Takeda Pharmaceutical Company: A Global Leader in Gastroenterology

Investor and Analyst Event
March 9th, 2015
W Hotel, New York City

Today's Presenters & Panel

Christophe Weber
President & Chief Operating Officer

Asit Parikh, M.D., Ph.D.
Head of GI Therapeutic Area Unit

Kirsten Detrick,
Vice President, Therapeutic Area Commercial Lead, GI, Global Commercial

Nicole Mowad-Nassar
Vice President, Marketing, Takeda Pharmaceuticals USA
Agenda for Today

09:00~10:00  **Session 1**  
Introduction: Strategic Roadmap for Profitable Growth  
Takeda's Position of Strength within the Gastroenterology Space  
Takeda's GI Portfolio  
Takeda's GI Drug Discovery Unit

10:00~10:20  break & refreshments

10:20~11:10  **Session 2**  
The IBD Market  
The US Launch of Entyvio®  
Entyvio® Global Launch  
Achieving >$2 Billion in Global Peak Sales  
The Road to GI Leadership

11:10~12:00  Q&A Session

12:00~13:00  lunch buffet

Forward-Looking Statements

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All forward-looking statements are based on judgments derived from the information available to the Company at this time.  Forward looking statements can sometimes be identified by the use of forward-looking words such as "may," "believe," "will," "expect," "project," "estimate," "should," "anticipate," "plan," "continue," "seek," "pro forma," "potential," "target," "forecast," or "intend" or other similar words or expressions of the negative thereof.  
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• For full indication and important safety information of marketed products featured in the presentation, please see from slide 104. Products may not be available in all countries, or may be available under different trademarks, for different indications, in different dosages, or in different strengths.

Introduction:
Strategic Roadmap for Profitable Growth

Takeda Pharmaceutical Company: A Global Leader in Gastroenterology
Takeda's strategic roadmap to deliver sustainable EPS growth

- **Takeda-ism**
  - Patient → Trust → Reputation → Business

- **Patient and customer centricity**

- **Global and agile organization fostering talent**

- **Focused world class innovation engine (R&D)**

- **Sustaining sales growth**
  - Innovation with leadership in GI & Oncology
  - Leverage value brands in Emerging Markets

- **Financial discipline**

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Two powerful growth engines

**INNOVATIVE PRODUCTS**

- 4 THERAPEUTIC AREAS and VACCINES

  - US, Europe, Japan and Emerging Markets

**VALUE BRANDS**

- BRANDED GENERICS and OTC

  - Emerging Markets
Promising portfolio that is increasingly focused, innovative and global

<table>
<thead>
<tr>
<th>New and Potential Product Approvals</th>
<th>Oncology</th>
<th>CNS</th>
<th>CVM</th>
<th>GI</th>
<th>Vaccine</th>
<th>Other TA</th>
</tr>
</thead>
<tbody>
<tr>
<td>FY2008 - 2012</td>
<td>ADCETRIS®</td>
<td>REMINYL®</td>
<td>NESINA®</td>
<td>DEXILANT®</td>
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<td>COLCRYS®</td>
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<td></td>
<td>VECTIBIX®</td>
<td></td>
<td>AZILVA®</td>
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<td>ULORIC®</td>
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<td></td>
<td>EDARBI®</td>
<td></td>
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<td>ALVESCO®</td>
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<td></td>
<td>LOTRIGA®</td>
<td></td>
<td></td>
<td>DAXAS®</td>
</tr>
<tr>
<td>FY2013 - 2017</td>
<td></td>
<td>ixazomib</td>
<td>BRINTELLIX®</td>
<td>ENTYVIO®</td>
<td>Norovirus</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>alisertib</td>
<td>CONTRAVE®</td>
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<td>trelagliptin</td>
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<td></td>
<td></td>
<td>TAK-375SL</td>
<td></td>
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</tr>
<tr>
<td>FY2018 - 2022</td>
<td>MLN0264</td>
<td>AD-4833/</td>
<td>TAK-114</td>
<td>TAK-003</td>
<td>Dengue</td>
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<td>TOMM40</td>
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</tbody>
</table>

Assets shown are in Phase 2 or later and have the most substantial financial expectations.

Takeda is a global GI leader

Major marketed products sales: 299 billion yen (FY2013)*

Launched in FY2014

Pipeline

TAK-114
Life-cycle management programs for Entyvio, Dexilant, Amitiza

*Includes royalty income
### Takeda’s Position of Strength within the Gastroenterology Space

**2014-2015: A pivotal time for Takeda gastroenterology**

<table>
<thead>
<tr>
<th>Gastroenterology (GI) positioned as a core Therapeutic Areas Unit (TAU)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Entyvio</strong> successfully launched in US and EU for the treatment of Ulcerative Colitis (UC) and Crohn’s Disease (CD) (June 2014)</td>
</tr>
<tr>
<td><strong>Takecab</strong> launched in Japan for acid-related diseases (Feb 2015)</td>
</tr>
<tr>
<td>Territory expansion agreement executed for <strong>Amitiza</strong></td>
</tr>
<tr>
<td><strong>GI Drug Discovery Unit</strong> to accelerate innovation and fuel pipeline</td>
</tr>
<tr>
<td>More than 40 ongoing <strong>GI trials</strong> with similar number anticipated for FY2015</td>
</tr>
<tr>
<td><strong>Significant R&amp;D investment</strong> in GI therapeutic area</td>
</tr>
</tbody>
</table>
How Takeda defines gastroenterology

Treating disorders of the digestive system:

- esophagus
- stomach
- small intestine
- large intestine (colon)
- rectum
- liver
- gallbladder and
- pancreas

Specialty GI market is projected to be nearly $28 billion in 2020

<table>
<thead>
<tr>
<th>Indication</th>
<th>Market forecast 2020 (global), $B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crohn’s disease</td>
<td>8.9</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>4.8</td>
</tr>
<tr>
<td>Irritable bowel syndrome</td>
<td>3.7</td>
</tr>
<tr>
<td>Slow transit/spinal inj. constipation</td>
<td>3.6</td>
</tr>
<tr>
<td>Nonalcoholic steatohepatitis</td>
<td>3.8</td>
</tr>
<tr>
<td>Hepatic encephalopathy</td>
<td>1.5</td>
</tr>
<tr>
<td>Primary biliary cirrhosis</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Functional dyspepsia</td>
<td>0.4</td>
</tr>
<tr>
<td>Primary sclerosing cholangitis</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td>Gastroparesis</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td>Ileus / ICU gastric stasis</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td>Celiac disease</td>
<td>&lt;0.1</td>
</tr>
</tbody>
</table>

Source: EvaluatePharma
The specialty GI category is growing faster than other therapeutic areas

Worldwide, 2014-2020

**Absolute dollar growth 2014-20**

$ billion

-10 0 10 20 30 40 50 60 70 80 90

Dollar Sales CAGR 2013-2020 %

- (2) 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15

*Defined as Inflammatory Bowel Disease and Hepato-Pancreato-Biliary sub-Therapeutic Areas and select specialty GI indications within motility (e.g., Irritable Bowel Syndrome, gastroparesis, functional dyspepsia)

Source: EvaluatePharma and Internal research and analysis

A strong legacy to build on
Past 25 years make today’s Takeda ideally poised for success

