

Horizon Pharma plc
Form 424B5
April 13, 2015
Table of Contents

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-198852

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 we are not soliciting offers to buy these securities, in any state or other jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED APRIL 13, 2015

PRELIMINARY PROSPECTUS SUPPLEMENT

(To Prospectus dated September 19, 2014)

12,000,000 Shares

Horizon Pharma plc

Ordinary Shares

\$ per share

We are offering 12,000,000 of our ordinary shares, nominal value \$0.0001 per share.

We intend to use a portion of the net proceeds of this offering, together with the net proceeds of the Debt Financings (as defined herein), to finance the Acquisition (as defined herein), refinance certain outstanding debt and to pay any prepayment premiums, related fees and expenses. Subsequent to this offering, we expect to conduct an unregistered offering of Senior Notes (as defined herein) and to enter into a new Term

Edgar Filing: Horizon Pharma plc - Form 424B5

Facility (as defined herein). This offering is not contingent on the completion of the Debt Financings, and the Debt Financings are not contingent on the completion of this offering. This offering is not contingent upon the completion of the Acquisition, which, if completed, will occur subsequent to the closing of this offering. This prospectus supplement is not an offer to sell or a solicitation of an offer to buy any debt being sold or placed in the Debt Financings. For more information, see Prospectus Supplement Summary About the Debt Financings in this prospectus supplement.

We have granted the underwriters the option to purchase up to an additional 1,800,000 of our ordinary shares to cover over-allotments, if any.

Our ordinary shares are listed on The NASDAQ Global Select Market under the symbol HZNP. The last reported sale price of our ordinary shares on The NASDAQ Global Select Market on April 10, 2015 was \$28.48 per share.

Investing in our ordinary shares involves risks. See Risk Factors beginning on page S-18.

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

| | Per share | Total |
|---------------------------------------|-----------|-------|
| Public Offering Price | \$ | \$ |
| Underwriting Discounts(1) | \$ | \$ |
| Proceeds to Horizon (before expenses) | \$ | \$ |

(1) We have agreed to reimburse the underwriters for certain expenses. See Underwriting.

The underwriters expect to deliver the ordinary shares to purchasers on or about _____, 2015 through the book-entry facilities of The Depository Trust Company.

Joint Book-Running Managers

**Citigroup
Cowen and Company**

**Jefferies
Morgan Stanley**

, 2015

Table of Contents

TABLE OF CONTENTS

Prospectus Supplement

| | Page |
|---|-------------|
| <u>About This Prospectus Supplement</u> | S-1 |
| <u>Market and Industry Data</u> | S-2 |
| <u>Non-GAAP Financial Measures</u> | S-3 |
| <u>Prospectus Supplement Summary</u> | S-4 |
| <u>Risk Factors</u> | S-18 |
| <u>Special Note Regarding Forward-Looking Statements</u> | S-76 |
| <u>Use of Proceeds</u> | S-77 |
| <u>Capitalization</u> | S-78 |
| <u>Dilution</u> | S-80 |
| <u>Price Range of Ordinary Shares and Dividend Policy</u> | S-82 |
| <u>Unaudited Pro Forma Combined Financial Information</u> | S-83 |
| <u>Material Tax Considerations</u> | S-98 |
| <u>Underwriting</u> | S-108 |
| <u>Legal Matters</u> | S-113 |
| <u>Experts</u> | S-113 |
| <u>Where You Can Find More Information</u> | S-113 |

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, we are offering to sell our ordinary shares using this prospectus supplement and the accompanying prospectus.

This prospectus supplement describes the terms of the offering 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 any free writing prospectus that we have authorized for use in connection with this offering in their entirety before making an investment decision.

We 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.

Table of Contents

MARKET AND INDUSTRY DATA

We obtained the industry, market and competitive position data in this prospectus supplement and the accompanying prospectus from our own internal estimates and research as well as from industry and general publications and research surveys and studies conducted by third parties. While we believe that each of these studies and publications is reliable, we have not independently verified market and industry data from third-party sources. In addition, while we believe our internal company research is reliable and the market definitions we use are appropriate, neither our internal research nor these definitions have been verified by any independent source.

S-2

Table of Contents

NON-GAAP FINANCIAL MEASURES

This prospectus supplement contains certain financial measures such as EBITDA, or earnings before interest, taxes, depreciation and amortization, Adjusted EBITDA, Adjusted EBITDA, Net of Royalties and Supplemental Adjusted EBITDA that include adjustments to GAAP figures. These adjustments to GAAP exclude the bargain purchase gain related to the acquisition of Vidara, acquisition transaction related expenses, loss on induced debt conversion, loss on debt extinguishment, secondary offering expenses as well as non-cash items such as stock compensation, depreciation and amortization, royalty accretion, non-cash interest expense, and other non-cash adjustments such as the increase or decrease in the fair value of the embedded derivative associated with the Company's convertible senior notes. Certain other special items or substantive events may also be included in the non-GAAP adjustments periodically when their magnitude is significant within the periods incurred. We believe that these non-GAAP financial measures, when considered together with the GAAP figures, can enhance an overall understanding of our financial performance. The non-GAAP financial measures are included with the intent of providing you with a more complete understanding of our operational results and trends. In addition, these non-GAAP financial measures are among the indicators our management uses for planning and forecasting purposes and measuring our performance. These non-GAAP financial measures should be considered in addition to, and not as a substitute for, or superior to, financial measures calculated in accordance with GAAP. The non-GAAP financial measures we use may be calculated differently from, and therefore may not be comparable to, non-GAAP financial measures used by other companies.

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 included and 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 or in-licensing 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), PENNSAID[®] (diclofenac sodium topical solution) 2% w/w, RAYOS[®] (prednisone) delayed-release tablets and VIMOVO[®] (naproxen/esomeprazole magnesium). We developed DUEXIS and RAYOS, acquired the U.S. rights to VIMOVO from AstraZeneca AB, or AstraZeneca, in November 2013, acquired the U.S. rights to ACTIMMUNE as a result of the merger with Vidara Therapeutics International plc in September 2014, or the Merger, and acquired the U.S. rights to PENNSAID 2% from Nuvo Research Inc., or Nuvo, in October 2014. We market our products in the United States through our field sales force of approximately 375 representatives. Our strategy is to utilize the commercial strength and infrastructure we have established in creating a fully-integrated U.S.-focused specialty biopharmaceutical company to continue the successful commercialization of our existing product portfolio while expanding and leveraging these capabilities further through the acquisition of biopharmaceutical products and companies.

On April 23, 2011, the U.S. Food and Drug Administration, or FDA, approved DUEXIS, a proprietary 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. We began marketing DUEXIS to physicians in December 2011.

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 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. We have been focusing our promotion of RAYOS in the United States on rheumatology indications, including RA and PMR, and currently are broadening the marketing efforts for RAYOS into multiple other indications. We began marketing 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, excluding Japan and Canada, 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 nonsteroidal anti-inflammatory drugs, or NSAIDs, in the United States. VIMOVO 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,

Table of Contents

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. We announced the availability of Horizon-labeled VIMOVO on January 2, 2014, at which time we also began marketing VIMOVO with our primary care sales force.

On September 19, 2014, as a result of the 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. We also plan to study ACTIMMUNE for potential additional indications, and the FDA has agreed to the primary endpoint for a Phase 3 study that will evaluate ACTIMMUNE in the treatment of Friedreich's Ataxia, or FA. We anticipate the Phase 3 clinical study related to FA will begin enrolling patients in the second quarter of 2015. In April 2015, the FDA granted Fast Track designation for ACTIMMUNE in FA.

On October 17, 2014, we acquired the U.S. rights to PENNSAID 2% from Nuvo for \$45.0 million in cash. 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 exclusive eight-year supply agreement with Nuvo under which Nuvo will supply us product. We began marketing PENNSAID 2% in January 2015. In connection with our PENNSAID 2% acquisition, we expanded our primary care sales force by 75 additional representatives. Our primary care representatives are now marketing DUEXIS, PENNSAID 2% and VIMOVO.

Another key part of our primary care commercial strategy is to encourage physicians to have their patients fill prescriptions through our Prescriptions-Made-Easy, or PME, specialty pharmacy program, which enables uninsured or commercially insured patients to have enhanced access to our products by providing financial assistance to reduce eligible patients' out of pocket costs for prescriptions filled via a PME-participating mail order pharmacy. Through PME, prescriptions for our products are filled by designated mail order specialty pharmacies, with the products shipped directly to the patient. Because our products when dispensed through the PME program do not require involvement of a traditional retail pharmacy, prescriptions filled through our PME program are less likely to be subject to the efforts of traditional pharmacies to switch a physician's intended 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 less expensive generic or over the counter brands instead of branded products increases. We believe the continued expansion of our PME program will allow us to largely mitigate the potential impact of our products being placed on the exclusion lists implemented by PBMs.

Recent Developments

Weekly prescriptions of our primary care products grew significantly during the first quarter of 2015. Despite being placed on certain formulary exclusion lists beginning on January 1, 2015, during the first 12 weeks of 2015, DUEXIS weekly prescriptions rose 42% and VIMOVO weekly prescriptions rose 26%. Compared to the first 12 weeks of 2014, DUEXIS weekly prescriptions rose 55% and VIMOVO weekly prescriptions rose 9%. With respect to PENNSAID 2%, during the first 12 weeks of 2015, weekly prescriptions grew each week, representing a 353% increase during the period. We also continued to increase PME activation for our primary care products in the first quarter of 2015, with the percentage of prescriptions filled through PME rising to 58%, 44% and 56% for DUEXIS, VIMOVO and PENNSAID 2%, respectively, for the week ended March 27, 2015.

We estimate that our cash and cash equivalents as of March 31, 2015 were approximately \$544 million. This amount is preliminary and is subject to completion of financial closing procedures. As a result, this amount may differ from the amount that will be reflected in our consolidated financial statements as of March 31, 2015. The

Table of Contents

preliminary financial data included in this preliminary prospectus supplement has been prepared by, and is the responsibility of our management. PricewaterhouseCoopers LLP has not audited, reviewed, compiled or performed any procedures with respect to the preliminary financial data. Accordingly, PricewaterhouseCoopers LLP does not express an opinion or any other form of assurance with respect thereto.

The estimated balance of cash and cash equivalents as of March 31, 2015 reflects cash outflows during the first quarter of 2015 resulting from our transition away from contracting with pharmacy benefit managers, or PBMs, increases in accounts receivable and normal seasonal outflows during the quarter. Prior to 2015, we would incur significant payment obligations to PBMs in the form of rebates, and these rebates were historically paid in arrears up to four months after incurrence. In connection with certain of our products being placed on PBM exclusion lists beginning on January 1, 2015, we no longer incur PBM rebates on these products. However, we are incurring increased copay assistance costs as the result of more patients who are on healthcare plans that no longer include certain of our products on their formularies. Under our copay assistance arrangements, we are generally obligated to pay copay amounts in advance or within weeks of being incurred. As a result of the transition from incurring PBM rebates to having additional patients receiving copay assistance and the relative timing of the related payments, in the first quarter of 2015, we were still experiencing normal cash outflows from rebate obligations that had accrued in the prior year, but also had an increase in cash outflows for copay assistance payments due to the short payment cycle for those obligations. We also experienced an increase in accounts receivable during the first quarter of 2015 due to the introduction of PENNSAID 2% and price increases we implemented for DUEXIS and VIMIVO, each of which occurred on January 1, 2015, and our normal collection cycle. Our estimated cash and cash equivalents balance as of March 31, 2015 was also impacted by the payment of annual incentive bonuses, which typically occurs during the first quarter of each year. We believe that the significant cash outflow in the first quarter of 2015 due to the transition from PBM rebates to copay assistance payments was a one-time event. We also do not expect to experience the same or similar increases in accounts receivable resulting from product introductions and price increases for the remainder of 2015.

The Hyperion Acquisition

On March 29, 2015, our indirect wholly-owned subsidiary, Ghria Acquisition Inc., or Purchaser, a Delaware corporation and a wholly owned subsidiary of Horizon Pharma, Inc., or HPI, and Hyperion Therapeutics, Inc., a Delaware corporation, or Hyperion, entered into a definitive Agreement and Plan of Merger, or the Merger Agreement, pursuant to which HPI, through Purchaser, has commenced an offer to acquire all of the outstanding shares of Hyperion's common stock, par value \$0.0001 per share, for \$46.00 per share in cash, without interest, subject to any required withholding of taxes, or the Offer Price. We refer to the proposed acquisition as the Acquisition.

We intend to use a portion of the net proceeds of this offering, together with the net proceeds of the proposed Debt Financings described below, to finance the Acquisition and to pay related fees and expenses. In the event that we do not consummate the Acquisition, we expect to use the net proceeds from this offering for future acquisitions and general corporate purposes. This offering is not contingent upon the completion of the Acquisition, which, if completed, will occur subsequent to the closing of this offering. We cannot assure you that the Acquisition will be completed or, if completed, that it will be completed within the time period or on the terms and with the anticipated benefits described in this prospectus supplement.

About Hyperion

Hyperion is a commercial biopharmaceutical company focused on the development and commercialization of novel therapeutics to treat orphan diseases. Hyperion's products, RAVICTAM (glycerol phenylbutyrate) Oral liquid, BUPHENYL® and AMMONAPS® (sodium phenylbutyrate) Tablets and Powder, are designed to lower ammonia in the blood. Ammonia is produced in the intestine after a person eats protein and is normally

Table of Contents

detoxified in the liver by conversion to urea. Elevated levels of ammonia are potentially toxic and can lead to severe medical complications which may include death. Hyperion has developed RAVICTI, which it launched during the first quarter of 2013, to treat most urea cycle disorders, or UCD, including seven of the eight and the most prevalent UCD subtypes. UCD is a disease in which blood ammonia is elevated. UCD are inherited rare genetic diseases caused by a deficiency of one or more enzymes or transporters that constitute the urea cycle, which in a healthy individual removes ammonia through its conversion to urea. Hyperion estimates there are approximately 2,100 cases of UCD in the United States of which approximately 1,100 have been diagnosed. However, we estimate that only about 680 patients are currently treated with medication approved by the FDA.

On February 1, 2013, the FDA granted approval of RAVICTI for chronic management of UCD in adult and pediatric patients greater than two years of age who cannot be managed by dietary protein restriction and/or amino acid supplementation alone. Limitations of use include treatment of patients with acute hyperammonemia, or HA, crises for whom urgent intervention is typically necessary, patients with N-acetylglutamate synthetase, or NAGS, deficiency for whom the safety and efficacy of RAVICTI has not been established, and UCD patients under two months of age for whom RAVICTI is contraindicated due to uncertainty as to whether newborns, who may have immature pancreatic function, can effectively digest RAVICTI.

In May 2013, Hyperion acquired BUPHENYL, an FDA-approved therapy for treatment of three of the most prevalent UCD subtypes, from Ucyclid Pharma Inc., or Ucyclid, a subsidiary of Valeant Pharmaceuticals International, Inc., or Valeant. In Europe and the Middle East, BUPHENYL is sold under the brand name AMMONAPS®. The active pharmaceutical ingredient in BUPHENYL and AMMONAPS is sodium phenylbutyrate, or NaPBA. References to BUPHENYL in this prospectus supplement include AMMONAPS when referring to the product in the Middle East and Europe. Subsequent to the acquisition, Hyperion began selling BUPHENYL within the United States to patients who have not transitioned to RAVICTI. In addition, Hyperion sells BUPHENYL in Canada based on Special Access Requests from Health Canada and through its distributors in other select regions outside the United States. References to NaPBA in this prospectus supplement include the generically available tablet and powdered forms of the drug, as well as our branded products in both powdered and tablet forms.

Although the price of BUPHENYL per gram is approximately one fifth that of RAVICTI and the prices for both therapies vary among patients because doses are individualized based on a patient's weight and disease severity, most patients cannot afford to pay for either medication themselves. Hyperion has engaged a dedicated team at a third party call center, which serves as an integrated resource for prescription intake and distribution, reimbursement adjudication, patient financial support, and ongoing compliance support for its UCD patients. Together with distribution via two specialty pharmacies, Hyperion believes these services provide important support to UCD patients and their physicians, and help them achieve more favorable outcomes in managing their disease. As part of Hyperion's ongoing commitment to the patient community, Hyperion provides its UCD products at no cost to patients as it helps them establish insurance coverage for its UCD products by donating to an independent foundation with an established track record of enabling patients to access medications affordably.

RAVICTI was granted orphan drug exclusivity in the United States for the maintenance treatment of patients with UCD shortly after its FDA approval in 2013. This exclusivity extends through February 1, 2020. RAVICTI has also received orphan drug designation in the European Union, or EU, although the right to marketing exclusivity cannot be determined until Hyperion is authorized to market it in the EU. In March 2013, U.S. Patent No. 8,404,215 entitled *Methods of Therapeutic Monitoring of Nitrogen Scavenging Drugs* issued from U.S. Patent Appl. No. 13/417,137 with claims directed to methods of optimizing the dosage of nitrogen scavenging drugs based on target fasting ammonia levels. This patent will expire in March 2032, and is currently listed in the FDA publication *Approved Drug Products with Therapeutic Equivalence Evaluations*, known as the Orange Book. In February 2014, U.S. Patent 8,642,012 entitled *Methods of Treatment Using Ammonia Scavenging Drugs* issued from U.S. Patent Appl. No. 12/350,111 with claims directed to methods of treating

Table of Contents

patients with UCD using phenylacetic acid, or PAA, prodrugs based in part on target urinary phenylacetylglutamine, or PAGN, levels. This patent will expire in September 2030 with Patent Term Extension, or PTE, and is listed in the Orange Book.

In March 2012, Hyperion entered into an amended and restated collaboration agreement, or the restated collaboration agreement, with Ucylyd pursuant to which Hyperion obtained an option to purchase all of Ucylyd's worldwide rights in BUPHENYL and AMMONUL, subject to Ucylyd's right to retain AMMONUL for an upfront payment of \$32.0 million, plus subsequent milestone and royalty payments. Hyperion exercised this option on April 29, 2013 and Ucylyd elected to retain AMMONUL, resulting in a net payment from Ucylyd to Hyperion of \$11.0 million upon close of the transaction. This net payment reflected the \$32.0 million purchase price to retain AMMONUL due to Hyperion and the \$19.0 million purchase price for BUPHENYL due to Ucylyd, less costs of approximately \$2.0 million for inventory Hyperion purchased from Ucylyd.

About the Debt Financings

In connection with the Merger Agreement, HPI entered into a commitment letter, or the Debt Commitment Letter, with Citigroup Global Capital Markets Inc., or Citi, and Jefferies Finance LLC, or Jefferies, on March 29, 2015, pursuant to which Citi and Jefferies have committed to provide up to \$900.0 million of secured term loans pursuant to a term loan facility, the proceeds of which, in addition to a portion of HPI's existing cash, would be available to (i) refinance the loans under our existing credit facility and certain outstanding debt of Hyperion, (ii) pay the Offer Price, and (iii) pay any prepayment premiums, fees and expenses in connection with any of the foregoing. The commitment to provide the term loans is subject to certain conditions, including the negotiation of definitive documentation for the term loans and other customary closing conditions consistent with the Merger Agreement. We will pay customary fees and expenses in connection with borrowings pursuant to the Debt Commitment Letter.

In lieu of borrowing pursuant to the Debt Commitment Letter, and subsequent to this offering, we or one or more of our subsidiaries expect to borrow up to an aggregate of approximately \$800.0 million pursuant to an offering of senior notes, or the Senior Notes, and the arrangement and syndication of a new senior unsecured term loan facility, or the Term Facility. The proceeds of the Senior Notes and Term Facility would be used to (i) refinance the loans under our existing credit facility and certain outstanding debt of Hyperion, (ii) pay the Offer Price, and (iii) pay any prepayment premiums, fees and expenses in connection with any of the foregoing. We refer to any debt financing that we expect to incur to fund the Acquisition and to pay related fees and expenses as the Debt Financings. **The foregoing description and any other information regarding the Debt Financings is included herein solely for informational purposes. The Debt Financings are not part of the offering to which this prospectus supplement relates. The Senior Notes will be offered only to qualified institutional buyers pursuant to Rule 144A under the Securities Act of 1933, as amended, or the Securities Act, and to persons outside the United States pursuant to Regulation S under the Securities Act. This prospectus supplement is not an offer to sell or a solicitation of an offer to buy any securities in such Debt Financings.**

The amount and terms and conditions of the Debt Financings will be subject to market conditions. There can be no assurance that we will be able to complete any Debt Financings on terms and conditions acceptable to us. This offering is not contingent on the consummation of the Debt Financings, and the Debt Financings are not contingent upon completion of this offering. The closing of the Debt Financings will be conditioned on the simultaneous closing of the Acquisition.

Completion of this offering is not contingent upon the closing of the Debt Financings or the completion of the Acquisition.

Table of Contents

We cannot assure you that we will complete the Acquisition, the Debt Financings or any of the other financing transactions on the terms contemplated by this prospectus supplement or at all.

After the closing of the Acquisition, if completed, we may also replenish our cash or repay any borrowings made in connection with the Acquisition with the proceeds of additional financings.

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 re-registered as a public limited company, Vidara Therapeutics International plc, and became the parent company of and successor to Horizon Pharma, Inc., or HPI, and we were re-named Horizon Pharma plc. Our principal executive offices are located at Connaught House, 1st Floor, 1 Burlington Road, Dublin 4, Ireland. Our telephone number is 011-353-1-772-2100. 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.

Horizon Pharma, Horizon Therapeutics, a stylized letter H, ACTIMMUNE, DUEXIS, LODOTRA, PENNSAID 2%, RAYOS, and are registered trademarks in the United States and/or certain other countries. RAVICTI and BUPHENYL are trademarks of Hyperion. This prospectus supplement and the accompanying prospectus also include references to trademarks and service marks of other entities and those trademarks and service marks are the property of their respective owners.

Table of Contents

The Offering

| | |
|---|--|
| Issuer | Horizon Pharma Public Limited Company |
| Ordinary shares offered by us | 12,000,000 shares |
| Option to purchase additional shares granted by us | 1,800,000 shares |
| Ordinary shares outstanding immediately after this offering | 145,287,015 shares |
| Use of proceeds | We estimate that the net proceeds to us from this offering, after deducting the underwriting discounts and estimated offering expenses payable by us, will be approximately \$325.4 million (or approximately \$374.3 million if the underwriters exercise their option to purchase additional ordinary shares in full), in each case assuming a public offering price of \$28.48 per share, the last reported sale price per ordinary share on The NASDAQ Global Select Market on April 10, 2015. We intend to use the net proceeds from this offering to fund a portion of the Acquisition and the remainder to fund additional acquisitions or investments in businesses, products and product candidates that are complementary to our own, although we have no present commitments or agreements to do so other than with respect to the Acquisition, and for general corporate purposes. If the Acquisition is not consummated, we expect to use the net proceeds from this offering for future acquisitions and general corporate purposes. See Use of Proceeds . |
| Risk factors | Investing in our ordinary shares involves risks. See Risk Factors beginning on page S-18, and in the documents which are incorporated by reference in this prospectus supplement and the accompanying prospectus. |
| NASDAQ Global Select Market symbol | HZNP |

Outstanding Shares

The number of ordinary shares outstanding immediately after this offering referenced above is as of March 31, 2015, and excludes, as of that date:

11,523,627 ordinary shares issuable upon the exercise of outstanding options, having a weighted average exercise price of \$14.35 per share;

Edgar Filing: Horizon Pharma plc - Form 424B5

3,163,702 ordinary shares issuable upon the settlement of outstanding restricted stock units;

2,571,000 ordinary shares issuable upon the settlement of outstanding performance stock units;

3,802,029 ordinary shares issuable upon the exercise of outstanding warrants, having a weighted average exercise price of \$5.42 per share;

S-10

Table of Contents

5,301,912 ordinary shares, all or a portion of which may be issued upon the conversion of our outstanding convertible senior notes;

13,959,160 ordinary shares, all or a portion of which may be issued upon the conversion of our outstanding exchangeable notes;

9,929,336 ordinary shares reserved for future issuance under our 2014 Employee Share Purchase Plan;

3,771,738 ordinary shares reserved for future issuance under our 2014 Equity Incentive Plan; and

2,386,242 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 1,800,000 ordinary shares.

