WE ARE A LEADING GI COMPANY

GASTROENTEROLOGY

OUR VISION
Restore Life to Living for patients suffering with GI and liver diseases

OUR MISSION
Deliver innovative, life-changing therapeutics for patients with GI and liver diseases
OUR STRATEGY EXPANDS THE PORTFOLIO ACROSS CORE DISEASE AREAS SUPPORTED BY PLATFORM TECHNOLOGIES

**IBD**
- Build upon success of Entyvio with new formulations
- Expand treatment options with Alofisel

**Celiac disease**
- Advance approaches for the prevention of immune responses to gluten

**Motility disorders**
- Focus on select high unmet medical need areas including gastroparesis and enteral feeding intolerance

**Liver diseases**
- Target early-stage investments in liver fibrosis

**Luminal platforms**
- Accelerate microbiome investments
- Invest in selective drug delivery technologies

Acid related diseases franchise will continued to be supported, but new pipeline investment will be deprioritized relative to above disease areas.

Abbreviations: IBD, Inflammatory Bowel Disease e.g., Ulcerative Colitis, Crohn’s disease

WE ARE EXECUTING ON OUR STRATEGY THROUGH A RICH, DIVERSIFIED PIPELINE FUELED BY STRONG EXTERNAL PARTNERSHIPS

<table>
<thead>
<tr>
<th>Discovery/preclinical*</th>
<th>Phase 1</th>
<th>Phase 2</th>
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Abbreviations: IBD, Inflammatory Bowel Disease e.g., Ulcerative Colitis (UC), Crohn’s disease (CD); SC, Subcutaneous; PPI, Proton pump inhibitor
WE ARE BUILDING ON THE SUCCESS OF ENTYVIO TO ADDRESS CONTINUED UNMET NEED IN IBD PATIENTS

Geographic expansion
New formulations
Expanded patient populations
New evidence generation

Abbreviations: IBD, Inflammatory Bowel Disease e.g., Ulcerative Colitis, Crohn’s disease

WE ARE CONTINUOUSLY IMPROVING THE VALUE OF ENTYVIO FOR PATIENTS

GEOGRAPHIC EXPANSION
• Japan NDA approval for UC
• Potential China approval in FY2020*
• Approved in 58 countries**
• Nearly 90,000*** IBD patients treated

NEW FORMULATIONS
ENTYVIO SUBCUTANEOUS
• Positive topline results from VISIBLE UC trial; filing Q4 FY2018 in US for UC, and in EU for both UC and CD
• Anticipate readout in H2 FY2019 from VISIBLE CD

EXPANDED PATIENT POPULATIONS
• GvHD prophylaxis Ph3 first patient expected Dec 2018
• GvHD prophylaxis Ph3 readout expected H1 FY2021
Phase 1b data (N = 21): 6 month incidence of intestinal aGVHD*  

* On Aug 8th 2018, a total of 48 products marketed outside of China were selected by the CDE based on urgent medical needs, companies are encouraged to apply for NDA with overseas data including data demonstrating lack of ethnic differences. Priority review/approval process will be applied.
** As of April 2018
*** As of FY 2017

* The safety profile of Entyvio in the GvHD patient population remains unchanged and is consistent with the approved US labelling
** Adjusted for patient population including allogeneic stem cell transplant characteristics with similar conditioning regimen

Abbreviations: IBD, Inflammatory Bowel Disease e.g., Ulcerative Colitis (UC), Crohn’s disease (CD); aGVHD, Acute Graft vs. Host Disease
ENTYVIO CONTINUES TO DELIVER AGAINST UNMET NEED FOR PATIENTS

NEW EVIDENCE GENERATION

MUCOSAL HEALING IN CROHN’S DISEASE – PREVIOUSLY A GAP FOR ENTYVIO

Vedolizumab can induce endoscopic remission and complete mucosal healing over 26 weeks of treatment1 at levels comparable to other biologic therapies

3 References for the VICTORY Consortium Studies:
Böhme et al—CD propensity; [https://academic.oup.com/ecco-jcc/article/12/supplement_1/S018/4807655](https://academic.oup.com/ecco-jcc/article/12/supplement_1/S018/4807655)
Faleck et al—UC propensity; [https://academic.oup.com/ecco-jcc/article/12/supplement_1/S019/4807661](https://academic.oup.com/ecco-jcc/article/12/supplement_1/S019/4807661)

Abbreviations: SES-CD, Simple Endoscopic Score for CD; TNFα, tumor necrosis factor alpha.

OTHER DATA

- Head-to-head vs. adalimumab readout expected in H1 FY2019
- Long-term safety data published in Gut2
- Real world propensity score matched analyses by the VICTORY Consortium3 tended favorable to superior profile for Entyvio vs. anti-TNFs

ALOFISEL: FIRST AND ONLY APPROVED (EU) MESENCHYMAL STEM CELL THERAPY FOR FISTULIZING CROHN’S DISEASE

ADDRESSES THE HIGHEST UNMET NEED IN IBD, PERIANAL CROHN’S

- ~5% of Crohn’s patients experience perianal fistulas, resulting in drainage, pain, and multiple surgeries
- Biologic therapies do not address the depth of unmet need
- Patients experience an average of 4 medical treatments and 5.4 surgeries with >50% failure rate and risk of permanent fecal incontinence
- Patient anxiety regarding maintenance of bodily function, shame, fear of unknown and depression
- ADMIRE-2 Phase 3 study for US registration ongoing in EU/Israel, first US patient expected Q1 FY2019