**Selected milestones:**

Prevpac Approved in US

Prevacid NapraPAC Approved in US

Tecta* Approved in Mexico

Amitiza IBS-C Indication Approved in US

Amitiza OIC Indication Approved -and- Entyvio BLA Filed

Prevacid Oral Suspension Approved in US

Amitiza** CIC Indication Approved in US

Dexilant Approved in US

Entyvio Approved in US and EU -and- Takecab Approved in Japan

CIC: Chronic Idiopathic Constipation; IBS-C: Irritable Bowel Syndrome with Constipation; OIC: Opioid-Induced Constipation; BLA: Biologics License Application

* Tecta was acquired by Takeda as part of the Nycomed acquisition in 2011
** In-licensed from Sucampo
Note: Indications are not written in full
### Takeda's GI Portfolio

#### Robust diversified portfolio and pipeline

<table>
<thead>
<tr>
<th>Product / Development code</th>
<th>Category</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Registration</th>
<th>Marketed</th>
</tr>
</thead>
<tbody>
<tr>
<td>pantoprazole</td>
<td>Acid-related diseases</td>
<td></td>
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<td></td>
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<tr>
<td>lansoprazole</td>
<td>Acid-related diseases</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>ulinastatin</td>
<td>Acute pancreatitis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dexilant</td>
<td>Acid-related diseases</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amitiza</td>
<td>CIC, IBS-C, OIC*</td>
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<tr>
<td></td>
<td>Pediatric functional constipation</td>
<td></td>
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<tr>
<td></td>
<td>New formulation</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Takecab</td>
<td>Acid-related diseases</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entyvio</td>
<td>Ulcerative colitis, Crohn's disease</td>
<td></td>
<td></td>
<td>Preparing for Phase 3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Primary Sclerosing Cholangitis</td>
<td></td>
<td></td>
<td>Preparing for Phase 3</td>
<td></td>
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<tr>
<td></td>
<td>Subcutaneous formulation</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>TAK-114</td>
<td>Ulcerative colitis</td>
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</tbody>
</table>

*Table shows most advanced stage of development, regardless of region
*CIC: Chronic Idiopathic Constipation, IBS-C: Irritable Bowel Syndrome with Constipation, OIC: Opioid Induced Constipation*
Takeda’s PPI portfolio totals 274 billion yen, with wide range of indications and formulations

- 1st and only Dual-Delayed Release Proton Pump Inhibitor (PPI) offers two releases in one pill
- US and Emerging Market launches driving growth
- Global growth CAGR of 33% from FY2011 to FY2014 (forecast)

- 120 billion yen in FY2013
- Lansoprazole is uniquely differentiated with multiple formulations

- 104 billion yen in FY2013
- IV formulation delivering strong growth in China

Amitiza is in-licensed from Sucampo Pharmaceuticals Inc. For full indication and important safety information please see from slide 110 in this presentation
Amitiza® (lubiprostone) activates intestinal chloride channels

- Locally acting chloride channel activator that enhances intestinal fluid secretion without altering serum sodium or potassium
- Specifically activates CIC-2, a normal constituent of the apical membrane of human intestine
- Bypasses the antisecretory action of opiates that results from suppression of secretomotor neuron excitability

Images are an artist's rendition and are for illustration purposes only

Amitiza® continues to show robust growth in the US

Amitiza Net Sales Growth
FYQ1-Q3 2013-2014
(billion yen) 22.9
18.5

April – December 2013
April – December 2014

+24%

Amitiza is approved in the U.S. for the treatment of chronic idiopathic constipation, irritable bowel syndrome with constipation and opioid-induced constipation
Recent territory expansion agreement bolsters our global GI position

- Original Territory FY2014 revenue forecast: 28 billion yen
  - Planned pediatric labeling and new formulation expected to fuel growth if approved
  - Canadian CIC* approval anticipated in 2015
- Expansion Territory: launches in key Emerging Markets starting in 2017-18
- Global Lifecycle management plan under evaluation

\*Chronic Idiopathic Constipation

Takecab (vonoprazan) is approved for acid-related diseases only in Japan
Takecab® (vonoprazan) is a potent, novel Potassium-Competitive Acid Blocker (P-CAB)

- Reversible inhibitor of proton pump
- Activation of drug by acid/food not needed
- Long half-life (~9h), linear pharmacokinetics up to 40mg
- High extent of 24 hour pH holding time >4
- Less affected by drug metabolism polymorphism (CYP2C19)

Takecab® demonstrates rapid gastric acid neutralization

Mean of Median Gastric pH Profiles for TAK-438 Treatment Groups on Day 7*

- Rapid gastric acid neutralization
- Fast onset of action and acid suppression from first dose
Takecab® phase 3 data, erosive esophagitis healing:
Takecab is clinically potent

High healing rate of Takecab at 2 weeks

- Secondary endpoints met

Endoscopic EE healing rate up to Week 2 and Week 4

<table>
<thead>
<tr>
<th>Healing rate at Week 2</th>
<th>70%</th>
<th>80%</th>
<th>90%</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Takecab 20 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lansoprazole 30 mg</td>
<td></td>
<td></td>
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</tbody>
</table>

- Post hoc analysis for superiority showed difference in favor of Takecab*

Endoscopic Erosive Esophagitis (EE) healing rates at Week 8 were confirmed in the non-inferiority analysis vs. lansoprazole

<table>
<thead>
<tr>
<th>Difference (%)</th>
<th>95% CI non-inferiority</th>
<th>z-value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.5</td>
<td>0.362 - 6.732</td>
<td>5.3945</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

TAK-438/CCT-002 study
CI: confidence interval
* (P = 0.0337; Fisher exact test)
Takecab®, EE maintenance phase 3 data
Endoscopic EE Recurrence rates at week 24

EE recurrence rate at Week 24

<table>
<thead>
<tr>
<th></th>
<th>15mg</th>
<th>10mg</th>
<th>20mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lansoprazole</td>
<td>16.8% (33/196)</td>
<td>5.1% (10/197)</td>
<td>2.0% (4/201)</td>
</tr>
</tbody>
</table>

- As per protocol testing, non-inferiority of Takecab 10mg and 20mg to lansoprazole 15mg was confirmed
- Post hoc analysis for superiority showed difference in favor of Takecab*

TAK-438/CCT-003 study
*(Takecab 20mg vs. lansoprazole P<0.0001, Takecab 10mg vs. lansoprazole P=0.0002; Fisher exact test)

Takecab® phase 3 data:
H. pylori high eradication rates

1st Line Eradication Rate

<table>
<thead>
<tr>
<th></th>
<th>20mg</th>
<th>30mg</th>
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</thead>
<tbody>
<tr>
<td>Takecab</td>
<td>92.6% (300/324)</td>
<td>75.9% (243/320)</td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>70%</td>
<td>80%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Difference (%)</th>
<th>95% CI</th>
<th>Non-inferiority test *</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Lower</td>
<td>Upper</td>
</tr>
<tr>
<td>Takecab</td>
<td>16.7</td>
<td>11.172</td>
<td>22.138</td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>11.70</td>
<td>22.35</td>
<td>8.7909</td>
</tr>
</tbody>
</table>

- Non-inferiority of triple therapy with Takecab/amoxicillin/clarithromycin vs Lansoprazole/amoxicillin/clarithromycin was confirmed
- Post hoc analysis for superiority showed difference in favor of Takecab**
The Japanese anti-acid market is large and still growing even after generic entries of classical PPIs.

