SCHEDULE 14A

RULE 14a-101
SCHEDULE 14A INFORMATION

Proxy Statement Pursuant to Section 14(a) of the Securities Exchange Act of 1934

Filed by the Registrant ☐  Filed by a Party other than the Registrant ☒

Check the appropriate box:
☐ Preliminary Proxy Statement
☐ Confidential, for Use of the Commission Only (as permitted by Rule 14a-6(e)(2))
☐ Definitive Proxy Statement
☒ Definitive Additional Materials
☐ Soliciting Material Pursuant to 240.14a-12

DEPOMED, INC.
(Name of Registrant as Specified in Its Charter)

HORIZON PHARMA PUBLIC LIMITED COMPANY
HORIZON PHARMA, INC.
(Name of Persons(s) Filing Proxy Statement, if Other Than the Registrant)

Payment of Filing Fee (Check the appropriate box):
☒ No fee required.
☐ Fee computed on table below per Exchange Act Rules 14a-6(i)(1) and 0-11.

(1)  Title of each class of securities to which transaction applies:

(2)  Aggregate number of securities to which transaction applies:

(3)  Per unit price or other underlying value of transaction computed pursuant to Exchange Act Rule 0-11 (set forth the amount on which the filing fee is calculated and state how it was determined):

(4)  Proposed maximum aggregate value of transaction:

(5)  Total fee paid:

☐ Fee paid previously with preliminary materials.

☐ Check box if any part of the fee is offset as provided by Exchange Act Rule 0-11(a)(2) and identify the filing for which the offsetting fee was paid previously. Identify the previous filing by registration statement number, or the Form or Schedule and the date of its filing.
Horizon Pharma plc ("Horizon Pharma") has filed a definitive proxy statement with the Securities and Exchange Commission (the "SEC") and accompanying WHITE and BLUE proxy cards to be used to solicit requests that Depomed, Inc. ("Depomed") call two related special meetings of shareholders.

This Schedule 14A filing consists of an investor presentation released by Horizon Pharma on November 9, 2015.

Forward-Looking Statements

This communication contains forward-looking statements, including, but not limited to, statements related to Horizon Pharma’s strategy, plans, objectives, expectations (financial or otherwise) and intentions, future financial results and growth potential, expected impact and potential benefits from recent and future transactions, development programs and clinical plans, and other statements that are not historical facts. These forward-looking statements are based on Horizon Pharma’s current expectations and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks related to Horizon Pharma’s ability to complete any future acquisitions on anticipated terms; risks associated with business combination transactions, such as the risk that the businesses will not be integrated successfully, that such integration may be more difficult, time-consuming or costly than expected or that the expected benefits of any acquisition will not be realized; risks related to future opportunities and plans for Horizon Pharma and/or the combined company, including, without limitation, uncertainty of the expected financial performance and results of Horizon Pharma and/or the combined company following completion of any acquisition; disruption from any future acquisition, making it more difficult to conduct business as usual or maintain relationships with customers, employees or suppliers; and the possibility that if the combined company does not achieve the perceived benefits of any future acquisition as rapidly or to the extent anticipated by financial analysts or investors, the market price of Horizon Pharma’s shares could decline, as well as other risks related to Horizon Pharma’s business, including the ability to grow sales and revenues from existing medicines and its ability to increase sales of its existing medicines; Horizon Pharma’s ability to successfully execute its commercial strategy and achieve projected financial results for 2015, 2016 and other long-term financial metrics; the fact that past financial or operating results are not a guarantee of future results; competition, including potential generic competition; the ability to protect intellectual property and defend patents; regulatory obligations and oversight, including potential changes in healthcare laws and regulations; the availability of coverage and adequate reimbursement and pricing from government and third-party payers and risks relating to the success of Horizon’s patient support program; risks associated with clinical development and
regulatory approvals, including the anticipated timing of initiating and completing studies and filing for and obtaining regulatory approvals, whether data from clinical studies will support regulatory approval, and whether clinical results will be consistent with data from animal models; and those risks detailed from time-to-time under the caption “Risk Factors” and elsewhere in Horizon Pharma’s and Depomed’s respective filings and reports with the SEC, including in their respective Annual Report on Form 10-K for the year ended December 31, 2014, and subsequent quarterly reports on Form 10-Q. Horizon Pharma undertakes no duty or obligation to update any forward-looking statements contained in this communication as a result of new information, except as required by applicable law or regulation.

Additional Information
This communication does not constitute an offer to buy or solicitation of any offer to sell or vote securities and is for informational purposes only. It relates to the offer commenced by Horizon Pharma to exchange each issued and outstanding share of Depomed common stock for 0.95 Horizon ordinary shares. The offer will be made only through the Tender Offer Statement on Schedule TO or the Prospectus/Offer to Exchange included in the Registration Statement on Form S-4 (including the Letter of Transmittal and related documents and as amended from time to time, the “Exchange Offer Documents”) that Horizon Pharma has filed with the SEC. This communication also relates to a solicitation by Horizon Pharma of Depomed’s shareholders to (i) call two special shareholder meetings (the “Special Meetings”) to consider the principal proposals described in the Special Meetings Solicitation Statement (as defined below) and (ii) vote in favor of the principal proposals described in the Special Meetings Proxy Statements (as defined below) if the two special shareholder meetings are called and held. This communication also relates to a solicitation by Horizon Pharma of its shareholders to vote in favor of the principal proposals described in the Extraordinary General Meeting Proxy Statement (as defined below). On September 8, 2015, Horizon Pharma filed a definitive solicitation statement and accompanying WHITE and BLUE proxy cards with the SEC with respect to the solicitation of proxies to call two related special meetings of shareholders (including any amendments and supplements, the “Special Meetings Solicitation Statement”). On October 13, 2015, Horizon Pharma also filed two preliminary proxy statements and accompanying WHITE and BLUE proxy cards for the two related special meetings of shareholders with the SEC with respect to the solicitation of proxies to vote in favor of the proposals described in the Special Meetings Solicitation Statement (including any amendments and supplements, the “Special Meetings Proxy Statements”). On October 15, 2015, Horizon Pharma filed a definitive proxy statement and accompanying proxy card for the extraordinary general meeting of Horizon Pharma shareholders (the “Extraordinary General Meeting”) with the SEC with respect to the solicitation of proxies to vote in favor of the proposals described therein (including any amendments and supplements, the “Extraordinary General Meeting Proxy Statement”). Subject to further developments, Horizon Pharma may file one or more further supplements to the Special Meetings Solicitation Statement, one or more amendments and supplements to the Special Meetings Proxy Statements, one or more amendments and supplements to the Extraordinary General Meeting Proxy Statement and additional solicitation statements and/or proxy statements or other documents with the SEC in connection with the Special Meetings and/or the Extraordinary General Meeting, and Horizon Pharma (and, if a negotiated transaction is agreed upon, Depomed) may file one or more registration statements, prospectuses, proxy statements,
Exchange Offer Documents or other documents with the SEC in connection with the offer or any other proposed transaction involving Horizon Pharma and Depomed. This communication is not a substitute for any solicitation statement, proxy statement or other document filed with the SEC in connection with the Special Meetings, the Extraordinary General Meeting or any registration statement, prospectus, proxy statement, Exchange Offer Documents or other documents Horizon Pharma and/or Depomed may file with the SEC in connection with the offer or any other proposed transaction involving Horizon Pharma and Depomed.

If your shares are held by a bank, broker or other nominee, you are considered the beneficial owner of shares held in “street name.” Only your broker or other nominee, as the holder of record of your shares, may submit a WHITE proxy card and/or a BLUE proxy card to join us in calling the Special Meetings, a WHITE proxy card and/or a BLUE proxy card to vote in favor of the proposals described in the Special Meetings Proxy Statements or a proxy card to vote in favor of the proposals described in the Extraordinary General Meeting Proxy Statement, as applicable, and your bank, broker or other nominee may do so only with your specific instructions to do so. YOUR BANK, BROKER OR OTHER NOMINEE HAS PROVIDED YOU WITH A SINGLE VOTING INSTRUCTION FORM FOR PURPOSES OF VOTING ON THE MATTERS SET FORTH IN BOTH THE WHITE PROXY CARD AND THE BLUE PROXY CARD ACCOMPANYING THE SPECIAL MEETINGS SOLICITATION STATEMENT. PLEASE READ AND FOLLOW SUCH SINGLE VOTING INSTRUCTION FORM CAREFULLY IF YOU WISH TO JOIN US IN CALLING ONE OR BOTH OF THE SPECIAL MEETINGS. PLEASE NOTE THAT THE SINGLE VOTING INSTRUCTION FORM PERMITS BENEFICIAL OWNERS TO “ABSTAIN” FROM VOTING ON THE MATTERS SET FORTH ON THE WHITE AND BLUE PROXY CARDS ACCOMPANYING THE SPECIAL MEETINGS SOLICITATION STATEMENT; IF YOU, AS A BENEFICIAL OWNER SO ABSTAIN ON EITHER OR BOTH PROXY CARDS ACCOMPANYING THE SPECIAL MEETINGS SOLICITATION STATEMENT, YOUR ABSTENTION WILL RESULT IN YOUR SHARES NOT BEING COUNTED TOWARDS OUR OBTAINING THE SPECIAL MEETING PERCENTAGE FOR CALLING THE APPLICABLE SPECIAL MEETING.

INVESTORS AND SECURITY HOLDERS OF HORIZON PHARMA AND DEPOMED ARE URGED TO READ CAREFULLY THE SPECIAL MEETINGS SOLICITATION STATEMENT (INCLUDING ANY AMENDMENTS AND SUPPLEMENTS), THE WHITE AND BLUE PROXY CARDS ACCOMPANYING THE SPECIAL MEETINGS SOLICITATION STATEMENT, THE SPECIAL MEETINGS PROXY STATEMENTS (INCLUDING ANY AMENDMENTS AND SUPPLEMENTS), THE WHITE AND BLUE PROXY CARDS ACCOMPANYING THE SPECIAL MEETINGS PROXY STATEMENTS, THE EXTRAORDINARY GENERAL MEETING PROXY STATEMENT (INCLUDING ANY AMENDMENTS AND SUPPLEMENTS), THE PROXY CARD ACCOMPANYING THE EXTRAORDINARY GENERAL MEETING PROXY STATEMENT AND OTHER SOLICITATION STATEMENTS, PROXY STATEMENTS AND DOCUMENTS FILED WITH THE SEC IN CONNECTION WITH THE SPECIAL MEETINGS AND THE EXTRAORDINARY GENERAL MEETING AND THE EXCHANGE OFFER DOCUMENTS (INCLUDING ANY AMENDMENTS AND SUPPLEMENTS) AND ANY OTHER REGISTRATION STATEMENTS, PROSPECTUSES, PROXY STATEMENTS AND OTHER
Special Note Regarding Litigation

As described in the Special Meetings Solicitation Statement, the Special Meetings Proxy Statements and the Extraordinary General Meeting Proxy Statement, Horizon Pharma is currently challenging Depomed’s bylaw-mandated process for calling a special meeting of shareholders as contrary to California law in a judicial proceeding seeking to protect Depomed shareholders’ franchise rights. With that judicial challenge pending, the Special Meetings Solicitation Statement and accompanying WHITE and BLUE proxy cards that have been distributed to Depomed shareholders and the Special Meetings Proxy Statements and accompanying WHITE and BLUE proxy cards that will be distributed to Depomed shareholders reflect Horizon Pharma’s good faith effort to nevertheless comply with what we believe is an onerous process for calling a special meeting of shareholders imposed by the Depomed board of directors. The Superior Court of the State of California, County of Santa Clara, where our judicial challenge is pending, calendared for November 5, 2015 a hearing on a preliminary injunction motion by a subsidiary of Horizon Pharma to enjoin, among other things, the enforcement of Depomed’s bylaws that mandate what we believe to be the onerous process for calling a special meeting of shareholders. The Court subsequently continued the hearing from November 5, 2015 to November 19, 2015. On that same date, the Court is also scheduled to hold a hearing on a preliminary injunction motion by Depomed for its claims against Horizon Pharma and its subsidiary.

Certain Information Regarding Participants

Horizon Pharma and/or Depomed and their respective directors, executive officers and certain other employees and the Horizon Pharma nominees may be deemed participants in the solicitations of proxies in connection with the requests to call the Special Meetings, to vote in favor of the principal proposals described in the Special Meetings Proxy Statements if the Special Meetings are called and held and to vote in favor of the principal proposals described in the Extraordinary General Meeting Proxy Statement. You can find information about Horizon
Pharma’s directors, executive officers and such certain other employees and any individuals Horizon Pharma is seeking to nominate for election to the Depomed board of directors, as described in the Special Meetings Solicitation Statement and the Special Meetings Proxy Statements, in Horizon Pharma’s Annual Report on Form 10-K for the year ended December 31, 2014, which was filed with the SEC on February 27, 2015, Horizon Pharma’s definitive proxy statement filed with the SEC on May 6, 2015, Horizon Pharma’s Current Report on Form 8-K/A filed with the SEC on July 27, 2015; the Special Meetings Solicitation Statement, the Special Meetings Proxy Statements and the Extraordinary General Meeting Proxy Statement and in such other solicitation statements, proxy statements or other documents that would be filed with the SEC in connection with the Special Meetings. You can find information about Depomed’s directors, executive officers and its employees who are participants in such solicitation in Depomed’s definitive proxy statement filed with the SEC on April 16, 2015, Depomed’s definitive revocation statement filed with the SEC on September 30, 2015 and as may be supplemented from time to time, the Special Meetings Solicitation Statement, the Special Meetings Proxy Statements and in such other solicitation statements, proxy statements or other documents that would be filed with the SEC in connection with the Special Meetings. These documents are available free of charge at the SEC’s web site at www.sec.gov and, with respect to Horizon Pharma, from Investor Relations at Horizon Pharma as described above. Additional information regarding the interests of such potential participants is included in the Special Meetings Solicitation Statement, the Special Meetings Proxy Statements and the Extraordinary General Meeting Proxy Statement and will be included in one or more registration statements, proxy statements or other documents filed with the SEC if and when they become available.
Introduction

John B. Thomas
Executive Vice President, Corporate Strategy and Investor Relations
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Note Regarding Use of Non-GAAP Financial Measures

Horizon Pharma provides certain financial measures such as adjusted non-GAAP net income (loss), adjusted non-GAAP net income (loss) per share, non-GAAP gross profit margins and non-GAAP cash from operations 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, 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 prior 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. EBITDA, or earnings before interest, taxes, depreciation and amortization, and adjusted EBITDA are also used and provided by Horizon as non-GAAP financial measures.

