ORIENTATION TO OUR ONCOLOGY R&D OVERVIEW

**Focused Oncology R&D Strategy**
- Building on foundational expertise in hematologic malignancies and a growing portfolio in lung cancer

**Novel Discovery Strategy in Immuno-Oncology (I/O) and Advance in Cell Therapies**
- Pursuing novel I/O targets and next-generation platforms with world class external partners
- Next-generation cell therapies will bring transformative potential to patients with cancer

**Near Term Inflections**
- FY2018-FY2020 will be highlighted by several submissions, approvals, pivotal trial starts, and novel assets entering clinical trials
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WE ASPIRE TO CURE CANCER

OUR MISSION
We endeavor to deliver novel medicines to patients with cancer worldwide through our commitment to science, breakthrough innovation, and passion for improving the lives of patients.
BUILDING ON THE TAKEDA ONCOLOGY FOUNDATION IN HEMATOLOGIC MALIGNANCIES

GROWING LEADERSHIP POSITION IN HEMATOLOGIC MALIGNANCIES

Next Generation I/O

- TAK-573
- TAK-981

MDS
- Phase 3
- pevonedistat

AML
- Phase 3
- alisertib

Lymphoma
- Chronic Myeloid Leukemia

Improved Patient Outcomes in Multiple Myeloma

- ADCETRIS® brentuximab vedotin
- ICLUSIG® (ponatinib) tablets

- VELCADE® (bortezomib)
- NINLARO® (ixazomib) capsules
RECENT PROGRESS AND NEXT STEPS

Current Status
Approved in 59 countries for Relapsed/Refractory Multiple Myeloma
First Phase 3 maintenance readout (post-transplant)

Looking Forward
2019 Data Inflections:
MM2 (newly diagnosed)
MM4 (non-transplant maintenance)
AL1 (amyloidosis)
Evolution of real world evidence

Ideal Maintenance Therapies in Multiple Myeloma:
✓ Easy to administer  ✓ Minimal toxicity  ✓ Maintain response

![Diagram showing progression of multiple myeloma stages and therapies.](image-url)
ADVANCE CD38 BIOLOGY FOR REFRACTORY MULTIPLE MYELOMA

**TAK-079**
- A fully human, anti-CD38 cytolytic IgG1 lambda antibody
- Potent and selective reduction of plasmablasts and NK cells
- Potential for convenient subcutaneous delivery
- Currently in Phase 1 for refractory multiple myeloma

**TAK-573**
- Novel immuno-cytokine approach
- Potential to overcome toxicity of unmodified interferon α and realize the true benefit in oncology
- Compelling pre-clinical data; Phase 1 enrolling for patients with refractory multiple myeloma

**TAK-169**
- 2nd generation Molecular Templates platform
- pM activity against CD38+ cells plus activity in daratumumab-resistant cells
- IND planned in 2019
TAK-079: IMPROVING UPON FIRST GENERATION ANTI-CD38 mAb FOR REFRACTORY MULTIPLE MYELOMA PATIENTS

A potent anti-CD38 mAb administered as a low volume subcutaneous (SC) injection

![Graphs showing Plasmablast depletion and NK cell depletion](image)

* After a single SC injection of 0.6 mg/kg into healthy volunteers (n=6)

Novel pharmacokinetic properties enhance potency and enable convenient administration
BRINGING NOVEL THERAPIES TO MDS AND AML

PEVONEDISTAT IN HR-MDS

1 in 3 MDS patients will progress to AML

Overall survival 1-1.5 years in the relapse setting

No new therapies in the last decade

Phase 3 trial initiated in 2018

ALISERTIB IN AML

AML: Current 5 year survival ~30%

Transplant remains only curative option

American Society of Hematology
ASH 2018: Phase 2 Data Submitted

• Alisertib is a novel, first in class mechanism for front-line AML in combination with chemotherapy

• Exploring initiation of Phase 3 registration enabling study in frontline AML in 2019

Unmet Need

Clinical Status

Next Steps

1 in 3 MDS patients will progress to AML

Overall survival 1-1.5 years in the relapse setting

No new therapies in the last decade

Phase 3 trial initiated in 2018

Potential accelerated filing based upon Phase II data in 2019

DUAL STRATEGY IN LUNG CANCER: TARGETING DRIVER MUTATIONS AND NEXT-GENERATION I/O

Molecularly-Targeted Precision Therapy

Tumor Mutational Burden

CURRENT PORTFOLIO

EMERGING ASSETS

Sapanisertib (TAK-228)

Next-generation kinase inhibitors

TAK-788

NEXT GENERATION TARGETS AND PLATFORM

SHATTUCK LABS

Crescendo biologics
ALUNBRIG ALTA 1L—POTENTIAL BEST-IN-CLASS PROFILE IN ALK+ NSCLC