Brands (Growth)  
Mar 14 MAT – Dec 2014 MAT*  
- Generics (25%)  
- Brand esomeprazole (33%)  
- Brand omeprazole (-24%)  
- Brand rabeprazole (-10%)  
- Brand lansoprazole (-13%)

*MAT: Moving Annual Total

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Takecab® now launched in Japan

Japan
- Phase III program focused only on Japan
- Just launched with 7 approved indications
- Takeda and Otsuka co-promotion, two leading GI companies
- Anticipated to be a top 3 revenue generator for Takeda in Japan (over 60 billion yen in sales)
- Patent protection until at least 2026

Rest of World
- Takeda is reviewing different options for development of Takecab in markets outside of Japan
For full indication and important safety information please see from slide 104 in this presentation.
Inflammatory Bowel Disease (IBD)

IBD includes two distinct inflammatory diseases of the gastrointestinal tract:

1. Ulcerative Colitis (UC) affects the innermost lining of the large intestine.
2. Crohn’s Disease (CD) affects any portion of the GI tract, involves all tissue layers.

- UC and CD are chronic conditions affecting 2.6 million patients in the G7 markets.
- Symptoms include abdominal pain, diarrhea, rectal bleeding, and weight loss.
- Lifelong condition that often affects young otherwise healthy individuals.
- Complications include strictures, bowel obstruction, need for surgery, and cancer.

Inflammatory Bowel Disease (IBD)
Stepwise treatment paradigm

- UC/CD severity at presentation
- Severe
- Moderate
- Mild

- Induction
- Maintenance
- Surgery
- Anti-TNF/Thiopurine
- Anti-TNF
- 5-ASA/Thiopurine/Methotrexate
- Steroids
- 5-ASA

Adapted from Kornbluth and Sachar, Am J Gastroenterol 2010; 105:501–523
Entyvio® (vedolizumab): An alternative for patients with UC and CD

- **First and only** biologic engineered for the treatment of moderately to severely active ulcerative colitis and Crohn’s disease
- **First and only** product in the US and Europe indicated for both anti-TNFα-naïve and anti-TNFα-failure patients, both in UC and CD
- **First and only** biologic with a specific binding action designed for a gut-homing inflammatory pathway
- **First and only** simultaneous launch in both UC and CD in US and Europe
- No boxed warning in label

Entyvio® is the first biologic to primarily inhibit homing of lymphocytes to the gut

![Artist's rendition](image)
The specific binding action of Entyvio® inhibits lymphocyte trafficking to inflamed gut

- Entyvio selectively inhibits the movement of a discrete subset of T lymphocytes that preferentially migrate into inflamed GI tissue
- Entyvio does not bind to or inhibit function of the α4β1 or αβ7 integrins

Entyvio® discovery and development
An incredible journey

1. Entyvio [prescribing information]. Deerfield, IL: Takeda Pharmaceuticals America, Inc.
Early publications

α4β7 integrin mediates lymphocyte binding to the mucosal vascular addressin MAdCAM-1
Cornelia Berlin1, 5, 7, Ellen L. Berg1, 7, Michael J. Briskin1, 7, David P. Andrew1, 7, Peter J. Kilshaw2, Bernhard Holzmann3, Irving L. Weissman4, 5, Alf Hamann6, Eugene C. Butcher1, 5, 7

Cell 1993

Attenuation of Colitis in the Cotton-top Tamarin by Anti–α4 integrin Monoclonal Antibody
Daniel K. Podolsky, * 7, Roy Lobb, 8, Norval King, 6, Christopher D. Benjamin, 8
Blake Pepinsky, 8, Prebit Sehgal, 6, and Michelle deBeaumont 7
*Gastrointestinal Unit, Massachusetts General Hospital and Department of Medicine, Harvard Medical School; 1Massachusetts General Hospital/New England Regional Primate Research Center for the Study of Inflammatory Bowel Disease, Boston Massachusetts 02114; 4Biogen, Inc., Cambridge, Massachusetts 02142; and 6New England Regional Primate Research Center, Southboro, Massachusetts 01772

JCI 1992

Rapid Resolution of Chronic Colitis in the Cotton-top Tamarin With an Antibody to a Gut-Homing Integrin α4β7

Gastroenterology 1996

Blocking α4β7 alleviates chronic diarrhea in monkeys

Entyvio® discovery and development
An incredible journey

- **2008**: Phase II proof of concept established in IBD
- **2012**: GEMINI data presented at Digestive Disease Week
- **2013**: Entyvio precursor discovered
- **2013**: Role of α4β7 integrin in cell trafficking elucidated
- **2013**: GEMINI Phase III studies initiated
- **2014**: FDA Advisory Committee
- **2014**: CHMP (EMA) positive opinion
- **2014**: Entyvio Approved by FDA and EMA
- **2013**: GEMINI UC and CD data published in New England Journal of Medicine
- **2013**: EMA and FDA Filings
- **2013**: Entyvio name accepted

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**GEMINI**

- **Phase III** studies initiated
- **2012**: GEMINI data presented at Digestive Disease Week
Entyvio® ulcerative colitis pivotal data
Powerful results in UC from GEMINI I

UC Primary and Secondary Outcomes at 52 Weeks (ITT)

- Clinical Remission
- Durable Clinical Response
- Mucosal Healing
- Durable Clinical Remission
- CS-Free Remissions

Note: Q4 dosing is not the recommended dosage regimen in the US

5.3
15.8
46.5
42.5
20.5
27.3

Patients With Prior Anti-TNFα Failure (n=121)

Patients Without Anti-TNFα Failure (n=224)

Note: Q4 dosing is not the recommended dosage regimen in the US
**Entyvio® UC Pivotal Data (GEMINI I)**

<table>
<thead>
<tr>
<th>Incidence, %</th>
<th>PLACEBO (n=149)</th>
<th>VEDOLIZUMAB (n=746)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE</td>
<td>46</td>
<td>45</td>
</tr>
<tr>
<td>Serious AE</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Common AEs (≥5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>UC exacerbation</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Infections</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>Serious</td>
<td>2</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Infusion related reaction</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Malignant neoplasm</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

AE: adverse event


**Entyvio® demonstrates favorable efficacy and safety in UC meta analysis**

### Clinical Remission with Induction Rx

<table>
<thead>
<tr>
<th>Study</th>
<th>Odds Ratio</th>
<th>OR</th>
<th>95% CI</th>
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<tbody>
<tr>
<td>Treatment = ADA NCT00833509</td>
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<tr>
<td>ULTRA 1 (ITT-A)</td>
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<tr>
<td>ULTRA 1 (ITT-E)</td>
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<tr>
<td>ULTRA 2</td>
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<tr>
<td>Random effects model</td>
<td></td>
<td></td>
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<tr>
<td>Heterogeneity: fixed-effects, I² = 0.0%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OR</td>
<td>95% CI</td>
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<tr>
<td>0.85</td>
<td>[0.33; 2.19]</td>
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<tr>
<td>2.23</td>
<td>[1.06; 4.67]</td>
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<tr>
<td>2.99</td>
<td>[0.91; 9.29]</td>
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</tr>
<tr>
<td>2.19</td>
<td>[1.14; 4.16]</td>
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</tr>
<tr>
<td>1.89</td>
<td>[1.18; 3.01]</td>
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<tr>
<td>Treatment = GLM PURSUIT-M</td>
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<tr>
<td>PURSUIT-SC (phase 2)</td>
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<tr>
<td>PURSUIT-SC (phase 2, additional)</td>
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<td>Random effects model</td>
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<tr>
<td>Heterogeneity: fixed-effects, I² = 0.0%</td>
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<tr>
<td>OR</td>
<td>95% CI</td>
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<td>1.90</td>
<td>[0.51; 7.05]</td>
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<td>2.24</td>
<td>[0.51; 9.91]</td>
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<td>3.46</td>
<td>[1.91; 6.27]</td>
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<tr>
<td>3.60</td>
<td>[1.80; 7.06]</td>
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<tr>
<td>Treatment = IFX ACT 1</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>ACT 2</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Random effects model</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Heterogeneity: fixed-effects, I² = 12.5%</td>
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<td>OR</td>
<td>95% CI</td>
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<tr>
<td>3.63</td>
<td>[1.99; 6.70]</td>
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<tr>
<td>8.49</td>
<td>[3.62; 19.80]</td>
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<tr>
<td>5.27</td>
<td>[2.31; 12.04]</td>
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</tr>
<tr>
<td>Treatment = VDZ GEMINI 1</td>
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<tr>
<td>Random effects model</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: not applicable</td>
<td></td>
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<tr>
<td>OR</td>
<td>95% CI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.26</td>
<td>[1.58; 11.51]</td>
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### Serious Adverse Events