Horizon believes that these non-GAAP financial measures, when considered together with the GAAP figures, can enhance an overall understanding of Horizon's financial performance. The non-GAAP financial measures are included with the intent of providing investors with a more complete understanding of the Company's operational results, trends and expectations. In addition, these non-GAAP financial measures are among the indicators Horizon's management uses for planning and forecasting purposes and measuring the Company's 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 used by the Company may be calculated differently from, and therefore may not be comparable to, non-GAAP financial measures used by other companies. The Company has not provided a reconciliation of full year 2015, 2016 or 2020 adjusted EBITDA outlook to a net income (loss) outlook because certain items that are a component of net income (loss) but not part of adjusted EBITDA, such as the gain (loss) on derivative revaluation associated with the convertible senior notes, stock compensation, acquisition related expenses and certain purchase accounting items such as intangibles and step-up inventory, cannot be reasonably projected, either due to the significant impact of changes in Horizon's stock price on derivative revaluation and stock compensation, or the variability associated with acquisition related expenses and purchase accounting items due to timing and other factors.
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Investors and security holders may obtain free copies of the Special Meetings Solicitation Statement, the Special Meetings Proxy Statements, the Extraordinary General Meeting Proxy Statement, the Exchange Offer Documents and any other related documents (when they are available) filed with the SEC at the SEC's website at www.sec.gov or by directing a request to Horizon Pharma's Investor Relations department at Horizon Pharma, Inc., Attention: Investor Relations, 520 Lake Cook Road, Suite 520, Deerfield, IL 60015 or to Horizon Pharma's Investor Relations department at 224-383-3400 or by email to investor-relations@horizonpharma.com. Investors and security holders may obtain free copies of the documents filed with the SEC on Horizon Pharma's website at www.horizonpharma.com under the heading "Investors" and then under the heading "SEC Filings."

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Executive Summary

Timothy P. Walbert
Chairman, President and Chief Executive Officer
Exceptional Net Sales Growth

Net Sales CAGR of 125%

($ in millions)

$250
$200
Sales $150 Net $100

$50
$0
$227
$173
$113 $104
$52
$30 $24
$9 $11


DUEXIS
RAYOS/LODOTRA
VIMOVO
ACTIMMUNE
PENNSAID 2%
BUPHENYL
RAVICITI

Strong quarterly net sales growth and diversification over the last 11 quarters

Non-Confidential Information – Horizon Pharma plc
Diversify Mix of Orphan and Primary Care/Specialty

- Continue transformation to a predominantly orphan business by 2020
- Complement orphan business with strong primary care / specialty business units providing significant cash flows to invest

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<td>1 Year Ago (Q3 2014)</td>
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<tr>
<td>Orphan</td>
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<td>4%</td>
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<tr>
<td>96%</td>
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Non-Confidential Information – Horizon Pharma plc
$2B+ in 2020 Net Sales in Long-Range Plan

(ann ($ in millions))

Net Sales
Adjusted EBITDA

2012: $19
2013: $(73)
2014: $(28)
2015(1): $74
2016(2): $297
2020(3): $975

Note: Excludes any future business development activities

(1) Estimate based on financial guidance issued November 6, 2015
(2) Estimate based on financial guidance issued November 9, 2015
(3) Horizon internal goals based on long-range plan presented November 9, 2015, does not include ACTIMMUNE in certain cancers

Non Confidential Information – Horizon Pharma plc
Today’s Focus

• Issuing first-time 2016 net sales and adjusted EBITDA guidance

• Company’s long-range plan estimates $2B+ in net sales in 2020\(^{(1)}\)
  
  – Orphan business and development pipeline with net sales potential of
    \(\sim$1 - $1.5B+\) in 2020, not including potential for ACTIMMUNE in cancer
  
  – Differentiated and clinically important Primary Care and Specialty medicines
    combined with innovative patient support should lead to \(\sim$800M - $1B\) in
    net sales in 2020

• HorizonCares – Patients receive the medicines their doctors prescribe

• Diversified growth strategy with expected 20%+ annual organic growth
  complemented with disciplined incremental business development

• Strong balance sheet and cash flows enable significant incremental
  financing capacity

Note: Horizon estimates do not include any incremental business development contribution

\(^{(1)}\) Horizon internal goals based on long-range plan presented November 9, 2015, does not include ACTIMMUNE in certain cancers

Non Confidential Information – Horizon Pharma plc
Orphan Business Unit Review
Business Overview and Update

George P. Hampton
Executive Vice President, Global Orphan Business Unit and International Operations
Evolve into a Leading Orphan Business

- **RAVICTI and ACTIMMUNE** address significant unmet needs
- Valuable, growing orphan business in current indications
  - $265M annual net sales run rate
  - Long-life assets
  - Expansion opportunities Ex-U.S.
  - Annual U.S. net sales opportunity of ~$500M\(^{(1)}\) in 2020
  - Attractive contribution margins
- Significant potential upside with additional indications
  - Friedreich’s ataxia Phase 3 trial underway\(^{(2)}\)
  - Combination therapy with PD-1/PD-L1s in cancer\(^{(3)}\)
  - Annual U.S. net sales opportunity of ~$800M - $1.5B\(^{(1)}\) in 2020

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\(^{(1)}\) Horizon estimate

\(^{(2)}\) Use of ACTIMMUNE in Friedreich’s ataxia (FA) is investigational only, and safety and efficacy has not been established for use in Friedreich’s ataxia (FA). For further information see [www.ACTIMMUNE.com](http://www.ACTIMMUNE.com).

\(^{(3)}\) Use of ACTIMMUNE with PD-1 and PD-L1 inhibitors is investigational only, and safety and efficacy has not been established for use with any PD-1 and PD-L1 inhibitor. For further information see [www.ACTIMMUNE.com](http://www.ACTIMMUNE.com).
### Global Orphan Disease Focus

<table>
<thead>
<tr>
<th>Current Indications</th>
<th>Urea cycle disorders (UCDs)</th>
<th>U.S., Canada, Japan, Sweden, other ex-U.S.: Approved (all ages)</th>
<th>Chronic granulomatous disease (CGD), Severe, malignant osteopetrosis (SMO)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marketing Status</td>
<td>U.S.: Approved (&gt;2 yrs)</td>
<td>U.S., Canada, Japan, Sweden, other ex-U.S.: Approved (all ages)</td>
<td>U.S.: Approved</td>
</tr>
<tr>
<td>Dev. Programs</td>
<td>EU: In Registration (&gt;2 months)</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Dev. Programs</td>
<td>FDA PMR Studies</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td></td>
<td>Label expansion:</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td></td>
<td>Birth – 2 months</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td></td>
<td>2 months – 2 years</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>IP Position</td>
<td>4 allowed and 3 OB listed patents with protection to 2032</td>
<td>n/a</td>
<td>2 U.S. patents to 2022; perpetual Genentech know-how license</td>
</tr>
<tr>
<td>Rights Owned</td>
<td>Global</td>
<td>U.S.; Ex-U.S. partnered</td>
<td>U.S., Canada, Japan</td>
</tr>
</tbody>
</table>

1. BUPHENYL is known as AMMONAPS outside the United States
2. Anticipated to begin before year-end 2015

Non-Confidential Information – Horizon Pharma plc
Attractive Global Market Opportunity in UCDs

- Patients born with genetic defect of urea synthesis
- Ultra-orphan disease with an estimated U.S. prevalence of about 2,000 cases and incidence of about 1 in every 8,500 to 25,000 newborns
- Europe and Japan prevalence of about 2,000 cases total
- Variable age of diagnosis (newborn to adulthood), with neurological deficits ranging from mild mental retardation to coma and death
- In general, with prompt diagnosis and careful management involving dietary restriction, alternative pathway therapy can lead to good clinical outcomes
- Outcomes are poor for untreated, severely affected individuals
# Superior Profile of RAVICTI Drives Improved Adherence

<table>
<thead>
<tr>
<th>Form</th>
<th>Oral liquid</th>
<th>Tablets or powder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max Daily Dose</td>
<td>3 teaspoons</td>
<td>40 tablets</td>
</tr>
<tr>
<td>Taste and Smell</td>
<td>Virtually none</td>
<td>Repellant</td>
</tr>
<tr>
<td>Sodium Content</td>
<td>None</td>
<td>High levels</td>
</tr>
</tbody>
</table>

Note: RAVICTI is based upon a non-inferiority study and conclusions between RAVICTI and BUPHENYL may not be made. The information provided are fixed properties in the respective labels and not meant as a comparator or statement of efficacy between the two medicines.

1. BUPHENYL is known as AMMONAPS outside the United States.
Significant Advancement for Patients with UCDs

1996
Up to 40 tabs/day

Buphenyl (Phenylbutyrate) tab 500 mg

2013
3 teaspoons/day

RAVICTI® (glycerol phenylbutyrate) Oral Liquid

(1) BUPHENYL is known as AMMONAPS outside the United States

Non-Confidential Information – Horizon Pharma plc
Chronic Granulomatous Disease (CGD)

- Disease of the immune system and described as a primary immunodeficiency disorder
- Patients are more likely to experience recurrent severe bacterial and fungal infections and chronic inflammatory conditions
- ~1,600 patients in the U.S.
- May become apparent any time from infancy to late adulthood
  - >75% are diagnosed before the age of five years
- Under-diagnosed and can be misdiagnosed
- Diagnostic testing is readily available
**ACTIMMUNE in CGD**

**Indications**
- Reducing the frequency and severity of serious infections associated with Chronic Granulomatous Disease (CGD)

**Dosing/Route of Administration**
- Subcutaneous injection three times weekly

**CGD Treatment Protocols**

<table>
<thead>
<tr>
<th>ADVANCES IN ANTINFECTIOUS PROPHYLACTIC THERAPY</th>
<th>POTENTIAL CURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single</td>
<td>Dual</td>
</tr>
<tr>
<td>Antibiotic OR antifungal</td>
<td>Antibiotic AND antifungal</td>
</tr>
<tr>
<td>Bone Marrow Transplant</td>
<td></td>
</tr>
</tbody>
</table>
Orphan Business Focus

*Find and Manage Patients*

- **Patient identification in conjunction with doctors**
  - 14 clinical sales associates
  - Covering key U.S. medical centers
- **Increase adherence rates**
  - Utilize a range of patient support programs
  - Nurse educators work directly with patients
- **HUB implementation**
  - Single point of contact for the patient
  - Help patients battle disease through education
  - Data capture and reporting in real-time
Patient Programs Drive Improved Adherence

ACTIMMUNE in CGD and SMO

76% 74% 79% 85% 80% 78% 84% 88% 81% 85% 81% 90%

Adherence Promotional Piece
Intense Adherence Outreach to HCPs, Monitor Patient “Watch List”
Clinical Nurse Program, Email Reminders, Total Text Reminders, Outbound Calls

14 percentage point improvement in adherence = $14M of annualized net sales

Note: Adherence defined as vials shipped vs. prescribed vials

Non-Confidential Information – Horizon Pharma plc
Orphan Business at $265M Annual Net Sales Run Rate

$300,000 $250,000 $200,000 $150,000 $100,000 $50,000 $0

BUPHENYL RAVICTI ACTIMMUNE

$23M $25M $3M

Hyperion close May 7th, 2015

$49M $66M

Q3 first full quarter of RAVICTI sales

$265M

Annual Run Rate Based on Q3 2015

28 Non Confidential Information – Horizon Pharma plc
# U.S. Orphan Growth Drivers

**2020 Annual Net Sales Opportunity of ~$500M\(^{(1)}\)**

<table>
<thead>
<tr>
<th>RAVICTI</th>
<th>ACTIMMUNE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continue to transition patients from BUPHENYL to RAVICTI</td>
<td>Increase diagnosis</td>
</tr>
<tr>
<td>Further penetration into diagnosed, PBA (phenylbutyrate) treatment naïve and newly diagnosed patient populations</td>
<td>- 30% penetrated in CGD</td>
</tr>
<tr>
<td>Label expansion in patients &lt;2 years</td>
<td>Increase adherence in existing patients</td>
</tr>
<tr>
<td>- Anticipate sNDA filing in Q2 2016 for 2 month - 2 years</td>
<td>Increase acceptance of triple prophylaxis (oral antibiotic + oral anti-fungal + ACTIMMUNE)</td>
</tr>
<tr>
<td>Increase diagnosis rates</td>
<td></td>
</tr>
</tbody>
</table>

\(^{(1)}\) Horizon estimate for current approved indications
Global Expansion

- Build or buy infrastructure to capitalize on current and future approvals and acquired medicines

<table>
<thead>
<tr>
<th>EU</th>
<th>RAVICTI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CHMP positive opinion – September 24, 2015</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Anticipate European Commission approval by year-end 2015</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Potential for significantly enhanced EU label</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Commercial launch expected in 2017</strong></td>
<td></td>
</tr>
</tbody>
</table>

Future Medicines

- Orphan and specialty focus
Friedreich’s Ataxia (FA)

~$500M - $1B\(^{(1)}\) U.S. Annual Net Sales Opportunity

- Debilitating and progressive genetic, neurological disease
  - 85% of diagnosed patients exhibit symptoms before the age of 25
- Life shortening
  - Life span is 30 to 40 years of age
- No FDA approved treatment
  - Monitor symptoms
  - Most patients take vitamins and antioxidants
- Neurological examinations and genetic testing in specialized care centers
- Prevalence: ~15,000 worldwide, ~3,700 U.S.
- Patients in FARA registry: 2,400 worldwide, 1,400 U.S.

Note: Use of ACTIMMUNE in Friedreich’s ataxia (FA) is investigational only and safety and efficacy has not been established for use in Friedreich’s ataxia (FA). For further information see www.ACTIMMUNE.com.

\(^{(1)}\) Horizon estimate
ACTIMMUNE with PD-1/PD-L1 Inhibitors

~$300M - $500M(1) U.S. Annual Net Sales Opportunity

- Analysts project PD-1/PD-L1 checkpoint inhibitors market >$30B
- Significant investments by pharma in PD-1/PD-L1 checkpoint inhibitors
- Two currently approved medicines
  - KEYTRUDA® (pembrolizumab) – Merck(2)
  - OPDIVO® (nivolumab) – BMS(3)
- Initial focus: combination therapy in selected bladder and renal cancers

Possible combination therapy with PD-1/PD-L1, which are considered among the most promising breakthroughs in cancer therapy

Note: Use of ACTIMMUNE with PD-1 and PD-L1 inhibitors is investigational only, and safety and efficacy has not been established for use with any PD-1 and PD-L1 inhibitor. For further information see www.ACTIMMUNE.com.