Table of Contents

Summary Historical and Pro Forma Consolidated Financial Data

The following table sets forth summary historical and pro forma consolidated financial data of Horizon as of and for the periods indicated. We have derived the summary historical consolidated financial data of Horizon for the years ended December 31, 2012, 2013 and 2014 and as of December 31, 2013 and 2014, from Horizon's audited consolidated financial statements for such periods which are incorporated by reference into this prospectus supplement. The summary historical consolidated financial data as of December 31, 2012 have been derived from Horizon's consolidated financial statements which are not incorporated by reference into in this prospectus supplement.

The unaudited pro forma condensed consolidated financial information presented illustrates the estimated effects of the following transactions, or collectively, the Transactions: (i) this offering of 12 million ordinary shares, or the Offering, (ii) the March 2015 private placement of the 2022 notes, (iii) the acquisition of Hyperion by the Company pursuant to a tender offer for all outstanding shares of Hyperion's common stock for the Offer Price, which was announced on March 30, 2015, or the Acquisition, (iv) the assumed funding of \$800 million principal amount of the term loans under a new senior secured term loan facility, or the Senior Secured Term Loans, the proceeds of which would be used, in addition to a portion of Horizon's existing cash and a portion of the proceeds of the Offering, to repay \$300 million principal amount of outstanding term loans under Horizon's existing senior secured credit facility, or the Existing Credit Facility, and certain existing debt of Hyperion, fund a portion of the Offer Price and pay any prepayment premium, fees and expenses in connection with the foregoing, (v) the Merger, and (vi) \$300 million of loans borrowed under the Existing Credit Facility in connection with the Merger.

The unaudited pro forma condensed consolidated statement of operations data of Horizon for the year ended December 31, 2014 give effect to the Transactions as if they had occurred on January 1, 2014. The unaudited pro forma condensed consolidated balance sheet data of Horizon give effect to the Transactions as if they had occurred on December 31, 2014. The pro forma adjustments are based upon available information and certain assumptions that Horizon's management believes are reasonable. The summary unaudited pro forma condensed consolidated financial data of Horizon are for informational purposes only and do not purport to represent what our actual results of operations or financial position actually would have been had the Hyperion acquisition and other Transactions occurred at any prior date, nor do such data purport to project the results of operations for any future period.

The summary historical and pro forma consolidated financial data presented below should be read in conjunction with Use of Proceeds, Capitalization, Unaudited Pro Forma Combined Financial Information, Selected Financial Data, Management's Discussion and Analysis of Financial Condition and Results of Operations and our consolidated financial statements and the related notes thereto included or incorporated by reference in this prospectus supplement.

Table of Contents

The Hyperion acquisition will be accounted for as a business combination using the acquisition method of accounting. The summary unaudited pro forma financial data presented is based on preliminary estimates of the fair value of tangible and intangible assets to be acquired and liabilities assumed, available information and assumptions and will be revised as additional information becomes available. The actual adjustments to our financial statements upon the closing of the Hyperion acquisition and other Transactions will depend on a number of factors, including additional information available and our net assets on the closing of the Hyperion acquisition. The result of the final purchase price allocation could be materially different from the preliminary allocation set forth in this prospectus supplement. See Unaudited Pro Forma Combined Financial Information.

| (in thousands) | Year Ended December 31, | | | Pro Forma |
|---|-------------------------|--------------|--------------|---|
| | 2012 | 2013 | 2014 | Year Ended December 31, 2014 (unaudited) |
| Condensed Consolidated Statement of Operations Data: | | | | |
| Net sales | \$ 18,844 | \$ 74,016 | \$ 296,955 | \$ 461,104 |
| Cost of goods sold | 11,875 | 14,625 | 78,753 | 247,523 |
| Gross profit (loss) | 6,969 | 59,391 | 218,202 | 213,581 |
| Operating expenses: | | | | |
| Research and development(1) | 16,837 | 10,084 | 17,460 | 40,560 |
| Sales and marketing(1) | 49,561 | 68,595 | 120,276 | 146,707 |
| General and administrative(1) | 19,444 | 23,566 | 88,957 | 79,659 |
| Goodwill impairment(2) | | | | 30,201 |
| Total operating expenses | 85,842 | 102,245 | 226,693 | 297,127 |
| Loss from operations | (78,873) | (42,854) | (8,491) | (83,546) |
| Other (expense) income, net: | | | | |
| Interest expense, net | (11,552) | (12,774) | (23,826) | (98,199) |
| Loss on derivative fair value | | (69,300) | (214,995) | (214,995) |
| Loss on induced conversion and debt extinguishment | (2,973) | (26,404) | (29,390) | (29,390) |
| Bargain purchase gain | | | 22,171 | |
| Foreign exchange (loss) gain | 489 | 1,206 | (3,905) | (3,894) |
| Other expense | (56) | | (11,251) | (4,026) |
| Loss before benefit for income taxes | (92,965) | (150,126) | (269,687) | (434,050) |
| Benefit for income taxes | (5,171) | (1,121) | (6,084) | (78,681) |
| Net loss | \$ (87,794) | \$ (149,005) | \$ (263,603) | \$ (355,369) |

| (in thousands) | Year Ended December 31, | | | Pro Forma |
|--|-------------------------|-----------|------------|--|
| | 2012 | 2013 | 2014 | Year Ended December 31, 2014 (unaudited) |
| Selected Condensed Consolidated Balance Sheet Data (as of the end of the period): | | | | |
| Cash and cash equivalents | \$ 104,087 | \$ 80,480 | \$ 218,807 | \$ 379,103 |

Edgar Filing: Horizon Pharma plc - Form 424B5

| | | | | |
|--------------------------------------|-----------|-----------|-----------|-----------|
| Working capital(3) | 79,983 | 67,455 | 106,833 | 277,662 |
| Total assets | 193,984 | 252,596 | 1,134,624 | 2,652,966 |
| Total Debt, net of debt discount | 48,801 | 110,762 | 345,503 | 1,109,254 |
| Accumulated deficit | (308,111) | (457,116) | (720,719) | (816,877) |
| Total shareholders' equity (deficit) | 105,978 | (49,082) | 540,204 | 888,507 |

S-13

Table of Contents

| (in thousands) | Year Ended December 31, | | | Pro Forma |
|--------------------------------------|-------------------------|--------------|--------------|---|
| | 2012 | 2013 | 2014 | Year Ended December 31, 2014 (unaudited) |
| Other Financial Data: | | | | |
| EBITDA(4) | \$ (75,875) | \$ (128,972) | \$ (192,412) | \$ (135,657) |
| Adjusted EBITDA(4) | (68,241) | (28,254) | 105,352 | 173,620 |
| Adjusted EBITDA, Net of Royalties(4) | (68,241) | (28,254) | 87,088 | 155,356 |
| Supplemental Adjusted EBITDA(4) | | | | 196,915 |

- (1) Includes stock-based compensation expenses as follows:

| | Year Ended December 31, | | |
|---|-------------------------|-----------------|------------------|
| | 2012 | 2013 | 2014 |
| Share-based compensation expense: | | | |
| Research and development | \$ 1,186 | \$ 1,054 | \$ 1,515 |
| Sales and marketing | 1,090 | 1,465 | 4,174 |
| General and administrative | 2,385 | 2,495 | 7,509 |
| Total share-based compensation expense | \$ 4,661 | \$ 5,014 | \$ 13,198 |

- (2) The impairment of goodwill of \$30.2 million relates to the impairment loss recognized by Hyperion with regards to its acquisition of Andromeda Biotech, Ltd. in 2014.
- (3) Working capital is defined as our current assets minus our current liabilities.
- (4) We have presented earnings before interest, taxes, depreciations and amortization, or, EBITDA (which is defined as net loss before (i) interest expense, net, (ii) income taxes, (iii) depreciation and (iv) amortization), Adjusted EBITDA (which is defined as EBITDA adjusted for the other items described in the footnotes below), Adjusted EBITDA, Net of Royalties (which is defined as Adjusted EBITDA further adjusted for royalties for the period that are not otherwise included in the statement of operations for the period) and Supplemental Adjusted EBITDA (which is defined as Adjusted EBITDA, Net of Royalties further adjusted for certain cost reductions and savings, impacting our results following the consummation of the Transactions described in the footnotes below), which are considered non-GAAP financial measures. EBITDA, Adjusted EBITDA, Adjusted EBITDA, Net of Royalties and Supplemental Adjusted EBITDA are included in this prospectus supplement as supplemental measures of our liquidity and performance and because we believe such measures are frequently used by securities analysts, investors and other interested parties in the evaluation of companies in our industry.

EBITDA, Adjusted EBITDA, Adjusted EBITDA, Net of Royalties and Supplemental Adjusted EBITDA are not measures of our liquidity or financial performance under GAAP and should not be considered in isolation as alternatives to net loss, operating loss or any other performance measures derived in accordance with GAAP, or as an alternative to cash flow from operating activities as a measure of our liquidity. The use of EBITDA, Adjusted EBITDA, Adjusted EBITDA, Net of Royalties and Supplemental Adjusted EBITDA, instead of net loss or an analysis of our results as reported under GAAP has limitations as an analytical tool, including the following:

EBITDA, Adjusted EBITDA, Adjusted EBITDA, Net of Royalties and Supplemental Adjusted EBITDA do not necessarily reflect changes in, or cash requirements for, our working capital needs;

EBITDA, Adjusted EBITDA, Adjusted EBITDA, Net of Royalties and Supplemental Adjusted EBITDA do not reflect our interest expense, or the cash requirements necessary to service interest or principal payments, on our debt;

Edgar Filing: Horizon Pharma plc - Form 424B5

EBITDA, Adjusted EBITDA, Adjusted EBITDA, Net of Royalties and Supplemental Adjusted EBITDA do not reflect our tax expense or the cash requirements to pay our taxes;

S-14

Table of Contents

although depreciation and amortization are non-cash charges, the assets being depreciated and amortized will often have to be replaced in the future, and EBITDA, Adjusted EBITDA, Adjusted EBITDA, Net of Royalties and Supplemental Adjusted EBITDA do not reflect any cash requirements for such replacements;

EBITDA, Adjusted EBITDA, Adjusted EBITDA, Net of Royalties and Supplemental Adjusted EBITDA do not reflect historical cash expenditures or future cash requirements for capital expenditures or contractual commitments; and

Adjusted EBITDA includes adjustments that represented a cash expense or that represented a non-cash charge that may relate to a future cash expense, and some of these expenses are of a type that we expect to incur in the future, although we cannot predict the amount of any such future charge.

Management compensates for these limitations by relying primarily on our GAAP results and by using EBITDA, Adjusted EBITDA, Adjusted EBITDA, Net of Royalties and Supplemental Adjusted EBITDA only supplementally. Other companies in our industry may calculate these measures differently than we do, limiting their usefulness as a comparative measure. See Non-GAAP Financial Measures.

The following is a reconciliation of net loss to EBITDA, Adjusted EBITDA, Adjusted EBITDA, Net of Royalties and Supplemental Adjusted EBITDA. Adjusted EBITDA, Adjusted EBITDA, Net of Royalties and Supplemental Adjusted EBITDA for the Pro Forma Year Ended December 31, 2014 column has been adjusted to give effect to the Transactions.

| (in thousands) | Year Ended December 31, | | | Pro Forma |
|--|-------------------------|--------------|--------------|------------------------------|
| | 2012 | 2013 | 2014 | Year Ended December 31, 2014 |
| Net loss | \$ (87,794) | \$ (149,005) | \$ (263,603) | \$ (355,369) |
| Depreciation(a) | 788 | 1,174 | 1,702 | 2,198 |
| Amortization and accretion: | | | | |
| Intangible amortization expense(b) | 4,750 | 8,136 | 32,306 | 189,620 |
| Accretion of royalty liabilities(c) | | | 9,020 | 9,020 |
| Amortization of deferred revenue(d) | | (930) | (644) | (644) |
| Amortization of inventory step-up adjustment(e) | | | 11,065 | |
| Interest expense, net (including amortization of debt discount and deferred financing costs) | 11,552 | 12,774 | 23,826 | 98,199 |
| Benefit for income taxes | (5,171) | (1,121) | (6,084) | (78,681) |
| EBITDA | \$ (75,875) | \$ (128,972) | \$ (192,412) | \$ (135,657) |
| Remeasurement of VIMOVO and ACTIMMUNE royalties(f) | | | 10,660 | 10,660 |
| Bargain purchase gain(g) | | | (22,171) | |
| Goodwill impairment(h) | | | | 30,201 |
| Loss on derivative revaluation(i) | | 69,300 | 214,995 | 214,995 |
| Vidara acquisition costs(j) | | | 48,427 | |
| PENNSAID acquisition costs(k) | | | 408 | 408 |
| Loss on induced debt conversion / debt extinguishment(l) | 2,973 | 26,404 | 29,390 | 29,390 |
| Secondary offering costs(m) | | | 2,857 | 2,857 |
| Share-based compensation(n) | 4,661 | 5,014 | 13,198 | 20,766 |
| Adjusted EBITDA | \$ (68,241) | \$ (28,254) | \$ 105,352 | \$ 173,620 |
| VIMOVO and ACTIMMUNE royalties for the period | | | (18,264) | (18,264) |

Edgar Filing: Horizon Pharma plc - Form 424B5

| | | | | |
|--|-------------|-------------|-----------|------------|
| Adjusted EBITDA, Net of Royalties | \$ (68,241) | \$ (28,254) | \$ 87,088 | \$ 155,356 |
| Estimated cost reductions and savings(o) | | | | \$ 41,559 |
| Supplemental Adjusted EBITDA | | | | \$ 196,915 |

S-15

Table of Contents

- (a) Depreciation expense related to the Company's property, equipment and leasehold improvements.
- (b) Intangible amortization expenses associated with the Company's intellectual property rights, developed technology and customer relationships of VIMOVO®, LODOTRA®, RAYOS® and ACTIMMUNE®, plus pro forma adjustments related to amortization of new intangible assets from the Acquisition.
- (c) Accretion expense associated with the liability for ACTIMMUNE and VIMOVO royalties.
- (d) Amortization of milestone payments related to LODOTRA between the Company and its European distribution partner, Mundipharma International Ltd.
- (e) In connection with the Merger, ACTIMMUNE inventory was stepped up in value to \$14,218 and during the year ended December 31, 2014, the Company recognized in cost of goods sold \$11,065 of amortization of step-up inventory costs related to ACTIMMUNE inventory sold.
- (f) At the time of the Company's acquisition of the U.S. rights to VIMOVO from AstraZeneca in the fourth quarter of 2013, the Company estimated the fair value of contingent royalties payable to Pozen, or the Pozen Royalty, using an income approach under the discounted cash flow method, which included revenue projections and other assumptions the Company made to determine the fair value. If the Company was to significantly overperform or underperform against its original revenue projections or it became necessary to make changes to assumptions as a result of a triggering event, the Company would be required to reassess the fair value of the contingent royalties payable to Pozen. Any adjustments to fair value would be recorded in the period such adjustment was made as either an increase or decrease to royalties payable, with a corresponding increase or decrease in cost of goods sold, in accordance with established accounting policies, and would impact the reported operating results in the period the adjustment was made. During the second quarter of 2014, based on higher sales of VIMOVO during the six months ended June 30, 2014 versus original expectations and adjusted expectations for future VIMOVO sales, the Company recorded a charge of \$13,033 to cost of goods sold to increase the amount of the contingent royalty liability to reflect the updated estimates. During the fourth quarter of 2014, the Company reassessed the current fair value of the contingent royalty based upon revised financial projections. For the three months ended December 31, 2014, the Company recorded a \$3,627 reduction in its contingent royalty payable and a corresponding decrease to cost of goods sold to properly reflect the carrying value of its contingent royalty liability. As a result of a price increase for ACTIMMUNE that was effective on January 1, 2015, the Company reassessed the estimated value of the ACTIMMUNE royalty liability as of December 31, 2014. Accordingly, during the three months ended December 31, 2014, the Company recorded a \$1,255 charge to increase the carrying value of the contingent royalties and a corresponding increase in cost of goods sold to reflect these updated estimates.
- (g) The bargain purchase gain of \$22,171 resulted from the application of purchase accounting for the Merger. Identifiable assets and liabilities of Vidara, including identifiable intangible assets, were recorded based on their estimated fair values as of the date of the closing of the merger. The excess of the fair value of the net assets acquired over the value of consideration paid was recorded as a bargain purchase gain.
- (h) The impairment of goodwill of \$30.2 million relates to the impairment loss recognized by Hyperion in 2014 with regards to its acquisition of Andromeda.
- (i) The Company recorded non-cash charges related to the increase in the fair value of the embedded derivative associated with its 5.00% convertible senior notes due 2018. The losses on the derivative revaluation were primarily due to an increase in the market value of the Company's common stock.
- (j) On September 19, 2014, the Company acquired Vidara through a reverse merger for stock and cash. Expenses, including investment banker, legal and consulting fees, financing commitment fees and other costs incurred in connection with the merger, have been excluded as non-recurring items.
- (k) On October 17, 2014, the Company acquired the U.S. rights to PENNSAID 2%. Expenses, including legal and consulting fees, incurred in connection with the acquisition have been excluded as non-recurring items.
- (l) During the year ended December 31, 2014, the Company recorded a loss on induced debt conversion for \$29,390, which represented the write-down of \$11,710 in debt discount and deferred financing costs, \$16,690 in additional exchange consideration to debt holders and \$990 in professional fees incurred in

Table of Contents

connection with the induced debt conversion. During the years ended December 31, 2012 and 2013, the Company recorded losses of \$2,973 and \$26,404, respectively, on the extinguishment of previous outstanding debt.

- (m) Represents legal fees, investment advisory fees and other costs associated with the secondary offering of the Company's ordinary shares by certain selling shareholders in November 2014.
- (n) Represents stock-based compensation expense associated with stock option and restricted stock unit grants to employees and non-employees and its employee stock purchase plan.
- (o) Represents management's current estimate of the amount by which Hyperion's expected 2015 operating expenses will be less than those incurred in 2014 as a result of reductions in research and development and selling, general and administrative costs.

S-17

Table of Contents

RISK FACTORS

An investment in our ordinary shares involves significant risks. Prior to making a decision about investing in our ordinary shares, and in consultation with your own financial and legal advisors, you should carefully consider, among other matters, the following risk factors together with the other information in this prospectus supplement, the information and documents incorporated by reference, and in any related term sheet that we deliver to you in connection with this offering. Any of these risks could seriously harm our consolidated business, financial condition, results of operations or cash flow, resulting in the decline of the value of our ordinary shares and a loss of all or part of your investment.

Risks Related to the Acquisition of Hyperion Therapeutics, Inc.

We may fail to realize all of the anticipated benefits of our proposed acquisition of Hyperion Therapeutics, Inc., or Hyperion, which we refer to as the Acquisition, or those benefits may take longer to realize than expected. We may also encounter significant difficulties in integrating Hyperion's business into our operations.

Our ability to realize the anticipated benefits of the Acquisition will depend, to a large extent, on our ability to integrate Hyperion's business into our existing operations. The combination of two independent businesses is a complex, costly and time-consuming process that will require significant management attention and resources. The integration process may disrupt the businesses and, if implemented ineffectively, would limit the expected benefits to us of the Acquisition. The failure to meet the challenges involved in integrating the two businesses and to realize the anticipated benefits of the Acquisition could cause an interruption of, or a loss of momentum in, the activities of the combined company and could adversely affect the results of operations of the combined company.

In addition, the overall integration of the businesses may result in material unanticipated problems, expenses, liabilities, competitive responses, loss of customer and other business relationships, and diversion of management's attention. The difficulties of combining the operations of the companies include, among others:

the diversion of management's attention to integration matters;

difficulties in achieving anticipated cost savings, synergies, business opportunities and growth prospects from the combination;

difficulties in the integration of operations and systems;

conforming standards, controls, procedures and accounting and other policies, business cultures and compensation structures between the two companies;

difficulties in the assimilation of employees and corporate cultures;

potential unknown liabilities, adverse consequences and unforeseen increased expenses associated with the Acquisition; and

challenges in attracting and retaining key personnel.

Many of these factors will be outside of our and Hyperion's control and any one of these factors could result in increased costs, decreases in the amount of expected revenues and additional diversion of management's time and energy, which could materially adversely impact the business, financial condition and results of operations of the combined company. In addition, even if the operations of our business and Hyperion's business are integrated successfully, the full benefits of the Acquisition may not be realized, including the synergies, cost savings, revenue growth or other benefits that are expected. These benefits may not be achieved within the anticipated time frame, or at all. Further, additional unanticipated costs may be incurred in the integration of our business with Hyperion's business. All of these factors could cause dilution to our earnings per share, decrease or delay the expected accretive effect of the Acquisition, and negatively impact the price of our ordinary shares. As a result, we cannot provide any assurance that acquisition of Hyperion will result in the realization of the full benefits anticipated from the transactions.

S-18

Table of Contents

The pendency of the Acquisition could cause disruptions in Hyperion's business, which could have an adverse effect on Hyperion's business and financial results, and consequently on the combined company.

We and Hyperion have operated and, until the completion of the Acquisition, will continue to operate, independently. Uncertainty about the effect of the Acquisition on Hyperion's employees, prescribing physicians, customers, distributors and suppliers may have an adverse effect on Hyperion and consequently on the combined company. These uncertainties may impair Hyperion's ability to retain and motivate key personnel and could cause disruptions to its existing business relationships or delay or reduce the use of its products, or otherwise impair the operations of Hyperion, which may materially and adversely affect Hyperion. Due to the limited termination rights agreed to by the parties in the definitive Agreement and Plan of Merger, or the Merger Agreement, we may be obligated to complete the Acquisition in spite of any adverse effects resulting from the disruption of Hyperion's ongoing business. Furthermore, this disruption could adversely affect the combined company's ability to maintain relationships with prescribing physicians, customers, distributors, suppliers and employees after the Acquisition or to achieve the anticipated benefits of the Acquisition. Each of these events could adversely affect Hyperion in the near term or the combined company thereafter if the Acquisition is completed.

We and Hyperion will incur substantial direct and indirect costs as a result of the Acquisition.

We and Hyperion will incur substantial expenses in connection with and as a result of completing the Acquisition and, over a period of time following the completion of the Acquisition, we expect to incur substantial additional expenses in connection with coordinating the businesses, operations, policies and procedures of the combined company. While we have assumed that a certain level of transaction expenses will be incurred, factors beyond our control could affect the total amount or the timing of these expenses. Many of the expenses that will be incurred, by their nature, are difficult to estimate accurately.

If the Acquisition is completed, we will incur a substantial amount of debt to finance the purchase price and certain other amounts to be paid in connection with the Acquisition, which could adversely affect our business, including by restricting our ability to engage in additional transactions or incur additional indebtedness.

In connection with the Merger Agreement, Horizon Pharma, Inc., or HPI, entered into a commitment letter, or the Debt Commitment Letter, with Citigroup Global Capital Markets Inc., or Citi, and Jefferies Finance LLC, or Jefferies, pursuant to which Citi and Jefferies have committed to provide up to \$900.0 million of secured term loans pursuant to a term loan facility, the proceeds of which, in addition to a portion of our existing cash, would be available to (i) refinance the loans under our existing credit facility and certain outstanding debt of Hyperion, (ii) fund the Acquisition, and (iii) pay any prepayment premiums, fees and expenses in connection with any of the foregoing. In lieu of borrowing pursuant to the Debt Commitment Letter, and subsequent to this offering, we or one or more of our subsidiaries expect to borrow up to an aggregate of approximately \$800.0 million pursuant to an offering of senior notes, or the Senior Notes, and the arrangement and syndication of a new senior unsecured term loan facility, or the Term Facility and together with the Senior Notes, the Debt Financings. We would intend to use the proceeds of the Debt Financings to (i) refinance the loans under our existing credit facility and certain outstanding debt of Hyperion, (ii) fund the Acquisition, and (iii) pay any prepayment premiums, fees and expenses in connection with any of the foregoing. The amount and terms and conditions of the Debt Financings will be subject to market conditions and there can be no assurance that we will be able to complete any Debt Financings on terms and conditions acceptable to us.

Regardless of whether borrowings occur under the Debt Commitment Letter or the expected Debt Financings, we will incur a substantial amount of new indebtedness in connection with completing the Acquisition. In addition, Horizon Limited, a wholly owned subsidiary of HPI, recently issued, and HPI guaranteed, \$400.0 million in aggregate principal amount of 2.50% Exchangeable Senior Notes due 2022, or 2022 notes, in March 2015 and an additional \$28.7 million aggregate principal amount of 5.00% Convertible

Table of Contents

Senior Notes due 2018, or 2018 notes, issued by HPI remained outstanding as of March 31, 2015. Consequently, following the completion of the Acquisition, we will have a significant amount of debt outstanding on a consolidated basis.