<table>
<thead>
<tr>
<th>Study</th>
<th>Odds Ratio</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment = ADA NCT00833509</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ULTRA 1</td>
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<td></td>
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<tr>
<td>ULTRA 2</td>
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</tr>
<tr>
<td>Random effects model</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: fixed-effects, I² = 0.0%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OR</td>
<td>95% CI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.96</td>
<td>[0.39; 2.11]</td>
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</tr>
<tr>
<td>0.51</td>
<td>[0.22; 1.17]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.82</td>
<td>[0.55; 1.22]</td>
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</tr>
<tr>
<td>Treatment = GLM PURSUIT-M</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PURSUIT-SC</td>
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</tr>
<tr>
<td>Random effects model</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: fixed-effects, I² = 0.0%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OR</td>
<td>95% CI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.94</td>
<td>[0.62; 1.42]</td>
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<tr>
<td>2.00</td>
<td>[0.95; 4.20]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment = IFX ACT 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACT 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Random effects model</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Heterogeneity: fixed-effects, I² = 9.1%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OR</td>
<td>95% CI</td>
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<tr>
<td>0.79</td>
<td>[0.44; 1.44]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.50</td>
<td>[0.24; 1.03]</td>
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<tr>
<td>0.66</td>
<td>[0.42; 1.04]</td>
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<td></td>
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<tr>
<td>Treatment = VDZ GEMINI 1 - induction</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>GEMINI 1 - maintenance</td>
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</tr>
<tr>
<td>Random effects model</td>
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<tr>
<td>Heterogeneity: fixed-effects, I² = 0.0%</td>
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<td></td>
</tr>
<tr>
<td>OR</td>
<td>95% CI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.32</td>
<td>[0.11; 0.94]</td>
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<tr>
<td>0.40</td>
<td>[0.25; 0.63]</td>
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</tr>
<tr>
<td>0.44</td>
<td>[0.25; 0.77]</td>
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</tr>
</tbody>
</table>

VDZ: vedolizumab (Entyvio), ADA: adalimumab (Humira), IFX: infliximab (Remicade), GLM: golimumab (Simponi)

Entyvio® Crohn's disease pivotal data
Impactful results in Crohn’s from GEMINI II

CD Primary and Secondary Outcomes through 52 Weeks (ITT)

- **Placebo**
- **VDZ Q8 Wks**
- **VDZ Q4 Wks**

% of patients

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Placebo</th>
<th>VDZ Q8 Wks</th>
<th>VDZ Q4 Wks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Remission</td>
<td>21.6</td>
<td>39.0</td>
<td>36.4</td>
</tr>
<tr>
<td>CDAI-100 Response</td>
<td>30.1</td>
<td>43.5</td>
<td>45.5</td>
</tr>
<tr>
<td>CS-Free Remission</td>
<td>15.9</td>
<td>31.7</td>
<td>28.8</td>
</tr>
<tr>
<td>Durable Remission</td>
<td>14.4</td>
<td>21.4</td>
<td>16.2</td>
</tr>
</tbody>
</table>

*P<0.05  **P<0.01  ***P<0.0001

Note: Q4 dosing is not the recommended dosage regimen in the US

Entyvio® CD pivotal data
Consistency irrespective of prior anti-TNFα exposure

Maintenance ITT Population

- Patients With Prior Anti-TNFα Failure (n=237)
  - VDZ/PBO
  - VDZ Q8W
  - VDZ Q4W

- Patients Without Prior Anti-TNFα Failure (n=224)

% of patients

<table>
<thead>
<tr>
<th>Outcome</th>
<th>VDZ/PBO</th>
<th>VDZ Q8W</th>
<th>VDZ Q4W</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Remission</td>
<td>12.8</td>
<td>28.0</td>
<td>27.3</td>
</tr>
<tr>
<td>CDAI-100 Response</td>
<td>20.5</td>
<td>29.3</td>
<td>37.7</td>
</tr>
<tr>
<td>Clinical Remission</td>
<td>30.7</td>
<td>51.4</td>
<td>45.5</td>
</tr>
<tr>
<td>CDAI-100 Response</td>
<td>40.0</td>
<td>59.7</td>
<td>53.2</td>
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</table>

Note: Exploratory sub-population not in the US label. Note: Q4 dosing is not the recommended dosage regimen in the US.
## Entyvio® CD Pivotal Data (GEMINI II)

<table>
<thead>
<tr>
<th>Incidence, %</th>
<th>PLACEBO (n=301)</th>
<th>VEDOLIZUMAB (n=814)</th>
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<tbody>
<tr>
<td>Any AE</td>
<td>82</td>
<td>87</td>
</tr>
<tr>
<td>Serious AE</td>
<td>15</td>
<td>24</td>
</tr>
<tr>
<td>Common AEs in ≥ 10%</td>
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<td></td>
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<tr>
<td>Crohn’s Disease</td>
<td>22</td>
<td>20</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>13</td>
<td>14</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>13</td>
<td>13</td>
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<tr>
<td>Headache</td>
<td>16</td>
<td>12</td>
</tr>
<tr>
<td>Nausea</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>19</td>
<td>23</td>
</tr>
<tr>
<td>Infections</td>
<td>40</td>
<td>44</td>
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<tr>
<td>Serious</td>
<td>3</td>
<td>6</td>
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<tr>
<td>Infusion reaction</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Malignant neoplasm</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

AE: adverse event

## Pivotal data from UC and CD published together

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 22, 2013 VOL. 369 NO. 8

Vedolizumab as Induction and Maintenance Therapy for Ulcerative Colitis

Brian G. Feagan, M.D., Paul Rutgeerts, M.D., Ph.D., Bruce E. Sands, M.D., Stephen Hanauer, M.D., Jean-Frédéric Colombel, M.D., William J. Sandborn, M.D., Gert Van Assche, M.D., Ph.D., Jeffrey Adler, M.D., Hyo-Jong Kim, M.D., Ph.D., Silvio D’Anese, M.D., Ph.D., Irving Fox, M.D., Catherine Milch, M.D., Serap Sankoh, Ph.D., Tim Wyatt, Ph.D., Jing Xu, Ph.D., and Asit Parikh, M.D., Ph.D., for the GEMINI 1 Study Group

Vedolizumab as Induction and Maintenance Therapy for Crohn’s Disease

William J. Sandborn, M.D., Brian G. Feagan, M.D., Paul Rutgeerts, M.D., Ph.D., Stephen Hanauer, M.D., Jean-Frédéric Colombel, M.D., Bruce E. Sands, M.D., Milan Lukas, M.D., Ph.D., Richard N. Fedorak, M.D., Scott Lee, M.D., Brian Bressler, M.D., Irving Fox, M.D., Maria Rosario, Ph.D., Serap Sankoh, Ph.D., Jing Xu, Ph.D., Kristin Stephens, B.A., Catherine Milch, M.D., and Asit Parikh, M.D., Ph.D., for the GEMINI 2 Study Group