(1) Horizon estimate in renal and bladder cancers
(2) Registered trademark of Merck
(3) Registered trademark of Bristol Myers Squibb
Orphan Business Long-Range Plan

$~1.3 - $2B+(1) Annual U.S. Net Sales Opportunity in 2020

Net Sales ($ in millions)

<table>
<thead>
<tr>
<th>Cancer</th>
<th>FA</th>
<th>Existing Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>~$300 - $500</td>
<td>~$500 - $1,000</td>
<td>~$1,300 - $2,000</td>
</tr>
</tbody>
</table>

Midpoint of ranges are represented on chart for FA and cancer

(1) Horizon estimate

Non-Confidential Information – Horizon Pharma plc
Jeffrey W. Sherman, M.D., FACP
Executive Vice President, Research and Development and Chief Medical Officer
Commitment to Clinical Development

- Clinical development is a vital part of our mission to provide innovative medicines to help patients live better lives
- Primary goals
  - Address unmet medical needs
  - Develop medicines with differentiated clinical features and benefits
  - Create sustainable long-term value through medicines we bring to market
- Comprehensive evaluation of our medicines for additional indications
- Engage regulatory agencies, health care professionals and patient groups to facilitate clinical development
### Robust Development Pipeline

**ACTHMUNE**
- Friedreich’s ataxia
- Autosomal Dominant Osteopetrosis
- Combo cancer therapy w/ PD-1/PD-L1
- Next-generation formulation

**RAVICTI**
- Urea Cycle Disorders
  - 2 months to 2 years of age
  - Birth to 2 months of age

**RAYOS**
- PMR (Dose-sparing)
- Lupus (Address fatigue)

### Collaborator Progression Table

<table>
<thead>
<tr>
<th>Collaborator</th>
<th>Pre-clinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Post-Market</th>
</tr>
</thead>
<tbody>
<tr>
<td>FARA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UCLA/Indiana U</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fox Chase</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UCDC</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>UCDC</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>OMERACT</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALR</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

Non-Confidential Information – Horizon Pharma plc
ACTIMMUNE (Interferon gamma-1b)

- Single-chain polypeptide containing 140 amino acids synthesized in the 1980s
  - Molecular weight: ~33 kDa
  - Expressed in E. coli bacterium
  - Specific activity of 20 million IU/mg
- Differs from other interferons (alpha and beta)
  - Treatment targets appear to not overlap
- Differs from natural human interferon gamma by the presence of an N-terminal methionine and lack of glycosylation
- Binds to interferon gamma cell surface receptor (Type II)
- 5.9 hours mean half-life in vivo for subcutaneous dosing with 100 mcg/m2; three times weekly dosing targeted for FA

Note: Use of ACTIMMUNE in Friedreich’s ataxia (FA) is investigational only, and safety and efficacy has not been established for use in Friedreich’s ataxia (FA). For further information see www.ACTIMMUNE.com.
What is FA?

- FA is a hereditary disease caused by a genetic mutation in the frataxin (FXN) gene
  - FXN gene first identified in 1996
- GAA triplet in the FXN gene is repeated 5-33 times in healthy subjects but 66-1000+ times in FA patients
- Abnormal GAA triplet repeat disrupts production of frataxin
- Low frataxin = mitochondrial dysfunction and energy deprivation = multi-system disease
Moderate Increases in Frataxin May Produce a Therapeutic Benefit

Carriers are asymptomatic and have approximately 50% of the frataxin levels of controls

Source: A rapid, noninvasive immunoassay for frataxin: Utility in assessment of Friedreich's ataxia; Eric C. Deutsch, Avni B. Santani, Susan L. Perlman, Jennifer M. Farmer, Catherine A. Stolle, Michael F. Marusich, and David R. Lynch, 2012
Why Interferon gamma-1b for FA?

Interferon gamma upregulates frataxin and corrects the functional deficits in a Friedreich ataxia model

Barbara Tomassini, Gaetano Arcuri, Silvia Fortuni, Chiranjeevi Sandi, Vahid Ezzatizadeh, Carlo Casali, Ivan Condò, Florence Malisan, Sahar Al-Mahdawi, Mark Pook and Roberto Testi

1. Laboratory of Immunology and Signal Transduction, University of Rome 'Tor Vergata', 00133 Rome, Italy, 2. Division of Biosciences, School of Health Sciences and Social Care, Brunel University, Uxbridge UB8 3PH, UK and 3. Department of Neurology, University of Rome 'La Sapienza', Polo Pontino, 04100 Latina, Italy

Received January 14, 2012; Revised and Accepted March 15, 2012

Note: Use of ACTIMMUNE in Friedreich’s ataxia (FA) is investigational only, and safety and efficacy has not been established for use in Friedreich’s ataxia (FA). For further information see www.ACTIMMUNE.com.

Source: A rapid, noninvasive immunoassay for frataxin: Utility in assessment of Friedreich’s ataxia; Eric C. Deutsch, Avni B. Santani, Susan L. Perlman, Jennifer M. Farmer, Catherine A. Stolle, Michael F. Marusich, and David R. Lynch, 2012

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Why Interferon gamma-1b for FA?

- **FRDA mouse model**
  - Half treated with interferon gamma (40 mcg/kg TIW)
  - Half with placebo for 10 weeks

- **Results**
  - IFNγ treated mice significantly improved both locomotor activity and motor coordination
  - IFNγ mechanism of action postulated to be upregulation of frataxin gene expression and neuronal preservation in dorsal root ganglion

Source: A rapid, noninvasive immunoassay for frataxin: Utility in assessment of Friedreich's ataxia; Eric C. Deutsch, Avni B. Santani, Susan L. Perlman, Jennifer M. Farmer, Catherine A. Stolle, Michael F. Marusich, and David R. Lynch, 2012

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ACTIMMUNE Phase 2 Trial in FA

Pilot Study in Children with FA

- Investigator-initiated study at CHOP
  - Goals
    - Safety and tolerability of IFNγ
    - Effect on frataxin protein levels
    - Effect on neurologic function
  
- Design: Open-label pilot study
  - 12 Individuals with genetic confirmation of FA, ages 5-17 enrolled September – December 2013
  - Dose-escalation every two weeks based on tolerability
    - 10mcg/m2, 25mcg/m2, 50mcg/m2 TIW– 3xwk
  - Overall treatment phase was 12 weeks
  - Reevaluation 1 month post treatment; last study visit March 2014

Note: Use of ACTIMMUNE in Friedreich’s ataxia (FA) is investigational only and safety and efficacy has not been established for use in Friedreich’s ataxia (FA). For further information see www.ACTIMMUNE.com.

### ACTIMMUNE Phase 2 Trial in FA

#### Demographics and Safety

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Safety and Tolerability</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 8 - 17 years old, mean age of 12</td>
<td>• No drug-related serious adverse events (SAE) occurred</td>
</tr>
<tr>
<td>• Mean GAA repeat length 835</td>
<td>• 11 of 12 subjects experienced at least 1 AE</td>
</tr>
<tr>
<td>• Mean age of onset was 6</td>
<td>• Low grade, not dose related</td>
</tr>
<tr>
<td>• 12 of 12 subjects screened met criteria</td>
<td>• Largely known side-effects of IFNγ</td>
</tr>
<tr>
<td>• Two subjects did not follow dose escalation protocol due to adverse events</td>
<td>• Two subjects were unable to continue with full dose-escalation of IFN-γ due to moderate to severe flu-like symptoms</td>
</tr>
<tr>
<td>• Two subjects withdrawn from the study for inability to complete study procedures due to travel challenges</td>
<td></td>
</tr>
</tbody>
</table>

Note: Use of ACTIMMUNE in Friedreich’s ataxia (FA) is investigational only, and safety and efficacy has not been established for use in Friedreich’s ataxia (FA). For further information see www.ACTIMMUNE.com.

ACTIMMUNE Phase 2 Trial in FA
Variable Frataxin Measurements - Buccal Cells as a Surrogate for Nerve Cells

Note: Use of ACTIMMUNE in Friedreich’s ataxia (FA) is investigational only, and safety and efficacy has not been established for use in Friedreich’s ataxia (FA). For further information see www.ACTIMMUNE.com.

Non-Confidential Information – Horizon Pharma plc
4.98 change in FARS score with a p-value of 0.0078 (equates to reversing 18 to 24 months of disease progression) plus patient decline upon therapy termination support initiation of Phase 3 Study

Note: Use of ACTIMMUNE in Friedreich’s ataxia (FA) is investigational only, and safety and efficacy has not been established for use in Friedreich’s ataxia (FA). For further information see www.ACTIMMUNE.com.

ACTIMMUNE Phase 2 Trial in FA

**Summary**

- **IFNγ** was considered safe and well-tolerated
- **Variable increase in frataxin levels**
  - Presence of increased levels through treatment
  - Sampling limited to unaffected tissue
  - Timing of sampling was variable - short half life of IFNγ
  - Limited to FDA approved dose for other diseases
- **Clinically significant neurologic improvement**
  - Probability of result occurring by chance < 1%
- **Limitations**
  - The small size of the study
  - Absence of a placebo group
  - Single center

Note: Use of ACTIMMUNE in Friedreich's ataxia (FA) is investigational only, and safety and efficacy has not been established for use in Friedreich’s ataxia (FA). For further information see www.ACTIMMUNE.com.

Randomized, Multicenter, Double-Blind, Placebo-Controlled, Efficacy, Safety, and Pharmacokinetic Study of ACTIMMUNE® (interferon γ-1b) in Children and Young Adults with Friedreich’s Ataxia

Short title:

STEADFAST

Safety, Tolerability and Efficacy of ACTIMMUNE Dose Escalation in Friedreich’s Ataxia Study

Clinicaltrials.gov: NCT02415127

Note: Use of ACTIMMUNE in Friedreich’s ataxia (FA) is investigational only, and safety and efficacy has not been established for use in Friedreich’s ataxia (FA). For further information see www.ACTIMMUNE.com.
ACTIMMUNE Phase 3 Trial in FA

STEADFAST Trial Design

- Patients randomized 1:1 to receive subcutaneous doses of either ACTIMMUNE or placebo three times a week for a total of 26 weeks
- Approximately 90 patients will be enrolled at four sites in the U.S. - CHOP, University of Florida, University of Iowa and UCLA
- Primary endpoint will measure the change in neurological outcome and evaluate the effect of ACTIMMUNE versus placebo as measured by the modified Friedreich’s Ataxia Rating Scale (FARS-mNeuro), focused on objective neurologic measures
  - FARS-mNeuro is a subset of the total FARS score removing components viewed by FDA to be more subjective and effort dependent
  - FARS-mNeuro score in the Phase 2 study (p=0.0117) is consistent with the previously reported total FARS score (p=0.0078)

Note: Use of ACTIMMUNE in Friedreich’s ataxia (FA) is investigational only and safety and efficacy has not been established for use in Friedreich’s ataxia (FA). For further information see www.ACTIMMUNE.com.
ACTIMMUNE Phase 3 Trial in FA
Progress Update & Milestones

• **Patient enrollment**
  – More than one-third enrolled to-date
    • In-line with our expectations
  – Target date for full enrollment of 90 patients: mid-year 2016
  – FARA collaboration to enroll through its patient registry

• **Potential clinical and regulatory milestones**
  – Data available: Late 2016
  – sBLA submission: Q1 2017
  – FDA approval: Q3 2017 (Fast Track designation)

Note: Use of ACTIMMUNE in Friedrich’s ataxia (FA) is investigational only, and safety and efficacy has not been established for use in Friedrich’s ataxia (FA). For further information see www.ACTIMMUNE.com.
Example of Clinical Response

Before Treatment

6 Months

- (200mcg 3x/week [2x CGD Dose])

10 Months

- (200mcg 3x/week [2x CGD Dose])


ACTIMMUNE is currently approved by the U.S. Food and Drug Administration (FDA) to reduce the frequency and severity of serious infections associated with Chronic Granulomatous Disease (CGD) and to slow the worsening of severe, malignant osteopetrosis (SMO). ACTIMMUNE is not approved for other indications including the treatment of Friedreich's ataxia (FA) and its use with patients suffering from FA is investigational as safety and efficacy have not been established in FA. For further information see www.ACTIMMUNE.com.
Checkpoint Inhibitors (PD-1/PD-L1 Immunotherapy)
Role in Cancer Therapy

- Normal immunologic surveillance mechanisms - programmed cell death
- Tumor cells up-regulate so-called “checkpoint inhibitors” with effect of turning off immune system’s ability to kill cells
- Allows cancer cells to multiply and divide “unchecked”
- Potential in multiple tumor types

Use of ACTIMMUNE with PD-1 and PD-L1 inhibitors is investigational only, and safety and efficacy has not been established for use with any PD-1 and PD-L1 inhibitor. For further information see [www.ACTIMMUNE.com](http://www.ACTIMMUNE.com).

Mechanistic Rationale Why ACTIMMUNE May Enhance Activity of PD-1/PD-L1 Inhibitors

- Interferon gamma (IFN-γ) may promote or enhance the effect of the PD-1 or PD-L1 inhibitors

- IFN-γ exhibited superior and more durable enhancement of PD-L1 expression in endothelial cell lines vs. IFN-α and IFN-β\(^{(1)}\)

- Tumor PD-L1 upregulation appears to be a factor most strongly correlated with response to PD-1 blockade\(^{(2)}\)

- Interferon gamma will be used to induce PD-L1 upregulation in tumor cells to increase the likelihood of response to a PD-1 inhibitor

Note: Use of ACTIMMUNE with PD-1 and PD-L1 inhibitors is investigational only, and safety and efficacy has not been established for use with any PD-1 and PD-L1 inhibitor. For further information see www.ACTIMMUNE.com.


ACTIMMUNE PD-1/PD-L1 Approach

Step #1

- Phase 1 trial in combination with PD-1 inhibitor in certain cancers
  - Collaboration with Fox Chase Cancer Center
  - Assess dose and sequencing of the combination of medicines
  - Initiate trial by year-end 2015

Step #2

- Advance to Phase 2/3 trials
  - Dependent upon Phase 1 results

Note: Use of ACTIMMUNE with PD-1 and PD-L1 inhibitors is investigational only, and safety and efficacy has not been established for use with any PD-1 and PD-L1 inhibitor. For further information see www.ACTIMMUNE.com.
RAVICTI (Glycerol Phenylbutyrate)

- Glycerol phenylbutyrate is a nitrogen-binding agent
  - Triglyceride containing 3 molecules of PBA linked to a glycerol backbone
- Glycerol is 7% of molecular weight
- Sodium and sugar free
- Nearly odorless and tasteless
- Requires “digestion” to release PBA in contrast to sodium phenylbutyrate that is a salt and releases PBA immediately after ingestion
- ~3 teaspoons = 40 tablets of Buphenyl (NaPBA)
**RAVICTI Label Expansion**

**Birth – 2 years of age**

- **Design:** Open label design to assess the safety, efficacy and PK of RAVICTI in pediatric patients under 2 years of age

- **Subjects:** UCD patients up to 2 years

- **Sites:** U.S. sites

- **Target dates:**
  - 2 months – 2 years
    - sNDA submission: Q2 2016
  - Birth – 2 months
    - sNDA submission: Q1 2018
Exploring Additional RAVICTI Indications

- Conducting assessment similar to what was done with ACTIMMUNE to determine possibilities for RAVICTI
  - IP feasibility
  - Technical hurdles
  - Commercial timing
  - Areas for collaboration with study consortia and patient groups to facilitate development such as with FARA in FA

Use of ACTIMMUNE in Friedreich’s ataxia (FA) is investigational only, and safety and efficacy has not been established for use in Friedreich’s ataxia (FA). For further information see www.ACTIMMUNE.com.
Key Takeaways – Clinical Development Opportunities

- We have a robust clinical development pipeline

- Multiple opportunities for possible expansion in use of our products
  - ACTIMMUNE for FA\(^{(1)}\)
    - Pre-clinical data supports mechanism of action
    - Clinical data is supportive of disease-modifying activity
    - Anecdotal data
  - Combination therapy with PD-1/PD-L1s in cancer\(^{(2)}\)
  - RAVICITI in younger patients (<2 years of age) with UCDs\(^{(3)}\) and other potential indications

---

\(^{(1)}\) Use of ACTIMMUNE in Friedreich’s ataxia (FA) is investigational only, and safety and efficacy has not been established for use in Friedreich’s ataxia (FA). For further information see www.ACTIMMUNE.com.