This substantial level of debt could have important consequences to our business, including, but not limited to:

reducing the benefits we expect to receive from the Acquisition;

making it more difficult for us to satisfy our obligations;

limiting our ability to borrow additional funds and increasing the cost of any such borrowing;

increasing our vulnerability to, and reducing our flexibility to respond to, general adverse economic and industry conditions;

limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we operate;

placing us at a disadvantage as compared to our competitors, to the extent that they are not as highly leveraged; and

restricting us from pursuing certain business opportunities.

Any credit rating we may receive will impact the cost and availability of future borrowings and, accordingly, our cost of capital. Our ratings at any time will reflect each rating organization's then opinion of our financial strength, operating performance and ability to meet our debt obligations. There can be no assurance that we will achieve a particular rating or maintain a particular rating in the future. Unfavorable initial ratings or a subsequent reduction in our credit ratings may limit our ability to borrow at acceptable interest rates. If our credit ratings were downgraded or put on watch for a potential downgrade, we may not be able to sell additional debt securities or borrow money in the amounts, at the times or interest rates or upon the more favorable terms and conditions that might otherwise be available. Any impairment of our ability to obtain future financing on favorable terms could have an adverse effect on our ability to refinance any of our then-existing debt and may severely restrict our ability to execute on our business strategy, which includes the continued acquisition of additional products or businesses.

If goodwill or other intangible assets that we record in connection with the Acquisition become impaired, we could have to take significant charges against earnings.

In connection with the accounting for the Acquisition, it is expected that we will record a significant amount of intangible assets and may also record goodwill. Under 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.

Our and Hyperion's actual financial positions and results of operations may differ materially from the unaudited pro forma financial data included in this prospectus supplement.

The pro forma financial information contained in this prospectus supplement is presented for illustrative purposes only and may not be an indication of what our financial position or results of operations would have been had the transactions been completed on the dates indicated. The pro forma financial information has been derived from our audited historical financial statements and the audited and unaudited financial data of certain companies previously acquired by us and certain adjustments and assumptions have been made regarding the

Table of Contents

combined company after giving effect to the indicated transactions. The assets and liabilities of Hyperion have been measured at fair value based on various preliminary estimates using assumptions that our management believes are reasonable utilizing information currently available. The process for estimating the fair value of acquired assets and assumed liabilities requires the use of judgment in determining the appropriate assumptions and estimates. These estimates may be revised as additional information becomes available and as additional analyses are performed. In addition, the pro forma financial information contained in this prospectus supplement is based upon certain assumptions with respect to our financing of the Acquisition. Whether the assumed financing sources are available and, if available, the terms of our future financings, will be subject to market conditions. The actual sources of financing and the terms on which it is obtained may not be as favorable as those reflected in the pro forma financial information. Differences between preliminary estimates in the pro forma financial information and the final acquisition accounting, as well as between the assumed and actual financing sources and terms, will occur and could have a material impact on the pro forma financial information and the combined company's financial position and future results of operations.

Other assumptions used in preparing the pro forma financial information may not prove to be accurate, and other factors may affect our financial condition or results of operations following the closing of the Acquisition and related transactions. Any potential decline in our financial condition or results of operations may cause significant variations in the price of our ordinary shares.

The Acquisition may not be accretive to our earnings per share, which may negatively affect the market price of our ordinary shares.

Although we currently anticipate that the Acquisition will be accretive to our earnings per share (on an adjusted earnings basis that is not pursuant to GAAP) from and after the Acquisition, this expectation is based on preliminary estimates, which may change materially. We could encounter additional transaction-related costs or other factors such as the failure to realize all of the operating synergies and other benefits anticipated in the Acquisition. These factors could cause a reduction in our earnings per share or decrease or delay the expected accretive effect of the Acquisition and cause a decrease in the market price of our ordinary shares.

Failure to consummate the Acquisition could negatively impact our share price and our future business and financial results.

We cannot guarantee that we will be able to complete the Acquisition. If the Acquisition is not completed, our ongoing business may be adversely affected and, without realizing any of the benefits of having completed the Acquisition, we will be subject to a number of risks, including the following:

the current prices of our ordinary shares may reflect a market assumption that the Acquisition will occur, meaning that a failure to complete the Acquisition could result in a decline in the price of our ordinary shares;

if the Merger Agreement is terminated under specified limited circumstances, we may be required to pay to Hyperion a termination fee equal to \$75 million;

we may be required to reimburse and indemnify Hyperion for certain expenses incurred by Hyperion in connection with its efforts to assist with our contemplated financing transactions; and

matters relating to the Acquisition (including integration planning) and related financings have required and will continue to require substantial commitments of time and resources by our management, which could otherwise have been devoted to other opportunities that may have been beneficial to us.

We also could be subject to litigation related to any failure to complete the Acquisition or to perform our obligations under the Merger Agreement, or related to any enforcement proceeding commenced against us. If the Acquisition is not consummated, these risks may materialize and may adversely affect our business, financial results and stock price. If the Acquisition is not completed, our expected use of the net proceeds from this offering would change and we may not use the proceeds in ways that increase shareholder value or that would be as beneficial to our shareholders as the Acquisition would be.

S-21

Table of Contents

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 payors.

Our current products, and other product or product candidates that we may develop, acquire, or in-license, such as RAVICTI and BUPHENYL upon the completion of the Acquisition, may not attain market acceptance among physicians, patients, healthcare payors or the medical community. In the U.S. market, we began marketing 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. VIMOVO was launched in the U.S. market in the fourth quarter of 2010 by AstraZeneca under its license from POZEN Inc., or Pozen. Following our acquisition of the U.S. rights to VIMOVO in November 2013, we began marketing VIMOVO in the first quarter of 2014. ACTIMMUNE was originally launched in the U.S. market in March 1991 by Genentech, Inc., or Genentech, and in June 2012, Vidara Therapeutics International Limited, or Vidara, acquired the intellectual property rights and certain assets related to the ACTIMMUNE product line. In September 2014, our business was combined with Vidara, and as a result we assumed the commercialization of ACTIMMUNE. In October 2014 we entered into an asset purchase agreement and ancillary agreements with Nuvo Research Inc., or Nuvo, to acquire the U.S. rights to PENNSAID 2%, and we began commercializing PENNSAID 2% in the United States in January 2015. 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 the 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 NSAIDs in Europe. There have been no sales of DUEXIS in the UK thus far. RAVICTI was launched in the United States by Hyperion in the first quarter of 2013, and BUPHENYL was originally launched in 1996 prior to being acquired by Hyperion. Neither product has ever been marketed by us to date. 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 products;

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 payors;

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

Edgar Filing: Horizon Pharma plc - Form 424B5

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 limitation of future product price increases;

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

S-22

Table of Contents

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 non-steroidal anti-inflammatory drugs, or 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 its competitors, would be more effective for their patients. With respect to each of DUEXIS, PENNSAID 2%, RAYOS/LODOTRA, VIMOVO and BUPHENYL, their higher cost compared to the generic or branded forms of their active ingredients alone may limit adoption by physicians, patients and healthcare payors. 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 and obtain marketing approval for additional indications. With respect to RAVICTI, which is also approved to treat a very limited patient population, in the event that the Acquisition is completed our ability to grow sales will depend in large part on our ability to transition urea cycle disorder, or UCD, patients from BUPHENYL or generic equivalents, which are comparatively much less expensive, to RAVICTI. If our current products 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 (including, possibly, the value of our ordinary shares).

Our current business plan is highly dependent upon our ability to successfully execute on our sales and marketing strategy for the commercialization of our products in the United States. 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 our products in the U.S. market. We may not be able to successfully commercialize ACTIMMUNE, DUEXIS, PENNSAID 2%, RAYOS or VIMOVO or, assuming completion of the Acquisition, BUPHENYL or RAVICTI, 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 375 sales representatives, consisting of 325 primary care sales representatives and 50 sales representatives in specialty and orphan diseases business areas, 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.

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

Table of Contents

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 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, PENNSAID 2%, RAYOS, VIMOVO and BUPHENYL 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 revenue 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 may not be able to commercialize our product candidates and execute on our business plan.

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 instructions from the prescribing physician. Because our products (other than BUPHENYL, if the Acquisition is consummated) do not currently have FDA-approved generic equivalents in the United States, we do not believe our products should be subject to mandatory generic substitution laws. However we understand that some pharmacies and payors may attempt to reduce costs by obtaining physician authorization to switch prescriptions for DUEXIS or VIMOVO to prescriptions for multiple generic products with similar active pharmaceutical ingredients. Accordingly, a key part of our commercial strategy is to encourage physicians to have their patients fill their prescriptions through Prescriptions-Made-Easy, or PME. Through PME, physicians can have their uninsured or commercially insured patients' prescriptions for our products shipped directly to the patient. Through the PME program, we provide financial assistance to reduce eligible patients' out of pocket costs for prescriptions filled via a participating mail order pharmacy. Because the patient's out of pocket cost for our products when dispensed through the PME program may be significantly lower than such costs when our products are dispensed outside of the PME program, prescriptions that are filled through our PME program are therefore less likely to be subject to the efforts of traditional pharmacies to switch a physician's intended prescription of our products to a generic or over the counter brand. We expect that continued adoption of our PME program by physicians and patients 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 less expensive 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, placed 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 or restrict coverage to situations where a generic or over-the-counter product has been tried first. To the extent we are unable to successfully encourage physicians to 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 and patient awareness and comfort with the program, and we have limited ability to influence whether physicians use our PME program to prescribe our products or whether patients will agree to receive our products through the PME program. In addition, the PME program is only available to patients with commercial insurance or who are uninsured, and is not available to federal health care program (such as Medicare and Medicaid) beneficiaries. 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. If these PME pharmacies are unable to process and fulfill the volume of patient prescriptions directed to them under the PME program, our ability to maintain or increase prescriptions for our products will be impaired. The commercialization of our products and our operating results could be affected should any of the PME pharmacies choose not to continue participation in our PME program or by any adverse events at any of those PME pharmacies. In addition, the PME program may implicate certain state laws related to, among other things, unlawful schemes to defraud, excessive fees for services, tortious

Table of Contents

interference with patient contracts and statutory or common law fraud. To the extent the PME program is found to be inconsistent with applicable laws, we may be required to restructure or discontinue such program, or be subject to other significant penalties.

If we are unable to successfully implement our commercial plans and facilitate 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 our current products, and we may not be able to successfully commercialize these products. Failure to do so would adversely impact our financial condition and prospects.

A substantial majority of our resources are focused on the commercialization of our current products. 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 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 and PENNSAID 2% in October 2014, our strategy has included bringing both products pricing in-line with DUEXIS, thereby significantly increasing the value we realize per prescription, and also increasing sales and marketing support to drive growth in prescriptions. We cannot guarantee that this strategy will continue to be effective generally, due to negative reactions to price increases or otherwise. Our 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. Our strategy with respect to ACTIMMUNE includes pricing increases, pursuing label expansion for additional indications, such as 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. 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. 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 our current and future products, 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.

If the Acquisition is completed, our strategy with respect to RAVICTI will include accelerating the transition of UCD patients from BUPHENYL or generic equivalents to RAVICTI and increasing the diagnosis of UCD and treatment of untreated UCD patients through patient and physician outreach. Part of our success in our strategy will be obtaining favorable results from an on-going study of the use of RAVICTI to treat UCD in patients less than two years of age, the timely submission of a supplemental NDA and approval of RAVICTI for

Table of Contents

the treatment in UCD in patients less than two years of age, and we cannot guarantee that any of these events will occur on our anticipated timeline or at all. In addition, RAVICTI is currently only approved for marketing in the United States. If required regulatory approvals in international markets are never obtained, are delayed or are not maintained, the market potential of RAVICTI will be limited. Additionally, if approval to market RAVICTI in Europe is not obtained prior to February 2016, when the RAVICTI composition of matter patent expires in European jurisdictions in which it is validated, we will not be eligible to apply to extend the patent's term, and we will have to rely on maintaining orphan designation to ensure marketing exclusivity in Europe. We cannot guarantee that we can maintain orphan designation for RAVICTI in Europe as we must demonstrate that the product provides significant benefit in those UCD subtypes for which AMMONAPS is approved.

We are solely dependent on third parties to commercialize certain of our products outside the United States. Failure of these third parties 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. Upon the closing of the Acquisition, we will rely on Hyperion's existing distributors for commercialization of BUPHENYL in certain territories outside the United States for which Hyperion currently has rights. We have limited contractual rights to force these third parties to invest significantly in commercialization of LODOTRA or BUPHENYL in our markets. In the event that Mundipharma, Hyperion's current ex-U.S. distributors, or any other third party with any future commercialization rights to any of our products or product candidates fail to adequately commercialize those products or product candidates because they lack adequate financial or other resources, decide 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 and Hyperion's agreements with its current ex-U.S. distributors 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 these third parties terminated their agreements, 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 or, after the consummation of the Acquisition, BUPHENYL, outside the United States would be materially harmed.

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 products and our product candidates are, and 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 or biologics 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.

Table of Contents

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 product 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.

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.

RAVICTI is currently only approved for marketing in the United States and, assuming the Acquisition is completed, our ability to expand our market potential will depend in part on our ability to obtain additional marketing approvals outside the United States. This is particularly true due to our expectation that, if we complete the Acquisition, we will not pursue approval in the United States for the treatment of hepatic

Edgar Filing: Horizon Pharma plc - Form 424B5

encephalopathy, or HE. On June 25, 2014 the European Medicines Agency, or EMA, accepted Hyperion's marketing authorization application, commencing its review process which is expected to be completed in the fourth quarter of 2015 or the first quarter of 2016. Hyperion has also submitted a New Drug Submission to Health Canada, or HC, for approval to market RAVICTI in Canada. However, in January 2015, Lucane Pharma

S-27

Table of Contents

announced that it had received approval from HC to market its taste-masked NaPBA granules in Canada. It is our understanding that in Canada only the first phenylbutyrate-containing product approved for any indication receives data protection which is similar to orphan drug exclusivity in the United States. Hyperion has been notified by HC that RAVICTI is not eligible for data protection. If we or Hyperion cannot successfully appeal this decision to obtain data protection, the application for marketing approval in Canada may be withdrawn. Regardless, we cannot be assured that Hyperion's applications to market RAVICTI in Europe and Canada will be approved nor can we be certain of the timelines for regulatory decisions to be made. If we or Hyperion are unable to obtain approvals for RAVICTI outside the United States or determine that commercializing RAVICTI outside the United States is not economically viable, the market potential of RAVICTI and the potential benefits of the Acquisition will be limited.

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 and our acquisition of the U.S. rights to PENNSAID 2% from Nuvo in October 2014, we have five 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. Upon completion of the Acquisition, we will have two additional products, both of which are approved in the United States and one of which, BUPHENYL, is approved in additional territories, including Europe. RAYOS/LODOTRA has been approved in the United States and over 37 other countries, including Australia, Columbia and select countries within Europe and Asia. 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. We began the commercial sale of DUEXIS in the United States in November 2011, 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 began commercializing PENNSAID 2% in the United States in January 2015. RAVICTI was launched in the United States by Hyperion in the first quarter of 2013, and BUPHENYL was originally launched in 1996 prior to being acquired by Hyperion, but neither product has ever been marketed by us to date. 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 limited history commercializing PENNSAID 2% and VIMOVO and, as a combined company, ACTIMMUNE, and lack of any history commercializing RAVICTI and BUPHENYL, makes it particularly difficult for us to predict our future operating results and appropriately budget for our expenses, particularly following completion of the Acquisition. 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 and Hyperion's, or to commercialize VIMOVO, ACTIMMUNE, PENNSAID 2%, and, following completion of the Acquisition, BUPHENYL and RAVICTI within our organization or not realize the benefits we expect to derive from our recent and pending acquisitions.

We have U.S. rights to ACTIMMUNE, PENNSAID 2% and VIMOVO but have no control over the activities of Boehringer Ingelheim to commercialize ACTIMMUNE outside the United States, Canada and Japan, AstraZeneca AB, or 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 ACTIMMUNE, PENNSAID 2% and VIMOVO 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 over Nuvo's or its future commercial partners' activities with respect to

Table of Contents

PENNSAID 2% outside of the United States, even though those activities could impact our ability to successfully commercialize PENNSAID 2% and VIMOVO in the United States. For example, Nuvo or its assignees or AstraZeneca or its assignees can make statements or use promotional materials with respect to PENNSAID 2% or VIMOVO, respectively, outside of the United States that are inconsistent with our positioning of the products in the United States, and could sell PENNSAID 2% or VIMOVO, respectively, in foreign countries, including Canada, at prices that are dramatically lower than the prices we 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 VIMOVO 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 PENNSAID 2% or VIMOVO 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 PENNSAID 2% and VIMOVO. We also rely on Nuvo and AstraZeneca or our assignees to provide us with timely and accurate safety information regarding the use of PENNSAID 2% or VIMOVO, 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 currently intend to rely on third parties to manufacture commercial supplies of any other approved products, including RAVICTI and BUPHENYL. 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, our manufacturing partner located in Laval, Canada for production of DUEXIS, and Jagotec AG, or Jagotec, a wholly-owned subsidiary of SkyePharma PLC, or SkyePharma, 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, or Bayer, 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, or BASF, 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.

In connection with our acquisition of the U.S. rights to VIMOVO, we 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, or Divis, and Minakem Holding SAS, or Minakem, 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) 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 our company. Furthermore, we do not have a

Table of Contents

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 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. We and Nuvo rely on a sole proprietary form of DMSO for which we maintain a substantial safety stock. However, should this supply become inadequate, damaged, destroyed or unusable, we and Nuvo may not be able to qualify a second source.

With respect to RAVICTI and BUPHENYL, Hyperion relies, and, assuming that the Acquisition is completed, we expect to continue to rely, on third parties for the manufacture of clinical and commercial supplies. Hyperion has bulk drug substance for the production of clinical and commercial supplies of RAVICTI manufactured for it by Helsinn Advanced Synthesis SA (Switzerland) and DPx Fine Chemicals Austria GmbH on a purchase order basis. Hyperion has bulk drug substance for the production of clinical and commercial supplies of BUPHENYL manufactured for it by CU Chemie Uetikon GmbH (Germany).

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 from 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.

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

Table of Contents

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 of RAYOS/LODOTRA, Bayer, 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. With respect to RAVICTI and BUPHENYL, Hyperion does not have any long-term commercial supply agreements in place for bulk drug product, and relies on safety stock to mitigate the risk of its current suppliers electing to cease producing bulk drug product or ceasing to do so at acceptable prices and quality. However, we can provide no assurance that, after completion of the Acquisition, such safety stocks would be sufficient to avoid supply shortfalls in the event we have to identify and qualify new contract manufacturers, and we may not be able to enter into long-term supply agreements with any manufacturers with respect to bulk drug substance for RAVICTI or BUPHENYL.

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. 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. Patheon supplies 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. Hyperion has clinical and commercial supplies of BUPHENYL finished product manufactured for it by Pharmaceutics International, Inc. on a purchase order basis. Hyperion has clinical and commercial supplies of RAVICTI finished drug product manufactured by Lyne Laboratories, Inc. under a commercial supply agreement and has an agreement in place with Halo Pharmaceutical, Inc. to serve as a secondary finished drug product supplier for RAVICTI.

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 our 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.

Table of Contents

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 expanded the size of our organization substantially in connection with our acquisition of the U.S. rights to VIMOVO in November 2013, our acquisition of Vidara in September 2014 and our acquisition of the U.S. rights to PENNSAID 2% in October 2014, and we may experience difficulties in managing this growth as well as potential additional growth in connection with future product acquisitions or company acquisitions, including the pending acquisition of Hyperion.

As of December 31, 2010, we employed approximately 40 full-time employees as a consolidated entity. In anticipation of the commercial launch of DUEXIS, we hired approximately 80 sales representatives during the period from September 2011 through October 2011. Recently, we further increased the size of our sales force in connection with our acquisition of PENNSAID 2% to a total of approximately 375 sales representatives. As of December 31, 2014 and 2013, we employed approximately 535 and 463 full-time employees, respectively, as a consolidated entity. If the Acquisition is completed, we will experience a further increase in headcount. We 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 continue to develop, we will need to continue to recruit and train 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 acquisitions of Vidara and PENNSAID 2%, as well as the pending acquisition of Hyperion. Our ability to manage any future growth effectively may require us to, among other things:

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.

Edgar Filing: Horizon Pharma plc - Form 424B5

In particular, the merger of our business with Vidara's business is subject to numerous uncertainties and risks and will require significant efforts and expenditures. For example, we have transitioned 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 us, 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 Vidara's business with our business;

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;

S-32

Table of Contents

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 continue to integrate our operations 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.

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 and PENNSAID 2% in the United States until the first quarter of 2014 and 2015, respectively, 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 our acquisition of Vidara, we have limited experience marketing ACTIMMUNE under our commercial organization. Likewise, while we expect to retain the substantial majority of Hyperion's sales force promoting RACTIVI and BUPHENYL if the Acquisition is completed, we may not be successful in retaining these employees and we otherwise have no experience marketing these products under its commercial organization. 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 we 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 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. 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,

Edgar Filing: Horizon Pharma plc - Form 424B5

experienced marketing and manufacturing organizations and well-established sales forces. Additional consolidations 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

S-33

Table of Contents

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% that are priced significantly less than the price we charge for PENNSAID 2% and Voltaren Gel, marketed by Endo Pharmaceuticals Solutions Inc., or 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 instructions from the prescribing physician. Because pharmacists often have economic and other incentives to prescribe lower-cost generics, if physicians prescribe DUEXIS, PENNSAID 2% or VIMOVO, 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, PENNSAID 2% and VIMOVO may suffer despite any success we may have in promoting DUEXIS, PENNSAID 2% or VIMOVO 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 the 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. Par retains the ability to challenge the enforceability and validity of the asserted patents as they relate to products other than DUEXIS.

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.

Table of Contents

Under the Par license agreement, we also agreed, on our behalf and on behalf of our affiliates, 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 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 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 court held a claim construction hearing on October 16, 2014, and issued its opinion and order on claim construction on November 10, 2014, adopting our proposed construction of both of the disputed claim terms. The court has scheduled expert discovery in the WLF action to be completed by June 2, 2015, and has set the pretrial conference for September 10, 2015. The trial date will be set following the pretrial conference.

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.

On November 13, 2014, we received a Paragraph IV Patent Certification from Watson advising that Watson had filed an ANDA with the FDA for a generic version of PENNSAID 2%. Watson has not advised us as to the timing or status of the FDA's review of its filing. On December 23, 2014, we filed suit in the United States District Court for the District of New Jersey against Watson seeking an injunction to prevent the approval of the ANDA. The lawsuit alleges that Watson has infringed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, and 8,871,809 by filing an ANDA seeking approval from the FDA to market generic versions of PENNSAID 2% 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 Watson's ANDA for 30 months or until an earlier district court decision that the subject patents are not infringed or are invalid. The court has not yet set a trial date for the Watson action.

Table of Contents

On December 2, 2014, we received a Paragraph IV Patent Certification against Orange Book listed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, and 8,741,956 from Paddock Laboratories, LLC, or Paddock, advising that Paddock had filed an ANDA with the FDA for a generic version of PENNSAID 2%. On January 9, 2015, we received from Paddock another Paragraph IV Patent Certification against newly Orange Book listed U.S. Patent No. 8,871,809. Paddock has not advised us as to the timing or status of the FDA's review of its filing. On January 13, 2015 and January 14, 2015, we filed suits in the United States District Court for the District of New Jersey and the United States District Court for the District of Delaware, respectively, against Paddock seeking an injunction to prevent the approval of the ANDA. The lawsuits alleged that Paddock has infringed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, and 8,871,809 by filing an ANDA seeking approval from the FDA to market generic versions of PENNSAID 2% 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 Paddock's ANDA for 30 months or until an earlier district court decision that the subject patents are not infringed or are invalid. The courts have not yet set trial dates for the Paddock actions.

Currently, patent litigation is pending in the United States District Court for 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 United States District Court for 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 Limited 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 United States District Court for the District of New Jersey against a fifth generic company, Anchen Pharmaceuticals Inc., or Anchen, was dismissed on June 9, 2014 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 amended and restated collaboration and license agreement for the United States with Pozen, or 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 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.

On February 25, 2015, Dr. Reddy's Laboratories, Inc. filed a Petition for *Inter Partes* Review of U.S. Patent No. 8,557,285, one of the patents in litigation in the above referenced VIMOVO cases. The Patent Trial and Appeal Board has not yet issued a decision with regard to whether or not the *Inter Partes* Review will be instituted.

