THERAPEUTIC AREA FOCUS IN GI WITH SPOTLIGHT ON CELIAC DISEASE

Asit Parikh, MD, PhD  
Head Gastroenterology Therapeutic Area Unit  
Takeda Pharmaceutical Company Limited  
Tokyo  
November 21, 2019

WE TARGET UNMET NEEDS THAT ALIGN WITH OUR STRENGTHS

AREAS OF FOCUS

- High unmet medical need
- Potential to advance SoC through innovative science – by being first or best in class
- Fit with internal strengths
- Ability to create a commercially viable path

GI WW RX SALES 2018 (USD BN)

- Total = $578Bn
- Acute GI Inflammation: 18.2
- GI Motility: 12.6
- GI Cancers: 3.9
- Liver Fibrosis: 6.5
- Viral Hepatitis: 0.3
- Other GI: 2.9

TAKEDA GI DISEASE AREAS

- GI Inflammation
- GI Motility
- Liver Fibrosis
- Acid Related Diseases

SOURCE: Evaluate Pharma indication-specific sales, accessed May 29, 2019. Other GI includes: pancreatic insufficiency, hepatic encephalopathy, diarrhea, bowel clearance, gallstones, hemorrhoids
WE STRENGTHEN ENTYVIO BY CONTINUOUSLY IMPROVING VALUE FOR PATIENTS

COMPETITIVE POSITIONING

VARSITY: 1st Head-to-Head study in IBD (UC)
- Vedolizumab was superior to adalimumab on the primary endpoint of clinical remission at wk 52
- Onset of action as rapid as anti-TNF

Expanding Patient Populations

Entyvio Subcutaneous Development
- Positive VISIBLE UC and CD trials
- Subject to regulatory approval, on track to launch exclusive, digital, needle-free jet-injector by 2022

Gut GvHD prophylaxis
- Could transform SoC for cancer patients undergoing allo stem-cell transplants

EXPECTED MILESTONES (FY)

2019
Entyvio (SC UC) US approval

2020
Entyvio (SC CD) US, EU approval
Entyvio (SC UC) EU, JP approval
Entyvio (IV) CN approval

2021
Entyvio IV GvHD Ph3 readout


IBD: Inflammatory Bowel Disease; UC: ulcerative colitis; CD: Crohn's Disease; IV=intravenous; SC=subcutaneous; TNF=tumour necrosis factor; SoC: standard of care; CN: China; JP: Japan; GvHD: graft versus host disease;

Clinical remission: Complete Mayo score of ≤2 points and no individual subscore >1 point

WE ARE POSITIONED TO DELIVER NEAR-TERM & SUSTAINED GROWTH

WAVE 1

TARGET APPROVAL
FY20
FY21
FY22
FY23
FY24

CLINICAL-STAGE NMEs

ONCOLOGY

TAK-784
2L NSCLC

TAK-924
AML

TAK-573
Multiple cancers

TAK-079
MG, ITP

RARE DISEASES

TAK-620
CMV reinf. in transplant

TAK-609
Hunter CNS (IT)

TAK-531
Hunter CNS

NEUROSCIENCE

TAK-954
POGD

TAK-951
Orexin2-R agonist

TAK-724
EoE

GASTRO-ENTEROLOGY

TAK-214
Zika Vaccine

VACCINES

TAK-003
Dengue Vaccine

WE ARE POSITIONED TO DELIVER NEAR-TERM & SUSTAINED GROWTH

WAVE 2

FY25 AND BEYOND

PLATFORMS

CELL THERAPY AND IMMUNE ENGAGERS

TARGETED IMMUNE MODULATION

NEXT-GEN CHECKPOINT MODULATORS

WAVE 1

WEAVE 11

TAK-788
R/R MM

WEAVE 22

WAVE 2

TAK-924
AML

TAK-531
Hunter CNS

1. Estimated dates as of November 14, 2019
2. Projected timing of approvals depending on data read-outs; some of these Wave 1 target approval dates assume accelerated approval
3. Some Wave 1 assets could be accelerated into Wave 2 if they have breakthrough data
4. Projected approval date assumes filing on Phase 2 data
5. TAK-079 to be developed in Rare Diseases indications myasthenia gravis (MG) and immune thrombocytopenic purpura (ITP) (FPI projected in each indication in 2H FY19)
6. Orphan potential in at least one indication