\(^{(2)}\) Use of ACTIMMUNE with PD-1 and PD-L1 inhibitors is investigational only, and safety and efficacy has not been established for use with any PD-1 and PD-L1 inhibitor. For further information see www.ACTIMMUNE.com.

\(^{(3)}\) Use of RAVICITI for patients less than two years of age is investigational only, and safety and efficacy has not been established in patients less than two years of age. For further information see www.ravicti.com.
Primary Care and Specialty Business Unit Review

Business Overview and Update

John Kody
Executive Vice President, Chief Commercial Officer
Primary Care/Specialty Commercial Business Model
*Patient Focused, Best-in-Class Execution*

- Clinically Differentiated Medicines
- Differentiated Commercial Execution
- Evolving Payer and PBM Environment
- Patient Support Program

**Primary Care Brands**

- **DUEXIS®**
  (ibuprofen and famotidine) Tablets
  800 mg/26.6 mg
- **VIMOVO®**
  (naproxen,esomeprazole magnesium)
  375/30-300/30 mg delayed-release tablets

**Specialty Brand**

- **RAYOS®**
  (Prednisone) Delayed-release Tablets
- **PENNSAID®**
  (Diclofenac sodium topical solution) 2% w/w
Our Objective is to Grow PC & Specialty Business into $800M - $1B in Annual Net Sales by 2020

<table>
<thead>
<tr>
<th>Year</th>
<th>RAYOS</th>
<th>PENNSAID 2%</th>
<th>VIMOVO</th>
<th>DUEXIS</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2015</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2020</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Estimate based on financial guidance issued November 6, 2015

Non Confidential Information – Horizon Pharma plc
Large and Growing NSAID Market

117M TRx/Year, Growing ~3%/year, Topical Market +15% Growth

Ibuprofen = 36M TRx/Year
Naproxen = 17M TRx/Year
Topical NSAIDs = 6M TRx/year
TRx Growth Driven By Commercial Model with Clinically Differentiated Medicines

Current State = 380k Doctors Rx NSAIDs Each Week

Qualifying
- No recent TRx (called on)

INITIAL Trial
- TRx in recent weeks

NICHE (Trial)
- 10k Prescribers
- TRx in most recent week

ADOPTION
- 1k Prescribers
- 5+ TRx in most recent week

Key Tactics
- Focus sales effort on PAR doctors:
  - Potential for high TRx
  - Access to call on weekly
  - Receptive to clinical message
- Apply Horizon differentiated sales model to drive acceleration of adopters

>$500M(1)
2015 PC/Specialty Sales

[1] Estimate based on financial guidance issued November 6, 2015
Effective Promotion + Differentiated Clinical Benefits Drive Rapid Acceleration of Adopters

The number of adopters (>5 TRx/week) has TRIpled in 2015

Source: IMS Xponent
(1) For Horizon’s four Primary Care and Specialty medicines

Non Confidential Information – Horizon Pharma plc
Primary Care/Specialty Volume +189% vs. Price +16%

Last 7 Quarter Net Sales Growth Driven by Volume Growth

- Average net realized price (ANRP) has increased 9% annualized, 16% cumulatively since Q1 2014
  - Prescription growth of 189% since Q1 2014

Quarterly ANRP and Prescription Volumes 1/1/14 to 9/30/15

(1) For Horizon’s four Primary Care and Specialty medicines

Non-Confidential Information – Horizon Pharma plc
Commercial Execution Expected to Drive Achievement of 2020 Long-Range Plan

- Doctor adoption via execution of commercial business model
- Education of the clinical benefit of our medicines
- Prescription growth with relatively constant net realized price should allow achievement of LRP
- Significant incremental market opportunity for each of our medicines
- Commitment to ensure commercially insured patients get the medicines their doctors prescribe at the lowest out-of-pocket cost possible
Alfonso E. Bello, M.D., MHS, FACP, FACR, DABPM
Rheumatologist
Objectives

- Background of NSAID use
- Review the scope of gastrointestinal (GI) related NSAID toxicities
- Compare and contrast current gastroprotective strategies
- DUEXIS® and VIMOVO® review

Please see Important Safety Information in appendix.
The Increasing Burden of Arthritis

- **Osteoarthritis (OA)** is the most common type of arthritis — 26.9 million adults (≥25 years of age) in the U.S. have clinical OA

- Approximately 2.8 million adults (≥18 years of age) in the US have rheumatoid arthritis (RA)
  - Prevalence in U.S. is expected to increase with the aging of the population

- **NSAIDs** are commonly prescribed to treat OA/RA

---


Incidence of Chronic Pain Compared with Other Disease States in the U.S.

Millions of Americans

<table>
<thead>
<tr>
<th>Disease</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic pain</td>
<td>116.0</td>
</tr>
<tr>
<td>Diabetes</td>
<td>25.8</td>
</tr>
<tr>
<td>CHD/Stroke</td>
<td>23.3</td>
</tr>
<tr>
<td>Cancer</td>
<td>11.7</td>
</tr>
</tbody>
</table>

Serious Consequences of NSAID Use

- As many as 25% of chronic NSAID users will develop ulcer disease¹
  - 2% to 4% will develop a bleed or perforation¹,²
- Serious GI complications such as inflammation, bleeding, ulceration and perforation can occur at any time, with or without warning symptoms²
- In patients with arthritis who are taking NSAIDs³:
  - >107,000 hospitalizations per year for serious GI complications
  - >16,500 deaths per year
- Managing and preventing NSAID-associated gastropathy has been estimated to cost more than $4 billion annually⁴

NSAID-Induced GI Damage

- Superficial damage (i.e., mucosal hemorrhages and erosions)
- Endoscopically documented non-symptomatic “silent” ulcers
- Ulcers causing complications, i.e., GI hemorrhage
Relative Risk of Upper GI Bleeding

- Past Complicated Ulcer: 13.5
- Multiple NSAIDs*: 8.9
- High-Dose NSAIDs: 7.0
- Anticoagulant: 6.4
- Past Uncomplicated Ulcer: 6.1
- Age 70-80 Years: 5.6
- Steroids: 2.2

* Including low dose aspirin

Mortality From NSAID-Induced GI Complications* Versus Other Diseases in the United States

Heroin
Viral Hepatitis
Opioid Analgesics
NSAID Induced Ulcers

Deaths (000's)

Sources
1. CDC Selected Causes of Death 2012 (Table 10) http://www.cdc.gov/nchs/data/nvsr/nvsr63/nvsr63_09.pdf
2. NSAID Induced Deaths - M. Wolfe, et.al.; Gastrointestinal Toxicity of Nonsteroidal Anti-inflammatory Drugs; NEJM; vol. 340; no. 24; June 1999
NSAID Gastroprotection Strategies and Issues
Prescribing guidelines for treating OA and RA call for gastroprotective agents to be taken along with NSAIDs to lessen the risk of serious GI side effects such as ulcers.

**Risk Factors Include:**
- Age >65 years
- High-dose NSAID therapy
- A history of uncomplicated ulcer
- Concurrent use of aspirin (including low dose), corticosteroids or anticoagulants

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>High Risk</th>
<th>Moderate Risk</th>
<th>Low Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;2 risk factors</td>
<td>1–2 risk factors</td>
<td>No risk factors</td>
<td></td>
</tr>
<tr>
<td>History of complicated ulcer, especially recent</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Use of Unprotected NSAIDs Post COX-2 Issues...Caused Increase in Serious GI Ulcers*

* G. Singh, 2007 American College of Rheumatology Annual Meeting Presentation

Gastroprotection Gap

Serious GI Ulcers/100,000 NSAID Users

NSAID Use with No Gastroprotection

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* G. Singh, 2007 American College of Rheumatology Annual Meeting Presentation
Utilization of Gastroprotective Strategies Among New NSAID Users

1 GI Risk Factor
0.1% 2.5% 10.8%

2 GI Risk Factors
0.2% 4% 14.7%

GPA: Gastroprotective agent
Provider Adherence To Recommended Guidelines For High Risk Patients*

- NSAID Alone: 9%
- NSAID+GPA: 18%
- COX-2 (i.e., Celebrex): 73%

GPA: Gastroprotective agent.

* Age ≥65, history of upper GI event, high dose NSAID, corticosteroid use and anticoagulant use.

Gastroprotective Non-adherence by Number of Repeat NSAID Prescriptions

GI Toxicity Associated With Traditional NSAIDs

Most Patients Are Asymptomatic

N = 1,921

- Without symptoms: 81%
- With symptoms: 19%

DUEXIS Overview

- DUEXIS is an innovative 2-in-1 combination tablet with 800 mg ibuprofen and 26.6 mg famotidine\(^1\)
- TID dosing provides 2400 mg ibuprofen and 80 mg famotidine\(^2\) daily\(^1\)

---


\(^2\): Generic famotidine is not approved to reduce upper GI ulcers

Please see Important Safety Information in appendix.
DUEXIS

Indications and Usage

DUEXIS is indicated for

- The relief of signs and symptoms of rheumatoid arthritis and osteoarthritis and to decrease the risk of developing upper gastrointestinal ulcers in patients who are taking ibuprofen for those indications
  - In the clinical trials, upper GI ulcer was defined as a gastric and/or duodenal ulcer
  - The clinical trials primarily enrolled patients <65 years of age without a prior history of GI ulcer. Controlled trials did not extend beyond 6 months

Please see Important Safety Information in appendix.
The primary objective was to evaluate the efficacy of DUEXIS in reducing the proportion of patients who develop endoscopically-diagnosed upper gastrointestinal ulcers during the 24-week treatment period, as compared to ibuprofen, in subjects at risk for NSAID-induced ulcers.
DUEXIS was evaluated in 2 randomized, double-blind, multicenter, comparator-controlled clinical trials enrolling more than 1500 patients with mild to moderate chronic pain\(^1\)\(^2\).

The trials compared the efficacy of DUEXIS with ibuprofen alone in reducing endoscopically diagnosed ulcers during a 24-week treatment period\(^1\)\(^2\).

*At week 24 or at early termination.


\(^2\) Data on file. Horizon Pharma, Inc.

Please see Important Safety Information in appendix.
# DUEXIS Phase 3: REDUCE-1 and REDUCE-2

## Patient Demographics and Risk Factors

### All Patients Characteristic (N=1533)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Patients (N=1533)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient Demographics</strong></td>
<td></td>
</tr>
<tr>
<td>Median age (range)</td>
<td>55 years (39 to 80)*</td>
</tr>
<tr>
<td>Female</td>
<td>68%</td>
</tr>
<tr>
<td>Race: Caucasian</td>
<td>79%</td>
</tr>
<tr>
<td><strong>GI Risk Factors</strong></td>
<td></td>
</tr>
<tr>
<td>≥65 years</td>
<td>18%</td>
</tr>
<tr>
<td>Use of low-dose aspirin</td>
<td>15%</td>
</tr>
<tr>
<td>Positive upper GI ulcer history</td>
<td>6%</td>
</tr>
</tbody>
</table>

* The clinical trials primarily enrolled patients <65 years of age without prior history of GI ulcers.

---

1. DUEXIS ([ibuprofen and famotidine] [package insert]. Pharmaceutics International, Inc; 2012. Please see Important Safety Information in appendix.)
DUEXIS significantly reduced the risk of developing ibuprofen-induced upper GI ulcers by ~50% in two 24-week pivotal trials.

- Patients without an endoscopic evaluation within 14 days of their last dose were not counted as having an ulcer.

* This analysis excludes patients who dropped out of the study prior to the first endoscopy (at 8 weeks).
† In REDUCE-1 (Study 303†), the secondary endpoint was incidence of upper GI ulcers.
‡ In REDUCE-2 (Study 301‡), the primary endpoint was incidence of upper GI ulcers.
§ See Prescribing Information for alternative statistical analyses relating to such patients.

Please see Important Safety Information in appendix.
In controlled clinical trials, DUEXIS was associated with ~40% ($P=0.0086$) fewer adverse event reports of dyspepsia vs. ibuprofen alone.

Although reported incidences of dyspepsia were 5% (DUEXIS) and 8% (ibuprofen), the discontinuation rate due to adverse events was similar for both groups.

The adverse events observed for DUEXIS are consistent with the known safety profiles of ibuprofen and famotidine.


Please see Important Safety Information in appendix.
## Adverse Events

**The Most Common Adverse Reactions in ≥2% of Patients in Clinical Trials**

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>DUEXIS (Ibuprofen and famotidine) (n=1022) %</th>
<th>Ibuprofen (n=511) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Constipation</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Upper abdominal pain</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Headache</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Gastroesophageal reflux disease</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>DUEXIS (Ibuprofen and famotidine) (n=1022) %</th>
<th>Ibuprofen (n=511) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomach discomfort</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Edema peripheral</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Influenza</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Cough</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Anemia</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Back pain</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Pharyngolaryngeal pain</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

   Please see Important Safety Information in appendix.
VIMOVO®
(naproxen/esomeprazole)
Clinical Development Program

Please see Important Safety Information in appendix.
VIMOVO Overview

- First and only, 2-in-1 tablet to combine an NSAID with a PPI
- BID dosing provides up to 1000 mg naproxen and 40 mg esomeprazole daily

A Smart Choice
375 mg or 500 mg NAPROXEN
VIMOVO inner core

Due to Gastroprotection
20 mg ESOMEPRAZOLE
MAGNESIUM VIMOVO outer layer

Please see Important Safety Information in appendix.
VIMOVO

Indications and Usage

VIMOVO is indicated for

- The relief of signs and symptoms of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis and to decrease the risk of developing gastric ulcers in patients at risk of developing NSAID-associated gastric ulcers

- VIMOVO is not recommended for initial treatment of acute pain because the absorption of naproxen is delayed compared to absorption from other naproxen-containing products. Controlled studies do not extend beyond 6 months

Please see Important Safety Information in appendix.
VIMOVO Phase 3 Study Design

Two randomized, double-blind, parallel-group, controlled, multicenter studies included *H. pylori*-negative patients

- With OA, RA, or any other condition requiring chronic NSAIDs
- Without GU or DU (≥3 mm diameter with depth) at baseline
- Aged ≥50 years or 18-49 years with a history of GU or DU within the past 5 years

Please see Important Safety Information in appendix.

