THERAPEUTIC AREA FOCUS IN GI WITH SPOTLIGHT ON CELIAC DISEASE

Asit Parikh, MD, PhD
Head Gastroenterology Therapeutic Area Unit
Takeda Pharmaceutical Company Limited
New York, NY
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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
- 18.2 Acid related diseases
- 12.6 GI Cancers
- 12.2 Other GI
- 3.9 GI inflammation
- 6.5 Viral hepatitis
- 0.3 Liver fibrosis
- 2.9 GI motility

**TAKEDA GI DISEASE AREAS**

- GI inflammation
- GI motility
- Liver fibrosis
- Acid related diseases

SOURCE: EvaluatePharma 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

EXPANDED 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

GEOGRAPHIC EXPANSION

Entyvio IV
- Approved in 68 countries
- Launched in Japan (UC: Nov 2018, CD: May 2019)

EXPECTED MILESTONES (FY)


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

TARGET APPROVAL

WAVE 1

CLINICAL-STAGE NMEs

WAVE 2

PLATFORMS

ONCOLOGY

TAK-788
2L NSCLC

TAK-924
AML

TAK-076
Hematologic malignancies

TAK-164
GI malignancies

TAK-252
Solid tumours

TAK-778
2L NSCLC

TAK-981
Multiple cancers

TAK-611
MCL (IT)

TAK-754
ITP

TAK-531
Hunter CA

TAK-755
cITP

TAK-079
MGI, ITP

TAK-755
cITP

TAK-924
DLE

TAK-015
Thrombosis

TAK-069
CNS (IT)

TAK-418
Kabuki Syndrome

TAK-104
CNS (IT)

TAK-341
Parkinson’s Disease

TAK-531
Hunter CNS

TAK-935
DLE

TAK-653
TMD

TAK-021
Endometriosis

TAK-117
Sleep Disorders

TAK-671
Acute Renal Failure

TAK-954
POD

TAK-906
Gastroenteritis

TAK-214
Neuralgia

TAK-426
Zika Vaccine

RARE DISEASES

Immunology

TAK-620
CMV reject. in Transplant

TAK-609
Hunter CNS (IT)

NEUROSCIENCE

Kuma062
Celiac Disease

TAK-003
Dengue Vaccine

GASTRO-ENTEROLOGY

TAK-721
EoE

TAK-214
Neuralgia

VACCINES

Estimated dates as of November 14, 2019

Source: Wave 1 clinical-stage NMEs

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)
TAK-721: ON TRACK TO BE THE FIRST FDA APPROVED AGENT TO TREAT EOSINOPHILIC ESOPHAGITIS (EOE)

ADRESSES 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) 2019 2020 2021
Q4: Maintenance TL results Q2: NDA filing Q1: Launch

INDUCTION DATA SHOWS SIGNIFICANT HISTOLOGIC AND SYMPTOM RESPONSE

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

<table>
<thead>
<tr>
<th>Proportion of patients (%)</th>
<th>Placebo (n = 105)</th>
<th>2 mg BID (n=213)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0%</td>
<td>1.0%</td>
<td>53.1%</td>
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</table>

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

<table>
<thead>
<tr>
<th>Proportion of patients (%)</th>
<th>Placebo (n = 105)</th>
<th>2 mg BID (n=213)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0%</td>
<td>39.1%</td>
<td>52.6%</td>
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</table>

p < 0.001
p = 0.024

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

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

2. Estimated number of patients projected eligible for treatment, in markets where the product is anticipated to be commercialized, subject to regulatory approval

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

Global population affected by celiac

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

Estimated global, eligible patient population

~1% ~40% ~1M

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

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

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
WE ARE FOCUSING ON THE NARROWEST POPULATION WITH HIGH UNMET NEED

- **40%** Uncontrolled* on GFD
- **60%** Controlled on Gluten Free Diet (GFD)

**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

Source: Green and Cellier, 2007

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
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 glutenases