Takeda Pharmaceutical Company Limited
**Entyvio® development (2007-2013)**
Exemplifies Takeda capabilities

- Studies enrolled ~3000 patients
- Largest IBD clinical program ever conducted, resulting in approval
- Addressed numerous challenges associated with novel mechanism
- Continued mechanistic studies performed during clinical development
  - No impact on peripheral lymphocyte counts in humans
  - No CNS immunosuppressive effect in macaques
  - No effect on human spinal fluid cell counts or number
  - Measurable effect on gut but not systemic immune function in vaccine challenge study in humans

---

**FDA and EMA approval achieved in the same week – historic in IBD**

1. Entyvio (vedolizumab) [package insert]. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; 2014;

---

**TAK-114 is an investigational oral STAT3 inhibitor for ulcerative colitis positioned pre-biologic**

- In-licensed from Natrogen in December 2013
- Positive results in Phase 2a (4 week ulcerative colitis study)
- Oral twice a day dosing
- For moderate to severe UC patients who fail 5-ASAs or other conventional oral therapies
TAK-114 in UC:
Positive results in a 4 week Phase II Study

Clinical Response at Week 4*

Δ=50.0
P=0.0016

Δ=58.6
P<0.0001

% of patients

n=22

Clinical Remission at Week 4*

Δ=22.7
P=0.1324

Δ=35.9
P=0.0132

% of patients

n=22

*Study phase 2a NCT02009UC1: Post-hoc analysis (Completers-Observed data). Percentage of subjects and exact 95% confidence intervals. P-value is derived from Fisher’s exact test.

Gastroenterology Drug Discovery Unit

- Innovative highly matrixed virtual DD
- Focused on collaborative innovation
- Leverages the best internal & external GI science wherever it exists
- Lean infrastructure provides agility
- Passionate & experienced leadership
- Ambition to be #1 partner of choice

Inflammatory / Immune GI Diseases

Functional Bowel Disorders

Liver Diseases

Motility Disorders

Key external partnerships established in 2014

MONASH University
Institute of Pharmaceutical Sciences
- A unique academic fully integrated preclinical drug discovery unit

Queen Mary
University of London
- Human GI tissue biology, *state of the art* target validation

THE UNIVERSITY of ADELAIDE
- World-leading visceral pain laboratories

ADVINUS
- Discovery CRO* - A major partnership with Takeda

*Contract Research Organization
**GI Leadership within Reach**

**GI is an attractive market for further investment**
- Global health burden of GI diseases remains substantial
- Key assets Takecab and Entyvio are cornerstones of a diversified portfolio

**Takeda will achieve global leadership in GI**
- Leveraging existing franchise and CMC/discovery/development capabilities
- Licensing/acquiring additional GI assets as good opportunities present

---

**Agenda for Today**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
</thead>
<tbody>
<tr>
<td>09:00~10:10</td>
<td><strong>Session 1</strong></td>
</tr>
<tr>
<td></td>
<td>Introduction: Strategic Roadmap for Profitable Growth</td>
</tr>
<tr>
<td></td>
<td>Takeda’s Position of Strength within the Gastroenterology Space</td>
</tr>
<tr>
<td></td>
<td>Takeda’s GI Portfolio</td>
</tr>
<tr>
<td></td>
<td>Takeda’s GI Drug Discovery Unit</td>
</tr>
<tr>
<td>10:10~10:20</td>
<td>break &amp; refreshments</td>
</tr>
<tr>
<td>10:20~11:20</td>
<td><strong>Session 2</strong></td>
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<tr>
<td></td>
<td>The IBD Market</td>
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<tr>
<td></td>
<td>The US Launch of Entyvio®</td>
</tr>
<tr>
<td></td>
<td>Entyvio® Global Launch</td>
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<tr>
<td></td>
<td>Achieving &gt;$2 Billion in Global Peak Sales</td>
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<tr>
<td></td>
<td>The Road to GI Leadership</td>
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<tr>
<td>11:20~12:00</td>
<td>Q&amp;A Session</td>
</tr>
<tr>
<td>12:00~13:00</td>
<td>lunch buffet</td>
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</tbody>
</table>
Takeda Pharmaceutical Company: A Global Leader in Gastroenterology

The IBD Market

IBD has a significant impact on patients and society

IBD Impacts the Lives of Patients
- Physical symptoms
- Increased risk of colorectal cancer
- Impact on quality of life including loved ones
- Lack of general public awareness

High Cost of Care
- High rates of surgery, hospitalizations, complications
- Over $12B in direct and indirect costs in the US\textsuperscript{1,2}
- Increased worker absenteeism, non-participation, and sick leave

Significant unmet needs remain

The UC and CD biologic treated segments of the IBD category are ripe for a new entrant.

IBD Patient Pool Dynamics (G7 data)

- **Ulcerative Colitis**
  - 1.26 million diagnosed patients¹
  - 76k patients on biologic therapy¹

- **Crohn's Disease**
  - 1.03 million diagnosed patients²
  - 242k patients on biologic therapy²

Patients currently on:

- 65% 1st Biologic
- 28% 2nd Biologic
- 7% 3rd Biologic

**UC Market Revenue ($millions)**

**CD Market Revenue ($millions)**

The UC and CD total market will total ~$10 billion by 2022, with biologics accounting for 80% of sales.

Projected Market Revenues (G7) 2012-2022

**Ulcerative Colitis**

**Crohn's Disease**

*acetylsalicylic acids

Source: Decision Resources Pharmacor G7 UC and CD Markets, 2014
The biologic treated segment of the UC and CD market will become more prevalent, biotherapy could be used more widely.

Projected CAGR, Treated Patients (G7)
2012-2022

- UC CAGR
- CD CAGR

The US Launch of Entyvio®
Takeda Pharmaceutical Company: A Global Leader in Gastroenterology
A stellar launch in the US, already generating over $112MM in net sales*  

Entyvio is now the 3rd largest IBD biologic with a volume share of 6%, surpassing two other biologics¹

- 32,000+ Vials shipped to accounts²
- 6,500+ Unique patients using Entyvio³
- 2,000+ Healthcare Professionals have utilized³
- Top 20 Specialty Launch since 2008, per IMS Health⁴

* June-December 2014
¹ Internal analysis, estimated claims and unit sales data as of Dec 2014
² Internal analysis of shipment and enrollment data, as of February 13th, 2014
³ Based on data from EntyvioConnect
⁴ Based on internal analysis of IMS Health, NSP (National Sales Perspectives), Nov 2014

There are nearly 1.5MM patients in the US with IBD, and the market is growing at 8% per year

IBD Patient Pool Dynamics (US data)

- ~200K patients on biologic therapy
- Higher penetration in CD vs. UC
- Biologic therapy used in patients with moderate-to-severe disease not controlled on conventional agents

Annual growth rate of 8% expected through 2020

UC growth is expected to be nearly 2x GREATER than CD

*Wholesale acquisition cost
¹ Datamonitor (2014), 2. Decision Resources (Aug 2014)
² Internal Research and Analysis (Aug 2014)
³ Based on data from EntyvioConnect
⁴ Based on internal analysis of IMS Health, NSP (National Sales Perspectives), Nov 2014
Initial customer response has been positive

- Physicians like Entyvio’s differentiated mechanism of action, remission data, safety profile
- Eager to have an alternative to the TNF class of biologics
- Expressing a desire for more education, research, and experience
- Physicians report that patients are responding well to the discussion of Entyvio as an option*