OA, osteoarthritis; RA, rheumatoid arthritis; GU, gastric ulcer; DU, duodenal ulcer
## Patient Demographics and Baseline Clinical Features

<table>
<thead>
<tr>
<th></th>
<th>Study 301</th>
<th></th>
<th>Study 302</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>VIMOVO</td>
<td>EC naproxen</td>
<td>VIMOVO</td>
<td>EC naproxen</td>
</tr>
<tr>
<td></td>
<td>(n=218)</td>
<td>(n=216)</td>
<td>(n=210)</td>
<td>(n=210)</td>
</tr>
<tr>
<td><strong>Age (years), mean (range)</strong></td>
<td>60.8 (30-90)</td>
<td>61.9 (43-90)</td>
<td>59.6 (27-85)</td>
<td>59.4 (29-82)</td>
</tr>
<tr>
<td><strong>LDA use at randomization, n (%)</strong></td>
<td>53 (24.3)</td>
<td>51 (23.6)</td>
<td>46 (21.9)</td>
<td>51 (24.3)</td>
</tr>
<tr>
<td><strong>Indication for NSAID use</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>172 (78.9)</td>
<td>186 (86.1)</td>
<td>173 (82.4)</td>
<td>166 (79.0)</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>22 (10.1)</td>
<td>8 (3.7)</td>
<td>11 (5.2)</td>
<td>9 (4.3)</td>
</tr>
<tr>
<td>Other</td>
<td>53 (24.3)</td>
<td>38 (17.6)</td>
<td>48 (22.9)</td>
<td>59 (28.1)</td>
</tr>
<tr>
<td><strong>Sex, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>150 (68.8)</td>
<td>149 (69.0)</td>
<td>132 (62.9)</td>
<td>142 (67.6)</td>
</tr>
<tr>
<td><strong>Race, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>184 (84.4)</td>
<td>181 (83.8)</td>
<td>183 (87.1)</td>
<td>190 (90.5)</td>
</tr>
</tbody>
</table>

Please see Important Safety Information in appendix.

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Please see Important Safety Information in appendix.

**VIMOVO**

Study 301 (n=218)
Study 302 (n=212)

**EC naproxen**

Study 301 (n=220)
Study 302 (n=211)

**ITT population**

Study 301 (n=218)
Study 302 (n=210)

Study 301 premature discontinuations (n=38)
- AE (n=14)
- Withdrew consent (n=13)
- Lost to follow up (n=5)
- DU (n=1)
- Other (n=5)

Study 302 premature discontinuations (n=61)
- AE (n=20)
- Withdrew consent (n=24)
- Lost to follow up (n=6)
- DU (n=2)
- Other (n=9)

Completed study
Study 301 (n=180)
Study 302 (n=151)

Study 301 premature discontinuations (n=67)
- AE (n=24)
- Withdrew consent (n=25)
- Lost to follow up (n=2)
- DU (n=10)
- Other (n=6)

Completed study
Study 301 (n=153)
Study 302 (n=153)

Study 302 premature discontinuations (n=58)
- AE (n=30)
- Withdrew consent (n=8)
- Lost to follow up (n=7)
- DU (n=8)
- Other (n=5)

**ITT, intent-to-treat population (received ≥1 dose of study drug and had no ulcer at screening)**
VIMOVO\textsuperscript{1} Showed a Significant Reduction in Gastric Ulcers

Cumulative observed incidence of Gastric Ulcers

**Study 301**

**Study 302**

\*\(P<0.001\) EC Naproxen vs. VIMOVO

\textsuperscript{1} VIMOVO (naproxen/esomeprazole magnesium) [package insert]. Horizon Pharma USA, Inc; December 2014.

Please see Important Safety Information in appendix.
VIMOVO Was Well Tolerated

- 4% of patients taking VIMOVO discontinued treatment\(^1\)
- 12% of patients taking EC naproxen discontinued treatment\(^1\)

67% LESS DISCONTINUATION DUE TO ANY UPPER GI ADVERSE EVENT, INCLUDING DUODENAL ULCERS

---

\(^1\) VIMOVO (naproxen/esomeprazole magnesium) [package insert]. Horizon Pharma USA, Inc; December 2014.

Please see Important Safety Information in appendix.
Most Common Treatment Emergent Adverse Events

<table>
<thead>
<tr>
<th>AE, n (%)</th>
<th>Study 301 PN 400 (n = 216)</th>
<th>Study 301 EC naproxen (n = 216)</th>
<th>Study 302 PN 400 (n = 210)</th>
<th>Study 302 EC naproxen (n = 210)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erosive gastritis</td>
<td>45 (20.6)</td>
<td>81 (37.5)</td>
<td>38 (18.1)</td>
<td>81 (38.6)</td>
</tr>
<tr>
<td>Gastritis</td>
<td>39 (17.9)</td>
<td>28 (13.0)</td>
<td>34 (16.2)</td>
<td>32 (15.2)</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>36 (16.5)</td>
<td>65 (30.1)</td>
<td>41 (19.5)</td>
<td>49 (23.3)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>14 (6.4)</td>
<td>13 (6.0)</td>
<td>12 (5.7)</td>
<td>9 (4.3)</td>
</tr>
<tr>
<td>Abdominal distension</td>
<td>11 (5.0)</td>
<td>10 (4.6)</td>
<td>5 (2.4)</td>
<td>6 (2.9)</td>
</tr>
<tr>
<td>Upper abdominal pain</td>
<td>9 (4.1)</td>
<td>18 (8.3)</td>
<td>15 (7.1)</td>
<td>19 (9.0)</td>
</tr>
<tr>
<td>Nausea</td>
<td>9 (4.1)</td>
<td>11 (5.1)</td>
<td>13 (6.2)</td>
<td>10 (4.8)</td>
</tr>
<tr>
<td>Hiatus hernia</td>
<td>8 (3.7)</td>
<td>14 (6.5)</td>
<td>10 (4.8)</td>
<td>11 (5.2)</td>
</tr>
<tr>
<td>Oesophagitis</td>
<td>7 (3.2)</td>
<td>17 (7.9)</td>
<td>8 (3.8)</td>
<td>15 (7.1)</td>
</tr>
<tr>
<td>Duodenitis</td>
<td>4 (1.8)</td>
<td>19 (8.8)</td>
<td>2 (1.0)</td>
<td>12 (5.7)</td>
</tr>
<tr>
<td>Erosive duodenitis</td>
<td>4 (1.8)</td>
<td>30 (13.9)</td>
<td>5 (2.4)</td>
<td>20 (9.5)</td>
</tr>
<tr>
<td>Erosive oesophagitis</td>
<td>0 (0.0)</td>
<td>12 (5.6)</td>
<td>2 (1.0)</td>
<td>12 (5.7)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>5 (2.3)</td>
<td>8 (3.7)</td>
<td>16 (7.6)</td>
<td>8 (3.8)</td>
</tr>
</tbody>
</table>

AE, adverse event; EC, enteric-coated.

1 VIMOVO (naproxen/esomeprazole magnesium) [package insert]. Horizon Pharma USA, Inc; December 2014.

Please see Important Safety Information in appendix.
U.S. Reimbursement Environment

Terry Evans
Senior Vice President and General Manager,
Managed Care and Trade

Horizon Pharma
Doing the Right Thing for Patients

- What you have heard today
  - The success of Horizon’s business model
  - The clinical differentiation of Horizon’s medicines
- The patient’s journey in the drug distribution channel is increasingly complex
- Multiple interested parties intervening between the doctors prescribing and the patients receiving the prescribed medicine
Ensure Patients with Commercial Insurance Receive the Medicine their Doctor Prescribed

- **Challenge**
  - Overcome payer/PBM attempts to prevent patients from receiving the medicine their doctor prescribed based on its clinical benefits

- **Our Mission**
  - Patients receive the medicine their doctor prescribed at the lowest out-of-pocket cost possible

- **Our Strategy**
  - Support doctor prescribing through education of the clinical benefits of our medicines
  - Remove the barriers put in place by payers, PBMs and pharmacies to access our medicines
  - Ensure patient receives medicine at the lowest out-of-pocket cost possible
  - Utilize open distribution through wholesalers to pharmacies
Preferred Patient Journey to Access

Access Strategy

- Support doctors prescribing through education of the clinical benefits of our medicines
- Ensure patient receives medicine at the lowest out-of-pocket cost possible
- Utilize open distribution through wholesalers to pharmacies
Five Stakeholders in Every Commercial Prescription...
...but their interests are not always aligned

<table>
<thead>
<tr>
<th>Patient</th>
<th>Doctor</th>
<th>Horizon</th>
<th>Payer/ PBM</th>
<th>Pharmacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Receive medicine doctor Rx’d</td>
<td>• Patient receives medicine doctor Rx’d</td>
<td>• Patient receives medicine doctor Rx’d</td>
<td>• Patient to receive a medicine approved by PBM</td>
<td>• Patient Rx filled quickly and efficiently</td>
</tr>
<tr>
<td>• Avoid hassle or wait at the pharmacy</td>
<td>• Avoid hassle by the pharmacy</td>
<td>• Doctor not hassled by pharmacy</td>
<td>• Receive largest rebate from Horizon</td>
<td>• Maximize return per visit</td>
</tr>
<tr>
<td>• Pay lowest copay</td>
<td>• Patient to pay lowest copay</td>
<td>• Patient to pay lowest copay</td>
<td>• Reimburse pharmacy based on their choice of formulary medicine</td>
<td></td>
</tr>
</tbody>
</table>
Horizon Pharma takes action when patients with commercial insurance are prevented from receiving the medicine prescribed by their doctor

- Ensure affordable copays and patient access to the medicine the doctor prescribed
- Align interest of doctor and patient to ensure adherence and improve outcomes
How Payers/PBMs Control Access

• **Exclusion**
  
  – Exclude certain medicines from formularies based on costs to PBM rather than clinical benefits and value to patient
  
  – Remove medicines from formulary, which limits the doctor’s choice of medicine

• **Medication Therapy Management**
  
  – Step Edits
  
  – Prior Authorization
  
  – Quantity Limits
  
  – Therapeutic Interchange
Cost of Medicines is the Smallest Component of the U.S. Healthcare Spend...

However, medicines costs are a convenient target

Robust pharmacy management systems make medicine spend easier to control and therefore a target for criticism


(1) Other includes government administration, net cost of private health insurance, government public health activities, investment.

Non Confidential Information – Horizon Pharma plc
While Avoidable Healthcare Costs Should be the Focus

Non-adherence to medicine by patients is the largest potentially avoidable cost in the healthcare system.

Source: Avoidable Costs in U.S. Healthcare Study by IMS Institute of HealthCare Informatics, 2012
(1) Other levers include delayed evidence-based treatment, antibiotic misuse.
Patient Support Programs

HorizonCares Overview

Steve Curtis
Vice President and General Manager

Horizon Pharma
Genesis of Horizon Patient Support Programs

Patients Often Do Not Receive the Medicines their Doctor Prescribes

Create barriers to patient care

Often the medicine the doctor prescribed was not being received by the patient

Source: Horizon internal market research and analysis post DUEXIS launch

Non-Confidential Information – Horizon Pharma plc
Patients Receive Horizon’s Clinically Differentiated Medicines with Minimal Out-of-Pocket Costs

**Primary Care & Specialty**

- Copay Assistance
- Minimal Patient Copays for Rejected Rx’s

**Orphan**

- Reimbursement Support
- Clinical Nurse Program
- Patient Assistance
- Copay Assistance

---

[1] Available to commercial patients only

Non-Confidential Information – Horizon Pharma plc
HorizonCares Patient Support Pathways

Traditional Pharmacies

Doctor → Rx → Pharmacy → Claim → Payer/PBM → Approved/Denials

Participating Pharmacies

Doctor → Rx → Pharmacy → Claim → Payer/PBM → Approved/Denials

HUB

Doctor → Rx → HUB → Denials

Primary Care & Specialty

Orphan

Note: Illustrative purposes only

Non-Confidential Information – Horizon Pharma plc
Medicine Flow to Patients

Open Distribution Model
- Horizon contracts with a broad number of wholesalers to deliver medicine to pharmacies
- Ensures medicine availability at pharmacies
- Enables continuity of care for patients

PBM Controls Cost of Rx
- Electronic claim is passed through PBM system for copay of patient
- Formulary position of medicine dictates copay
- HorizonCares assists commercially insured patients to receive an affordable copay or free medicine
## Relationship with Pharmacies

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of pharmacies in which Horizon has ownership or option for ownership</td>
<td>0</td>
</tr>
<tr>
<td>Number of pharmacies that are exclusive to Horizon</td>
<td>0</td>
</tr>
<tr>
<td>Number of pharmacies that have ever purchased Horizon medicines on consignment</td>
<td>0</td>
</tr>
</tbody>
</table>
## Evolution of Horizon Patient Access Programs

<table>
<thead>
<tr>
<th>Year</th>
<th>Pilot</th>
<th>Expand</th>
<th>Optimize</th>
<th>Execute</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013</td>
<td>Initiated PME access program with two pharmacies</td>
<td>Launched in all Primary Care and Specialty territories</td>
<td>Improved rep training</td>
<td>HorizonCares established to expand patient access</td>
</tr>
<tr>
<td></td>
<td>Expanded to ~75 territories and additional pharmacies in the 2nd half of 2014</td>
<td>Established the support team</td>
<td>Improved doctor targeting</td>
<td>Increase the number of participating pharmacies</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Added additional participating pharmacies</td>
<td>Assess and implement alternative routes of ensuring patient access</td>
</tr>
</tbody>
</table>
Business Development Strategy

Robert F. Carey
Executive Vice President, Chief Business Officer
Successful Acquisition Track Record

<table>
<thead>
<tr>
<th>Product</th>
<th>Acquired From</th>
<th>Acquisition Date</th>
<th>Enterprise Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAYOS®</td>
<td>Vidara Therapeutics</td>
<td>May 2015</td>
<td>$958M</td>
</tr>
<tr>
<td>Vimovo®</td>
<td>AstraZeneca</td>
<td>November 2013</td>
<td>$35M</td>
</tr>
<tr>
<td>ACTIMMUNE®</td>
<td>Nuvo Research</td>
<td>October 2014</td>
<td>$45M</td>
</tr>
<tr>
<td>Pennsaid®</td>
<td>Hyperion Therapeutics</td>
<td>May 2015</td>
<td>$958M</td>
</tr>
<tr>
<td>Buphenyl®</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: Dollar figures represent enterprise or asset values and do not include fees and other expenses associated with the respective acquisition.

1. RAYOS is known as LODOTRA outside the United States.
2. Medicine was re-launched by Horizon sales force in January 2015.
3. Buphenyl is known as AMMONAPHS outside the United States.
4. Fair value of consideration paid less cash and cash equivalents, short-term investments, and long-term investments.

Non-Confidential Information – Horizon Pharma plc
~$2.1B in Value Created Through Organic Growth and Acquisitions

Acquired $1.6B in assets from 11/6/2013 to 11/6/2015

EV 11/6/2013(1)  VIMOVO  Vidara  PENNSAID 2%  Hyperion  Value Created  EV 11/6/2015(1)

$2,086  $958  $45  $567  $35  $2,086  $3,934

DUEXIS & RAYOS  $1,605 Value Acquired

(1) Approximate implied enterprise value based on November 6th closing share price and September 30th basic shares outstanding for respective years.