On or about December 19, 2014, we filed a Notice of Opposition to a European patent, EP 2611457, to Roberto Testi, et al., covering compositions and methods for treating FA with interferon gamma, e.g., ACTIMMUNE. In the European Union, or EU, the grant of a patent may be opposed by one or more private parties.

On February 2, 2015, we received a Paragraph IV Patent Certification against Orange Book listed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, 8,741,956, and 8,871,809 from Taro

Table of Contents

Pharmaceuticals USA, Inc. and Taro Pharmaceutical Industries, Ltd., or collectively, Taro, advising that Taro had filed an ANDA with the FDA for a generic version of PENNSAID 2%. Taro has not advised us as to the timing or status of the FDA's review of its filing. On March 13, 2015, we filed suit in the United States District Court for the District of New Jersey against Taro seeking an injunction to prevent the approval of the ANDA. The lawsuit alleges that Taro has infringed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, and 8,871,809 by filing an ANDA seeking approval from the FDA to market generic versions of PENNSAID 2% 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 Taro's ANDA for 30 months or until an earlier district court decision that the subject patents are not infringed or are invalid. The court has not yet set a trial date for the Taro action.

On March 18, 2015, we received a Paragraph IV Patent Certification against Orange Book listed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, 8,741,956, and 8,871,809 from Lupin Limited advising that Lupin Limited had filed an ANDA with the FDA for generic version of PENNSAID 2%. Lupin Limited has not advised us as to the timing or status of the FDA's review of its filing. We are still in the process of evaluating the Paragraph IV Patent Certification, and we expect that we will file suit against Lupin Limited within the statutorily prescribed 45 day time limit.

On March 17, 2014, Hyperion received notice from Par Pharmaceutical, Inc. that it had filed an ANDA with the FDA seeking approval for a generic version of our product RAVICTI. The ANDA contained a Paragraph IV Patent Certification alleging that two of Hyperion's patents covering RAVICTI, U.S. Patent No. 8,404,215, titled "Methods of therapeutic monitoring of nitrogen scavenging drugs," which expires in March 2032, and U.S. Patent No. 8,642,012, titled "Methods of treatment using ammonia scavenging drugs," which expires in September 2030, are invalid and/or will not be infringed by Par's manufacture, use or sale of the product for which the ANDA was submitted. Par Pharmaceutical, Inc. did not challenge the validity, enforceability, or infringement of Hyperion's primary composition of matter patent for RAVICTI, U.S. Patent No. 5,968,979 titled "Triglycerides and ethyl esters of phenylalkanoic acid and phenylalkenoic acid useful in treatment of various disorders," which would have expired on February 7, 2015, but as to which Hyperion has been granted an interim term of extension until February 7, 2016. Hyperion filed suit against Par Pharmaceutical, Inc. on April 23, 2014 and assuming the Acquisition is completed, we will take over and will be responsible for this patent litigation.

If we are unsuccessful in any of the on-going patent litigations, we will likely face generic competition with respect to VIMOVO, PENNSAID 2% and/or RAYOS and our sales of VIMOVO, PENNSAID 2% and/or RAYOS will be substantially harmed. If Par Pharmaceutical, Inc. were to prevail in the patent litigation with respect to RAVICTI and its ANDA were to receive FDA approval, RAVICTI would likely face generic competition in the United States when its orphan exclusivity expires (currently scheduled to occur in February 2020), and its sales would likely materially decline.

ACTIMMUNE is the only product 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 products 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

Table of Contents

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 products 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.

BUPHENYL's composition of matter patent protection and orphan drug exclusivity have expired. Because BUPHENYL has no regulatory exclusivity or listed patents, there is nothing to prevent a competitor from submitting an ANDA for a generic version of BUPHENYL and receiving FDA approval. In November 2011, Ampolgen Pharmaceuticals, LLC received FDA approval for a generic version of NaPBA tablets, which may compete with RAVICTI and BUPHENYL in treating UCD. In March 2013, SigmaPharm Laboratories, LLC received FDA approval for a generic version of NaPBA powder, which competes with BUPHENYL and may compete with RAVICTI in treating UCD. In July 2013, Lucane received marketing approval from the EMA for taste-masked NaPBA and has announced a distribution partnership in Canada. In January 2015, Lucane announced it had received marketing approval for its taste masked NaPBA in Canada. We believe Lucane is also seeking approval via an ANDA in the United States. If this ANDA is approved, this formulation may compete with RAVICTI and BUPHENYL in treating UCD in the United States. Generic versions of BUPHENYL to date have been priced at a discount relative to BUPHENYL or RAVICTI, and physicians, patients, or payors may decide that this less expensive alternative is preferable to BUPHENYL and RAVICTI. If this occurs, sales of BUPHENYL and/or RAVICTI could be materially reduced, but Horizon Pharma would nevertheless be required to make royalty payments to Ucyclyd Pharma Inc., or Ucyclyd, and Brusilow Enterprises, LLC, or Brusilow, at the same royalty rates. While Ucyclyd and its affiliates are generally contractually prohibited from developing or commercializing new products, anywhere in the world, for the treatment of UCD or HE, which are chemically similar to RAVICTI, they may still develop and commercialize products that compete with RAVICTI. For example, products approved for indications other than UCD and HE may still compete with RAVICTI if physicians prescribe such products off-label for UCD or HE. We are also aware that Orphan Europe is conducting a clinical trial of carglumic acid to treat some of the UCD enzyme deficiencies for which RAVICTI was approved. Promethera has successfully completed Phase I/II trials of its cell-based therapy for the treatment of UCD and plans to conduct a Phase IIb/III clinical trial. Aeglea Biotherapeutics, Inc., or Aeglea Biotherapeutics, has a degrading enzyme treatment in preclinical development for arginase 1 deficiency. Carglumic acid is approved for maintenance therapy for chronic hyperammonemia and to treat HA crises in N-acetylglutamate synthase deficiency, a rare UCD subtype, and is sold under the name Carbaglu. If the results of this trial are successful and Orphan Europe is able to complete development and obtain approval of Carbaglu to treat additional UCD enzyme deficiencies, RAVICTI would face additional competition from this compound.

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

Edgar Filing: Horizon Pharma plc - Form 424B5

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

S-38

Table of Contents

If we are unable to maintain or realize the benefits of orphan drug exclusivity for RAVICTI for the treatment of UCD in the United States, we may face increased competition.

Under the Orphan Drug Act of 1983, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition affecting fewer than 200,000 people in the United States. A company that first obtains FDA approval for a designated orphan drug for the specified rare disease or condition receives orphan drug marketing exclusivity for that drug for a period of seven years from the date of its approval. RAVICTI was granted orphan drug exclusivity by the FDA in May 2013, which we expect will provide the drug with orphan drug marketing exclusivity in the United States until February 2020, seven years from the date of its approval. However, despite orphan drug exclusivity, the FDA can still approve another drug containing the same active ingredient and used for the same orphan indication if it determines that a subsequent drug is safer, more effective or makes a major contribution to patient care, and orphan exclusivity can be lost if the orphan drug manufacturer is unable to assure that a sufficient quantity of the orphan drug is available to meet the needs of patients with the rare disease or condition. Orphan drug exclusivity may also be lost if the FDA later determines that the initial request for designation was materially defective. In addition, orphan drug exclusivity does not prevent the FDA from approving competing drugs for the same or similar indication containing a different active ingredient. Assuming the Acquisition is completed, if orphan drug exclusivity is lost and we were unable to successfully enforce any remaining patents covering RAVICTI, we could be subject to generic competition and revenues from RAVICTI could decrease materially. In addition, if the Acquisition is completed and a subsequent drug is approved for marketing for the same or a similar indication as RAVICTI despite orphan drug exclusivity we may face increased competition and lose market share with respect to RAVICTI. RAVICTI does not have orphan drug exclusivity in the EU or other regions of the world.

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 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 and assuming the closing of the Acquisition, we will assume responsibility for the on-going Hatch Waxman litigation with Par related to RAVICTI. 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 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. In 2014, 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

Table of Contents

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 and March 9, 2015, we received letters 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 has claimed that we owe approximately \$68 million in past price protection and utilization rebates related to VIMOVO and DUEXIS and 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 one of our National Drug Codes, or NDCs. Based upon the terms of the agreement and the PBM's actions, we believe that the PBM's claims in its November 6, 2014 and March 9, 2015 letters 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 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 our company.

On June 12, 2014, Hyperion acquired Andromeda Biotech Ltd, or Andromeda, an Israeli company developing DiaPep277 for the treatment of recent onset Type 1 diabetes, from Clal Biotechnology Industries Ltd., or CBI. On September 8, 2014, Hyperion announced the termination of further development of DiaPep277® beyond completion of the ongoing clinical trial as a result of evidence Hyperion uncovered that certain employees of Andromeda engaged in serious misconduct that compromised clinical trial results. Hyperion subsequently terminated the Andromeda employees involved in the misconduct and became involved in a legal dispute with CBI related to Andromeda. On February 16, 2015 Hyperion reached an agreement with CBI and Yeda Research and Development Company Ltd, or Yeda, the company from which Andromeda licenses the underlying DiaPep277 technology, to resolve DiaPep277-related claims against one another, and Hyperion granted CBI an option to acquire all of the outstanding stock of Andromeda. In connection with the agreement, the parties appointed a steering committee to oversee the completion of an on-going clinical trial of DiaPep277 with representatives of CBI and Yeda and a non-voting member appointed by Hyperion. Also on February 16, 2015, Hyperion entered into a release with Evotec International GmbH, or Evotec, pursuant to which Evotec released its previously asserted claims that it was entitled to a milestone payment from Hyperion in connection with Hyperion's acquisition of Andromeda and that it had suffered harm from recent incidents in relation to DiaPep277 in exchange for a payment of \$500,000 from Hyperion. In connection with the closing, CBI transferred to Hyperion beneficial ownership of 96,612 shares of Hyperion common stock. CBI cannot complete the transfer of shares to Hyperion until it obtains a valid tax certificate from the tax authority in Israel exempting CBI from an obligation to withhold Israeli taxes in connection with the transfer. It is possible that this transfer will be delayed and it is possible Hyperion may owe taxes in Israel in connection with this transfer.

Although the Andromeda release agreements resolved the disputes among the parties relating to DiaPep277, we cannot be certain that additional legal disputes will not arise with respect to Andromeda, including in connection with the on-going Phase 3 clinical trial of DiaPep277, the sale of Andromeda back to CBI if the option is exercised or, assuming the Acquisition is completed, the potential termination of DiaPep277 development by us and the return of related intellectual property to Yeda if CBI's option is not exercised. Further, under the terms of the release agreement, Hyperion agreed to retain certain liabilities relating to its ownership of Andromeda, including any liability related to or based on the misconduct of certain former Andromeda employees that led to its decision to terminate further development of DiaPep277. For example, in February 2015, one of the former employees of Andromeda sued Hyperion in Israeli labor court for wrongful dismissal and related employment causes of action. In addition to these potential liabilities, if the Acquisition is

Table of Contents

completed we may incur currently unknown liabilities related to Hyperion's acquisition of Andromeda. If the Acquisition is completed, any such potential legal dispute could lead to costly litigation, divert management's attention from our core business and harm our business.

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, Bermuda, Luxembourg, Switzerland and Germany and Hyperion has foreign operations in Canada and Israel (through Andromeda). 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 is in the registration process for the commercialization of DUEXIS in Latin America. BUPHENYL is currently marketed in various territories outside the United States by third party distributors and Hyperion's MAA is pending with the EMA for marketing approval of RAVICTI in the EU. 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 and, assuming the Acquisition is completed, will be subject to additional risks associated with Hyperion's international activities upon completion of the Acquisition, 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 over-indebtedness, 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, commercialization of BUPHENYL in select countries throughout Europe, the Middle East, and the Asia-Pacific Region, and commercialization of DUEXIS in Latin America, increased dependence on the commercialization efforts and regulatory compliance of third party 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;

compliance with Israeli laws with respect to Andromeda;

foreign government taxes, regulations and permit requirements;

U.S. and foreign government tariffs, trade restrictions, price and exchange controls and other regulatory requirements;

Edgar Filing: Horizon Pharma plc - Form 424B5

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;

S-41

Table of Contents

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.

Our business activities outside of the United States are subject to the Foreign Corrupt Practices Act, or FCPA, and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate, including the UK's Bribery Act 2010, or the UK Bribery Act. The FCPA and similar anti-corruption laws generally prohibit the offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to non-U.S. government officials in order to improperly influence any act or decision, secure any other improper advantage, or obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the company and to devise and maintain an adequate system of internal accounting controls. The UK Bribery Act prohibits giving, offering, or promising bribes to any person, including non-UK government officials and private persons, as well as requesting, agreeing to receive, or accepting bribes from any person. In addition, under the UK Bribery Act, companies which carry on a business or part of a business in the UK may be held liable for bribes given, offered or promised to any person, including non-UK government officials and private persons, by employees and persons associated with the company in order to obtain or retain business or a business advantage for the company. Liability is strict, with no element of a corrupt state of mind, but a defense of having in place adequate procedures designed to prevent bribery is available. Furthermore, under the UK Bribery Act there is no exception for facilitation payments. As described above, our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, any dealings with these prescribers and purchasers may be subject to regulation under the FCPA. Recently the SEC and the U.S. Department of Justice have increased their FCPA enforcement activities with respect to pharmaceutical companies. In addition, under the Dodd-Frank Wall Street Reform and Consumer Protection Act, private individuals who report to the SEC original information that leads to successful enforcement actions may be eligible for a monetary award. We are engaged in ongoing efforts that are designed to ensure our compliance with these laws, including due diligence, training, policies, procedures and internal controls. However, there is no certainty that all employees and third party business partners (including our distributors, wholesalers, agents, contractors, and other partners) will comply with anti-bribery laws. In particular, we do not control the actions of manufacturers and other third party agents, although we may be liable for their actions. Violation of these laws may result in civil or criminal sanctions, which could include monetary fines, criminal penalties, and disgorgement of past profits, which could have a material adverse impact on our business and financial condition.

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 products or product candidates in addition to our current products, through business or product acquisitions such as the proposed acquisition of Hyperion. Because we do not engage in proprietary drug discovery, 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 approved or clinically enabled product candidates for therapeutic indications that complement or augment our current products, or that otherwise fit into our development or strategic plans on terms that are acceptable to our company. Identifying,

Table of Contents

selecting, acquiring or licensing promising products or 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 or 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 products or product candidates from third parties or acquire businesses at valuations and on other terms acceptable to us, or if we are unable to raise capital required to acquire or in-license businesses or new products, our business and prospects will be limited.

Moreover, any product candidate we acquire or license may require additional, time-consuming development or regulatory efforts prior to commercial sale or prior to expansion into other indications, 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 or be able to acquire other products to expand our existing portfolio, and our business and prospects would be harmed.

Our November 2013 acquisition of the U.S. rights to VIMOVO, the September 2014 acquisition of Vidara and our October 2014 acquisition of the U.S. rights to PENNSAID 2%, and our pending acquisition of Hyperion 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 our business with Vidara's business in September 2014 and acquired the U.S. rights to PENNSAID 2% in October 2014, and executed the Merger Agreement to acquire Hyperion in March 2015. 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 products or product candidates or technologies that we believe will complement or augment our existing business, including the proposed acquisition of Hyperion. 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, assuming the Acquisition is completed, we will also assume responsibility for the existing patent infringement litigation with respect to RAVICTI upon the closing of the Acquisition and will assume responsibility for completing post-marketing clinical trials of RAVICTI that are required by the FDA and are ongoing. We expect that Hyperion litigation will result in substantial on-going expenses and potential distractions to our management team. Moreover, we face significant competition in seeking appropriate strategic transaction opportunities 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 may be insufficient and/or third parties may not view our commercial and development capabilities as being adequate. 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

Table of Contents

acquisition of the U.S. rights to VIMOVO, the acquisition of Vidara, our acquisition of the U.S. rights to PENNSAID 2%, the completion of the potential Acquisition or any other strategic transaction, we will achieve the anticipated revenues, net income or tax benefits that we believe justify such transactions. 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 current advantageous tax status and resulting 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 Ireland, the United States, Switzerland, Luxembourg, Germany and Bermuda. Prior to the acquisition of Vidara, Vidara was able to achieve a favorable 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 we are 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 we are an Irish incorporated entity, we 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.

Under Section 7874, and as a result of the fact that the former shareholders of HPI owned (within the meaning of Section 7874) less than 80% (by both vote and value) of the combined entity's stock immediately after the acquisition of Vidara, we believe we qualify as a foreign corporation for U.S. federal income tax purposes following the acquisition of Vidara. 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 acquisition Vidara would be nullified and we may not be able to recoup the significant investment in completing the transaction.

Table of Contents

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

Under current law, we expect to be treated as a foreign corporation for U.S. federal income tax purposes. 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 to our shareholders. On May 20, 2014 Senator Carl Levin and Representative Sander M. Levin introduced The Stop Corporate Inversions Act of 2014, or 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 HPI owning 50% or more of the combined entity's stock immediately following the acquisition of Vidara. 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. Additionally, in September 2014, legislation was introduced in the U.S. Senate that seeks to address the practice of earnings stripping by inverted companies and the Treasury and the IRS announced that they would issue regulations to curb such practices.

In addition, the Organization for Economic Co-operation and Development, the EU, the United States and other governments have been placing increasing pressure on the governments of Ireland, Switzerland and Luxembourg to eliminate certain tax ruling practices and reform their tax rules that have allowed multinational corporations to significantly reduce their world-wide tax burdens. As a result, the tax ruling practices and tax laws in these jurisdictions and other countries in which we and our affiliates are organized have changed and could change significantly in the future on a prospective or retroactive basis, and any such changes could materially and adversely affect our company.

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 executive committee comprised of 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, Company Secretary and Managing Director, Ireland, David Kelly; our Executive Vice President and Chief Commercial Officer, John J. Kody; our Executive Vice President, Corporate Development, Barry J. Moze; and our Executive Vice President, Research and Development and Chief Medical Officer, Jeffrey W. Sherman, M.D. In order to retain valuable employees at our company, in addition to salary and cash incentives, we provide incentive stock options and restricted stock units that vest over time. The value to employees of stock options and restricted stock units that vest over time will be significantly affected by movements in the 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 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

Table of Contents

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 our current products, and will be, with respect to any other product or product candidate for which we obtain FDA approval or which we acquires 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, with respect to our currently FDA-approved products (and with respect to our product candidates, if approved), the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product are 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. For example, Hyperion has recently engaged the FDA in discussions related to a change it made to an analytical method for RAVICTI without obtaining the FDA's prior approval. If the FDA determines that prior approval was required and the Acquisition is completed, we could face sanctions and other regulatory consequences with respect to RAVICTI following completion of the Acquisition based on Hyperion's prior changes to the analytical method. 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. With respect to RAVICTI, the FDA imposed several post-marketing requirements and a post-marketing commitment, which include remaining obligations to conduct studies in UCD patients during the first two months of life and from two months to two years of age, including a study of the pharmacokinetics in both age groups, and a randomized study to determine the safety and efficacy in UCD patients who are treatment naïve to phenylbutyrate treatment.

In addition, the FDA closely regulates the marketing and promotion of drugs and biologics. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturers' promotional communications. A significant number of pharmaceutical companies have been the target of inquiries and investigations by various U.S. federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of products for off-label uses and other sales practices. These investigations have alleged violations of various U.S. federal and state laws and regulations, including claims asserting antitrust violations, violations of the Food, Drug and Cosmetic Act, false claims laws, the Prescription Drug Marketing Act, anti-kickback laws, and other alleged violations in connection with the promotion of products for unapproved uses, pricing and Medicare and/or Medicaid reimbursement. 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.

Table of Contents

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 exclusion, debarment or suspension from government healthcare programs.

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.

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 payor 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 payors 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 EU and other significant or potentially significant markets for our products and product candidates, government authorities and third-party payors 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 EU 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.

Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved products for a particular indication. Moreover, a third-party payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Additionally, one third-party payor's decision to cover a particular product does not ensure that other payors will also provide coverage for the product, or will provide coverage at an adequate reimbursement rate. Even though we have contracts with some PBMs in the United States, that does not guarantee that they will perform in accordance with the contracts, nor does that preclude them from taking adverse actions against us, which could materially adversely affect our operating results. In

Table of Contents

addition, the existence of such PBM contracts does not guarantee coverage by such PBM's contracted health plans or adequate reimbursement to their respective providers for our products. For example, two significant PBMs placed DUEXIS and VIMOVO on their exclusion lists beginning in 2015, which has resulted in a loss of coverage for patients whose healthcare plans have adopted these PBM lists. Also, as noted above, we are currently in an ongoing contract and rebate dispute with a U.S. PBM involving VIMOVO and DUEXIS, the outcome of which we cannot at this time determine, and which has the potential to negatively impact our relationship with that PBM, which could affect their coverage and/or reimbursement treatment of our other products. Additional healthcare plan formularies may also exclude our products from coverage due to the actions of these PBMs, future price increases we may implement, our use of the PME program or any other 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, as well as BUPHENYL and, if approved outside the United States, RAVICTI, 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. BUPHENYL is marketed in select countries throughout Europe, the Middle East, and the Asia-Pacific Region. 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 EU 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.

In light of such policies and the uncertainty surrounding proposed regulations and changes in the coverage and reimbursement policies of governments and third-party payors, we cannot be sure that coverage and reimbursement will be available for any of our products 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 are not available or are 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 payors and healthcare providers to use generic drugs that contain the active ingredients found in DUEXIS, PENNSAID 2%, RAYOS/LODOTRA and VIMOVO or any other product candidates that we may develop, acquire or in-license, including BUPHENYL. 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 payors concerning certain promotional approaches that we may implement such as PME program or any other co-pay programs whereby we assist

Table of Contents

qualified patients with certain out-of-pocket expenditures for our product. In addition, pharmaceutical manufacturer co-pay initiatives are the subject of evolving interpretations of applicable regulatory requirements, and any change in the regulatory or enforcement environment regarding such programs could impact our ability to offer such programs. If we are unsuccessful with our PME program or any other co-pay initiatives, we would be at a competitive disadvantage in terms of pricing versus preferred branded and generic competitors, or be subject to significant penalties.

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 U.S. 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 our company for violation of these laws, even if we ultimately are successful in our defense, will cause it 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 Reconciliation Act, or collectively, the ACA, 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 potential developments resulting from the ACA, such as an increase in the number of people with health insurance and an increased focus on preventive medicine, may provide Our additional revenue to offset the annual excise tax (on certain drug product sales) enacted under the ACA, subject to limited exceptions. It is possible that the tax burden, if ours is 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 payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to 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 and similar state laws, 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 our Annual Report on Form 10-K for the fiscal year ended December 31, 2014, which is incorporated by reference herein. These laws may impact, among other things, our company's current and proposed sales, marketing and

Table of Contents

educational programs, as well as other possible relationships with customers, pharmacies, physicians, payors, and patients.

Compliance with these laws, including the development of a comprehensive compliance program, is difficult, costly and time consuming. Because of the breadth of these laws and the narrowness of available statutory and regulatory exemptions, it is possible that some of our company's business activities could be subject to challenge under one or more of such laws. These risks may be increased where there are evolving interpretations of applicable regulatory requirements, such as those applicable to manufacturer co-pay initiatives. We are engaged in various business arrangements with current and potential customers, and we can give no assurance that such arrangements would not be subject to scrutiny under such laws, despite our company's efforts to properly structure such arrangements. 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. Further, we cannot give any assurances that business activities or arrangements of Hyperion prior to the Acquisition will not be scrutinized or subject to enforcement or litigation.

There has also been a recent trend of increased federal and state regulation of payments made to physicians and other healthcare providers. The ACA, among other things, imposed new reporting requirements on drug manufacturers for payments made by them to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information may result in significant civil monetary penalties.

We are unable to predict whether we or Hyperion as our subsidiary upon completion of the Acquisition could be subject to actions under any of these or other healthcare laws, or the impact of such actions. If we are found to be in violation of, or to encourage or assist the violation by third parties of any of the laws described above or other applicable state and federal fraud and abuse laws, we may be subject to penalties, including administrative, civil and criminal penalties, damages, fines, withdrawal of regulatory approval, imprisonment, exclusion from government healthcare reimbursement programs, contractual damages, reputational harm, diminished profits and future earnings, injunctions and other associated remedies, or private qui tam actions brought by individual whistleblowers in the name of the government, and the curtailment or restructuring of our operations, all of which could have a material adverse effect on our business and results of operations. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business.