“We expect vedolizumab (Takeda’s Entyvio) will... earn gold-standard status for moderate to severe UC in 2018”
Decision Resources, Feb 2015

“The introduction of vedolizumab as an additional option will offer the possibility of increasing disease-free remission for a greater proportion of patients with... active UC and CD”
Gastroenterology & Hepatology, Dec 2014

Initial penetration into the biologic-naïve segment is encouraging, and physicians are open to expanding use

Around two-thirds of current use is with patients that have failed an ant-TNFα

Nearly 80% of physicians state they will expand Entyvio use... higher than any other IBD biologic†

*Internal Research and Analysis (Aug 2014)
† Internal Research and Analysis, ATU quantitative research, Nov 2014, n=151
Entyvio® is being used in both the UC and CD patient populations

### US - Entyvio Usage by Indication

<table>
<thead>
<tr>
<th>Month</th>
<th>UC</th>
<th>CD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jul-14</td>
<td>71%</td>
<td>28%</td>
</tr>
<tr>
<td>Aug-14</td>
<td>67%</td>
<td>33%</td>
</tr>
<tr>
<td>Sep-14</td>
<td>67%</td>
<td>33%</td>
</tr>
<tr>
<td>Oct-14</td>
<td>65%</td>
<td>35%</td>
</tr>
<tr>
<td>Nov-14</td>
<td>65%</td>
<td>34%</td>
</tr>
<tr>
<td>Dec-14</td>
<td>68%</td>
<td>32%</td>
</tr>
<tr>
<td>Jan-15</td>
<td>64%</td>
<td>36%</td>
</tr>
</tbody>
</table>

Source: Internal research and analysis, Feb 2015

Takeda will capitalize on market opportunities to continue growing Entyvio® in the US

- **DISRUPT**
  - Raise awareness to allow doctors to utilize Entyvio with appropriate new or failing patients

- **DIFFERENTIATE**
  - Address gaps in clinical knowledge through expanded programs and education initiatives

- **EXPAND**
  - Grow use in ideal patient types where Entyvio may offer a positive benefit-risk profile

- **DELIVER**
  - A positive brand experience and develop reputation as a partner in IBD care
In the US our approach is to meet the unique needs of customers; establishing Takeda as an IBD partner.

**Specialty Infrastructure:** developed to support customers with 8 field-based roles and over 200 individuals.

- Regional Access Managers
- National Account Managers
- Medical Science Liaisons
- Field Medical Educators
- Field Medical Directors
- Specialty Sales Representatives
- Specialty Account Managers
- Field Reimbursement Specialists
- Entyvio Connect Case Managers
EntyvioConnect™ is a centralized program offering an integrated portfolio of access services and support.

**Access Support Services**
- Insurance Verification and Prior Authorization Support
- Billing and Coding Support
- Claims Denial Investigations
- Specialty Pharmacy Coordination

**Patient Coverage Support**
- Commercial Co-pay Program
- Uninsured Patient Assistance
- Insurance Foundation Referrals
- National and International Infusion Coordination

EntyvioConnect™ new patient enrollments continue to grow by approx. 200 each week.
Market Access is in line with launch expectations

Commercial Insured Market
- ~80% of IBD biologic patients are commercially insured\(^1\)
- Medicare reimbursement has been secured

Reaction to Entyvio Positive
- Payers respond positively to the clinical and economic profile
- Over 94% of health plans are covering Entyvio\(^1\)

Future efforts to gain more access
- Disease management education and programs
- Exploration of partnerships to pilot value-add services

Supporting and Activating the Patient Community

Engage | Activate | Enable

Resources

In-Office Education | Digital | Access & Support

1 Source: Internal research and analysis, Feb 2014
Working closely with the leading advocacy organization

Aligning with the CCFA Mission:
To cure Crohn’s disease and ulcerative colitis, and to improve the quality of life of children and adults affected by these diseases

For Patients…
Sponsorships for:
• Educational Webcasts and Materials
• Fundraising Walks and Runs
• Various local fundraisers

For Professionals…
Support for:
• Quality of Care Partnerships
• Practitioner Education
• Conference Sponsorship

Entyvio® start in the US supports global >$2 billion target

Strong and encouraging launch results…

…a commitment to the IBD Community…

…positioned for continued success
Entyvio® has had a promising launch to date, with Europe also contributing significantly to sales.

¥16.4 billion launch-to-date ($154 million)*

@Constant currency

Monthly Revenue (billion yen)

- Europe
- US

*Converted at average rate of 107 yen = $1
The strong uptake of Entyvio® due to a variety of factors

Current IBD treatment options still not adequate to meet need

Regulatory labelling
- Broad indication with descriptive clinical trial sections
- No boxed warning or Risk Evaluation & Mitigation Strategy
- Mechanism of action explanation
- Dose flexibility for some patients (EU only)

Access and reimbursement, due to:
- Early access programs
- Country-level reimbursement assessments (eg, Health Technology Assessment)

Market access results for Entyvio® are encouraging and balanced

UK
Entyvio became the first biologic to receive a provisional “yes” as a maintenance therapy in UC
- Recommended for patients who have not received an anti-TNF or could not tolerate an anti-TNF

Germany
Entyvio is classified at least “as good as” comparable biologic therapies (and can be prescribed without restrictions)

Israel
National Health Basket Committee granted full reimbursement per the Entyvio label for both TNF-naïve and TNF-failure patients in both UC and CD

Sweden
TLV officially reimbursed Entyvio for patients not suitable for anti-TNF therapy or who have not reached treatment goals with 1st anti-TNF therapy

Estonia
Fully reimbursed as of Jan. 1, 2015

Switzerland
BAG granted unrestricted reimbursement for anti-TNF naïve and experienced patients in both UC and CD as of Mar 1, 2015
Entyvio® sales from 14 countries so far

Sweden, Denmark, Finland
First markets to combat biosimilars

Norway

United States
$112M net sales (to Dec ’14)
>11,500 MDs reached

Ireland

UK

Netherlands
>90% of key accounts ordered

Spain

France
Early Patient Access Program

Early Patient Access programs with near-term full commercial launches

Spain

France

Austria
6% UC patient share

Germany
€21M in net sales (to Dec ’14)

Switzerland
Non-restricted reimbursement @ premium price

Austria

Germany

UK

Ireland

United States

Netherlands

Norway

Norway

Sweden, Denmark, Finland

First markets to combat biosimilars

Early launch countries in Europe are delivering strong Entyvio® uptake

GERMANY
Market Share and Sales, by Fiscal Quarter

Market Share

Market Sales (million €)

Q3/’13
Q4/’13
Q1/’14
Q2/’14
Q3/’14

95
96
103
114
124

TNF A
TNF B
TNF C
Entyvio

Source: Internal research and analysis; Germany Retail + Hospital sales, calculated based on data provided by IMS Health (DKM+NPA);
The benefits of Entyvio® are clear to EU physicians in both the UC and CD segments

**GERMANY**
Cited positive characteristics, all GEs
UC and CD

- New MoA/therapeutic option for IBD: 46.7%
- Good tolerability profile: 16.7%
- Few side effects: 15.0%
- Good efficacy/good study data: 13.3%
- Gut-selective MoA: 13.3%
- New therapeutic option for anti-TNFα failures: 8.3%
- Easy application/IV: 6.7%

Source: Internal Research and Analysis, Germany ATU (Oct. – Nov. 2014, n=60 gastroenterologists)

Q35. What do you think are some of the positive product characteristics of Entyvio® (vedolizumab) – independent of whether or not you have already used this biologic? – May choose more than one.