Non-Confidential Information – Horizon Pharma plc
Business Development Strategy has Contributed to Net Sales Increasing Tenfold over the Past Two Years

- Based on current guidance, net sales will increase tenfold from 2013 to 2015
  - Addition of five medicines and accelerated organic growth
- Significant revenue diversification
  - No single medicine expected to be more than 23% of total net revenues
  - DUEXIS was ~81% of net revenues in 2013 and will be ~23% in 2015

[1] Horizon estimate based on 2015 run rate net revenues (Q3 2015 annualized for RAVCITI / BUPHENYL, YTD Q3 2015 annualized for all other medicines)
Significant Value Created through Acquisitions

- **Diversification of net sales**
  - Expected that no single medicine contributes more than 23% of total 2015 net sales\(^{(1)}\)

- **Enhanced growth rate in net sales and adjusted EBITDA**
  - 165% and 360%, respectively, YTD Q3 2015 over YTD Q3 2014

- **Enhanced operating margins**
  - Adjusted EBITDA margin from 27% YTD Q3 2014 to 47% YTD Q3 2015

- **Substantially increased commercial and financial scale**
  - Approaching ~$1 billion in net sales in 2016\(^{(2)}\)

- **Lowered cost of and improved access to capital**
  - Raised ~$1.75 billion in 2015
  - Average borrowing rate is 4.7%

---

\(^{(1)}\) Based on 2015 run rate net sales (Q3 2015 annualized for RAVICTI / BUPHENYL, YTD Q3 2015 annualized for all other medicines)

\(^{(2)}\) Horizon issued financial guidance, including net revenues of $950 - $975 for 2016
### Business Development Focus

<table>
<thead>
<tr>
<th>BD Criteria</th>
<th>Prior Focus</th>
<th>Today’s Focus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimum Net Sales</td>
<td>$20M</td>
<td>$20M</td>
</tr>
<tr>
<td>Product Profile</td>
<td>Clinically differentiated</td>
<td>Clinically differentiated</td>
</tr>
<tr>
<td>Other Financial Metrics</td>
<td>Immediate accretion, positive NPV</td>
<td>Immediate accretion, positive NPV(1)</td>
</tr>
<tr>
<td>IP Life</td>
<td>Long-life focus</td>
<td>Increased focus on extending avg. LOE</td>
</tr>
<tr>
<td>Business Unit Priority</td>
<td>Agnostic</td>
<td>1. Orphan, 2. Specialty, 3. PC</td>
</tr>
<tr>
<td>Geography</td>
<td>U.S. only</td>
<td>WW for Orphan</td>
</tr>
<tr>
<td>Stage of Development</td>
<td>Marketed only</td>
<td>Late-stage dev. + marketed</td>
</tr>
</tbody>
</table>

Business model execution enables an expansion and evolution in BD focus and priorities

---

Development stage orphan opportunities may not be immediately accretive
Long Range Plan Plus Possible Acquisitions

~20% Annual Organic Growth Plus Acquire ~25% of Prior Year’s Net Sales

Annual Net Sales
($ in millions)

- Acquisition Net Sales
- Organic Net Sales

<table>
<thead>
<tr>
<th>Year</th>
<th>Acquisition Net Sales</th>
<th>Organic Net Sales</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>$750 - $760 (1)</td>
<td></td>
</tr>
<tr>
<td>2016</td>
<td>$950 - $975 (2)</td>
<td></td>
</tr>
<tr>
<td>2017</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2018</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2019</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2020</td>
<td>$2,000 (3)</td>
<td></td>
</tr>
</tbody>
</table>

Note: Unlabeled bars are illustrative only.

(1) Estimate based on financial guidance issued November 6, 2015
(2) Estimate based on financial guidance issued November 9, 2015
(3) Horizon internal goals based on long-range plan presented November 9, 2015
Current Enterprise Value Doesn’t Reflect Sum-of-the-Parts

11/6/2015 Enterprise Value

Fixed Orphan Multiple at Median of 8.0x Net Sales

$1,889 3.8x 48%
$2,046 8.0x 52%

Implied 31% Discount to Comparable Company Multiples

Fixed Primary Care / Specialty Multiple at Median of 5.5x Net Sales

$1,204 4.7x 31%
$2,730 5.5x 69%

Implied 59% Discount to Comparable Company Multiples

~18%, or ~$800M, Discount to the EV Based on Median Multiples for Each of Orphan and Primary Care / Specialty

$2,046
8.0x
43%

$2,730
5.5x
57%

(1) Based on $3.9 billion enterprise value as of November 6, 2015 and median EV / Net Revenue trading multiples

Non-Confidential Information – Horizon Pharma plc
Future Value Primarily Driven by Orphan Growth\(^{(1)}\)

Potential 2020 Enterprise Value Allocation

- Orphan: \(~5.5\times\) ~33%
- Primary Care / Specialty: \(~8.0\times\) ~67%

\(^{(1)}\) Based on Horizon internal goals from the long-range plan presented November 9, 2015 and comparable company market multiples.
Financial Review

Paul W. Hoelscher
Executive Vice President, Chief Financial Officer

Horizon Pharma
**Third Quarter Net Sales**

**Strong Y-o-Y and sequential growth from Q2 2015**

- Net sales up 202% compared to Q3 2014 and 31% sequential vs Q2 2015
- Strong sales growth across all three business units

<table>
<thead>
<tr>
<th></th>
<th>Q3 2015</th>
<th>Q3 2014</th>
<th>Y-o-Y % Change</th>
<th>Q2 2015</th>
<th>Q-o-Q % Change</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Care</strong></td>
<td>$147,649</td>
<td>$65,959</td>
<td>124</td>
<td>$113,441</td>
<td>30</td>
</tr>
<tr>
<td>DUEXIS*</td>
<td>56,902</td>
<td>22,753</td>
<td>150</td>
<td>44,205</td>
<td>29</td>
</tr>
<tr>
<td>VIMOVO*</td>
<td>46,855</td>
<td>43,206</td>
<td>8</td>
<td>39,805</td>
<td>18</td>
</tr>
<tr>
<td>PENNSAID* 2% (1)</td>
<td>43,892</td>
<td>0</td>
<td>NM</td>
<td>29,431</td>
<td>49</td>
</tr>
<tr>
<td><strong>Orphan</strong></td>
<td>66,126</td>
<td>2,707</td>
<td>2,343</td>
<td>48,688</td>
<td>36</td>
</tr>
<tr>
<td>ACTIMMUNE* (2)</td>
<td>28,737</td>
<td>2,707</td>
<td>962</td>
<td>25,835</td>
<td>11</td>
</tr>
<tr>
<td>RAVICTI* (3)</td>
<td>33,427</td>
<td>0</td>
<td>NM</td>
<td>18,993</td>
<td>76</td>
</tr>
<tr>
<td>BUPHENYL* (3)</td>
<td>3,962</td>
<td>0</td>
<td>NM</td>
<td>3,860</td>
<td>3</td>
</tr>
<tr>
<td><strong>Specialty</strong></td>
<td>12,769</td>
<td>6,460</td>
<td>98</td>
<td>10,692</td>
<td>19</td>
</tr>
<tr>
<td>RAYOS*</td>
<td>11,670</td>
<td>5,652</td>
<td>106</td>
<td>10,316</td>
<td>13</td>
</tr>
<tr>
<td>LODOTRA*</td>
<td>1,099</td>
<td>808</td>
<td>36</td>
<td>376</td>
<td>192</td>
</tr>
<tr>
<td><strong>Total net sales</strong></td>
<td>$226,544</td>
<td>$75,126</td>
<td>202</td>
<td>$172,821</td>
<td>31</td>
</tr>
</tbody>
</table>

(1) PENNSAID 2% was acquired on October 17, 2014
(2) ACTIMMUNE was acquired on September 19, 2014.
(3) RAVICTI and BUPHENYL were acquired on May 7, 2015.
# Third Quarter 2015 Overview

- Adjusted EBITDA was $131M for Q3 2015; LTM adjusted EBITDA was at $274M
- Non-GAAP diluted EPS was 70 cents up 268% compared to Q3 2014
- Non-GAAP operating cash flow of $101M up 183% compared to Q3 2014

<table>
<thead>
<tr>
<th>($ in millions except share and per share amounts)</th>
<th>Q3 2015</th>
<th>Q3 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>U.S. GAAP</td>
<td>Adjustments</td>
</tr>
<tr>
<td>Net sales</td>
<td>$226.5</td>
<td>-</td>
</tr>
<tr>
<td>Adjusted EBITDA</td>
<td>99.0</td>
<td>32.1</td>
</tr>
<tr>
<td>Net income</td>
<td>3.3</td>
<td>113.7</td>
</tr>
<tr>
<td>Basic EPS</td>
<td>$0.23</td>
<td>$0.72</td>
</tr>
<tr>
<td>Diluted EPS</td>
<td>$0.23</td>
<td>$0.68</td>
</tr>
<tr>
<td>Operating Cash Flow</td>
<td>$88.4</td>
<td>$12.4</td>
</tr>
</tbody>
</table>

(1) EBITDA is a non-GAAP measure

See Non-GAAP reconciliations in the appendix.
Exceptional Net Sales Growth

*Net Sales CAGR of 125%*

<table>
<thead>
<tr>
<th>Quarter</th>
<th>Net Sales</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1 2013</td>
<td>$59</td>
</tr>
<tr>
<td>Q2 2013</td>
<td>$11</td>
</tr>
<tr>
<td>Q3 2013</td>
<td>$24</td>
</tr>
<tr>
<td>Q4 2013</td>
<td>$30</td>
</tr>
<tr>
<td>Q1 2014</td>
<td>$52</td>
</tr>
<tr>
<td>Q2 2014</td>
<td>$66</td>
</tr>
<tr>
<td>Q3 2014</td>
<td>$75</td>
</tr>
<tr>
<td>Q4 2014</td>
<td>$104</td>
</tr>
<tr>
<td>Q1 2015</td>
<td>$113</td>
</tr>
<tr>
<td>Q2 2015</td>
<td>$173</td>
</tr>
<tr>
<td>Q3 2015</td>
<td>$227</td>
</tr>
</tbody>
</table>

*Strong quarterly net sales growth and diversification over the last 11 quarters*
Increasing Diversification of Net Sales
Q3 2015 Net Sales of $226.5 million

Q3 2014
Q3 2015

57%

30%

9%

4%

21%

5%

15%

2%

19%

25%

13%

5%

57%

30%

9%

4%

21%

5%

15%

2%

19%

25%

13%

5%

ACTIMMUNE
DUEXIS
PENNSAID 2%
BUPHENYL
RAVICITI
RAYOS / LODOTRA
VIMOVO

Significant diversification of net sales over past year with no single medicine greater than 25% in Q3 2015
Transformational Growth in Net Sales and EBITDA in 2015

*Increased full-year 2015 guidance on November 5, 2015*

- Increased sales guidance to $750 - $760M from $660 - $680M
- Increased adjusted EBITDA guidance to $350 - $360M (47% margin) from $265 - $280M (41% margin)

Note: Excludes any future business development activities

(1) Estimate based on financial guidance issued November 6, 2015

---

Net Sales Adjusted EBITDA

2012 2013 2014 2015(1)

- $19 $(73)
- $74 $(28)
- $297 $87
- $750 - $760 $350 - $360

Note: Excludes any future business development activities

(1) Estimate based on financial guidance issued November 6, 2015
Fiscal Year 2016 Guidance

*Significant Growth with Additional Margin Expansion Expected in 2016*

- **Sales guidance of $950 - $975M (increase of 28% at midpoint)**
- **Adjusted EBITDA guidance of $460 - $475M (margin of 49% at midpoint)**

Note: Excludes any future business development activities

(1) Estimate based on financial guidance issued November 6, 2015
(2) Estimate based on financial guidance issued November 9, 2015

Non-Confidential Information – Horizon Pharma plc
2020 Long Range Plan

Business Doubles Over Next Five Years with Orphan Becoming Majority

- Sales potential could exceed $2.0 billion(1)
- Adjusted EBITDA margin expected to reach ~60% by 2020(2)

($ in millions)

<table>
<thead>
<tr>
<th>Year</th>
<th>Net Sales</th>
<th>Adjusted EBITDA</th>
<th>Adjusted EBITDA %</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>$297</td>
<td>$87</td>
<td>28%</td>
</tr>
<tr>
<td>2015(1)</td>
<td>$750 - $760</td>
<td>47%</td>
<td></td>
</tr>
<tr>
<td>2016(2)</td>
<td>$950 - $975</td>
<td>~49%</td>
<td></td>
</tr>
<tr>
<td>2020(3)</td>
<td>$2,000+</td>
<td>~60%</td>
<td></td>
</tr>
</tbody>
</table>

Note: Excludes any future business development activities
(1) Estimate based on financial guidance issued November 6, 2015
(2) Estimate based on financial guidance issued November 9, 2015
(3) Horizon internal goals based on long range plan presented November 9, 2015, does not include ACTIMMUNE in certain cancers

Non-Confidential Information – Horizon Pharma plc
Adjusted EBITDA Margins Expected to Expand as Orphan Becomes Majority of Business

• Potential $2B+ business from existing portfolio of medicines
  – Assumes sales from potential approval of ACTIMMUNE for FA
  – Does not include $300 - $500M of potential sales for ACTIMMUNE in various cancer treatments if approved in cancer indications
  – Does not include any acquisition net sales

• Adjusted EBITDA margin expected to expand to ~60% driven by decreases in:
  – Sales and marketing as a percent of sales, assuming the Orphan business unit becomes a majority of the business
  – G&A as a percent of sales, as the G&A infrastructure that we are currently building is leveraged

Note: Use of ACTIMMUNE in Friedreich’s ataxia (FA) is investigational only, and safety and efficacy has not been established for use in Friedreich’s ataxia (FA). For further information see www.ACTIMMUNE.com.