2020
Entyvio IV GvHD Ph3 readout

2021
Entyvio IV CN approval


IBD: Inflammatory Bowel Disease; UC: ulcerative colitis; CD: Crohn's Disease; IV=intravenous; SC=subcutaneous; TNF=tumour necrosis factor; SoC: standard of care; CN: China; JP: Japan; GvHD: graft versus host disease;

Clinical remission: Complete Mayo score of ≤2 points and no individual subscore >1 point

1. Projected timing of approvals depending on data read-outs; some of these Wave 1 target approval dates assume accelerated approval
2. Some Wave 2 assets could be accelerated into Wave 1 if they have breakthrough data
3. Projected approval date assumes filing on Phase 2 data
4. TAK-079 to be developed in Rare Diseases indications myasthenia gravis (MG) and immune thrombocytopenic purpura (ITP) (FPI projected in each indication in 2H FY19)
5. Orphan potential in at least one indication

Estimated dates as of November 14, 2019
**TAK-721: ON TRACK TO BE THE FIRST FDA APPROVED AGENT TO TREAT EOSINOPHILIC ESOPHAGITIS (EOE)**

**ADDRESSES SIGNIFICANT UNMET NEED**

- Chronic, allergic, inflammatory condition of the esophagus that results in swallowing dysfunction
- Diagnosed prevalence is expected to increase significantly

No approved US medication  
SOC is food elimination, off-label use

TAK-721 granted breakthrough therapy designation by FDA in 2016

**EXPECTED MILESTONES (FY)**

<table>
<thead>
<tr>
<th>2019</th>
<th>2020</th>
<th>2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q4: Maintenance TL results</td>
<td>Q2: NDA filing</td>
<td>Q1: Launch</td>
</tr>
</tbody>
</table>

**INDUCTION DATA SHOWS SIGNIFICANT HISTOLOGIC AND SYMPTOM RESPONSE**

Results presented at presidential plenary at ACG, Texas, Oct 2019

**Histologic Response at 12 Weeks** (peak ≤ 6 eosinophils/hpf on biopsy)

<table>
<thead>
<tr>
<th>Proportion of patients (%)</th>
<th>0</th>
<th>20</th>
<th>40</th>
<th>60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (n = 105)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 mg BID (n = 213)</td>
<td>1.0%</td>
<td>53.1%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Symptom Response at 12 Weeks** (≥ 30% reduction in DSQ score)

<table>
<thead>
<tr>
<th>Proportion of patients (%)</th>
<th>0</th>
<th>20</th>
<th>40</th>
<th>60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (n = 105)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 mg BID (n = 213)</td>
<td>39.1%</td>
<td>52.6%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. Swallowed use of glucocorticoids intended for asthma (e.g., home or compounded thickening of budesonide solution, or swallowing fluticasone aerosol).

**TAK‐721 granted breakthrough therapy designation by FDA in 2016**

**EXPECTED MILESTONES (FY)**

<table>
<thead>
<tr>
<th>Q4: Maintenance TL results</th>
<th>Q2: NDA filing</th>
<th>Q1: Launch</th>
</tr>
</thead>
</table>

**CELIA DISEASE IS AN EXAMPLE OF A HIGH UNMET NEED AREA WITH NO THERAPIES**

**Global population affected by celiac**

~1%

**Patients still suffer from symptoms despite being on a gluten-free diet**

~40%

**Estimated global, eligible patient population**

~1M

- Overlooked disease, growing prevalence
- Chronic symptoms
- Higher risk of certain cancers
- High treatment burden affecting the whole family
- No current pharmacologic therapies

---

1. Pooled global prevalence; Clin Gastroenterol Hepatol. 2018 Jun;16(6):823-836
2. Estimated number of patients projected eligible for treatment, in markets where the product is anticipated to be commercialized, subject to regulatory approval

---

"Some of us are so extremely sensitive that one little crumb will make us extremely sick. I’m one of those people, and there is really nothing I can do about it."