Emerging market physicians are interested in using Entyvio as a 1st line biologic

<table>
<thead>
<tr>
<th>Placement of Entyvio</th>
<th>UC</th>
<th>CD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Emerging Markets (n=286)</td>
<td>Emerging Markets (n=286)</td>
</tr>
<tr>
<td>Before immunomodulators and anti-TNFα</td>
<td>24%</td>
<td>22%</td>
</tr>
<tr>
<td>After immunomodulators, before anti-TNFα</td>
<td>38%</td>
<td>39%</td>
</tr>
<tr>
<td>TOTAL pre anti-TNF</td>
<td>62%</td>
<td>61%</td>
</tr>
<tr>
<td>After 1st anti-TNFα therapy</td>
<td>26%</td>
<td>29%</td>
</tr>
<tr>
<td>Alternative to Surgery</td>
<td>11%</td>
<td>10%</td>
</tr>
<tr>
<td>Would not consider to use</td>
<td>1%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Source: Internal Research and Analysis, Takeda IBD treatment landscape and evaluation of Biologics in Emerging Markets Market Research – October 2012

Question: Assuming no reimbursement restrictions, where would you most likely use ProductP in your current treatment paradigm?
Biologic penetration into Japan CD segment is greater than penetration in UC

Total and anti-TNFα treated patients in Japan

Source: Japan Medical Data Center

Takeda Pharmaceutical Company Limited
Achieving >$2B in global peak sales requires aligned execution against these strategic drivers

<table>
<thead>
<tr>
<th>Strategic Driver</th>
<th>Entyvio Executional Mandatory</th>
</tr>
</thead>
</table>
| Penetrate biologic naive patient pool                                           | • Expand IBD efficacy data set  
• Reinforce safety profile  
• Facilitate product experience                                                  |
| Raise awareness of Entyvio as an alternative treatment for existing biologic patients | • Increase recognition sub-optimal response  
• Support evaluative tactics to assess real-world anti-TNFα performance |
| Lead category in “switch to” preference in anti-TNFα switch patients            | • Over-index on share gain in anti-TNFα failures                                               |
| Enter new segments, deliver new data                                            | • Explore new scientific frontiers                                                             |

Takeda has an ambitious life-cycle management plan for Entyvio®

UC head-to-head vs Adalimumab
Primary Sclerosing Cholangitis
Subcutaneous Formulation
CD Mucosal Healing
Japan UC and CD

all plans subject to regulatory feedback and evolving marketplace dynamics
Planned CD Mucosal Healing trial could provide gold standard data for Entyvio®

Objective:
• To explore the correlation between endoscopy (mucosal healing) with histology (biopsy) and imaging (MRI) in vedolizumab treated patients

Rationale:
• Mucosal healing is increasingly seen as the “gold standard” clinical objective
• Correlates strongly with prolonged remission¹
• Entyvio would benefit from mucosal healing data in Crohn’s disease

Subcutaneous (SC) program will address patient preference as a strategic LCM opportunity

• SC formulation, if approved, would represent a meaningful convenience for patients, particularly as maintenance therapy
• SC bioavailability confirmed; dose selected for the Phase 3 program will deliver similar exposure with SC as with IV administration.
• Phase 3 trials in both UC and CD are planned to investigate the efficacy, safety, and clinical pharmacology of the SC formulation
• Customers like injections while IV retains key segment appeal¹

Entyvio could be the only IBD biologic to offer both infusion and subcutaneous administration

¹ Source: Internal Research and Analysis, Physician Conjoint (Europe & Canada and Emerging Markets) (Nov. 2013)
Life Cycle Plans include UC head to head

<table>
<thead>
<tr>
<th>Treatment Duration</th>
<th>Entyvio + Placebo</th>
<th>Follow-up</th>
<th>Safety Follow-up</th>
</tr>
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<tbody>
<tr>
<td>52 weeks</td>
<td></td>
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Randomization

Primary sclerosing cholangitis (PSC)
Evidence for Entyvio® mechanism in area of high unmet need

- PSC is a progressive inflammatory liver disease resulting in scarring of bile ducts, fibrosis and cirrhosis; patients at risk of liver failure and death with many requiring transplant
- To date, no therapy has been shown to prevent disease progression
- Lymphocyte migration to liver via a4b7-MAdCAM binding (Entyvio mechanism) has been implicated in pathophysiology of PSC

The UC and CD biologics market is large and growing significantly, particularly in UC

Achieving a 15-20% global patient share will result in $2 billion in Entyvio® revenues

Evolution of UC Patient Share (G7 Markets)

Evolution of CD Patient Share (G7 Markets)

Source: Decision Resources Pharmacor UC and CD Markets, 2014

Source: Internal research and analysis
Achieving a 15-20% global patient share will result in $2 billion in Entyvio® revenues

Scenario 1 - Entyvio Patient Share by Line of Therapy (2023)

- Ulcerative Colitis: TNF-naïve share 11%, TNF-failure share 27%
- Crohn's Disease: TNF-naïve share 10%, TNF-failure share 23%

Scenario 2 – Entyvio Patient Share by Line of Therapy (2023)

- Ulcerative Colitis: TNF-naïve share 3%, TNF-failure share 38%
- Crohn's Disease: TNF-naïve share 3%, TNF-failure share 30%

Entyvio® has a unique opportunity to position itself optimally now and will compete aggressively in future

- No new branded IBD competition expected for 2 years
- Strong patent protection with market exclusivity into next decade
- Biosimilar anti-TNFαs will target current brand anti-TNFs, but Entyvio will be positioned differently
- Anti-migration therapies - Although they may offer subcutaneous delivery, Entyvio will have first-mover advantage
- Biologic-like orals - Emerging orals have unknown efficacy/safety profiles

CURRENT OPPORTUNITY

FUTURE DYNAMICS

Source: Internal research and analysis
Takeda will realize the exciting commercial promise of Entyvio® by bringing its therapeutic benefits to patients worldwide.

Takeda Pharmaceutical Company: A Global Leader in Gastroenterology

The Road to GI Leadership
GI products contribute significantly to growth

GI contribution to sales*

FY2014
- GI contribution: 22%

FY2017
- GI contribution: 28%

*Sales from Japan OTC, non-pharmaceutical businesses, etc. are excluded from the calculation. Numbers are shown in circa %.

The road to GI leadership

To be Number 1 in GI

2014

- TAK-114
- Entyvio
- LCM
- Evaluate Business Development Opportunities
- External Partnerships
- GI DDU Pipeline Projects
Entyvio® (vedolizumab) Indication:
(US label)

**Adult Ulcerative Colitis (UC)**
Adult patients with moderately to severely active UC who have had an inadequate response with, lost response to, or were intolerant to a tumor necrosis factor (TNF) blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids:
- inducing and maintaining clinical response
- inducing and maintaining clinical remission
- improving the endoscopic appearance of the mucosa
- achieving corticosteroid-free remission

**Adult Crohn’s Disease (CD)**
Adult patients with moderately to severely active CD who have had an inadequate response with, lost response to, or were intolerant to a TNF blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids:
- achieving clinical response
- achieving clinical remission
- achieving corticosteroid-free remission

Please click [here](http://www.entyvio.com) for full prescribing information, or visit [www.entyvio.com](http://www.entyvio.com)
ENTYVIO Important Safety Information

(US label)

- ENTYVIO for injection is contraindicated in patients who have had a known serious or severe hypersensitivity reaction to ENTYVIO or any of its excipients.