Note: Use of ACTIMMUNE with PD-1 and PD-L1 inhibitors is investigational only, and safety and efficacy has not been established for use with any PD-1 and PD-L1 inhibitor. For further information see www.ACTIMMUNE.com.
Diversify Mix of Orphan and Primary Care/Specialty

- Continue transformation to a predominantly orphan business by 2020
- Complement orphan business with strong primary care / specialty business units providing significant cash flows to invest

**Net Sales Mix**

<table>
<thead>
<tr>
<th></th>
<th>1 Year Ago (Q3 2014)</th>
<th>Today (Q3 2015)</th>
<th>Future (2020 LRP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orphan</td>
<td>4%</td>
<td>29%</td>
<td>40%</td>
</tr>
<tr>
<td>Primary Care / Specialty</td>
<td>96%</td>
<td>71%</td>
<td>60%</td>
</tr>
</tbody>
</table>

Non-Confidential Information – Horizon Pharma plc
## Strong Financial Position

### September 30, 2015

<table>
<thead>
<tr>
<th>(in millions)</th>
<th>September 30, 2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash and cash equivalents</td>
<td>$684</td>
</tr>
<tr>
<td>Senior secured term loans - Due 2021</td>
<td>399</td>
</tr>
<tr>
<td>2.5% exchangeable senior notes - Due 2022</td>
<td>400</td>
</tr>
<tr>
<td>Senior notes - Due 2023</td>
<td>475</td>
</tr>
<tr>
<td>Total Debt (Face Amount)</td>
<td>$1,274</td>
</tr>
<tr>
<td>Less debt discount</td>
<td>(133)</td>
</tr>
<tr>
<td>Total Debt (Book Value)</td>
<td>$1,141</td>
</tr>
<tr>
<td>Shares outstanding</td>
<td>159,267,370</td>
</tr>
</tbody>
</table>

*Strong capital structure with net debt of $590M at September 30, 2015*
## Strong Cash Flows Improving Leverage Position

*Significant Acquisition Funding from Existing Cash and Borrowing Capacity*(1)

<table>
<thead>
<tr>
<th>($ in millions)</th>
<th>LTM</th>
<th>2015</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Leverage Position:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted EBITDA</td>
<td>$274</td>
<td>$350 - $360</td>
<td>$460 - $475</td>
</tr>
<tr>
<td>Leverage ratio based on 9/30/15 debt and cash balances:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL DEBT</strong></td>
<td>4.6x</td>
<td>3.6x</td>
<td>2.7x</td>
</tr>
<tr>
<td><strong>NET DEBT</strong></td>
<td>2.1x</td>
<td>1.7x</td>
<td>1.3x</td>
</tr>
<tr>
<td><strong>Acquisition Funding Available</strong>(2):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Senior secured debt maximum at 3.5x EBITDA(3)</td>
<td>$959</td>
<td>$1,242</td>
<td>$1,636</td>
</tr>
<tr>
<td>Current senior secured debt</td>
<td>(399)</td>
<td>(399)</td>
<td>(399)</td>
</tr>
<tr>
<td>Incremental senior secured debt available</td>
<td>$560</td>
<td>$843</td>
<td>$1,237</td>
</tr>
<tr>
<td>Total debt at 5.75x EBITDA(3)</td>
<td>$1,576</td>
<td>$2,041</td>
<td>$2,688</td>
</tr>
<tr>
<td>Current total debt</td>
<td>(1,274)</td>
<td>(1,274)</td>
<td>(1,274)</td>
</tr>
<tr>
<td>Incremental total debt available</td>
<td>$302</td>
<td>$767</td>
<td>$1,414</td>
</tr>
<tr>
<td>Current cash and cash equivalents</td>
<td>684</td>
<td>684</td>
<td>684</td>
</tr>
<tr>
<td>Total potential stand-alone acquisition funding available</td>
<td>$986</td>
<td>$1,451</td>
<td>$2,098</td>
</tr>
</tbody>
</table>

---

1. Subject to Horizon’s ability to meet various covenants, as well as market conditions.
2. Does not include any post Q3 2015 cash flow generation or the EBITDA from any acquired medicines or businesses.
3. 3.5x senior secured and 5.75x total are covenants in our current debt agreement.
Timothy P. Walbert
Chairman, President and Chief Executive Officer

HORIZON PHARMA
Today’s Focus

• Issuing first-time 2016 net sales and adjusted EBITDA guidance

• Company’s long-range plan estimates $2B+ in net sales in 2020\(^1\)
  – Orphan business and development pipeline with net sales potential of ~$1 - $1.5B+ in 2020, not including potential for ACTIMMUNE in cancer
  – Differentiated and clinically important Primary Care and Specialty medicines combined with innovative patient support should lead to ~$800M - $1B in net sales in 2020

• HorizonCares – Patients receive the medicines their doctors prescribe

• Diversified growth strategy with expected 20%+ annual organic growth complemented with disciplined incremental business development

• Strong balance sheet and cash flows enable significant incremental financing capacity

Note: Horizon estimates do not include any incremental business development contribution

\(^1\) Horizon internal goals based on long-range plan presented November 9, 2015, does not include ACTIMMUNE in certain cancers
<table>
<thead>
<tr>
<th>GAAP to Non-GAAP Reconciliation</th>
<th>Net Income</th>
<th></th>
<th>Three Months Ended Sept. 30</th>
<th>Nine Months Ended Sept. 30</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2015</td>
<td>2014</td>
<td>2015</td>
<td>2014</td>
</tr>
<tr>
<td>Adjusted Non-GAAP Net Income:</td>
<td></td>
<td></td>
<td>(Unaudited)</td>
<td>(Unaudited)</td>
</tr>
<tr>
<td>Net Income (Loss) GAAP Adjustments:</td>
<td></td>
<td></td>
<td>$3,277</td>
<td>$2,063</td>
</tr>
<tr>
<td>- Revaluation of intangibles for products acquired through business combinations</td>
<td>-</td>
<td>-</td>
<td>$26,877</td>
<td>$20,081</td>
</tr>
<tr>
<td>- Acquisition-related costs</td>
<td>14,498</td>
<td>15,477</td>
<td>64,981</td>
<td>49,061</td>
</tr>
<tr>
<td>- Loss on debt extinguishment</td>
<td>-</td>
<td>-</td>
<td>7,824</td>
<td>3,695</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>(13,171)</td>
<td>-</td>
<td>(23,173)</td>
</tr>
<tr>
<td></td>
<td>Amortization and accretion</td>
<td>61,307</td>
<td>6,413</td>
<td>91,217</td>
</tr>
<tr>
<td></td>
<td>- Depreciation expense</td>
<td>4,163</td>
<td>4,261</td>
<td>9,302</td>
</tr>
<tr>
<td></td>
<td>- Amortization of inventory step up</td>
<td>4,180</td>
<td>1,349</td>
<td>32,635</td>
</tr>
<tr>
<td></td>
<td>- Share-based compensation</td>
<td>36,459</td>
<td>3,094</td>
<td>67,766</td>
</tr>
<tr>
<td></td>
<td>Disposition gains</td>
<td>1,378</td>
<td>413</td>
<td>2,286</td>
</tr>
<tr>
<td></td>
<td>- Royalties for products acquired through business combinations</td>
<td>8,834</td>
<td>9,336</td>
<td>20,890</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total pre-tax non-GAAP adjustments</td>
<td>91,557</td>
<td>20,415</td>
<td>325,207</td>
</tr>
<tr>
<td>Income tax adjustments</td>
<td>22,178</td>
<td>(3,042)</td>
<td>(137,328)</td>
<td>(3,267)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total non-GAAP adjustments</td>
<td>113,735</td>
<td>17,373</td>
<td>187,879</td>
</tr>
<tr>
<td>Adjusted Non-GAAP Net Income</td>
<td>$117,012</td>
<td>$19,436</td>
<td>$203,417</td>
<td>$46,240</td>
</tr>
</tbody>
</table>

Adjusted Non-GAAP Earnings Per Share:

| Weighted average shares Basic | 159,035,880 | 79,169,901 | 984,198,981 | 75,169,901 |
| Adjusted Non-GAAP earnings Per Share - Basic: | | | | |
| - GAAP earnings (loss) per share - Basic | $0.02 | $0.03 | $0.11 | (3.17) |
| - Non-GAAP adjustments | 0.72 | 0.22 | 1.29 | 3.80 |
| Adjusted Non-GAAP earnings per share - Basic | $0.74 | $0.25 | $1.40 | $0.63 |

| Weighted average shares - Diluted | 166,830,809 | 80,161,367 | 984,198,981 | 75,169,901 |
| Adjusted Non-GAAP Net Income - Diluted | $117,012 | $19,436 | $203,417 | $46,240 |
| Adjusted Non-GAAP earnings Per Share - Diluted: | | | | |
| - GAAP earnings (loss) per share - Diluted | $0.02 | $0.02 | $0.10 | (3.17) |
| - Non-GAAP adjustments | 0.68 | 0.20 | 1.22 | 3.81 |
| Diluted earnings per share effect of ordinary share equivalents | (0.03) | (0.16) | - | - |
| Adjusted Non-GAAP earnings per share - Diluted | $0.70 | $0.19 | $1.32 | $0.48 |

(1) Royalties for products acquired through business combinations relate to VIMOVO, ACTIMMUNE, RAVICTI and BUPHENYL.
(2) Adjustments to convert the income tax benefit/expense to the estimated amount of taxes that are payable in cash.
### GAAP to Non-GAAP Reconciliation

**EBITDA**

<table>
<thead>
<tr>
<th></th>
<th>Three Months Ended Sept. 30</th>
<th>Nine Months Ended Sept. 30</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2015</td>
<td>2014</td>
</tr>
<tr>
<td></td>
<td>(Unaudited)</td>
<td>(Unaudited)</td>
</tr>
<tr>
<td><strong>EBITDA and Adjusted EBITDA:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAAP Net Income (Loss)</td>
<td>$ 3,277</td>
<td>$ 2,063</td>
</tr>
<tr>
<td>Depreciation</td>
<td>1,578</td>
<td>413</td>
</tr>
<tr>
<td>Amortization and accretion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intangible amortization expense</td>
<td>41,527</td>
<td>6,413</td>
</tr>
<tr>
<td>Accretion of royalty liabilities</td>
<td>4,326</td>
<td>2,664</td>
</tr>
<tr>
<td>Amortization of deferred revenue adjustment</td>
<td>(99)</td>
<td>(794)</td>
</tr>
<tr>
<td>Intangible amortization (COGS only)</td>
<td>41,006</td>
<td>3,386</td>
</tr>
<tr>
<td>Interest expense, net (excluding amortization of debt discount and deferred financing costs)</td>
<td>20,300</td>
<td>5,194</td>
</tr>
<tr>
<td>EBITDA</td>
<td>$ 99,042</td>
<td>$ 15,089</td>
</tr>
<tr>
<td>Adjusted EBITDA</td>
<td>$ 131,143</td>
<td>$ 22,053</td>
</tr>
<tr>
<td><strong>Non-GAAP Gross Profit:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAAP net sales</td>
<td>$ 226,544</td>
<td>$ 75,126</td>
</tr>
<tr>
<td>GAAP cost of goods sold</td>
<td>61,250</td>
<td>13,644</td>
</tr>
<tr>
<td>GAAP gross profit</td>
<td>$ 165,294</td>
<td>$ 61,482</td>
</tr>
<tr>
<td>GAAP gross profit %</td>
<td>73.0%</td>
<td>81.8%</td>
</tr>
<tr>
<td><strong>Non-GAAP Gross Profit:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAAP gross profit</td>
<td>$ 165,294</td>
<td>$ 61,482</td>
</tr>
<tr>
<td>Non-GAAP gross profit adjustments</td>
<td>43,408</td>
<td>4,314</td>
</tr>
<tr>
<td>GAAP gross profit</td>
<td>$ 208,702</td>
<td>$ 65,796</td>
</tr>
<tr>
<td>Non-GAAP gross profit %</td>
<td>92.1%</td>
<td>87.6%</td>
</tr>
<tr>
<td><strong>Non-GAAP Cash Provided by Operating Activities:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAAP cash (used in) provided by operating activities</td>
<td>$ 88,383</td>
<td>$ 1,466</td>
</tr>
<tr>
<td>Cash payments of acquisition related costs</td>
<td>12,464</td>
<td>34,142</td>
</tr>
<tr>
<td>Cash payments for induced conversion</td>
<td>45,367</td>
<td></td>
</tr>
<tr>
<td>Non-GAAP cash provided by operating activities</td>
<td>$ 100,847</td>
<td>$ 35,608</td>
</tr>
<tr>
<td>Non-GAAP cash provided by operating activities %</td>
<td>53.0%</td>
<td>41.2%</td>
</tr>
</tbody>
</table>

1. Remeasurement of royalties for products acquired through business combinations relate to VIMOVO, ACTIMMUNE, RAVICTI and BUPHENYL.
### GAAP to Non-GAAP Reconciliation

**EBITDA (Continued)**

<table>
<thead>
<tr>
<th>EBITDA and Adjustments</th>
<th>Three Months Ended December 31</th>
<th>Twelve Months Ended December 31</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(‘000)</td>
<td>(‘000)</td>
</tr>
<tr>
<td><strong>EBITDA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAAP Net Loss</td>
<td>$ (31,647)</td>
<td>$ (10,191)</td>
</tr>
<tr>
<td>Depreciation</td>
<td>390</td>
<td>335</td>
</tr>
<tr>
<td>Amortization and attr.</td>
<td>15,814</td>
<td>3,118</td>
</tr>
<tr>
<td>Intangible asset impair.</td>
<td>318</td>
<td>8,002</td>
</tr>
<tr>
<td>Accrued interest income</td>
<td>318</td>
<td>(917)</td>
</tr>
<tr>
<td>Non-operating income</td>
<td>9,636</td>
<td>11,185</td>
</tr>
<tr>
<td>Issuance expenses, net (including amortization of</td>
<td>18,216</td>
<td>21,308</td>
</tr>
<tr>
<td>debt discount and deferred financing costs</td>
<td>12,813</td>
<td>(3,122)</td>
</tr>
<tr>
<td><strong>EBITDA</strong></td>
<td>$ 6,982 (1)</td>
<td>$ (5,415)</td>
</tr>
</tbody>
</table>

**Non-GAAP Adjustments:**

<table>
<thead>
<tr>
<th>Non-GAAP Adjustments</th>
<th>Three Months Ended December 31</th>
<th>Twelve Months Ended December 31</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(‘000)</td>
<td>(‘000)</td>
</tr>
<tr>
<td>Reinvestment of USGAAP and ACC/DSM/US royalty liabilities</td>
<td>$ 2,372</td>
<td>$ 2,372</td>
</tr>
<tr>
<td>Less: proceeds from royalty escrow liability</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Less: non-cash interest</td>
<td>60,300</td>
<td>21,409</td>
</tr>
<tr>
<td>Less: income tax costs</td>
<td>344</td>
<td>2,170</td>
</tr>
<tr>
<td>Less: acquired tax credits</td>
<td>868</td>
<td>408</td>
</tr>
<tr>
<td>Less: revaluation of debt</td>
<td>36,405</td>
<td>36,405</td>
</tr>
<tr>
<td>Less: deferred interest</td>
<td>2,857</td>
<td>-</td>
</tr>
<tr>
<td><strong>Non-GAAP Adjustments</strong></td>
<td>$ 11,185</td>
<td>$ 11,185</td>
</tr>
</tbody>
</table>

**Adj. to EBITDA:**

<table>
<thead>
<tr>
<th>Adj. to EBITDA</th>
<th>Three Months Ended December 31</th>
<th>Twelve Months Ended December 31</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(‘000)</td>
<td>(‘000)</td>
</tr>
<tr>
<td>USGAAP and ACC/DSM/US royalty liabilities</td>
<td>$ 48,605</td>
<td>$ 19,242</td>
</tr>
<tr>
<td><strong>Adj. to EBITDA</strong></td>
<td>$ 49,787</td>
<td>$ 20,427</td>
</tr>
</tbody>
</table>

**Adjusted EBITDA (Net of Reconciliation):**

<table>
<thead>
<tr>
<th>Adjusted EBITDA</th>
<th>Three Months Ended December 31</th>
<th>Twelve Months Ended December 31</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(‘000)</td>
<td>(‘000)</td>
</tr>
<tr>
<td><strong>Adjusted</strong> EBITDA</td>
<td>$ 43,614</td>
<td>$ 18,272</td>
</tr>
</tbody>
</table>