CX601 MEANINGFULLY IMPROVES STANDARD OF CARE IN ACHIEVING REMISSION (52 WK)*

<table>
<thead>
<tr>
<th>Control group (Placebo + SOC; n=101)</th>
<th>CX601 group (Cx601 + SOC; n=103)</th>
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<tbody>
<tr>
<td>COMBINED** REMISSION</td>
<td>CLINICAL REMISSION</td>
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<tr>
<td>38.6%</td>
<td>41.6%</td>
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<td>56.30%</td>
<td>59.20%</td>
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</table>

(95% CI): 17.7% (4.2-31.2)p=0.010 (95% CI): 17.6% (4.1-31.1)p=0.013

* Panes J, et al., Gastroenterology. Published online 18th December 2017.
** Combined = clinical + radiologic.
Abbreviations: SOC, Standard of care.
TAK-906: DISTINCTIVE MECHANISM OF ACTION (ORAL D2/D3 RECEPTOR ANTAGONIST) THAT FILLS A LARGE UNMET NEED IN GASTROPARESIS

CURRENT THERAPIES DO NOT MEET THE SIGNIFICANT UNMET NEED IN GASTROPARESIS

- Gastroparesis affects ~45M people globally
- Key symptoms are nausea, vomiting
- No drug approved in the US to treat all forms of gastroparesis, inadequate options elsewhere

TAK-906: PHASE 2A STUDY DEMONSTRATES TARGET ENGAGEMENT AND ENABLES DOSE SELECTION

- No QTc prolongation in Healthy Volunteer study
- No QTc prolongation or drug-related neurological AEs in Phase 2a study in GP patients*
- Phase 2b dose-range finding study expected to initiate in Q4 2018

Abbreviations: AE, Adverse event; HV, healthy volunteer; GP, Gastroparesis

* Other AEs observed in Phase 2a study not related to TAK-906 administration included a case of tremor in a subject with history of depression, anxiety, T2DM and Neurontin use. Also, acute kidney insufficiency in a patient with urinary tract infection and in a patient with prior chronic renal failure.

KUMA062: A HIGHLY POTENT ORAL GLUTENASE THAT COULD CHANGE THE STANDARD OF CARE IN CELIAC DISEASE

CELIAC DISEASE

- Affects ~1% of the population, rising prevalence
- Triggered by exposure to omnipresent gluten peptides
- Manifests via immune reaction in gut causing distressing symptoms
- Only existing treatment is a gluten free diet (GFD)

GLUTEN RECOVERY FROM RAT STOMACHS 30MINS AFTER DIGESTION OF A HIGH-GLUTEN BREAD SLURRY

- Kuma062 is a computationally engineered super glutenase
- Proof-of-mechanism (POM) study enabling go/no-go decision initiated July 2018, readout anticipated H1 FY2019

Abbreviations: POM, Proof of mechanism

References:
1. Pooled global prevalence; Clin Gastroenterol Hepatol. 2018 Jun;16(6):823-836

As little as 50-100mg of gluten exposure per day can trigger celiac disease

% Gluten Degraded

99.67% 99.72% >99.9%
WE HAVE STRENGTHENED OUR COMMITMENT TO ADDRESSING LIVER DISEASES THROUGH EARLY RESEARCH PARTNERSHIPS

TARGETING LIVER FIBROSIS PREVENTION AND REVERSAL THROUGH NEW PLATFORMS, NEW PROJECTS AND BUSINESS DEVELOPMENT FOCUSED ON PERI-IND OPPORTUNITIES

**Abbreviations:** MOA, Mechanism of action

Human cell system for new target identification and validation for liver fibrosis

Liver-targeted delivery of nucleotide therapeutics with anti-fibrotic MOAs

Takeda co-founded with Third Rock Ventures to focus on cell and gene therapy for end-stage liver diseases

*Series A announced August 2018*

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**EXPECTED KEY GI PORTFOLIO INFLECTIONS AND MILESTONES**

Dates in fiscal year (FY) starting April 1st

<table>
<thead>
<tr>
<th>Timeframe</th>
<th>Events</th>
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<tbody>
<tr>
<td>2H FY 2018</td>
<td>TAK-906 (Gastroparesis) Ph2b start</td>
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<tr>
<td>1H FY 2019</td>
<td>Kuma062 (Celiac disease) US Ph3 FSI; Entryvio H2H with adalimumab Ph3 readout; TIMP-GLIA (Celiac disease) Ph1 readout; Alofasel (Perianal Crohn’s) US Ph3 FSI</td>
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<tr>
<td>2H FY 2019</td>
<td>TAK-438 (Acid disorders) Flash results from H2H with Esomeprazole</td>
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<tr>
<td>FY 2020</td>
<td>Entryvio (SC UC) JAPAN FILING; TAK-954 (EFI) Ph2b complete; Entryvio (SC UC) US FILING; TAK-906 (Gastroparesis) Ph2b complete</td>
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<td>Entyvio (IV CD) JAPAN LAUNCH; Entryvio (SC CD) US Ph3 readout</td>
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<td>Entryvio (SC UC) JAPAN FILING</td>
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**Abbreviations:** FSI, First subject in; SC, Subcutaneous; IV, Intravenous; UC, Ulcerative colitis; CD, Crohn’s disease; GvHD, Graft vs. host disease; POM, Proof of mechanism; EFI, Enteral feeding intolerance; H2H, head to head.

Projected timelines as of September 23, 2018, subject to change.
## CONCLUSION

1. Maximizing the potential of ENTYVIO and delivering ALOFISEL to global markets
2. Progressing several early to mid-stage assets including TAK-906 for gastroparesis and KUMA062 for celiac disease
3. Continuing to capture opportunities early through industry-leading scientific talent, sophisticated in-house evaluation capabilities and rapid decision-making