– Delisi, Celiac disease patient
WE ARE FOCUSING ON THE NARROWEST POPULATION WITH HIGH UNMET NEED

**Our focus:**
- Niche patient segment with the highest unmet need
- Severe symptoms with villous atrophy
- Continue to suffer despite the GFD and are highly likely to take a therapy

*Uncontrolled defined as ongoing chronic moderate to severe symptoms with villous atrophy*

---

OUR APPROACH TO TREATING CELIAC DISEASE

**TREATMENT OPPORTUNITIES FOR CELIAC DISEASE**

1. Enzymatic digestion of gluten
2. Reduce intestinal permeability
3. Microbiome modulation
4. Cytokine inhibition
5. Transglutaminase inhibition
6. Promote immune tolerance

**Kuma062** promises greatly increased enzymatic efficiency and improved formulation over predecessors

**TAK-101 (TIMP-GLIA)** has the potential to be a first in class, tolerizing immune therapy for celiac disease

*Source: Green and Cellier, 2007*
KUMA062: A HIGHLY POTENT ORAL GLUTENASE THAT COULD CHANGE THE STANDARD OF CARE IN CELIAC DISEASE

ABOUT KUMA062

• Kuma062 is an oral, computationally-engineered super glutenase
• Enhanced catalytic activity compared to other glutanases

CLINICAL DATA SHOWS KUMA062 CAN DEGRADE >95% OF INGESTED GLUTEN

Gluten recovery in gastric contents aspirated 30mins after meal containing 3g of gluten

- Kuma well-tolerated, no identified safety concern
- Decision to acquire PVP Biologics expected Q3 FY2019

TAK-101: POTENTIAL BEST-IN-CLASS, INTRAVENOUS THERAPY FOR CELIAC DISEASE DESIGNED TO MODIFY T CELL RESPONSE

ABOUT TAK-101*

• Biodegradable polymer encapsulating antigen
• Designed to induce tolerance to gluten, reduce T cell responses to gliadin

TAKEDAC ACQUIRED EXCLUSIVE GLOBAL LICENSE TO TAK-101

*Formerly TIMP-GLIA
Source: https://www.courpharma.com/our-technology/
WE ARE LEADING THE SCIENCE IN CELIAC DISEASE WITH A NEW AI-BASED TOOL AND INGESTIBLE DEVICE

PIONEERING AT BOUNDARIES OF CLINICAL MEDICINE

- Innovative, non-invasive, patented method of measuring total burden of intestinal disease

INNOVATIVE USE OF TECHNOLOGY

- Ingestible high resolution camera pill
- Modern machine-learning/AI based image processing

PRECISION MEASUREMENT USING AI

- Pioneering Automated Image assessment quantifies disease burden

TAKEDA IS THE BEST COMPANY TO BRING CELIAC THERAPIES TO PATIENTS

World-class, fully connected GI commercial infrastructure across 65+ countries that supports $6bn+ revenues

- Extensive GI clinical footprint
- Strong reputation for scientific excellence
- Lauded for calculated risk-taking by the GI community
- Experience with redefining guidelines and treatment paths
NME MILESTONES ACHIEVED IN FY19 AND LOOKING AHEAD TO OTHER POTENTIAL MILESTONES\(^1\) THROUGH FY20

<table>
<thead>
<tr>
<th>PIVOTAL STUDY STARTS, APPROVALS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1H FY 2019</strong></td>
</tr>
<tr>
<td>TAK-621</td>
</tr>
<tr>
<td>TAK-755</td>
</tr>
<tr>
<td>TAK-721</td>
</tr>
<tr>
<td>TAK-101</td>
</tr>
<tr>
<td>PEVONEDISTAT</td>
</tr>
<tr>
<td>TAK-924</td>
</tr>
<tr>
<td>TAK-925</td>
</tr>
<tr>
<td>TAK-721</td>
</tr>
<tr>
<td>TAK-101</td>
</tr>
</tbody>
</table>

**KEY DATA READOUTS**

1. Potential key milestone dates as of November 14, 2019. The dates included herein are estimates based on current data and are subject to change.
2. Potentially registration enabling

---

**SUMMARY**

1. We have built an industry-leading portfolio rooted in unparalleled scientific excellence and outstanding global commercial strength.
2. We are well positioned to bring the first therapies to celiac patients that could change the standard of care.
3. We have multiple milestones, including expected key approvals in the next 2 years that will be transformative for patients.