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. With respect to BUPHENYL, the most common side effects are change in the frequency of breathing, lack of or irregular menstruation, lower back, side, or stomach pain, mood or mental changes, muscle pain or twitching, nausea or vomiting, nervousness or

Table of Contents

restlessness, swelling of the feet or lower legs, unpleasant taste and unusual tiredness or weakness. With respect to RAVICTI, the most common side effects are diarrhea, nausea, decreased appetite, gas, vomiting, high blood levels of ammonia, headache, tiredness and dizziness.

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

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;

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; and

we may be subject to increased exposure to product liability and/or personal injury claims.

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, and we expect to continue to rely on CROs for the completion of on-going and planned clinical trials of RAVICTI. 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. In connection with our planned Phase 3 study to evaluate ACTIMMUNE in the treatment of Friedreich's Ataxia, or FA, we are working with the Clinical Trials Coordination Center, an academic research organization that is part of the Center for Human Experimental Therapeutics at the University of Rochester to conduct the FA Phase 3 study as well as collaborating with the Friedreich's Ataxia Research Alliance, or FARA, and select investigators of FARA's Collaborative Clinical Research Network in FA. 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

S-51

Table of Contents

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 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 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.

In addition, 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 Idiopathic Arthritis for which the FDA recently granted an extension with a final report due date of December 2015. If the Acquisition is completed, upon closing the Acquisition we will also assume Hyperion's post-marketing obligations and commitments to conduct studies in UCD patients during the first two months of life and from two months to two years of age. 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 development of drugs and biologics 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 our 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.

With respect to our planned Phase 3 clinical trial to evaluate ACTIMMUNE for the treatment of FA, and to the extent that we are required to conduct additional clinical development of any of our existing or later acquired products or we conduct clinical development of earlier stage product candidates or for other 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;

Edgar Filing: Horizon Pharma plc - Form 424B5

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;

S-52

Table of Contents

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.

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 or biologics that may be approved for the indications we are investigating. Furthermore, we rely and expect to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our future clinical trials and while we have and 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 product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If our experiences 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.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA. The FDA may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. FDA may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

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

Table of Contents

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. We conduct significant management operations at both our global headquarters located in Dublin, Ireland and our U.S. office 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 and third-party logistics partners to ship 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 third-party suppliers or logistics partners 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 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 itself 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 resources;

substantial monetary awards to trial participants or patients;

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

loss of revenue;

Edgar Filing: Horizon Pharma plc - Form 424B5

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 our current products in the United States, and/or the potential commercial launches of DUEXIS and LODOTRA or following the closing of

S-54

Table of Contents

the Acquisition, RAVICTI, 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 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, independent contractors, principal investigators, consultants, vendors, distributors and CROs may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that our employees, independent contractors, principal investigators, consultants, vendors, distributors and CROs may engage in fraudulent or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or unauthorized activities that violate FDA regulations, including those laws that require the reporting of true, complete and accurate information to the FDA, manufacturing standards, federal and state healthcare fraud and abuse laws and regulations, and laws that require the true, complete and accurate reporting of financial information or data. 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. Misconduct by our employees and other third parties may also include 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 misconduct by our employees and other third parties, 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 itself or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare programs and imprisonment.

Risks Related to our Financial Position and Capital Requirements

We have incurred significant operating losses since our inception, and have not yet achieved profitability.

Edgar Filing: Horizon Pharma plc - Form 424B5

We have a limited operating history and even less history operating as a combined organization following the acquisition of Vidara, and have no history operating as a combined organization that would result from

S-55

Table of Contents

completing the Acquisition. We have financed our operations primarily through equity and debt financings, including the issuance of convertible notes, and have incurred significant operating losses since our inception. We have net losses of \$263.6 million, \$149.0 million and \$87.8 million for the years ended December 31, 2014, 2013 and 2012, respectively. As of December 31, 2014, we have an accumulated deficit of \$720.7 million. Our losses have resulted principally from costs incurred in our development activities for our products and product candidates, commercialization activities related to our products and costs associated with derivative liability accounting. 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. While we anticipate that we will become profitable in the future, whether and when we achieve this will depend on the revenues we generate from the sale of our products being sufficient to cover our operating expenses, and we have not achieved profitability to date.

We have limited sources of revenues and significant expenses. Even if we achieve profitability in the future, we cannot be certain that we will 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. 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 the HPI 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 began commercializing PENNSAID 2% in the United States in January 2015. If the Acquisition is completed, our businesses and the business of Hyperion will be combined and we will assume the commercialization of RAVICTI and BUPHENYL. We may never be able to successfully commercialize our products 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:

continued commercialization of our existing products and any other product candidates for which we obtain approval;

obtaining FDA approvals for additional indications for ACTIMMUNE;

securing additional foreign regulatory approvals for LODOTRA and DUEXIS and, if the Acquisition is completed, RAVICTI; and

developing, acquiring or in-licensing and commercializing a portfolio of other product candidates in addition to our current products.

Even if we do generate additional product sales, we may not be able to 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 fund additional acquisitions.

Edgar Filing: Horizon Pharma plc - Form 424B5

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

S-56

Table of Contents

VIMOVO and the additional expansion of our sales force in connection with our acquisition of U.S. rights to PENNSAID 2%;

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

potentially acquire other businesses or additional complementary products or products that augment our current product portfolio, including costs associated with refinancing debt of acquired companies; and

conduct clinical trials with respect to ACTIMMUNE for FA and any other potential indications beyond GCD or SMO, as well as conduct post-marketing requirements and commitments with respect to our products and products we acquire, including RAVICTI.

While we believe that our expected cash and cash equivalents following the completion of the Acquisition and related financing transactions, including the Debt Financings, will be sufficient to fund our operations to the point of generating continuous 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 presently anticipates, if we develop, acquires or in-licenses additional products or acquires companies, or if our revenue does 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, or delay, cut back or abandon our plans to grow the business through acquisition or in-licensing. 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

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

In addition, if we are 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 over-indebtedness that require Horizon Pharma AG to maintain assets in excess of its liabilities. As of December 31, 2014, Horizon Pharma AG was not over-indebted. However, Horizon Pharma AG has previously been over-indebted, including at December 31, 2013. We will continue to monitor and review Horizon Pharma AG's financial position and, as necessary, will address any over-indebtedness, 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 our company 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

Table of Contents

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, we expect to incur a substantial amount of additional indebtedness to finance the Acquisition, which will subject us to significant additional fixed payment obligations in the future as we become obligated to repay the debt, and we expect that we will continue to be subject to 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 our products, to potentially fund additional regulatory approvals of DUEXIS, ACTIMMUNE and RAYOS/LODOTRA and, following the closing of the Acquisition, RAVICTI, 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 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 carry forwards and certain other tax attributes may be limited.

Under Section 382 of the Code, 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 pre-change net operating loss carry forwards and other pre-change tax attributes to offset post-change income may be limited. In September 2014, the acquisition of Vidara triggered an ownership change limitation and, as a result, we will be subject to annual limits on our ability to utilize net operating loss carry forwards of Horizon Pharma Holdings USA Inc. and its subsidiary. We estimate this will result in annual limits of \$91.1 million, \$84.0 million and \$84.0 million in 2015, 2016 and 2017, respectively. The net operating loss carry forward limitation is cumulative such that any use of the carry forwards 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 acquisition of Vidara. As a result, it is not currently expected that HPI 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 acquisition of Vidara. Notwithstanding this limitation, we expect that HPI 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 HPI 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 us from fully utilizing our U.S. tax attributes prior to their expiration if HPI does not generate taxable income consistent with our expectations.

Table of Contents

Any limitation on our ability to use our net operating loss carry forwards, including any carry forwards of Hyperion following the closing of the Acquisition, 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.

At December 31, 2014, we had \$218.8 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 December 31, 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. GAAP 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.

Covenants under our existing and expected future debt agreements currently restrict or will 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.

Our existing senior secured credit facility, or Existing Credit Facility, imposes, and the similar agreements that we will enter into in connection with our expected borrowings to finance the Acquisition may impose, 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;

pay dividends or distributions or redeem or repurchase capital stock;

S-59

Table of Contents

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 that are currently imposed on us and that may be imposed in connection with our expected borrowings to finance the Acquisition:

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 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 our credit agreements, which could permit the administrative agent to, or permit the 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 our credit agreements. An event of default under our credit agreements could also lead to an event of default under the terms of the 2018 notes and the 2022 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 acquisitions of the U.S. rights to VIMOVO and PENNSAID 2% and the acquisition of Vidara become impaired, we could have to take significant charges against earnings.

In connection with the accounting for acquisitions of the U.S. rights to VIMOVO and PENNSAID 2% and the acquisition of Vidara, we have recorded significant amounts of intangible assets. Under 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 markets.

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 our products in the United States or in other foreign countries. If this were to occur, early generic competition could be expected against our current products 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. In addition, claims directed to dosing and dose adjustment may be substantially less likely to issue in light of the Supreme Court decision in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, where the court held that claims directed to methods of determining whether to adjust drug dosing levels based on drug metabolite levels in the red blood cells were not patent eligible because they were directed to a law of nature. This decision may have wide-ranging implications on the validity and scope of pharmaceutical method claims.

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 the 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. Par retains the ability to challenge the enforceability and validity of the asserted patents as they relate to products other than DUEXIS.

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. 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.

Edgar Filing: Horizon Pharma plc - Form 424B5

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

S-61

Table of Contents

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, on behalf of ourselves and our affiliates, 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. Together with Jagotec, we 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 court held a claim construction hearing on October 16, 2014, and issued its opinion and order on claim construction on November 10, 2014, adopting our proposed construction of both of the disputed claim terms. The court has scheduled expert discovery in the WLF action to be completed by June 2, 2015, and has set the pretrial conference for September 10, 2015. The trial date will be set following the pretrial conference.

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.

On November 13, 2014, we received a Paragraph IV Patent Certification from Watson advising that Watson had filed an ANDA with the FDA for a generic version of PENNSAID 2%. Watson has not advised us as to the timing or status of the FDA's review of its filing.

On December 23, 2014, we filed suit in the United States District Court for the District of New Jersey against Watson seeking an injunction to prevent the approval of the ANDA. The lawsuit alleges that Watson has infringed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, and 8,871,809 by filing an

Table of Contents

ANDA seeking approval from the FDA to market generic versions of PENNSAID 2% 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 Watson's ANDA for 30 months or until an earlier district court decision that the subject patents are not infringed or are invalid. The court has not yet set a trial date for the Watson action.

On December 2, 2014, we received a Paragraph IV Patent Certification against Orange Book listed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, and 8,741,956 from Paddock advising that Paddock had filed an ANDA with the FDA for a generic version of PENNSAID 2%. On January 9, 2015, we received from Paddock another Paragraph IV Patent Certification against newly Orange Book listed U.S. Patent No. 8,871,809. Paddock has not advised us as to the timing or status of the FDA's review of its filing. On January 13, 2015 and January 14, 2015, we filed suits in the United States District Court for the District of New Jersey and the United States District Court for the District of Delaware, respectively, against Paddock seeking an injunction to prevent the approval of the ANDA. The lawsuits allege that Paddock has infringed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, and 8,871,809 by filing an ANDA seeking approval from the FDA to market generic versions of PENNSAID 2% 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 Paddock's ANDA for 30 months or until an earlier district court decision that the subject patents are not infringed or are invalid. The courts have not yet set trial dates for the Paddock actions.

Currently, patent litigation is pending in the United States District Court for 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 United States District Court for 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 United States District Court for the District of New Jersey against a fifth generic company, Anchen, was dismissed on June 9, 2014 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 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.

On February 25, Dr. Reddy's Laboratories, Inc. filed a Petition for *Inter Partes* Review of U.S. Patent No. 8,557,285, one of the patents in litigation in the above referenced VIMOVO cases. The Patent Trial and Appeal Board has not yet issued a decision with regard to whether or not the *Inter Partes* Review will be instituted.

On or about December 19, 2014, we filed a Notice of Opposition to a European patent, EP 2611457, to Roberto Testi, et al., covering compositions and methods for treating FA with interferon gamma, e.g., ACTIMMUNE. In the EU, the grant of a patent may be opposed by one or more private parties.

Table of Contents

On February 2, 2015, we received a Paragraph IV Patent Certification against Orange Book listed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, 8,741,956, and 8,871,809 from Taro Pharmaceuticals USA, Inc. and Taro Pharmaceutical Industries, Ltd., or collectively, Taro, advising that Taro had filed an ANDA with the FDA for a generic version of PENNSAID 2%. Taro has not advised us as to the timing or status of the FDA's review of its filing. On March 13, 2015, we filed suit in the United States District Court for the District of New Jersey against Taro seeking an injunction to prevent the approval of the ANDA. The lawsuit alleges that Taro has infringed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, and 8,871,809 by filing an ANDA seeking approval from the FDA to market generic versions of PENNSAID 2% 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 Taro's ANDA for 30 months or until an earlier district court decision that the subject patents are not infringed or are invalid. The court has not yet set a trial date for the Taro action.

On March 18, 2015, we received a Paragraph IV Patent Certification against Orange Book listed U.S. Patent Nos. 8,217,078, 8,252,838, 8,546,450, 8,563,613, 8,618,164, 8,741,956, and 8,871,809 from Lupin Limited advising that Lupin Limited had filed an ANDA with the FDA for generic version of PENNSAID 2%. Lupin Limited has not advised us as to the timing or status of the FDA's review of its filing. We are still in the process of evaluating the Paragraph IV Patent Certification, and we expect that we will file suit against Lupin Limited within the statutorily prescribed 45 day time limit.

On March 17, 2014, Hyperion received notice from Par Pharmaceutical, Inc. that it had filed an ANDA with the FDA seeking approval for a generic version of our product RAVICTI. The ANDA contained a Paragraph IV Patent Certification alleging that two of Hyperion's patents covering RAVICTI, U.S. Patent No. 8,404,215, titled "Methods of therapeutic monitoring of nitrogen scavenging drugs," which expires in March 2032, and U.S. Patent No. 8,642,012, titled "Methods of treatment using ammonia scavenging drugs," which expires in September 2030, are invalid and/or will not be infringed by Par's manufacture, use or sale of the product for which the ANDA was submitted. Par did not challenge the validity, enforceability, or infringement of Hyperion's primary composition of matter patent for RAVICTI, U.S. Patent No. 5,968,979 titled "Triglycerides and ethyl esters of phenylalkanoic acid and phenylalkenoic acid useful in treatment of various disorders," which would have expired on February 7, 2015, but as to which Hyperion has been granted an interim term of extension until February 7, 2016. Hyperion filed suit against Par on April 23, 2014, and, following the closing of the Acquisition, we will take over and will be responsible for this patent litigation.

We intend to vigorously defend our intellectual property rights relating to DUEXIS, VIMOVO, ACTIMMUNE, PENNSAID 2% and RAYOS and, if the Acquisition is completed, RAVICTI, 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, the Watson and Paddock cases related to PENNSAID 2%, or the Par Pharmaceutical matter related to RAVICTI. 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, PENNSAID 2%, RAYOS or RAVICTI 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, PENNSAID 2% and/or RAYOS and, if the Acquisition is completed, RAVICTI, 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%, or that Hyperion holds with respect to RAVICTI, 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

Table of Contents

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.

With respect to RAVICTI, the composition of matter patent Hyperion holds would have expired in the United States in February 2015 without term extension. However, Hyperion has applied for a term extension of approximately four years for this patent under the Drug Price Competition and Patent Term Restoration Act, or the Hatch-Waxman Act. Hyperion recently received notice that it has been granted an interim extension of this patent's term through February 7, 2016 while the United States Patent and Trademark Office makes a final determination as to the length of the extension. We cannot be certain that the full four year term of extension for which Hyperion has applied will be granted, or that there will be any extension beyond the one year interim extension. We cannot guarantee that pending patent applications related to RAVICTI will result in additional patents or that other existing and future patents related to RAVICTI will be held valid and enforceable or will be sufficient to deter generic competition in the United States. Therefore, it is possible that upon expiration of the RAVICTI composition of matter patent, we would need to rely on forms of regulatory exclusivity, to the extent available, to protect against generic competition.

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 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 ACA 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

Table of Contents

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, in a given country, of a patent to us, 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 us 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 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 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

Table of Contents

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 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'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 if 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 and results of operations.

Hyperion relies on a license from Ucylyd with respect to technology developed by Ucylyd in connection with the manufacturing of RAVICTI. The purchase agreement under which Hyperion purchased the worldwide rights to RAVICTI contains obligations to pay Ucylyd regulatory and sales milestone payments relating to RAVICTI, as well as royalties on the net sales of RAVICTI. On May 31, 2013, when Hyperion acquired BUPHENYL, under a restated collaboration agreement with Ucylyd, Hyperion received a license to use some of the manufacturing technology developed by Ucylyd in connection with the manufacturing of BUPHENYL. The restated collaboration agreement also contains obligations to pay Ucylyd regulatory and sales milestone payments, as well as royalties on net sales of BUPHENYL. Following the completion of the Acquisition, if we fail to make a required payment to Ucylyd and do not cure the failure with the required time period, Ucylyd may be able to terminate the license to use its manufacturing technology for RAVICTI and BUPHENYL. If we lose access to the Ucylyd manufacturing technology, we cannot guarantee that an acceptable alternative method of manufacture could be developed or acquired. Even if alternative technology could be developed or acquired, the loss of the Ucylyd technology could still result in substantial costs and potential periods where we would not

Table of Contents

be able to market and sell RAVICTI and/or BUPHENYL. Hyperion also licenses intellectual property necessary for commercialization of RAVICTI from Brusilow Enterprises. Following the completion of the Acquisition, Brusilow may be entitled to terminate the license if we breach the agreement, including failure to pay required royalties on net sales of RAVICTI, or we do not meet specified diligence obligations in our development and commercialization of RAVICTI, and we do not cure the failure within the required time period. If the license from Brusilow is terminated, it may be difficult or impossible for us to continue to commercialize RAVICTI, which would have a material adverse effect on our business, financial condition and results of operations.

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 one of our patents, or a patent of one of 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.

There are numerous post grant review proceedings available at the U.S. PTO (including inter partes review, post-grant review and ex-parte reexamination) and similar proceedings in other countries of the world that could be initiated by a third party that could potentially negatively impact our issued patents.

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.

Edgar Filing: Horizon Pharma plc - Form 424B5

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 licensors that control the prosecution and maintenance of our licensed patents fail to

S-68

Table of Contents

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 us 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 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 for our ordinary shares will be sustained or what the market price of our ordinary shares will be and as a result it may be difficult to sell our ordinary shares.

Although our ordinary shares are listed on The NASDAQ Global Select Market, an active trading market for our shares may never be sustained. 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 any investment in our ordinary shares.

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 prospectus, 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;

actions or announcements by third party or government payors with respect to coverage and reimbursement of our products;

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;

Edgar Filing: Horizon Pharma plc - Form 424B5

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;

S-69

Table of Contents

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 that we may provide to the public;

actual or anticipated variations in quarterly operating results;

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;

Edgar Filing: Horizon Pharma plc - Form 424B5

significant lawsuits, including patent or shareholder litigation;

changes in the market valuations of similar companies to us;

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 Select 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 have never declared or paid dividends on our share capital and we do not anticipate paying dividends in the foreseeable future.

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 that are currently imposed by the Existing Credit Facility and that we expect to be imposed by the credit agreements associated

S-70

Table of Contents

with our expected borrowings to finance the Acquisition. Any return to shareholders will therefore be limited to the increase, if any, of our ordinary share price.

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 2000, 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 are exacerbated by our transition to an Irish company and the integration of Vidara's business and operations into our historical business and operating structure, and would be further exacerbated by the integration of Hyperion's business and operations following the closing of the Acquisition. 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 that 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 Select 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 its internal controls over financial reporting that are deemed to be material weaknesses. Our compliance with Section 404 requires that we incur substantial expense and expend significant management efforts, particularly because of our Irish parent company structure and international operations. In particular, prior to the acquisition of Vidara, Vidara and its affiliate entities were not subject to the requirements of the Sarbanes-Oxley Act. We are taking 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. 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. In addition, while Hyperion has been subject to some of the requirements of Section 404 of the Sarbanes-Oxley Act, our independent registered public accounting firm has never been required to provide an attestation report on the effectiveness of Hyperion's internal control over financial reporting, and we may otherwise encounter difficulties in integrating Hyperion's internal controls within our current internal control framework. 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

Table of Contents

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 as we respond to their requirements.

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 such 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 of 1933, as amended, or 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 our affiliates. For example, we are subject to a registration rights agreement with certain former Vidara shareholders that acquired our ordinary shares in connection with our acquisition of Vidara. Pursuant to this agreement, we filed and are required to maintain a registration statement covering the resale of 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. 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.

In addition, any conversion or exchange of our existing convertible notes, whether pursuant to their terms or pursuant to privately negotiated transactions between the issuer and/or us and a holder of such securities could depress the market price for our ordinary shares. In the fourth quarter of 2014 and the first quarter of 2015, we entered into separate, privately-negotiated conversion agreements with certain holders of the 2018 notes. Under the conversion agreements, the holders agreed to convert an aggregate principal amount of \$121.3 million of 2018 notes held by them and we agreed to settle such conversions by issuing 22,606,336 ordinary shares. In addition, pursuant to the conversion agreements, we made an aggregate cash payment of \$22.0 million to the holders for additional exchange consideration and \$2.2 million of accrued and unpaid interest. As of March 31, 2015, approximately \$28.7 million in aggregate principal amount of the 2018 notes remained outstanding. We may enter into additional conversion agreements with respect to the 2018 notes or may enter into similar agreements with respect to the 2022 notes from time to time.

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 or securities convertible into or exchangeable for ordinary shares, our shareholders may experience substantial dilution. We may sell ordinary shares, and we may sell convertible or exchangeable 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 such ordinary shares, convertible or exchangeable securities or other equity securities in subsequent transactions, existing shareholders may be materially diluted. New investors in such subsequent transactions could gain rights, preferences and privileges senior to those of holders of ordinary shares. We also maintain equity incentive plans, including our 2014 Equity Incentive Plan, 2014 Non-Employee

Table of Contents

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 our 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 U.S. 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 differ 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 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 of directors;

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 at a meeting of shareholders to amend or repeal our articles of association.

In addition, several mandatory provisions of Irish law could prevent or delay an acquisition of us. For example, Irish law does not permit shareholders of an Irish public limited company to take action by written consent with less than unanimous consent. We are also subject to various provisions of Irish law relating to mandatory bids, voluntary bids, requirements to make a cash offer and minimum price requirements, as well as substantial acquisition rules and rules requiring the disclosure of interests in our ordinary shares in certain circumstances.

Edgar Filing: Horizon Pharma plc - Form 424B5

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 our other shareholders to elect directors other than the candidates nominated by our board of directors, and could depress the market price of our ordinary shares.

S-73

Table of Contents

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 from this stamp duty is available to transfers by shareholders who hold 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 or to a record holder who holds 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 one of our subsidiaries 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 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 such 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 such subsidiary for the amount of stamp duty paid. Our lien shall extend to all dividends paid on those ordinary shares.

Dividends paid by us may be subject to Irish dividend withholding tax

In certain circumstances, as an Irish tax resident company, we will be required to deduct Irish dividend withholding tax (currently at the rate of 20%) from dividends paid to our shareholders. Shareholders that are resident in the United States, EU countries (other than Ireland) or other countries with which Ireland has signed a tax treaty (whether the treaty has been ratified or not) generally should not be subject to Irish withholding tax so long as the shareholder has provided its broker, for onward transmission to our qualifying intermediary or other designated agent (in the case of shares held beneficially), or our or its transfer agent (in the case of shares held directly), with all the necessary documentation by the appropriate due date prior to payment of the dividend. However, some shareholders may be subject to withholding tax, which could adversely affect the price of our 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 our company regularly, demand for our ordinary shares could decrease, which might cause our share price and trading volume to decline.

We may become involved in securities class action litigation that could divert our 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,

Edgar Filing: Horizon Pharma plc - Form 424B5

litigation could result in substantial costs and may be a distraction to our management, and may result in unfavorable results that could adversely impact our financial condition and prospects.

S-74

Table of Contents

Risks Related to this Offering

Our management will have broad discretion as to the use of the net proceeds from this offering, and we may not use the proceeds effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our ordinary shares. This offering is not contingent upon the closing of the Acquisition, and we cannot guarantee that the Acquisition will close. If the Acquisition does not close, we will not use the net proceeds from this offering for that purpose and will have discretion to use the net proceeds for other purposes. Our failure to apply these funds effectively could have a material adverse effect on our business and cause the price of our ordinary shares to decline.