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

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

- Placebo (n=13)
- 900mg Kuma062 (n=12)
- 900mg Kuma062 + Nexium (n=13)

- 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

• Expected to provide durable (3 months or longer) down regulation of T cell responses to immunogenic gliadin peptides

TAK-101 REDUCES IMMUNE ACTIVATION AFTER GLUTEN EXPOSURE

Interferon-gamma ELISPOT measurement of gluten-responsive T cells

- Placebo n=16
- TIMP-GLIA n=13

Treatment with TAK-101 reduced immune activation by >85%

*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

PIioneerIng 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

PIVOTAL STUDY STARTS, APPROVALS

**1H FY 2019**
- **TAK-621**: MDL Ph 2 start
- **TAK-755**: ITP Ph 3 start
- **PEVONEDISTAT**: ANL Ph 3 start
- **TAK-788**: tMLD GC Ph 3 start

**2H FY 2019**
- **TAK-925**: Neurology POC
- **TAK-721**: Eot Ph 3 data (induction)
- **TAK-101**: AAA Disease POC
- **PEVONEDISTAT**: tMLD Ph 2 Overall Survival
- **TAK-607**: Inm. Malignancies POC
- **TAK-609**: Urea Ph 3 data 2yr extension

**1H FY 2020**
- **TAK-788**: tMLD GC Ph 2 Pivotal
- **TAK-573**: R/R-MM, Solid Tumor POC

**2H FY 2020**
- **TAK-721**: Eot Approval
- **mHTT ASO**: Huntington’s Disease Pivotal start
- **TAK-620**: R/R CMV SOT & HSCT Ph 3 data
- **TAK-788**: 1L NSCLC Ph 3 start
- **TAK-925**: Narcolepsy POC
- **TAK-721**: Eot Ph 3 data (maintenance)

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**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.

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**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.
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<thead>
<tr>
<th>TIME</th>
<th>AGENDA</th>
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<tbody>
<tr>
<td>12:30 – 12:35</td>
<td>Welcome and Opening Remarks</td>
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<tr>
<td></td>
<td>Sheelagh Cowley-Knopf, Head R&amp;D Global Portfolio Strategy</td>
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<tr>
<td>12:35 – 12:45</td>
<td>Takeda: A Global Values-Based, R&amp;D-Driven Biopharmaceutical Leader</td>
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<tr>
<td></td>
<td>Christophe Weber, President &amp; CEO Takeda</td>
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<tr>
<td>12:45 – 13:20</td>
<td>Translating Science into Highly Innovative, Life-changing Medicines</td>
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<tr>
<td></td>
<td>Andy Plump, President R&amp;D</td>
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<tr>
<td>13:20 – 13:45</td>
<td>Oncology and Cell Therapies with Spotlight on CAR-NK</td>
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<tr>
<td></td>
<td>Chris Arendt, Head Oncology Drug Discovery Unit</td>
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<td>13:45 – 14:05</td>
<td>Spotlight on Oncology Opportunities</td>
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<tr>
<td></td>
<td>• TAK-788 : Rachael Brake, Global Program Lead</td>
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<td></td>
<td>• Pevonedistat : Phil Rowlands, Head Oncology Therapeutic Area Unit</td>
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<td>14:05 – 14:20</td>
<td>Break</td>
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<td>14:20 – 14:45</td>
<td>Rare Diseases &amp; Gene Therapy</td>
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<td>Dan Curran, Head Rare Disease Therapeutic Area Unit</td>
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<td>14:45 – 15:00</td>
<td>Spotlight on Orexin2R agonists</td>
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<td>Deborah Hartman, Global Program Lead</td>
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<tr>
<td>15:00 – 15:20</td>
<td>Therapeutic Area Focus in GI with Spotlight on Celiac Disease</td>
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<td>Asit Parikh, Head GI Therapeutic Area Unit</td>
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<tr>
<td>15:20 – 16:00</td>
<td>Panel Q&amp;A Session</td>
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<tr>
<td>16:00</td>
<td>Drinks reception</td>
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