- Infusion-related reactions and hypersensitivity reactions including anaphylaxis have occurred. Allergic reactions including dyspnea, bronchospasm, urticaria, flushing, rash, and increased blood pressure and heart rate have also been observed. If anaphylaxis or other serious allergic reactions occur, discontinue administration of ENTYVIO immediately and initiate appropriate treatment.

- Patients treated with ENTYVIO are at increased risk for developing infections. Serious infections have been reported in patients treated with ENTYVIO, including anal abscess, sepsis (some fatal), tuberculosis, salmonella sepsis, Listeria meningitis, giardiasis, and cytomegaloviral colitis. ENTYVIO is not recommended in patients with active, severe infections until the infections are controlled. Consider withholding ENTYVIO in patients who develop a severe infection while on treatment with ENTYVIO. Exercise caution in patients with a history of recurring severe infections. Consider screening for tuberculosis (TB) according to the local practice.

Please click here for full prescribing information, or visit www.entyvio.com

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ENTYVIO Important Safety Information

(US label)

- Although no cases of PML have been observed in ENTYVIO clinical trials, JC virus infection resulting in progressive multifocal leukoencephalopathy (PML) and death has occurred in patients treated with another integrin receptor antagonist. A risk of PML cannot be ruled out. Monitor patients for any new or worsening neurological signs or symptoms. Typical signs and symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes. If PML is suspected, withhold dosing with ENTYVIO and refer to a neurologist; if confirmed, discontinue ENTYVIO dosing permanently.

- There have been reports of elevations of transaminase and/or bilirubin in patients receiving ENTYVIO. ENTYVIO should be discontinued in patients with jaundice or other evidence of significant liver injury.

- Prior to initiating treatment with ENTYVIO, all patients should be brought up to date with all immunizations according to current immunization guidelines. Patients receiving ENTYVIO may receive non-live vaccines and may receive live vaccines if the benefits outweigh the risks.

- Most common adverse reactions (incidence ≥3% and ≥1% higher than placebo): nasopharyngitis, headache, arthralgia, nausea, pyrexia, upper respiratory tract infection, fatigue, cough, bronchitis, influenza, back pain, rash, pruritus, sinusitis, oropharyngeal pain, and pain in extremities.

Please click here for full prescribing information, or visit www.entyvio.com
Dexilant (dexlansoprazole) Indications:
(US label)

- Healing all grades of erosive esophagitis (EE) for up to 8 weeks (60 mg once daily)
- Maintaining healing of EE and relief of heartburn for up to 6 months (30 mg once daily)
- Treating heartburn associated with symptomatic non-erosive gastroesophageal reflux disease (GERD) for 4 weeks (30 mg once daily)

Please see full Prescribing Information, including Medication Guide for DEXILANT.

Dexilant Important Safety Information:
(US label)

- DEXILANT is contraindicated in patients with known hypersensitivity to any component of the formulation. Hypersensitivity and anaphylaxis have been reported with DEXILANT use.
- Symptomatic response with DEXILANT does not preclude the presence of gastric malignancy.
- PPI therapy may be associated with increased risk of *Clostridium difficile* associated diarrhea.
- Long-term and multiple daily dose PPI therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist, or spine. Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.
- Hypomagnesemia has been reported rarely with prolonged treatment with PPIs.
- Most commonly reported adverse reactions were diarrhea (4.8%), abdominal pain (4.0%), nausea (2.9%), upper respiratory tract infection (1.9%), vomiting (1.6%), and flatulence (1.6%).

Please see full Prescribing Information, including Medication Guide for DEXILANT.
Dexilant Important Safety Information:
(US label)

- Do not co-administer atazanavir with DEXILANT because atazanavir systemic concentrations may be substantially decreased. DEXILANT may interfere with absorption of drugs for which gastric pH is important for bioavailability (e.g., ampicillin esters, digoxin, iron salts, ketoconazole, erlotinib).

- Patients taking concomitant warfarin may require monitoring for increases in international normalized ratio (INR) and prothrombin time. Increases in INR and prothrombin time may lead to abnormal bleeding and even death. Concomitant tacrolimus use may increase tacrolimus whole blood concentrations. DEXILANT may increase serum levels of methotrexate.

- DEXILANT 30 mg should be considered for patients with moderate hepatic impairment.

Please see full Prescribing Information, including Medication Guide for DEXILANT.

Amitiza (lubiprostone) Indications:
(US label)

AMITIZA (lubiprostone) capsules are indicated for the treatment of Chronic Idiopathic Constipation (CIC) in adults and Opioid-Induced Constipation (OIC) in adults with chronic, non-cancer pain (24 mcg twice daily). The effectiveness in patients with OIC taking diphenylheptane opioids (e.g., methadone) has not been established. AMITIZA is also indicated for Irritable Bowel Syndrome with Constipation (IBS-C) in women ≥ 18 years old (8 mcg twice daily).

Please click here for complete Prescribing Information.
Amitiza Important Safety Information:

(US label)

- AMITIZA ( lubiprostone ) is contraindicated in patients with known or suspected mechanical gastrointestinal obstruction. Patients with symptoms suggestive of mechanical gastrointestinal obstruction should be thoroughly evaluated by the treating healthcare provider (HCP) to confirm the absence of such an obstruction prior to initiating AMITIZA treatment.

- Patients taking AMITIZA may experience nausea. If this occurs, concomitant administration of food with AMITIZA may reduce symptoms of nausea. Patients who experience severe nausea should inform their HCP.

- AMITIZA should not be prescribed to patients that have severe diarrhea. Patients should be aware of the possible occurrence of diarrhea during treatment. Patients should be instructed to discontinue AMITIZA and inform their HCP if severe diarrhea occurs.

- Patients taking AMITIZA may experience dyspnea within an hour of first dose. This symptom generally resolves within three hours, but may recur with repeat dosing. Patients who experience dyspnea should inform their HCP. Some patients have discontinued therapy because of dyspnea.

- In clinical trials of AMITIZA (24 mcg twice daily vs placebo; N=1113 vs N=316, respectively) in patients with CIC, the most common adverse reactions (incidence > 4%) were nausea (29% vs 3%), diarrhea (12% vs 1%), headache (11% vs 5%), abdominal pain (8% vs 3%), abdominal distension (6% vs 2%), and flatulence (6% vs 2%).

Please click here for complete Prescribing Information.

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Amitiza Important Safety Information:

(US label)

- In clinical trials of AMITIZA (24 mcg twice daily vs placebo; N=860 vs N=632, respectively) in patients with OIC, the most common adverse reactions (incidence >4%) were nausea (11% vs 5%) and diarrhea (8% vs 2%).

- In clinical trials of AMITIZA (8 mcg twice daily vs placebo; N=1011 vs N=435, respectively) in patients with IBS-C the most common adverse reactions (incidence > 4%) were nausea (8% vs 4%), diarrhea (7% vs 4%), and abdominal pain (5% vs 5%).

- Concomitant use of diphenylheptane opioids (e.g., methadone) may interfere with the efficacy of AMITIZA.

- The safety of AMITIZA in pregnancy has not been evaluated in humans. Based on animal data, AMITIZA may cause fetal harm. AMITIZA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Caution should be exercised when AMITIZA is administered to a nursing woman. Advise nursing women to monitor infants for diarrhea.

- Reduce the dosage in CIC and OIC patients with moderate and severe hepatic impairment. Reduce the dosage in IBS-C patients with severe hepatic impairment.

Please click here for complete Prescribing Information.