If you purchase the ordinary shares sold in this offering, you will experience immediate and substantial dilution in your investment. You will experience further dilution if we issue additional equity securities in the future.

Because the price per share of our ordinary shares being offered is substantially higher than the net tangible book value per share of our ordinary shares, you will suffer substantial dilution with respect to the net tangible book value of the ordinary shares you purchase in this offering. Based on the assumed public offering price of \$28.48 per share (the last reported sale price per ordinary share on The NASDAQ Global Select Market on April 10, 2015) and our net tangible book value as of December 31, 2014, if you purchase ordinary shares in this offering, you will suffer immediate and substantial dilution of \$27.54 per share with respect to the net tangible book value of our ordinary shares. See [Dilution](#) for a more detailed discussion of the dilution you will incur if you purchase ordinary shares in this offering.

In addition, we have a significant number of stock options, restricted stock units, convertible promissory notes and warrants outstanding. To the extent that these securities have been or may be exercised or converted or other shares are issued, investors purchasing our ordinary shares in this offering may experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our shareholders or result in downward pressure on the price of our ordinary shares.

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, including RAVICTI and BUPHENYL if we complete the Acquisition;

our business strategy and plans to acquire biopharmaceutical products and companies;

the pending Acquisition, including the expected timing, impact and benefits to be derived therefrom;

financing plans, including to fund the Acquisition;

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

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, and the negative of these terms and similar expressions in the prospectus supplement. 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** in this prospectus supplement, 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.

Table of Contents

USE OF PROCEEDS

We estimate that the net proceeds to us from this offering, after deducting the underwriting discounts and estimated offering expenses payable by us, will be approximately \$325.4 million (or approximately \$374.3 million if the underwriters exercise their option to purchase additional ordinary shares in full), based upon an assumed public offering price of \$28.48 per share (the last reported sale price of our ordinary shares on The NASDAQ Global Select Market on April 10, 2015). A \$1.00 increase (decrease) in the assumed public offering price of \$28.48 per share would increase (decrease) the net proceeds to us from this offering by approximately \$11.5 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus supplement, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, a one million share increase (decrease) in the number of shares offered by us, as set forth on the cover page of this prospectus supplement, would increase (decrease) the net proceeds to us by \$27.2 million, assuming the assumed public offering price of \$28.48 per share (the last reported sale price of our ordinary shares on the Nasdaq Global Select Market on April 10, 2015) remains the same, and after deducting the estimated underwriting discounts and estimated offering expenses payable by us. We intend to use the net proceeds from the offering to fund a portion of the Acquisition and the remainder to fund additional acquisitions or investments in businesses, products and product candidates that are complementary to our own, although we have no present commitments or agreements to do so other than with respect to the Acquisition, and for general corporate purposes. If the Acquisition is not consummated, we expect to use the net proceeds from this offering for future acquisitions and general corporate purposes.

S-77

Table of Contents**CAPITALIZATION**

The following table sets forth our cash and cash equivalents and capitalization as of December 31, 2014:

on an actual basis;

on an as adjusted basis after giving effect to our issuance of the 2022 notes;

on an as further adjusted basis after giving effect to this offering, assuming a public offering price of \$28.48 per ordinary share, which is the last reported sale price of our ordinary shares on The NASDAQ Global Select Market on April 10, 2015;

on an as further adjusted basis to also give effect to the anticipated borrowings pursuant to the Debt Financings;

on an as further adjusted basis after giving effect to the proposed extinguishment of our existing senior secured credit facility; and

on a pro forma as adjusted basis to give effect to the consummation of the Acquisition and the application of a portion of the net proceeds from this offering and the proposed Debt Financings.

The following data are qualified in their entirety by our financial statements and other information included and incorporated by reference herein. You should read this table in conjunction with Prospectus Supplement Summary The Hyperion Acquisition, Prospect Supplement Summary About the Debt Financings, Risk Factors, Use of Proceeds and Unaudited Pro Forma Combined Financial Information. Investors in our ordinary shares should not place undue reliance on the as adjusted or pro forma as adjusted information included in this prospectus supplement because this offering is not contingent upon any of the transactions reflected in the adjustments included in the following information. Whether the assumed financing sources are available and, if available, the terms of our future financings, will be subject to market conditions. The actual sources of financing and the terms on which it is obtained may not be as favorable as those reflected in the following data. Differences between the assumed and actual financing sources and terms will occur and could have a material impact on the as adjusted and pro forma as adjusted financial information and the combined company's financial position and future results of operations.

| | As of December 31, 2014 | | | | | |
|--|-------------------------|---|---|--|---|---|
| | Actual | As Adjusted for Issuance of 2022 Notes (unaudited) | As Further Adjusted for this Offering (unaudited) | As Further Adjusted for the Proposed Debt Financings (unaudited) | As Further Adjusted for the Proposed Extinguishment of Senior Secured Credit Facility (unaudited) | Pro Forma As Adjusted for the Acquisition (unaudited) |
| (In thousands, except share and per share data) | | | | | | |
| Cash and cash equivalents | \$ 218,807 | \$ 606,135 | \$ 931,516 | \$ 1,706,516 | \$ 1,361,956 | \$ 379,103 |
| Long-term debt, including current portion: | | | | | | |
| 5.0% convertible senior notes due 2018(1)(2) | 48,334 | 48,334 | 48,334 | 48,334 | 48,334 | 48,334 |
| 2.5% exchangeable senior notes due 2022(1)(3) | | 268,920 | 268,920 | 268,920 | 268,920 | 268,920 |
| Senior secured credit facility(4) | 297,169 | 297,169 | 297,169 | 297,169 | | |
| Secured term loans(5) | | | | 792,000 | 792,000 | 792,000 |

Edgar Filing: Horizon Pharma plc - Form 424B5

| | | | | | | |
|--|------------|--------------|--------------|--------------|--------------|--------------|
| Total long-term debt, including current portion | \$ 345,503 | \$ 614,423 | \$ 614,423 | \$ 1,406,423 | \$ 1,109,254 | \$ 1,109,254 |
| Shareholders' equity: | | | | | | |
| Ordinary shares, nominal value \$0.0001 per share, 300,000,000 shares authorized; 124,425,853 shares issued and 124,041,487 shares outstanding, actual and as adjusted; 136,041,487 shares outstanding, pro forma as adjusted(6) | | | | | | |
| | \$ 13 | \$ 13 | \$ 13 | \$ 13 | \$ 13 | \$ 13 |
| Treasury shares, 384,366 ordinary shares | (4,585) | (4,585) | (4,585) | (4,585) | (4,585) | (4,585) |
| Additional paid-in capital(1)(3) | 1,269,858 | 1,388,938 | 1,714,319 | 1,714,319 | 1,714,319 | 1,714,319 |
| Accumulated other comprehensive loss | (4,363) | (4,363) | (4,363) | (4,363) | (4,363) | (4,363) |
| Accumulated deficit | (720,719) | (720,719) | (720,719) | (720,719) | (777,577) | (816,877) |
| Total shareholders' equity | 540,204 | 659,284 | 984,665 | 984,665 | 927,807 | 888,507 |
| Total capitalization(1)(3) | \$ 885,707 | \$ 1,273,707 | \$ 1,599,088 | \$ 2,391,088 | \$ 2,037,061 | \$ 1,997,761 |

S-78

Table of Contents

- (1) In accordance with ASC 470-20, convertible debt instruments that may be settled entirely or partially in cash upon conversion are required to be separated into a liability and an equity component, such that interest expense reflects the issuer's non-convertible debt interest rate. Upon issuance, the original issue discount is recognized as a decrease in debt and an increase in equity. The debt component will accrete up to the principal amount over the expected term of the debt. Such accounting guidance does not affect the actual amount that we are required to repay.
- (2) Amounts shown reflect the application of ASC 470-20 with respect to the 2018 notes. As of December 31, 2014, \$61.0 million principal amount of the 2018 notes remained outstanding.
- (3) Amounts shown reflect the application of ASC 470-20 with respect to the 2022 notes with a total principal amount of \$400.0 million.
- (4) The amounts shown reflect the carrying value of the debt under our existing senior secured credit facility. Actual principal amount outstanding as of December 31, 2014 was \$300.0 million.
- (5) Amounts shown reflect the application of ASC 470-20 with respect to the debt anticipated to be issued in conjunction with the Debt Financings.
- (6) Ordinary shares shown as issued and outstanding in the table above exclude ordinary shares to be issued in conjunction with this offering, and also exclude, as of December 31, 2014: (i) 7,027,683 ordinary shares issuable upon the exercise of outstanding options, having a weighted average exercise price of \$8.95 per share; (ii) 1,618,502 ordinary shares issuable upon the vesting of outstanding restricted stock units; (iii) 6,683,811 ordinary shares issuable upon the exercise of outstanding warrants, having a weighted average exercise price of \$5.01 per share; and (iv) 11,369,398 ordinary shares, all or a portion of which may be issued upon the conversion of the 2018 notes; and (v) an aggregate of 26,579,579 ordinary shares reserved for future issuance under our equity incentive, employee share purchase and non-employee equity plans.

Table of Contents**DILUTION**

If you invest in our ordinary shares in this offering, your ownership interest will be immediately diluted to the extent of the difference between the public offering price per share and the pro forma as adjusted net tangible book value per share of our ordinary shares immediately after this offering.

Our historical net tangible book deficit as of December 31, 2014 was \$(250.9) million, or \$(2.02) per ordinary share. Our historical net tangible book value (deficit) is the amount of our total tangible assets less our liabilities. Historical net tangible book value (deficit) per share is our historical net tangible book value divided by the number of ordinary shares outstanding as of December 31, 2014.

After giving pro forma effect to our issuance of the 2022 notes, and the anticipated borrowings pursuant to the Debt Financings and repayment of existing indebtedness, our pro forma net tangible book deficit as of December 31, 2014 would have been approximately \$(196.9) million, or \$(1.58) per ordinary share.

After giving further effect to the sale of 12,000,000 shares of our ordinary shares in this offering at an assumed public offering price of \$28.48 per share (the last reported sale price of our ordinary shares on the Nasdaq Global Select Market on April 10, 2015), and after deducting the estimated underwriting discounts and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of December 31, 2014 would have been approximately \$128.5 million, or \$0.94 per ordinary share. This represents an immediate increase in pro forma net tangible book value of \$2.52 per share to our existing stockholders and an immediate dilution of \$27.54 per share to new investors purchasing ordinary shares in this offering at the assumed public offering price. The following table illustrates this dilution on a per share basis:

| | |
|--|-----------|
| Assumed public offering price per share | \$ 28.48 |
| Historical net tangible book deficit per share as of December 31, 2014 | \$ (2.02) |
| Increase in net tangible book deficit per share attributable to pro forma transactions described above | \$ 0.43 |
| Pro forma net tangible book deficit per share before giving effect to this offering | \$ (1.59) |
| Further increase in pro forma net tangible book value per share attributable to new investors participating in this offering | \$ 2.53 |
| Pro forma as adjusted net tangible book value per share after this offering | \$ 0.94 |
| Dilution per share to new investors participating in this offering | \$ 27.54 |

A \$1.00 increase (decrease) in the assumed public offering price of \$28.48 per share (the last reported sale price of our ordinary shares on the Nasdaq Global Select Market on April 10, 2015) would increase (decrease) the as adjusted pro forma net tangible book value per share after this offering by \$0.09 per share and the dilution per share to new investors participating in this offering by \$0.91 per share, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. A one million share increase or decrease in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase or decrease, respectively, the as adjusted pro forma net tangible book value per share after this offering by \$0.20 and decrease or increase, respectively, the dilution per share to new investors participating in this offering by \$0.20, assuming the assumed public offering price of \$28.48 per share (the last reported sale price of our common stock on The Nasdaq Global Select Market on April 10, 2015) remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Edgar Filing: Horizon Pharma plc - Form 424B5

If the underwriters exercise their option in full to purchase an additional 1,800,000 of our ordinary shares in this offering, the as adjusted pro forma net tangible book value will increase to \$1.30 per share, representing an immediate increase to existing stockholders of \$2.88 per share and an immediate dilution of \$22.98 per share to new investors participating in this offering.

S-80

Table of Contents

The foregoing discussion is based on 124,041,487 ordinary shares issued and outstanding as of December 31, 2014 and excludes as of that date:

7,027,683 ordinary shares issuable upon the exercise of outstanding options, having a weighted average exercise price of \$8.95 per share;

1,618,502 ordinary shares issuable upon the settlement of outstanding restricted stock units;

6,683,811 ordinary shares issuable upon the exercise of outstanding warrants, having a weighted average exercise price of \$5.01 per share;

11,369,368 ordinary shares, all or a portion of which may be issued upon the conversion of our outstanding convertible senior notes;

9,929,336 ordinary shares reserved for future issuance under our 2014 Employee Share Purchase Plan;

14,264,001 ordinary shares reserved for future issuance under our 2014 Equity Incentive Plan; and

2,386,242 ordinary shares reserved for future issuance under our 2014 Non-Employee Equity Plan.

Table of Contents**PRICE RANGE OF ORDINARY SHARES AND DIVIDEND POLICY**

Our ordinary shares are listed on The NASDAQ Global Select Market under the symbol HZNP . The following table sets forth, for the periods indicated, the high and low last sale prices per ordinary share as reported on The NASDAQ Global Select Market and dividends paid per ordinary share.

| | High | Low |
|--|-------------|------------|
| Fiscal year ended December 31, 2015 | | |
| First quarter | \$ 26.46 | \$ 12.64 |
| Second quarter (through April 10, 2015) | \$ 28.90 | \$ 25.26 |
| Fiscal year ended December 31, 2014 | | |
| First quarter | \$ 18.30 | \$ 7.40 |
| Second quarter | \$ 16.72 | \$ 11.50 |
| Third quarter | \$ 16.56 | \$ 7.85 |
| Fourth quarter | \$ 13.55 | \$ 10.15 |

On April 10, 2015, the last reported sale price of our ordinary shares on The NASDAQ Global Select Market was \$28.48 per share. On March 31, 2015, there were 133,287,015 of our ordinary shares outstanding.

We have never paid or declared any cash dividends.

Table of Contents

UNAUDITED PRO FORMA COMBINED FINANCIAL INFORMATION

The following unaudited pro forma combined financial information is presented to illustrate the estimated effects of the following transactions (collectively, the Transactions): (i) this offering of 12 million ordinary shares (the Offering) by Horizon Pharma plc (Horizon or the Company), (ii) the March 2015 private placement of \$400 million in aggregate principal amount of 2.5% Exchangeable Senior Notes due 2022 (the Exchangeable Notes), (iii) the acquisition of Hyperion Therapeutics (Hyperion) by the Company pursuant to a tender offer for all outstanding shares of Hyperion's common stock for \$46.00 per share (the Offer Price), which was announced on March 30, 2015 (the Acquisition), (iv) the assumed funding of \$800 million principal amount of the term loans under a new senior secured term loan facility (the Senior Secured Term Loans), the proceeds of which would be used, in addition to a portion of Horizon's existing cash and a portion of the proceeds of the Offering, to repay \$300 million principal amount of outstanding term loans under Horizon's existing senior secured credit facility (the Existing Credit Facility) and certain existing debt of Hyperion, fund a portion of the Offer Price and pay any prepayment premium, fees and expenses in connection with the foregoing, (v) the acquisition of Vidara Therapeutics International Public Limited (Vidara) by the Company which closed on September 19, 2014, (the Merger) and (vi) \$300 million of loans borrowed under the Existing Credit Facility in connection with the Merger.

The historical pro forma combined balance sheet information as of December 31, 2014 is based upon and derived from the historical financial information of the Company and Hyperion and gives effect to the Transactions as if such transactions had occurred on December 31, 2014 except for the acquisition of Vidara and its related financings, which are already reflected in Horizon's historical balance sheet as of December 31, 2014. The unaudited pro forma combined statement of operations for the year ended December 31, 2014 is based upon and derived from the historical financial information of the Company, Hyperion and Vidara and gives effect to the Transactions as if they occurred on January 1, 2014.

The Acquisition will be accounted for as a business combination using the acquisition method of accounting under the provisions of Accounting Standards Codification (ASC) 805, Business Combinations, (ASC 805). The Merger has been accounted for as a reverse acquisition under the acquisition method of accounting under the provisions of ASC 805. The unaudited pro forma combined financial information set forth below primarily give effect to the following:

The application of the acquisition method of accounting in connection with the acquisitions referred to above;

The Offering;

The issuance of the Exchangeable Notes;

The borrowing under the Senior Secured Term Loans; and

Transaction costs in connection with the acquisitions and financings.

The pro forma adjustments are preliminary and are based upon available information and certain assumptions, as described in the accompanying notes to the unaudited pro forma combined financial information, that Horizon management believes are reasonable under the circumstances and which are described in the accompanying notes to the unaudited pro forma combined financial information. Actual results and valuations may differ materially from the assumptions within the accompanying unaudited pro forma combined financial information.

Edgar Filing: Horizon Pharma plc - Form 424B5

Under ASC 805, assets acquired and liabilities assumed are generally recorded at their acquisition date fair value. The fair value of identifiable tangible and intangible assets acquired and liabilities assumed from the Acquisition are based on a preliminary estimate of fair value as of December 31, 2014. Any excess of the purchase price over the fair value of identified assets acquired and liabilities assumed will be recognized as

S-83

Table of Contents

goodwill. Significant judgment is required in determining the estimated fair values of developed technology intangible assets and certain other assets and liabilities. Such a valuation requires estimates and assumptions including, but not limited to, estimating future cash flows and direct costs in addition to developing the appropriate discount rates and current market profit margins. Horizon's management believes the fair values recognized for the assets to be acquired and the liabilities to be assumed are based on reasonable estimates and assumptions. After the closing of the Acquisition, we will complete the appraisals necessary to finalize the required purchase price allocation based upon the fair market values as of the actual closing date of the Acquisition, at which time the final allocation of the purchase price will be determined. The final purchase price allocation will be different than that reflected in the unaudited pro forma purchase price allocation, and those differences could be material.

The unaudited pro forma combined financial information has been prepared by Horizon management in accordance with SEC Regulation S-X Article 11 for illustrative purposes only and is not necessarily indicative of the combined financial position or results of operations that would have been realized had the transactions been completed as of the dates indicated, nor is it meant to be indicative of any anticipated combined financial position or future results of operations that Horizon will experience after the Transactions are completed. In addition, the accompanying unaudited pro forma combined statement of operations do not include any pro forma adjustments to reflect expected cost savings or restructuring actions which may be achievable or the impact of any non-recurring activity and one-time transaction related costs.

Certain financial information of Hyperion and Vidara, as presented in their respective consolidated financial statements, has been reclassified to conform to the historical presentation in Horizon's consolidated financial statements for purposes of preparation of the unaudited pro forma combined financial information. See Notes 4 and 5 for additional information on the reclassifications that were made to derive the Historical Hyperion (after conforming reclassifications) and Historical Vidara (after conforming reclassifications) columns in the unaudited pro forma combined financial statements.

The unaudited pro forma combined financial statements, including the notes thereto, should be read in conjunction with the historical consolidated financial statements of Horizon included in its Annual Report on Form 10-K for the year ended December 31, 2014, the historical consolidated financial statements of the Hyperion included in its Annual Report on Form 10-K for the year ended December 31, 2014, and Vidara's Quarterly Report on Form 10-Q for the quarter ended June 30, 2014, all of which are incorporated by reference herein.

The pro forma financial information contained in this prospectus supplement is based upon certain assumptions with respect to our financing of the Acquisition. Whether the assumed financing sources are available and, if available, the terms of our future financings, will be subject to market conditions. The actual sources of financing and the terms on which it is obtained may not be as favorable as those reflected in the pro forma financial information. Differences between preliminary estimates in the pro forma financial information and the final acquisition accounting, as well as between the assumed and actual financing sources and terms, will occur and could have a material impact on the pro forma financial information and the combined company's financial position and future results of operations.

Table of Contents**Unaudited Pro Forma Combined Balance Sheet**

As of December 31, 2014

(In thousands)

| | Historical Horizon Pharma plc | Historical Hyperion (after conforming reclassifications) (see Note 4) | Pro Forma Adjustments | | Pro Forma Combined |
|---|----------------------------------|--|--------------------------|-------------|-----------------------|
| Assets | | | | | |
| Current Assets: | | | | | |
| Cash and cash equivalents | \$ 218,807 | \$ 102,796 | \$ (344,560) | 6(B) | \$ 379,103 |
| | | | 775,000 | 6(A) | |
| | | | 387,328 | 6(C) | |
| | | | (1,071,938) | 6(D) | |
| | | | (38,800) | 6(E) | |
| | | | 43,713 | 6(F) | |
| | | | (18,624) | 6(I) | |
| | | | 325,381 | 6(H) | |
| Short-term investments | | 34,487 | (34,487) | 6(F) | |
| Restricted cash | 738 | | | | 738 |
| Accounts receivables, net | 73,915 | 14,864 | | | 88,779 |
| Inventories, net | 16,865 | 4,621 | 11,806 | 6(G) | 33,292 |
| Prepaid expenses and other current assets | 14,370 | 2,632 | 17,000 | 6(A) | 34,674 |
| | | | 672 | 6(C) | |
| Deferred tax asset | 1,530 | | | | 1,530 |
| Total current assets | \$ 326,225 | \$ 159,400 | \$ 52,491 | | \$ 538,116 |
| Long-term assets: | | | | | |
| Long-term investments | | 9,226 | (9,226) | 6(F) | |
| Property, plant and equipment, net | 7,241 | 1,116 | | | 8,357 |
| Developed technology, net | 696,963 | | 1,006,900 | 6(G) | 1,703,863 |
| In process research and development | 66,000 | | | | 66,000 |
| Other intangibles, net | 7,870 | 8,816 | (8,816) | 6(G) | 7,870 |
| Goodwill | | | 306,044 | 6(G) | 306,044 |
| Deferred tax asset | 18,761 | | | | 18,761 |
| Other assets | 11,564 | 1,858 | (9,467) | 6(B) | 3,955 |
| Total assets | \$ 1,134,624 | \$ 180,416 | \$ 1,337,926 | | \$ 2,652,966 |
| Liabilities and Shareholders' Equity | | | | | |
| Current liabilities: | | | | | |
| Accounts payable | 21,011 | 4,669 | | | 25,680 |
| Accrued expenses | 46,625 | 13,287 | | | 59,912 |
| Accrued trade, discounts and rebates | 76,115 | 10,142 | | | 86,257 |
| Accrued royalties - current portion | 25,325 | 2,080 | 6,493 | 6(G) | 33,898 |
| Deferred revenues - current portion | 1,261 | 224 | | | 1,485 |
| Notes payable - current portion | 48,334 | | | | 48,334 |
| Deferred tax liabilities | 721 | | 4,167 | 6(G) | 4,888 |
| Total current liabilities | \$ 219,392 | \$ 30,402 | \$ 10,660 | | \$ 260,454 |
| Long-Term liabilities: | | | | | |
| Long-term debt, net | 297,169 | 18,124 | (297,169) | 6(B) | 1,060,920 |
| | | | 792,000 | 6(A) | |
| | | | 268,920 | 6(C) | |
| | | | (18,124) | 6(I) | |
| Accrued royalties, net of current | 48,887 | | 75,707 | 6(G) | 124,594 |

Edgar Filing: Horizon Pharma plc - Form 424B5

| | | | | | |
|---|--------------|------------|--------------|-------------|--------------|
| Deferred revenues, net of current | 8,144 | | | | 8,144 |
| Deferred tax liabilities, net | 19,570 | | 289,181 | 6(G) | 308,751 |
| Other long term liabilities | 1,258 | 338 | | | 1,596 |
| Total Long-term liabilities | \$ 375,028 | \$ 18,462 | \$ 1,110,515 | | \$ 1,504,005 |
| Shareholders' Equity | | | | | |
| Ordinary shares, \$0.0001 nominal value; 300,000,000 shares authorized; 124,425,853 shares issued and 124,041,487 shares outstanding at December 31, 2014; 136,425,853 shares issued and 136,041,487 shares outstanding at December 31,2014 pro forma | 13 | 2 | (2) | 6(J) | 13 |
| Treasury stock, 384,366 ordinary shares | (4,585) | | | | (4,585) |
| Additional paid-in capital | 1,269,858 | 260,225 | 119,080 | 6(C) | 1,714,319 |
| | | | 325,381 | 6(H) | |
| | | | (260,225) | 6(J) | |
| Accumulated other comprehensive loss | (4,363) | (50) | 50 | 6(J) | (4,363) |
| Accumulated deficit | (720,719) | (128,625) | 128,625 | 6(J) | (816,877) |
| | | | (96,158) | 6(K) | |
| Total shareholders' equity | \$ 540,204 | \$ 131,552 | \$ 216,751 | | \$ 888,507 |
| Total liabilities and shareholders' equity | \$ 1,134,624 | \$ 180,416 | \$ 1,337,926 | | \$ 2,652,966 |

See the accompanying notes to the unaudited pro forma combined financial information, which are an integral part of these pro forma financial statements.