**Non-GAAP Gross Profit:**

<table>
<thead>
<tr>
<th>Non-GAAP Gross Profit</th>
<th>Three Months Ended December 31</th>
<th>Twelve Months Ended December 31</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(‘000)</td>
<td>(‘000)</td>
</tr>
<tr>
<td><strong>Non-GAAP Gross Profit</strong></td>
<td>$ 71,161</td>
<td>$ 69,391</td>
</tr>
</tbody>
</table>

**Non-GAAP Gross profit %:**

<table>
<thead>
<tr>
<th>Non-GAAP Gross profit %</th>
<th>Three Months Ended December 31</th>
<th>Twelve Months Ended December 31</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td><strong>Non-GAAP Gross profit %</strong></td>
<td>80%</td>
<td>80%</td>
</tr>
</tbody>
</table>

**Non-GAAP Cash Provided (Used) in Operating Activities:**

<table>
<thead>
<tr>
<th>Non-GAAP Cash Provided (Used) in Operating Activities</th>
<th>Three Months Ended December 31</th>
<th>Twelve Months Ended December 31</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(‘000)</td>
<td>(‘000)</td>
</tr>
<tr>
<td><strong>Non-GAAP Cash Provided (Used) in Operating Activities</strong></td>
<td>$ 22,025</td>
<td>$ 22,382</td>
</tr>
</tbody>
</table>

**Non-GAAP Cash Provided (Used) in Operating Activities:**

<table>
<thead>
<tr>
<th>Non-GAAP Cash Provided (Used) in Operating Activities</th>
<th>Three Months Ended December 31</th>
<th>Twelve Months Ended December 31</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(‘000)</td>
<td>(‘000)</td>
</tr>
<tr>
<td><strong>Non-GAAP Cash Provided (Used) in Operating Activities</strong></td>
<td>$ 22,025</td>
<td>$ 22,382</td>
</tr>
</tbody>
</table>
Important Safety Information for DUEXIS and VIMOVO
Selected Safety Information

WARNING: RISK OF SERIOUS CARDIOVASCULAR AND GASTROINTESTINAL EVENTS

See full Prescribing Information for complete boxed warning.

- Ibuprofen, a component of DUEXIS, may increase the risk of serious cardiovascular (CV) thrombotic events, myocardial infarction, and stroke, which can be fatal. Risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk.
- DUEXIS is contraindicated for the treatment of perioperative pain in the setting of coronary artery bypass graft (CABG) surgery.
- NSAIDs, including ibuprofen, a component of DUEXIS, increase the risk of serious gastrointestinal (GI) adverse reactions, including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. Reactions can occur at any time without warning symptoms. Elderly patients are at greater risk.

- NSAIDs, including ibuprofen, which is a component of DUEXIS tablets, can lead to onset of new hypertension or worsening of preexisting hypertension, either of which may contribute to the increased incidence of cardiovascular events. Monitor blood pressure closely during treatment with DUEXIS.
- As with other NSAIDs, the use of aspirin and DUEXIS may increase the risk of adverse events, including GI bleeding.
- The most common adverse reactions (≥1% and greater than ibuprofen alone) were nausea, diarrhea, constipation, upper abdominal pain, and headache.

DUEXIS®
(Ibuprofen and famotidine) Tablets
800 mg/26.6 mg
**Selected Safety Information (cont’d)**

- **DUEXIS** should not be given to patients who have experienced asthma, urticaria, or allergic reactions after taking aspirin or other NSAIDs. Severe, rarely fatal, anaphylaxis with NSAIDs has been reported in such patients. **DUEXIS** is contraindicated for the treatment of perioperative pain in the setting of coronary artery bypass graft surgery. **DUEXIS** is contraindicated in patients in late stages of pregnancy as premature closure of the ductus arteriosus in the fetus may occur. **DUEXIS** should not be administered to patients with a history of hypersensitivity to other H₂-receptor antagonists. Cross sensitivity with other H₂-receptor antagonists has been observed.

- When active and clinically significant bleeding from any source occurs in patients receiving **DUEXIS**, the treatment should be withdrawn.

- Fluid retention and edema have been observed in some patients taking NSAIDs. **DUEXIS** should be used with caution in patients with fluid retention or heart failure.
DUEXIS—
Indications and Usage

DUEXIS is indicated for:

- The relief of signs and symptoms of rheumatoid arthritis and osteoarthritis and to decrease the risk of developing upper gastrointestinal ulcers in patients who are taking ibuprofen for those indications
- In the clinical trials, upper GI ulcer was defined as a gastric and/or duodenal ulcer
- The clinical trials primarily enrolled patients <65 years of age without a prior history of GI ulcer. Controlled trials did not extend beyond 6 months
WARNING: RISK OF SERIOUS CARDIOVASCULAR AND GASTROINTESTINAL EVENTS
See full Prescribing Information for complete boxed warning.

- Ibuprofen, a component of DUEXIS, may increase the risk of serious cardiovascular (CV) thrombotic events, myocardial infarction, and stroke, which can be fatal. Risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk.
- DUEXIS is contraindicated for the treatment of perioperative pain in the setting of coronary artery bypass graft (CABG) surgery.
- NSAIDs, including ibuprofen, a component of DUEXIS, increase the risk of serious gastrointestinal (GI) adverse reactions, including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. Reactions can occur at any time without warning symptoms. Elderly patients are at greater risk.
DUEXIS Important Safety Information (cont’d)

- DUEXIS should not be given to patients who have experienced asthma, urticaria, or allergic reactions after taking aspirin or other NSAIDs. Severe, rarely fatal, anaphylaxis with NSAIDs has been reported in such patients. DUEXIS is contraindicated for the treatment of perioperative pain in the setting of coronary artery bypass graft surgery. DUEXIS is contraindicated in patients in late stages of pregnancy as premature closure of the ductus arteriosus in the fetus may occur. DUEXIS should not be administered to patients with a history of hypersensitivity to other H₂-receptor antagonists. Cross sensitivity with other H₂-receptor antagonists has been observed.
- When active and clinically significant bleeding from any source occurs in patients receiving DUEXIS, the treatment should be withdrawn.
- NSAIDs, including ibuprofen, which is a component of DUEXIS tablets, can lead to onset of new hypertension or worsening of preexisting hypertension, either of which may contribute to the increased incidence of cardiovascular events. Monitor blood pressure closely during treatment with DUEXIS.
DUEXIS Important Safety Information (cont’d)

- Fluid retention and edema have been observed in some patients taking NSAIDs. DUEXIS should be used with caution in patients with fluid retention or heart failure.
- Long-term administration of NSAIDs, including ibuprofen, which is a component of DUEXIS tablets, has resulted in renal papillary necrosis and other renal injury. Use DUEXIS with caution in patients at risk (e.g., the elderly; those with renal impairment, heart failure, or liver impairment; and those taking diuretics or ACE inhibitors).
- Hepatic injury ranging from transaminase elevations to liver failure can occur. If clinical signs and symptoms consistent with liver disease develop, if abnormal liver tests persist or worsen, or if systemic manifestations occur, DUEXIS should be discontinued immediately.
- Anaphylaxis may occur in patients with the aspirin triad or in patients without prior exposure to DUEXIS. If an anaphylactoid reaction occurs, DUEXIS should be discontinued immediately.

DUEXIS®
(Ibuprofen and famotidine) Tablets
800 mg/26.6 mg
Serious skin reactions, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, which can be fatal, can occur. Discontinue DUEXIS if rash or other signs of local skin reaction occur.

Nursing mothers should use DUEXIS with caution, as it is not known if ibuprofen is excreted in human milk, and famotidine is excreted in human milk.

The most common adverse reactions (≥1% and greater than ibuprofen alone) were nausea, diarrhea, constipation, upper abdominal pain, and headache.

For further information on DUEXIS, please see full Prescribing Information at www.DUEXIS.com/PI.
REDUCING THE RISK OF GASTRIC ULCERS FROM NAPROXEN
THE SMARTER NAPROXEN DUE TO ADDED GASTROPROTECTION

VIMOVO®
(naproxen/esomeprazole magnesium)
375/20-500/20 mg delayed-release tablets
VIMOVO Important Safety Information

WARNING: CARDIOVASCULAR AND GASTROINTESTINAL RISKS

Cardiovascular Risk
- Naproxen, a component of VIMOVO, may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk.
- VIMOVO is contraindicated for the treatment of perioperative pain in the setting of coronary artery bypass graft (CABG) surgery.

Gastrointestinal Risk
- NSAIDs, including naproxen, a component of VIMOVO, cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious gastrointestinal (GI) events.
Selected Safety Information (cont’d)

- Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals.

- There is no consistent evidence that concurrent use of aspirin mitigates the increased risk of serious CV thrombotic events associated with NSAID use. As with all NSAIDs, concurrent administration of VIMOVO and aspirin is not generally recommended because of the potential of increased adverse events.

- NSAIDs, including VIMOVO, can cause serious GI adverse events, which can be fatal. The risk is greater in patients with a prior history of ulcer disease or GI bleeding, and in patients at high risk for GI events, especially the elderly. VIMOVO should be used with caution in these patients.

- Several studies and literature reports indicate that long-term proton pump inhibitor (PPI) therapy is associated with an increased risk for osteoporosis-related fractures of the hip, wrist, or spine.

- The most commonly observed adverse events in clinical trials (experienced by >5% patients in the VIMOVO group) were erosive gastritis, dyspepsia, gastritis, diarrhea, gastric ulcer, upper abdominal pain, and nausea.
VIMOVO—THE SMARTER NAPROXEN DUE TO ADDED GASTROPROTECTION

INDICATIONS

- VIMOVO is indicated for the relief of signs and symptoms of osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis and to decrease the risk of developing gastric ulcers in patients at risk of developing NSAID-associated gastric ulcers.

- VIMOVO is not recommended for initial treatment of acute pain because the absorption of naproxen is delayed compared to absorption from other naproxen-containing products. Controlled studies do not extend beyond 6 months.
VIMOVO Dosing and Administration

- The recommended dose of VIMOVO is 1 tablet administered orally twice daily (BID)\(^1\)
  - Available as 375 mg/20 mg and 500 mg/20 mg of naproxen and esomeprazole magnesium\(^1\)
- VIMOVO tablets should be swallowed whole, with liquid\(^1\)
  - Do not split, chew, crush or dissolve tablets\(^1\)
- VIMOVO should be taken at least 30 minutes before meals\(^1\)
VIMOVO Important Safety Information (cont’d)

- VIMOVO is contraindicated in patients with known hypersensitivity to any component of VIMOVO or substituted benzimidazoles; in patients with a history of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs; in patients during the perioperative period in the setting of coronary artery bypass graft (CABG) surgery; or in patients in the late stages of pregnancy.
- Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals.
- Treatment should be withdrawn when active and clinically significant bleeding from any source occurs.
As with all NSAIDs, VIMOVO can lead to the onset of new hypertension or worsening of preexisting hypertension, either of which may contribute to the increased incidence of CV events. Blood pressure should be monitored closely. NSAIDs, including VIMOVO, may diminish the antihypertensive effect of angiotensin converting enzyme (ACE) inhibitors and angiotensin II antagonists, beta-blockers, and in some patients can reduce the natriuretic effect of furosemide and thiazides.

Fluid retention and edema have been observed in some patients taking NSAIDs, including VIMOVO. NSAIDs should be used with caution in patients with fluid retention or heart failure.

Two large, controlled, clinical trials of a COX-2 selective NSAID for the treatment of pain in the first 10-14 days following CABG surgery found an increased incidence of myocardial infarction and stroke.
There is no consistent evidence that concurrent use of aspirin mitigates the increased risk of serious CV thrombotic events associated with NSAID use. As with all NSAIDs, concurrent administration of VIMOVO and aspirin is not generally recommended because of the potential of increased adverse events.

NSAIDs, including VIMOVO, can cause serious GI adverse events, which can be fatal. The risk is greater in patients with a prior history of ulcer disease or GI bleeding, and in patients at high risk for GI events, especially the elderly. VIMOVO should be used with caution in these patients.
Epidemiological studies have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. In two studies, concurrent use of an NSAID, COX-2 inhibitor, or aspirin potentiated the risk of bleeding. Although these studies focused on upper gastrointestinal bleeding, bleeding at other sites cannot be ruled out.

- NSAIDs should be given with care to patients with a history of inflammatory bowel disease (ulcerative colitis, Crohn’s disease) as their condition may be exacerbated.
- Symptomatic response to esomeprazole, a component of VIMOVO, does not preclude the presence of gastric malignancy.
- Atrophic gastritis has been noted occasionally in gastric corpus biopsies from patients treated long-term with omeprazole, of which VIMOVO contains an enantiomer.
- Anaphylactoid reactions may occur in patients without known prior exposure to either component of VIMOVO. NSAIDs should not be given to patients with aspirin triad.
**VIMOVO Important Safety Information (cont’d)**

- NSAIDs can cause serious skin adverse reactions such as exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, which can be fatal. These serious events may occur without warning. Discontinue VIMOVO at first appearance of skin rash or any other sign of hypersensitivity.

- In late pregnancy, as with other NSAIDs, VIMOVO should be avoided because it may cause premature closure of the ductus arteriosus.

- VIMOVO is not recommended in patients with moderate or severe renal insufficiency. In addition, NSAIDs may cause renal toxicity.

- VIMOVO is not recommended in patients with severe hepatic insufficiency. Consider dose reduction in mild/moderate hepatic insufficiency. If abnormal liver enzymes persist or worsen, discontinue use immediately.

- Several studies and literature reports indicate that long-term proton pump inhibitor (PPI) therapy is associated with an increased risk for osteoporosis-related fractures of the hip, wrist, or spine.

- PPI therapy may be associated with increased risk of *Clostridium difficile* associated diarrhea.
VIMOVO Important Safety Information (cont’d)

- Avoid concomitant use of esomeprazole with clopidogrel due to a reduction in plasma concentrations of the active metabolite of clopidogrel. When using esomeprazole consider alternative anti-platelet therapy.
- Hypomagnesemia has been reported rarely with prolonged treatment with PPIs.
- Avoid concomitant use of VIMOVO with St John’s Wort or rifampin due to the potential reduction in esomeprazole levels.
- Esomeprazole, a component of VIMOVO, inhibits gastric acid secretion and may interfere with the absorption of drugs where gastric pH is an important determinant of bioavailability (e.g., ketoconazole, iron salts, and digoxin).
- Concomitant use of VIMOVO and warfarin may result in increased risk of bleeding complications. Monitor for increases in INR and prothrombin time.
- The most commonly observed adverse events in clinical trials (experienced by >5% patients in the VIMOVO group) were erosive gastritis, dyspepsia, gastritis, diarrhea, gastric ulcer, upper abdominal pain, and nausea.

For further information on VIMOVO, please see the full Prescribing Information at www.VIMOVO.com/PI.