. The SEC's Internet site can be found at <http://www.sec.gov>.

Table of Contents

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 another document that we or HPI have filed with the SEC. You should read the information incorporated by reference because it is an important part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we or HPI filed with the SEC prior to the date of this prospectus, while information that we file later with the SEC will automatically update and supersede the information in this prospectus. We incorporate by reference the following information or documents that we and HPI have filed with the SEC:

HPI's Annual Report on Form 10-K for the fiscal year ended December 31, 2013, filed with the SEC on March 13, 2014;

the information specifically incorporated by reference into HPI's Annual Report on Form 10-K for the fiscal year ended December 31, 2013 from HPI's definitive proxy statement on Schedule 14A, filed with the SEC on May 20, 2014;

HPI's Quarterly Reports on Form 10-Q for the quarters ended March 31, 2014 and June 30, 2014 filed with the SEC on May 9, 2014 and August 7, 2014, respectively;

HPI's Current Reports on Form 8-K filed with the SEC on January 16, 2014, February 6, 2014, March 4, 2013, March 19, 2014, March 20, 2014, April 17, 2014, May 9, 2014, June 18, 2014, June 19, 2014, July 2, 2014, July 28, 2014, August 7, 2014 and September 18, 2014;

Vidara's Quarterly Report on Form 10-Q for the quarter ended June 30, 2014 filed with the SEC on August 26, 2014;

the following information from HPI's definitive proxy statement on Schedule 14A filed with the SEC on August 7, 2014:

the information under the sections entitled Risk Factors, Selected Historical Financial Data of Vidara and The ACTIMMUNE Business of InterMune, Management's Discussion and Analysis of Financial Condition and Results of Operations of Vidara, Unaudited Pro Forma Combined Financial Information, The Business of Vidara, Management and Other Information of New Horizon, Executive Compensation, and Certain Relationships and Related Party Transactions ;

the audited combined financial statements of Vidara Therapeutics International Limited and subsidiaries and Vidara Therapeutics, Inc., including the combined balance sheets as of December 31, 2013 and 2012, and the related audited combined statements of operations, changes in shareholders equity and cash flows for each of the years in the two-year period ended December 31, 2013, and the notes related thereto, and the report of Habif, Arogeti & Wynne, independent registered public

accounting firm, included on pages F-1 to F-23;

the unaudited interim combined financial statements of Vidara Therapeutics International Limited and subsidiaries and Vidara Therapeutics, Inc., including the unaudited interim combined balance sheets as of March 31, 2014 and the unaudited interim combined statements of operations and cash flows for the three months ended March 31, 2014 and 2013 and the notes related thereto, including on pages F-24 to F-30; and

the audited statements of revenues and direct expenses of the ACTIMMUNE Product Line of InterMune, Inc. for the year ended December 31, 2011 and the period from January 1, 2012 to June 18, 2012 and the report of Ernst & Young LLP, an independent registered public accounting firm, included on pages F-31 to F-36; and

our Current Report on Form 8-K filed with the SEC on September 19, 2014 (which evidences the registration of our ordinary shares under Section 12(b) of the Exchange Act and includes therein a description of our ordinary shares).

Table of Contents

Any information in any of the foregoing documents will automatically be deemed to be modified or superseded to the extent that information in this prospectus or in a later filed document that is incorporated or deemed to be incorporated herein by reference modifies or replaces such information.

We also incorporate by reference any future filings (other than current reports or portions of 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) made with the SEC by us pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act until we file a post-effective amendment that indicates the termination of the offering of the ordinary shares made by this prospectus. Information in such future filings updates and supplements the information provided in this prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document that we or HPI 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 furnish without charge to each person, including any beneficial owner, to whom a prospectus is delivered, upon written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents. Any such request may be made by writing or telephoning us at the following address or phone number:

Horizon Pharma plc

Attn: Investor Relations

c/o Horizon Pharma Holdings USA, Inc.

520 Lake Cook Road, Suite 520

Deerfield, IL 60015

Telephone: +1 (224) 383-3000

Table of Contents