Table of Contents**Unaudited Pro Forma Combined Statement of Operations**

For the Year December 31, 2014

(In thousands, except for share data)

| | Historical Horizon Plc | Historical Vidara (after reclassifications) (see Note 5) | Historical Hyperion (after reclassifications) (see Note 4) | Vidara Acquisition Accounting Adjustments | Hyperion Acquisition Accounting Adjustments | Pro Forma Combined |
|---|---------------------------|--|--|--|--|-----------------------|
| Net sales | \$ 296,955 | \$ 50,565 | \$ 113,584 | | | \$ 461,104 |
| Cost of sales | 78,753 | 11,290 | 18,353 | 28,955 7(A) | 121,237 7(I) | 247,523 |
| | | | | (11,065) 7(L) | | |
| Gross profit | \$ 218,202 | \$ 39,275 | \$ 95,231 | \$ (17,890) | \$ (121,237) | \$ 213,581 |
| Operating Expenses: | | | | | | |
| Research and development | 17,460 | 2,799 | 20,715 | (414) 7(M) | | 40,560 |
| Sales and marketing | 120,276 | 17,664 | 17,367 | (8,600) 7(M) | | 146,707 |
| General and administrative | 88,957 | 8,253 | 31,155 | (40,227) 7(C) | | 79,659 |
| | | | | (5,102) 7(M) | | |
| | | | | (3,377) 7(B) | | |
| Goodwill impairment | | | 30,201 | | | 30,201 |
| Depreciation and amortization | | 487 | | (487) 7(E) | | |
| Total operating expenses | \$ 226,693 | \$ 29,203 | \$ 99,438 | \$ (58,207) | \$ | \$ 297,127 |
| Operating income (loss) | \$ (8,491) | \$ 10,072 | \$ (4,207) | \$ 40,317 | \$ (121,237) | \$ (83,546) |
| OTHER (EXPENSE) INCOME, NET: | | | | | | |
| Interest expense, net | (23,826) | (605) | (1,046) | | (72,167) 7(F) | (98,199) |
| | | | | | (555) 7(K) | |
| Loss on induced debt conversion and debt extinguishment | (29,390) | | | | | (29,390) |
| Foreign exchange loss | (3,905) | 11 | | | | (3,894) |
| Loss on derivative fair value | (214,995) | | | | | (214,995) |
| Other (expense) income, net | (11,251) | (298) | (699) | 8,222 7(D) | | (4,026) |
| Bargain purchase gain | 22,171 | | | (22,171) 7(G) | | |
| Total other expense, net | \$ (261,196) | \$ (892) | \$ (1,745) | \$ (13,949) | \$ (72,722) | \$ (350,504) |
| (Loss) income before income tax (benefit) expense | (269,687) | 9,180 | (5,952) | 26,368 | (193,959) | (434,050) |
| INCOME TAX (BENEFIT) EXPENSE | (6,084) | 881 | 303 | (77) 7(H) | (73,704) 7(J) | (78,681) |
| NET INCOME (LOSS) | \$ (263,603) | \$ 8,299 | \$ (6,255) | \$ 26,445 | \$ (120,255) | \$ (355,369) |
| Weighted average shares | 83,751,129 | | | | | 95,751,129 |

Edgar Filing: Horizon Pharma plc - Form 424B5

| | | | | |
|--------------------------------|----|--------|----|--------|
| Basic & Diluted EPS | \$ | (3.15) | \$ | (3.71) |
|--------------------------------|----|--------|----|--------|

See the accompanying notes to the unaudited pro forma combined financial information, which are an integral part of these pro forma financial statements.

S-86

Table of Contents

1. Description of transactions

The Acquisition: On March 29, 2015, Horizon Pharma, Inc. (HPI), a Delaware corporation and indirect wholly-owned subsidiary of Horizon Pharma plc, Ghria Acquisition Inc., a Delaware corporation and a wholly owned subsidiary of HPI (Purchaser) and Hyperion entered into a definitive Agreement and Plan of Merger (the Merger Agreement), pursuant to which HPI, through Purchaser, has commenced an offer (the Offer) to acquire all of the outstanding shares of the Hyperion s common stock, par value \$0.0001 per share (the Shares), for \$46.00 per share in cash, without interest, subject to any required withholding of taxes (the Offer Price).

The Company plans to pay for the Acquisition with its existing cash, which includes net proceeds from the completed offering of \$400 million in aggregate principal amount of the Exchangeable Notes and the anticipated proceeds from this Offering and the Senior Secured Term Loans described below or other debt incurred in lieu thereof.

Exchangeable Notes. On March 13, 2015, Horizon Pharma Investment Limited, a wholly-owned subsidiary of Horizon Pharma plc, completed its private placement of \$400 million aggregate principal amount of the Exchangeable Notes to several investment banks acting as initial purchasers who subsequently resold the Exchangeable Notes to qualified institutional buyers as defined in Rule 144A under the Securities Act.

Senior Secured Term Loans: In connection with the Acquisition, on March 29, 2015, the Company entered into a commitment letter (the Debt Commitment Letter) with Citigroup Global Capital Markets Inc. (Citi) and Jefferies Finance LLC (Jefferies), pursuant to which Citi and Jefferies have committed to provide up to \$900 million of senior secured term loans pursuant to a term loan facility, the proceeds of which, in addition to a portion of Horizon s existing cash, would be used to (i) refinance the loans under Existing Credit Facility and certain outstanding debt of the Target (the Refinancing), (ii) pay the Offer Price, and (iii) pay any prepayment premiums, fees and expenses in connection with any of the foregoing. The commitment to provide the Senior Secured Term Loans is subject to certain conditions, including the negotiation of definitive documentation for the Senior Secured Term Loans and other customary closing conditions consistent with the Merger Agreement. HPI will pay customary fees and expenses in connection with obtaining the Debt Commitment Letter and the senior secured term loans and has agreed to indemnify the lenders if certain losses are incurred by the lenders in connection therewith. Proceeds the Company receives from the Offering will not reduce the total amount committed under the Debt Commitment Letter.

Merger: On September 19, 2014, the Company acquired Vidara for \$601.4 million, comprised of \$387.8 million market value of the 31,350,000 Horizon ordinary shares that were held by prior Vidara shareholders immediately following the closing of the Merger plus cash consideration of \$213.6 million.

2. Basis of presentation

The historical consolidated financial information of the Company has been adjusted in the accompanying unaudited pro forma combined financial information to give effect to pro forma events that are (i) directly attributable to the Transactions, (ii) factually supportable, and (iii) with respect to the unaudited pro forma combined statements of operations, are expected to have a continuing impact on the results of operations.

The Acquisition will be accounted for as a business combination using the acquisition method of accounting under the provisions ASC 805. The unaudited pro forma combined financial information was prepared using the acquisition method of accounting, which requires, among other

Edgar Filing: Horizon Pharma plc - Form 424B5

things, that assets acquired and liabilities assumed in a business combination be recognized at their fair values as of the acquisition date. The adjustments to reflect the acquisition method of accounting are preliminary and are based upon available information and certain assumptions which management believes are reasonable under the circumstances.

The acquisition method of accounting uses the fair value concepts defined in ASC 820, Fair Value Measurement, (ASC 820) as the price that would be received to sell an asset or paid to transfer a liability in

S-87

Table of Contents

an orderly transaction between market participants at the measurement date. This is an exit price concept for the valuation of an asset or liability. Market participants are assumed to be buyers or sellers in the most advantageous market for the asset or liability. Fair value measurement for an asset assumes the highest and best use by these market participants. Fair value measurements can be highly subjective and it is possible the application of reasonable judgment could develop different assumptions resulting in a range of alternative estimates using the same facts and circumstances.

Cash and cash equivalents, investments, and other tangible assets and liabilities: The carrying amounts of tangible assets and liabilities were assumed to approximate current fair value.

Inventories: Inventories acquired included raw materials and finished goods. Inventories are recorded at their current fair values. Fair value of finished goods has been determined based on the estimated selling price, net of selling costs and a margin on the selling costs. Fair value of raw materials has been estimated to equal the replacement cost.

Developed technology: Developed technology intangible assets reflect the estimated value of Hyperion's rights to its currently marketed products. The fair value of developed technology was determined using an income approach. The income approach explicitly recognizes that the fair value of an asset is premised upon the expected receipt of future economic benefits such as earnings and cash inflows based on current sales projections and estimated direct costs for Hyperion's product line. Indications of value are developed by discounting these benefits to their present worth at a discount rate that reflects the current return requirements of the market. The fair value of developed technology will be capitalized as of the acquisition date and subsequently amortized over the 8 years, which is the period in which over 90% of the estimated cash flows are expected to be realized.

Goodwill: Goodwill represents the excess of the preliminary acquisition consideration over the estimated fair values of net assets acquired.

Deferred tax assets and liabilities: Deferred tax assets and liabilities arise from acquisition accounting adjustments where book values of certain assets and liabilities differ from their tax bases. Deferred tax assets and liabilities are recorded at the currently enacted rates which will be in effect at the time when the temporary differences are expected to reverse in the country where the underlying assets and liabilities are located. Hyperion's developed technology as of the acquisition date was located in the United States where a U.S. tax rate of 38% is being utilized and a deferred tax liability is recorded. Upon consummation of the Acquisition, Hyperion will be a member of the Company's U.S. tax consolidation group. As such, its tax assets and liabilities need to be considered in determining the appropriate amount (if any) of valuation allowance that should be recognized in assessing the realizability of the group's deferred tax assets. The Hyperion acquisition adjustments resulted in the recording of significant net deferred tax liabilities. Per ASC 740-10-130-18, future reversals of existing taxable temporary differences must be considered in determining the amount of valuation allowance to record. As of year end, the Company has a significant valuation allowance which must be reduced to reflect the addition of Hyperion's deferred tax liabilities that will provide taxable temporary differences that will be realized within the carryforward period of the group's available net operating losses and other deferred tax assets. Accordingly, the result will be to recognize the release of the existing Company's U.S. valuation allowance.

Pre-existing contingencies: The Company has identified a contingent liability potentially payable under previously existing royalty and licensing agreements. The initial fair value of this liability was determined using a discounted cash flow analysis incorporating the estimated future cash flows of royalty payments based on future sales. The liability will be periodically assessed based on events and circumstances related to the underlying milestones, and any change will be recorded in the Company's consolidated statement of operations.

Table of Contents

The preliminary determination of the fair value of the acquired net assets, assuming the Acquisition had closed on December 31, 2014, is as follows (in thousands, except share and per share data):

| | |
|--|--------------|
| Fully diluted equity value (24,369,000 shares at \$46 per share) | \$ 1,120,974 |
| Proceeds from exercise of stock options, restricted stock and performance stock units (3.12 million stock options at a weighted average exercise price of \$15.75 per share) | (49,036) |
| Consideration paid | \$ 1,071,938 |
| Book value of assets acquired and liabilities assumed (excluding historical intangible assets of \$8,816) | 122,736 |
| Step up adjustments: | |
| Inventory step-up | 11,806 |
| Developed technology | 1,006,900 |
| Accrued royalties, current portion | (6,493) |
| Accrued royalties, net of current | (75,707) |
| Short-term deferred tax liability | 4,167 |
| Long-term deferred tax liability | (289,181) |
| Goodwill | 306,044 |
| | \$ 1,071,938 |

3. Accounting policies

Following the Acquisition, the Company will conduct a review of accounting policies of Hyperion in an effort to determine if differences in accounting policies require restatement or reclassification of results of operations or reclassification of assets or liabilities to conform to the Company's accounting policies and classifications. As a result of that review, the Company may identify differences among the accounting policies of the Company and Hyperion that, when conformed, could have a material impact on this unaudited pro forma combined financial information. During the preparation of this unaudited pro forma combined financial information, the Company was not aware of any material differences between accounting policies of the Company and Hyperion, except for certain reclassifications necessary to conform to the Company's financial presentation, and accordingly, this unaudited pro forma combined financial information does not assume any material differences in accounting policies among the Company and Hyperion.

4. Historical Hyperion

Financial information of Hyperion in the Historical Hyperion (after conforming reclassifications) column in the unaudited pro forma combined balance sheet represents the historical consolidated balance sheet of Hyperion as of December 31, 2014. Financial information presented in the Historical Hyperion (after conforming reclassifications) column in the unaudited pro forma combined statement of operations represents the historical consolidated statement of earnings of Hyperion for the year ended December 31, 2014, which includes the operations from Andromeda Biotech Ltd. (Andromeda) since June 12, 2014, the date of acquisition. The Company does not believe that the operating results for Andromeda prior to its acquisition by Hyperion on June 12, 2014 are material to the combined entity and as such have not been included in the unaudited pro forma combined statement of operations. Such financial information has been reclassified or classified to conform to the historical presentation in the Company's consolidated financial statements as set forth below. Unless otherwise indicated, defined line items included in the footnotes have the meanings given to them in the historical financial statements of Hyperion.

Table of Contents

Reclassifications in Hyperion's unaudited pro forma combined balance sheet for the year ended December 31, 2014 are as follows (in thousands, except share data):

| | Historical Hyperion (before conforming reclassifications) | Reclassifications | | Historical Hyperion (after conforming reclassifications) |
|--|---|-------------------|-------------|--|
| Assets | | | | |
| Current assets: | | | | |
| Cash and cash equivalents | \$ 102,796 | | | \$ 102,796 |
| Short-term investments | 34,487 | | | 34,487 |
| Accounts receivables, net | 14,864 | | | 14,864 |
| Inventories, net | 4,621 | | | 4,621 |
| Prepaid expenses and other current assets | 2,632 | | | 2,632 |
| Total current assets | \$ 159,400 | \$ | | \$ 159,400 |
| Long-term assets: | | | | |
| Long-term investments | 9,226 | | | 9,226 |
| Property, plant and equipment, net | 1,116 | | | 1,116 |
| Other intangibles, net | 8,816 | | | 8,816 |
| Other assets | 1,858 | | | 1,858 |
| Total assets | \$ 180,416 | \$ | | \$ 180,416 |
| Liabilities and Stockholders' Equity | | | | |
| Current liabilities: | | | | |
| Accounts payable | 4,669 | | | 4,669 |
| Accrued expenses | 25,509 | (12,222) | 4(A) | 13,287 |
| Accrued trade, discounts and rebates | | 10,142 | 4(A) | 10,142 |
| Accrued royalties-current portion | | 2,080 | 4(A) | 2,080 |
| Deferred revenues-current portion | 224 | | | 224 |
| Total current liabilities | \$ 30,402 | \$ | | \$ 30,402 |
| Long-term liabilities: | | | | |
| Long-term debt, net | 18,124 | | | 18,124 |
| Deferred rent | 338 | (338) | 4(B) | |
| Other long-term liabilities | | 338 | 4(B) | 338 |
| Total long-term liabilities | \$ 18,462 | \$ | | \$ 18,462 |
| Stockholders' equity: | | | | |
| Common stock, par value \$0.0001 100,000,000 shares authorized at December 31, 2014; 20,747,013 shares issued and outstanding at December 31, 2014 | 2 | | | 2 |
| Additional paid-in capital | 260,225 | | | 260,225 |
| Accumulated other comprehensive loss | (50) | | | (50) |
| Accumulated deficit | (128,625) | | | (128,625) |
| Total stockholders' equity | \$ 131,552 | \$ | | \$ 131,552 |
| Total liabilities and stockholders' equity | \$ 180,416 | \$ | | \$ 180,416 |

Edgar Filing: Horizon Pharma plc - Form 424B5

- (A) Accrued trade, discounts and rebates of \$10,142 and accrued royalties of \$2,080 have been reclassified out of accrued expenses and into separate financial statement line items to conform to the Company's presentation.
- (B) Represents the reclassification of \$338 from deferred rent to other long-term liabilities to conform to the Company's presentation.

S-90

Table of Contents

Reclassifications in Hyperion's unaudited pro forma combined statement of operations for the year ended December 31, 2014 are as follows (in thousands):

| | Historical Hyperion (before conforming reclassifications) | Reclassifications | Historical Hyperion (after conforming reclassifications) |
|-------------------------------------|--|-------------------|---|
| Net sales | \$ 113,584 | \$ | \$ 113,584 |
| Cost of sales | 13,727 | 4,626 | 18,353 |
| Gross profit | \$ 99,857 | \$ (4,626) | \$ 95,231 |
| Operating Expenses: | | | |
| Research and development | 20,715 | | 20,715 |
| Sales and marketing | | 17,367 | 17,367 |
| General and administrative | | 31,155 | 31,155 |
| Goodwill impairment | 30,201 | | 30,201 |
| Depreciation and amortization | 4,626 | (4,626) | (4,626) |
| Selling general and administrative | 48,522 | (48,522) | (48,522) |
| Total operating expenses | \$ 104,064 | \$ (4,626) | \$ 99,438 |
| Operating income (loss) | \$ (4,207) | \$ | \$ (4,207) |
| Other (expense) income, net: | | | |
| Interest expense, net | (1,601) | 555 | (1,046) |
| Interest income | 555 | (555) | (555) |
| Other (expense) income, net | (699) | | (699) |
| Total other expense, net | \$ (1,745) | \$ | \$ (1,745) |
| Loss before income tax expense | (5,952) | | (5,952) |
| Income tax expense | 303 | | 303 |
| Net loss | \$ (6,255) | \$ | \$ (6,255) |

- (C) Intangible amortization expense of \$4,626 in Hyperion's historical statement of operations has been reclassified to cost of sales to conform to the Company's presentation.
- (D) Selling, general and administrative expenses in Hyperion's historical statement of earnings included \$17,367 of sales and marketing expenses and \$31,155 of general and administrative expenses that has been reclassified to conform to the Company's presentation.
- (E) Interest income of \$555 in Hyperion's historical statement of operations has been reclassified to interest expense, net to conform to the Company's presentation.

5. Historical Vidara

Financial information presented in the Historical Vidara (after conforming reclassifications) column in the unaudited pro forma combined statement of operations for the year ended December 31, 2014 represents Vidara results of operations as a stand-alone entity for the period from January 1, 2014 to September 18, 2014, which were derived from its unaudited combined financial statements included in its Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2014 and the stub period from July 1, 2014 to September 18, 2014. Financial information of Vidara subsequent to September 18, 2014 is included in the statement of operations of the Company for the year ended December 31, 2014.

Table of Contents

Reclassifications and classifications in Vidara's unaudited pro forma combined statement of operations for the year ended December 31, 2014 are as follows (in thousands):

| | Historical Vidara (for the six months ended June 30, 2014) | Historical Vidara Stub Period (July 1, 2014 to September 18, 2014) | Historical Vidara (January 1, 2014 to September 18, 2014) | Reclassifications | Historical Vidara (after conforming reclassifications) |
|--|---|---|--|-------------------|---|
| Net sales | \$ 35,746 | \$ 14,819 | \$ 50,565 | \$ | \$ 50,565 |
| Cost of sales | 1,660 | 630 | 2,290 | 2,497 | 11,290 |
| | | | | 6,503 | 5(B) |
| Gross profit | \$ 34,086 | \$ 14,189 | \$ 48,275 | \$ (9,000) | \$ 39,275 |
| Operating Expenses: | | | | | |
| Research and development | | | | 2,799 | 2,799 |
| Sales and marketing | | | | 17,664 | 17,664 |
| General and administrative | 6,134 | 4,760 | 10,894 | (2,799) | 8,253 |
| | | | | 158 | 5(E) |
| Selling expenses | 3,792 | 13,872 | 17,664 | (17,664) | 5(D) |
| Depreciation and amortization | 2,272 | 870 | 3,142 | (2,497) | 487 |
| | | | | (158) | 5(E) |
| Royalty expense | 4,935 | 1,568 | 6,503 | (6,503) | 5(B) |
| Total operating expenses | \$ 17,133 | \$ 21,070 | \$ 38,203 | \$ (9,000) | \$ 29,203 |
| Operating income (loss) | \$ 16,953 | \$ (6,881) | \$ 10,072 | \$ | \$ 10,072 |
| Other (expense) income, net: | | | | | |
| Interest expense, net | (516) | (89) | (605) | | (605) |
| Foreign exchange gain | | 11 | 11 | | 11 |
| Other (expense) income | (22) | (276) | (298) | | (298) |
| Total other expense, net | \$ (538) | \$ (354) | \$ (892) | \$ | \$ (892) |
| Income (loss) before income tax (benefit) expense | 16,415 | (7,235) | 9,180 | | 9,180 |
| Income tax (benefit) expense | 724 | 157 | 881 | | 881 |
| Net income (loss) | \$ 15,691 | \$ (7,392) | \$ 8,299 | \$ | \$ 8,299 |

- (A) Intangible amortization expense of \$2,497 in Vidara's historical statement of operations has been reclassified to cost of sales to conform to the Company's presentation.
- (B) Royalty expense of \$6,503 in Vidara's historical statement of operations has been reclassified from operating expenses to cost of sales to conform to the Company's presentation.
- (C) Represents \$2,799 of general and administrative expenses in Vidara's historical statement of operations that has been reclassified to research and development expenses to conform to Horizon's presentation.
- (D) Represents \$17,664 of selling expenses in Vidara's historical statement of operations that has been reclassified to sales and marketing to conform to the Company's presentation.
- (E) Depreciation expense of \$158 in Vidara's historical statement of operations has been reclassified to general and administrative expense to conform to the Company's presentation.

Table of Contents**6. Unaudited Pro Forma Combined Balance Sheet Adjustments**

- A. Assumes that the Company will incur \$800 million principal amount of debt in the form of the Senior Secured Term Loans (the terms of which are based on those set forth in Debt Commitment Letter), the proceeds of which would be used, in addition to a portion of the Company's existing cash and a portion of the proceeds of the Offering, to repay the outstanding term loans under the Existing Credit Facility (see Note 6(B)) and certain existing debt of Hyperion, fund a portion of the Offer Price and pay any prepayment premium, fees and expenses in connection with the foregoing. Financing fees associated with the Senior Secured Term Loans are estimated to be \$17 million.

For the Senior Secured Term Loans, the following adjustments are included:

| | |
|---------------------------------|-------------|
| Debt | \$ 800,000 |
| Original Issue Discount (OID) | \$ (8,000) |
| Debt, net of OID | \$ 792,000 |
| Deferred financing fees | \$ (17,000) |
| Cash proceeds | \$ 775,000 |

- B. For the extinguishment of the \$300 million principal amount of term loans under the Existing Credit Facility, the following adjustments are included:

| | |
|--|------------|
| Liability net of OID | \$ 297,169 |
| OID (See Note 6(K)) | \$ 2,831 |
| Existing Credit Facility | \$ 300,000 |
| Penalty for early payment (See Note 6(K)) | \$ 44,560 |
| Cash payment | \$ 344,560 |
| Write-off of deferred financing fees (See Note 6(K)) | \$ 9,467 |

As disclosed elsewhere, in lieu of borrowing the committed amounts under the Debt Commitment Letter and subsequent to the Offering, the Company may borrow up to an aggregate of \$800 million pursuant to an offering of senior notes and the arrangement of term loans, the terms of which may deviate from those included in the Debt Commitment Letter.

- C. Reflects the \$400 million aggregate principal amount of Exchangeable Notes issued in March 2015 for general corporate purposes, including financing new acquisitions, which includes the following adjustments (in thousands):

| | |
|---------------------------|--------------|
| Exchangeable Notes | \$ 400,000 |
| OID (contra debt account) | \$ (131,080) |
| Long term debt, net | \$ 268,920 |
| APIC (conversion feature) | \$ 119,080 |
| Deferred financing fees | \$ (672) |

Edgar Filing: Horizon Pharma plc - Form 424B5

Cash proceeds

\$ 387,328

The foregoing adjustments reflect the application of ASC 470-20, Debt with Conversion and Other Options, Cash Conversion , which requires issuers to separately account for the debt and equity components of certain types of convertible debt instruments.

- D. Represents the cash consideration to be paid for the Acquisition of \$1,121 million, net of \$49 million of cash proceeds related to the assumed exercise of Hyperion stock options (see Note 6(G)).

S-93

Table of Contents

E. Represents the cash to be paid for the following estimated transaction fees associated with the Acquisition (in thousands):

| | |
|-------------------------------------|---------------|
| Horizon advisory expenses | \$ 17,200 |
| Hyperion advisory expenses | \$ 17,600 |
| Horizon and Hyperion legal expenses | \$ 4,000 |
| (See Note 6(K)) | \$ 38,800 |

F. Represents the liquidation of the short-term and long-term investments and conversion into cash to fund a portion of the Acquisition, payoff Hyperion's existing debt and the net settlement of Hyperion stock options, restricted stock units and performance stock units.

G. Reflects the preliminary purchase price adjustments for the Acquisition based upon the following preliminary purchase price allocation (in thousands, except share and per share data):

| | |
|--|------------------|
| Fully diluted equity value (24,369,000 shares at \$46.00 per share) | \$ 1,120,974 |
| Proceeds from exercise of stock options, restricted stock and performance stock units (3.12 million stock options at a weighted average exercise price of \$15.75 per share) | (49,036) |
| Consideration paid | \$ 1,071,938 |
| Book value of assets acquired and liabilities assumed (excluding historical intangible assets of \$8,816) | 122,736 |
| Step up adjustments: | |
| Inventory step-up | 11,806 |
| Developed technology | 1,006,900 |
| Accrued royalties, current | (6,493) |
| Accrued royalties, net of current | (75,707) |
| Short-term deferred tax liability | 4,167 |
| Long-term deferred tax liability | (289,181) |
| Goodwill | 306,044 |
| | |
| | \$ 1,071,938 |

H. Represents the estimated net proceeds of \$325.4 million from the Offering (in thousands, except share data):

| | |
|---------------------------------------|----------------|
| Number of ordinary shares | 12,000,000 |
| Offer price per share (as of 4/10/15) | \$ 28.48 |
| Gross proceeds | \$ 341,760 |
| Underwriter fees (4.5%) | \$ (15,379) |
| Other estimated expenses | \$ (1,000) |
| Net proceeds | \$ 325,381 |

A \$1.00 increase (decrease) in the assumed public offering price of \$28.48 per share would increase (decrease) the net proceeds to the Company from the Offering by approximately \$11.5 million, assuming that the number of shares offered by the Company, as set forth on the cover page of this prospectus supplement, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by the Company.

Edgar Filing: Horizon Pharma plc - Form 424B5

Pro forma earnings per share gives effect to the issuance of 12 million ordinary shares from the Offering and the adjustments to the unaudited pro forma combined statement of operations described in Note 7.

S-94

Table of Contents

- I. Represents the cash used to retire the existing Hyperion debt of \$18.1 million and \$0.5 million (see Note 6(K)) of penalties for early payment.
- J. Represents the elimination of Hyperion's stockholders' equity.
- K. Represent the elimination of estimated future Acquisition costs and penalties for early payment of debts as follows (in thousands):

| | |
|---|-----------|
| Estimated future Acquisition costs (See Note 6(E)) | \$ 38,800 |
| Penalty for early payment of Existing Credit Facility (See Note 6(B)) | \$ 44,560 |
| Write-off of deferred financing fees for Existing Credit Facility (See Note 6(B)) | \$ 9,467 |
| OID of Existing Credit Facility (See Note 6(B)) | \$ 2,831 |
| Penalty fees for Hyperion Debt (See Note 6(I)) | \$ 500 |
| | \$ 96,158 |

7. Unaudited Pro Forma Combined Statement of Operations

- A. Reflects the amortization expense related to the fair value of identifiable intangible assets recognized related to the Merger, as follows (in thousands):

| Type of Intangible | Fair Value Adjustment | Useful Lives (Years) | For the Period Ending 9/18/2014 |
|---|--------------------------|-------------------------|---------------------------------------|
| Customer Relationship | \$ 8,100 | 10 | \$ 580 |
| Developed Technology | \$ 560,000 | 13 | \$ 30,872 |
| | \$ 568,100 | | \$ 31,452 |
| Historical Amortization expense | | | \$ (2,497) |
| Increase to pro forma amortization expense | | | \$ 28,955 |

- B. Reflects the elimination of Vidara transaction costs related to the Merger of \$3.4 million. The impact of transaction costs already incurred has not been reflected in the unaudited pro forma combined statement of operations since these costs are expected to be nonrecurring in nature. These charges include financial advisory fees, legal, accounting, other professional fees incurred by Vidara directly related to the Merger.
- C. Reflects the elimination of the Company's transaction costs related to the Merger of \$40.2 million. The impact of transaction costs already incurred has not been reflected in the unaudited pro forma combined statement of operations since these costs are expected to be nonrecurring in nature. These charges include financial advisory fees, legal, accounting, other professional fees incurred by the Company directly related to the Merger.
- D. Reflects the \$5.0 million of commitment fees incurred on a bridge loan commitment prior to executing the Existing Credit Facility and \$3.2 million of commitment fees incurred on the Existing Credit Facility prior to its funding on September 19, 2014. The impact of these fees is not included in the unaudited pro forma combined statement of operations since this cost is expected to be nonrecurring in nature.

Edgar Filing: Horizon Pharma plc - Form 424B5

- E. The pro forma adjustment reflects the elimination of \$487 related to historical Vidara amortization of deferred financing fees.

S-95

Table of Contents

- F. This pro forma adjustment reflects the interest expense, amortization of OID and deferred financing fees on (a) \$400 million principal amount of 2.5% Exchangeable Notes issued in March 2015 and (b) \$800 million principal amount of Senior Secured Term Loans assumed to have been entered into to finance in part the Acquisition. The adjustment also reflects the elimination of any historical interest expense for debt that will be extinguished as part of the Acquisition (in thousands):

| Description of Debt | Principal Amount | Interest Rate | Interest Payment | Amortization of OID | Amortization of Deferred Financing Fees | Interest Expense |
|--|------------------|---------------|------------------|---------------------|---|------------------|
| Exchangeable Notes | \$ 400,000 | 2.50% | \$ 10,000 | \$ 17,477 | \$ 90 | \$ 27,567 |
| Senior Secured Term Loan | \$ 800,000 | 6.375% | \$ 51,000 | \$ 1,334 | \$ 2,833 | 55,167 |
| New interest expense | | | \$ 61,000 | \$ 18,811 | \$ 2,923 | \$ 82,734 |
| Less historical interest expense of Existing Credit Facility to be prepaid | | | | | | \$ (8,460) |
| Less historical Vidara interest expense | | | | | | (506) |
| Less historical Hyperion interest expense | | | | | | (1,601) |
| Increase to pro forma interest expense | | | | | | \$ 72,167 |

Based on the Debt Commitment Letter, the interest rate on the Senior Secured Term Loans is assumed to be equal to the LIBOR rate, plus an applicable margin of 5.375% per annum (subject to a 1.00% LIBOR floor). This adjustment also includes the amortization of OID and deferred financing costs. Deferred financing costs include bank fees, financial advisory, legal, and other professional fees. These costs are deferred and recognized over the six-year term of the debt agreement using the straight-line method.

The interest rate used for purposes of preparing the accompanying unaudited pro forma combined statement of operations was 6.375%, which was derived by utilizing the 5.375% per annum applicable margin plus the 1.00% LIBOR floor rate. This rate may be considerably different from the actual interest rates incurred based fluctuations in the LIBOR rate.

In lieu of borrowing the committed amounts under the Debt Commitment Letter and subsequent to the Offering, the Company may borrow up to an aggregate of \$800 million pursuant to an offering of senior notes and the arrangement of term loans, the terms of which may deviate from those included in the Debt Commitment Letter. As a result, actual interest rates on the Company's debt may be considerably different. If the interest rate on the Company's \$800 million debt were to increase or decrease by 0.125%, the Company's annual pro forma interest expense would increase or decrease by \$1.0 million.

- G. Reflects the elimination of the bargain purchase gain recorded as part of the Merger.
- H. Represents the income tax benefit associated with the nonrecurring charges associated with the Merger removed from the pro forma statement of operations, using a combined federal and state statutory tax rate of 0%. The tax effect of the transaction related costs in the transition period was a blended rate of 0% due to the non-deductibility of certain costs. The tax effect of the incremental amortization expense of Vidara's customer-related intangible assets and the amortization of the developed technology step up to estimated fair value was based on a blended statutory tax rate of approximately 1% based on jurisdictions where these assets reside. The Company has assumed a 0% tax rate when estimating the tax impacts of the additional expense on incremental debt to finance the Merger because the debt is an obligation of a U.S. entity and taxed at the estimated combined effective U.S. federal statutory and state rate; however, the entity has a full valuation allowance. The Company has assumed a 1.5% tax rate expense when estimating the tax impacts on the intercompany debt obligation due to Horizon Pharma Finance S.a.r.L from Horizon Pharma Holdings USA, Inc. The Company has assumed that any intercompany interest expense which is nondeductible under Code Section 163(j) would be a timing matter and would be deductible in

future years based on future earnings.

S-96

Table of Contents

- I. Reflects amortization expense adjustments related to the fair value of identifiable intangible assets recognized related to the Acquisition, as follows (in thousands):

| Type of Intangible | Fair Value Adjustment | Useful Lives (Years) | For the Year Ending 12/31/2014 |
|---|-----------------------|----------------------|--------------------------------|
| Developed technology | \$ 1,006,900 | 8 | \$ 125,863 |
| Historical Hyperion amortization expense | | | \$ (4,626) |
| Increase to pro forma amortization expense | | | \$ 121,237 |

- J. Represents the income tax benefit associated with the non-recurring charges removed from the pro forma statement of income related to the Hyperion acquisition, using a combined federal and state statutory tax rate of 38%.
- K. Reflects the elimination of Hyperion interest income as all short-term and long-term investments will be converted into cash and will be used to fund the a portion of the Acquisition, all of Hyperion s existing debt will be repaid and Hyperion stock options, restricted stock units and performance stock units will be net settled.
- L. Reflects the elimination of the \$11.1 million charge to recognize additional cost of goods sold attributable to the stepped-up market value of Vidara inventory.
- M. Represents a total of \$14.1 million in option cancellation payments, one-time bonuses and severance payments incurred as a result of the Merger.

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;

Edgar Filing: Horizon Pharma plc - Form 424B5

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.

S-98

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 different 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 beneficial owner of ordinary shares that, 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 the trust 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 (including the amount of any foreign taxes withheld therefrom) 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

Edgar Filing: Horizon Pharma plc - Form 424B5

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. Such foreign currency gain or loss will generally be treated as ordinary income or loss and as income or loss from United States sources for United States foreign tax credit purposes.

Dividends received by a non-corporate U.S. Holder are eligible to be taxed at reduced rates if we are a qualified foreign corporation and certain other applicable requirements, including holding period requirements,

S-99

Table of Contents

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, 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 Select 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 Select 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 Issuer, 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, dividends paid by us 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 Taxable Disposition of Ordinary Shares

For U.S. federal income tax purposes, gain or loss recognized on the sale or other taxable 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. Such gain or loss will be generally treated as U.S. source. 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. There are limitations on the deductibility of capital losses.

If the consideration received for the ordinary shares is paid in foreign currency, the amount realized will be the U.S. dollar value of the payment received translated at the spot rate of exchange on the date of disposition. If the ordinary shares are treated as traded on an established securities market and the relevant holder is either a cash basis taxpayer or an accrual basis taxpayer who has made a special election (which must be applied consistently from year to year and cannot be changed without the consent of the IRS), such holder will determine the U.S. dollar value of the amount realized in a foreign currency by translating the amount received at the spot rate of exchange on the settlement date of the disposition. If the ordinary shares are not treated as traded on an established securities market, or the relevant U.S. Holder is an accrual basis taxpayer that is not eligible to or does not elect to determine the amount realized using the spot rate on the settlement date, such U.S. Holder will recognize foreign currency gain or loss to the extent of any difference between the U.S. dollar amount realized on the date of disposition (as determined above) and the U.S. dollar value of the currency received at the spot rate on the settlement date. Any such foreign currency gain or loss will generally be U.S. source ordinary income or loss.

Table of Contents

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. Assets that produce or are held for the production of passive income include cash, 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, is generally determined based on 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 were a PFIC in our previous taxable year or will be a PFIC in our current taxable year or any subsequent taxable 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 our current taxable year 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 which if made would result in different tax consequence than those described above if we are a PFIC for any taxable year. However, if we are a PFIC in any taxable year, U.S. Holders may be entitled to make a mark-to-market election which would also result in tax consequences different than those described above. A mark-to-market election can be made only if our ordinary shares are regularly traded on a qualified exchange. Our ordinary shares will be regularly traded during any calendar year if they are traded, other than in *de minimis* quantities, on at least 15 days in each calendar quarter. Because trading of our ordinary shares has met this threshold in the past and we expect that it will meet this threshold within the foreseeable future, and because our ordinary shares are listed on NASDAQ, a qualified exchange, we anticipate that U.S. Holders will be entitled to make mark-to-market elections with respect to our ordinary shares in the current taxable year and within the foreseeable future in the event we are or become a PFIC. There can be no assurance however, that these requirements will be satisfied for the current taxable year or in the future. You should consult your tax advisor concerning the tax consequences to you if we are a PFIC, the PFIC annual reporting requirement 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.

Medicare Tax on Net Investment Income

Certain U.S. Holders who are individuals, estates or trusts are subject to a 3.8% tax on all or a portion of their net investment income, which generally includes dividends on ordinary shares and net gains from the sale or other taxable disposition of ordinary shares. U.S. Holders that are individuals, estates or trusts should consult their tax advisors regarding the applicability of the Medicare tax to any dividends and gains in respect of ordinary shares.

Table of Contents

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 (and certain entities) are required to report on IRS 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. 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.

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 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.

Edgar Filing: Horizon Pharma plc - Form 424B5

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 &

S-102

Table of Contents

Herzegovina; Botswana; Bulgaria; Canada; Chile; China; Croatia; Cyprus; Czech Republic; Denmark; Egypt; Estonia; Ethiopia; 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.

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.

Table of Contents

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.

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

Edgar Filing: Horizon Pharma plc - Form 424B5

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

S-104

Table of Contents

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.

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.

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).

S-105

Table of Contents

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 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 willful 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.

Table of Contents

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.

Table of Contents

UNDERWRITING

Citigroup Global Markets Inc., Jefferies LLC, Cowen and Company, LLC and Morgan Stanley & Co. LLC are acting as joint book-running managers of the offering. Subject to the terms and conditions stated in the underwriting agreement dated the date of this prospectus supplement, each underwriter named below has severally agreed to purchase, and we have agreed to sell to that underwriter, the number of ordinary shares set forth opposite the underwriter's name.

| Underwriter | Number of Ordinary Shares |
|-------------------------------|--------------------------------------|
| Citigroup Global Markets Inc. | |
| Jefferies LLC | |
| Cowen and Company, LLC . | |
| Morgan Stanley & Co. LLC | |
| Total | 12,000,000 |

The underwriting agreement provides that the obligations of the underwriters to purchase the ordinary shares included in this offering are subject to approval of legal matters by counsel and to other conditions. The underwriters are obligated to purchase all the ordinary shares (other than those covered by the underwriters' option to purchase additional ordinary shares described below) if they purchase any of the ordinary shares. The offering of the ordinary shares by the underwriters is subject to the underwriters' right to reject any order in whole or in part.

The underwriters have advised us that they propose to offer the ordinary shares to the public at the public offering price set forth on the cover page of this prospectus supplement, and to certain dealers, which may include the underwriters, at that price less a concession not in excess of \$ _____ per ordinary share. The underwriters may allow, and such dealers may allow, a concession not in excess of \$ _____ per ordinary share to certain other dealers.

If the underwriters sell more ordinary shares than the total number set forth in the table above, we have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus supplement, to purchase up to 1,800,000 additional ordinary shares at the public offering price less the underwriting discount. To the extent the option is exercised, each underwriter must purchase a number of additional ordinary shares approximately proportionate to that underwriter's initial purchase commitment. Any ordinary shares issued or sold under the option will be issued and sold on the same terms and conditions as the other ordinary shares that are the subject of this offering.

We, our officers and directors have agreed that, for a period of 90 days from the date of this prospectus supplement, we and they will not, without the prior written consent of the underwriters and subject to certain customary exceptions, dispose of or hedge any ordinary shares or any securities convertible into or exchangeable for our ordinary shares. The underwriters may release any of the securities subject to these lock-up agreements at any time without notice.

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

The following table shows the underwriting discounts and commissions that we are to pay to the underwriters in connection with this offering. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional ordinary shares.

| | Paid by Horizon Pharma plc | |
|--------------------|-----------------------------------|----------------------|
| | No Exercise | Full Exercise |
| Per ordinary share | \$ | \$ |
| Total | \$ | \$ |

S-108

Table of Contents

We estimate that our portion of the total expenses of this offering will be \$1.0 million.

In connection with the offering, the underwriters may purchase and sell ordinary shares in the open market. Purchases and sales in the open market may include short sales, purchases to cover short positions, which may include purchases pursuant to the underwriters' option to purchase additional ordinary shares, and stabilizing purchases.

Short sales involve secondary market sales by the underwriters of a greater number of ordinary shares than they are required to purchase in the offering.

Covered short sales are sales of ordinary shares in an amount up to the number of ordinary shares represented by the underwriters' option to purchase additional ordinary shares.

Naked short sales are sales of ordinary shares in an amount in excess of the number of ordinary shares represented by the underwriters' option to purchase additional ordinary shares.

Covering transactions involve purchases of ordinary shares either pursuant to the underwriters' option to purchase additional ordinary shares or in the open market in order to cover short positions.

To close a naked short position, the underwriters must purchase ordinary 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 ordinary shares in the open market after pricing that could adversely affect investors who purchase in the offering.

To close a covered short position, the underwriters must purchase ordinary shares in the open market or must exercise the option to purchase additional ordinary shares. In determining the source of ordinary shares to close the covered short position, the underwriters will consider, among other things, the price of ordinary shares available for purchase in the open market as compared to the price at which they may purchase ordinary shares through the underwriters' option to purchase additional ordinary shares.

Stabilizing transactions involve bids to purchase ordinary shares so long as the stabilizing bids do not exceed a specified maximum.

Purchases to cover short positions and stabilizing purchases, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of the ordinary shares. They may also cause the price of the ordinary shares to be higher than the price that would otherwise exist in the open market in the absence of these transactions. The underwriters may conduct these transactions on The NASDAQ Global Select Market, in the over-the-counter market or otherwise. If the underwriters commence any of these transactions, they may discontinue them at any time.

In addition, in connection with this offering, some of the underwriters (and selling group members) may engage in passive market making transactions in the ordinary shares on The NASDAQ Select Global Market, prior to the pricing and completion of the offering. Passive market making consists of displaying bids on The NASDAQ Global Select Market no higher than the bid prices of independent market makers and making purchases at prices no higher than those independent bids and effected in response to order flow. Net purchases by a passive market maker on each day are 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 that limit is reached. Passive market making may cause the price of the ordinary shares to be higher than the price that otherwise would exist in the open market in the absence of those transactions. If the underwriters commence passive market making transactions, they may discontinue them at any time.

Edgar Filing: Horizon Pharma plc - Form 424B5

We have agreed to indemnify the several underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make because of any of those liabilities.

S-109

Table of Contents

Conflicts of Interest

The underwriters are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, principal investment, hedging, financing and brokerage activities. The underwriters and their respective affiliates have in the past performed commercial banking, investment banking and advisory services for us from time to time for which they have received customary fees and reimbursement of expenses and may, from time to time, engage in transactions with and perform services for us in the ordinary course of their business for which they may receive customary fees and reimbursement of expenses. 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 (which may include bank loans and/or credit default swaps) 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 investments and securities activities may involve securities and/or instruments of ours or our affiliates. In addition, affiliates of some of the underwriters are lenders, and in some cases agents or managers for the lenders, under our credit facility. Certain of the underwriters or their affiliates that have a lending relationship with us routinely hedge their credit exposure to us consistent with their customary risk management policies. A typical such hedging strategy would include these underwriters or their affiliates hedging such exposure by entering into transactions which consist of either the purchase of credit default swaps or the creation of short positions in our securities. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Notice to Prospective Investors in the European Economic Area

In relation to each member state of the European Economic Area that has implemented the Prospectus Directive (each, a relevant member state), with effect from and including the date on which the Prospectus Directive is implemented in that relevant member state (the relevant implementation date), an offer of ordinary shares described in this prospectus supplement may not be made to the public in that relevant member state other than:

to any legal entity which is a qualified investor as defined in the Prospectus Directive;

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 relevant Dealer or Dealers nominated by us for any such offer; or

in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of ordinary shares shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive.

For purposes of this provision, the expression an offer of securities to the public 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 the ordinary shares to be offered so as to enable an investor to decide to purchase or subscribe for the ordinary shares, as the expression may be varied in that member state by any measure implementing the Prospectus Directive in that member state, and 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. The expression 2010 PD Amending Directive means Directive 2010/73/EU.

Edgar Filing: Horizon Pharma plc - Form 424B5

The sellers of the ordinary shares have not authorized and do not authorize the making of any offer of ordinary shares through any financial intermediary on their behalf, other than offers made by the underwriters

S-110

Table of Contents

with a view to the final placement of the ordinary shares as contemplated in this prospectus supplement. Accordingly, no purchaser of the ordinary shares, other than the underwriters, is authorized to make any further offer of the ordinary shares on behalf of the sellers or the underwriters.

Notice to Prospective Investors in the United Kingdom

This prospectus supplement is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, or the Order, or (ii) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (each such person being referred to as a relevant person). This prospectus supplement and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

Notice to Prospective Investors in France

Neither this prospectus supplement nor any other offering material relating to the ordinary 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 ordinary 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 ordinary shares has been or will be:

released, issued, distributed or caused to be released, issued or distributed to the public in France; or

used in connection with any offer for subscription or sale of the ordinary shares to the public in France.

Such offers, sales and distributions will be made in France only:

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*;

to investment services providers authorized to engage in portfolio management on behalf of third parties; or

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*).

Edgar Filing: Horizon Pharma plc - Form 424B5

The ordinary 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*.

Notice to Prospective Investors in Hong Kong

The ordinary 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 ordinary 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

S-111

Table of Contents

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 ordinary 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.

Notice to Prospective Investors in Japan

The ordinary shares offered in this prospectus supplement have not been and will not be registered under the Financial Instruments and Exchange Law of Japan. The ordinary 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.

Notice to Prospective Investors in 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 ordinary shares may not be circulated or distributed, nor may the ordinary 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.

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

a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire ordinary share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

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,

ordinary shares, debentures and units of ordinary 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 ordinary shares pursuant to an offer made under Section 275 of the SFA except:

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 ordinary shares, debentures and units of ordinary 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

Edgar Filing: Horizon Pharma plc - Form 424B5

other assets, and further for corporations, in accordance with the conditions specified in Section 275 of the SFA;

where no consideration is or will be given for the transfer; or

where the transfer is by operation of law.

S-112

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 will be passed upon for the underwriters by Latham & Watkins 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 our Annual Report on Form 10-K for the year ended December 31, 2014 have been so incorporated in reliance on the report 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 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 audited historical consolidated financial statements of Hyperion Therapeutics, Inc. incorporated in this prospectus by reference to the Current Report on Form 8-K dated April 13, 2015 filed by Horizon Pharma plc have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and 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>.

Edgar Filing: Horizon Pharma plc - Form 424B5

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 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:

our Annual Report on Form 10-K for the fiscal year ended December 31, 2014, filed with the SEC on February 27, 2015, as amended on March 2, 2015 and April 10, 2015;

S-113

Table of Contents

The information specifically incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended December 31, 2014 from our definitive proxy statement on Schedule 14A, filed with the SEC on April 7, 2015;

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

our Current Reports on Form 8-K (other than information furnished rather than filed) filed with the SEC on February 27, 2015, March 6, 2015, March 13, 2015, March 16, 2015, March 27, 2015, March 30, 2015, March 31, 2015, April 9, 2015 and April 13, 2015 (including Exhibit 99.3 thereto containing portions of the Annual Report of Hyperion Therapeutics, Inc. on Form 10-K for the year ended December 31, 2014); and

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," and "The Business of Vidara";

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; and

the audited statements of revenues and direct expenses of the ACTIMMUNE Product Line of InterMune, Inc. for 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.

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

Edgar Filing: Horizon Pharma plc - Form 424B5

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-114

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

12,000,000 Shares

Horizon Pharma plc

Ordinary Shares

PRELIMINARY PROSPECTUS SUPPLEMENT

, 2015

Citigroup

Jefferies

Cowen and Company

Morgan Stanley