- Primary endpoint hazard ratio compelling relative to competition
- Risk/benefit profile consistent with the expectations of a best-in-class therapy
  - Primary endpoint (PFS) hazard ratio is 0.49
  - Clear superiority to crizotinib and early separation in PFS curve
  - Risk/benefit profile consistent with the expectations of a best-in-class therapy

Camidge R., WCLC 2018
TAK-788: ADDRESSING UNMET NEED IN EGFR EXON20 MUTATIONS

**RESPONSE TO CURRENT EGFR TKIs in EXON 20 INSERTIONS**

- **Median PFS**
  - EGFR Ex20 insertion (N=9): 2 months
  - Classical EGFR mut (N=129): 14 months

**Percent Survival**

- HR = 12.3
- p < 0.0001

**Overall survival <6 months for exon 20 insertions**

**Current therapies ineffective for these mutations**

**ANTITUMOR ACTIVITY IN ALL PATIENTS TREATED WITH TAK-788 AT A TOTAL DAILY DOSE OF ≥80–160 mg**

- **BEST CHANGE IN TARGET LESIONS (%)**
  - EGFR exon 20 insertion mutation
  - HER2 mutation

**Expected to begin registration-enabling Phase 2 trial in FY2018**

Robichaux et al. WCLC 2016

Neal et al., WCLC 2018
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WORLD CLASS PARTNERS FUELING THE I/O PIPELINE

Key Academic Collaborations in CAR-T

Re-directed immunity

Targeted payloads

Tumor micro-environment

- Memorial Sloan Kettering Cancer Center (2018)
- HaemaLogix (2017)
- Noile-Immune Biotech
- Shattuck Labs Heidelberg Pharma
- Gamma Delta Therapeutics Maverick Therapeutics
- Teva Crescendo Biologics Mersana Therapeutics

NOILE-IMMUNE BIOTECH
GAMMADELTA THERAPEUTICS
MAVERICK THERAPEUTICS
HaemaLogix
Heidelberg PHARMA
Mersana THERAPEUTICS
Teva
TAK-573: BRINGING A NOVEL IMMUNO-CYTOKINE APPROACH TO MULTIPLE MYELOMA

Targeted delivery of attenuated interferon α to CD38 - a known target in multiple myeloma

Binds to CD38

Human IgG4 Fc

Attenuated IFNα2b with 2 point mutations

NCI-H929 Myeloma Model

Highly compelling pre-clinical data with TAK-573 in a core area of our clinical development expertise in multiple myeloma

Ph 1 currently enrolling for patients with refractory multiple myeloma

Pogue et al. PLOS ONE 2016
TAKEDA ONCOLOGY AIMS TO BECOME A LEADER IN CELL THERAPIES

TRANSFORMATIVE POTENTIAL UTILIZING NEXT GENERATION CELL THERAPY PLATFORMS

Cell therapy engine for Takeda R&D

FY2019: Differentiated CAR-Ts in Phase I
FY2020+: Other Hematologic Malignancy and Solid Tumor CAR-Ts

Key Academic Collaborations in CAR-T
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<thead>
<tr>
<th>Discovery/preclinical*</th>
<th>Phase 1</th>
<th>Phase 2</th>
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<th>Approved**</th>
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<tbody>
<tr>
<td><strong>Hematologic</strong></td>
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<td>Malignancies</td>
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<tr>
<td>TAK-169</td>
<td>TAK-579</td>
<td>TAK-659</td>
<td>Pevonedistat</td>
<td>NINLARO</td>
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<tr>
<td>CD38 SLTA</td>
<td>RR MM, SLE</td>
<td>Lymphoma SYK, FLT-3</td>
<td>HR-MDS/AML</td>
<td>Amyloidosis, ND MM,</td>
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<tr>
<td></td>
<td>CD38 mAB</td>
<td>Small Molecule</td>
<td>NEDD 8</td>
<td>R/R MM dara combo,</td>
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<td>Alisertib</td>
<td>Small Molecule</td>
<td>R/R MM Ninlaro/dex,</td>
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<td>AML</td>
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<td>Maint. MM post-SCT</td>
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<td>Small Molecule</td>
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<td>ADCETRIS</td>
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<td>FL HL, FL PTCL, CTCL (JP)</td>
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<td>R/R HL (CN), SALCL (CN)</td>
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<td>CD30 mAB ADC</td>
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<td>ALUNBRRIG</td>
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<td>2L post-crizotinib ALK+NSCLC</td>
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<td>(EU, JP, CN), FL ALK+ NSCLC</td>
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<td>Small Molecule</td>
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<td><strong>Solid Tumors</strong></td>
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<td>Small Molecule</td>
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</tbody>
</table>

**Assets shown in discovery/preclinical and Phases 1-3 explicitly refer to new molecular entities**

**With active development seeking new or supplemental indications, or approvals in new territories**

***In pivotal trial for Japan approval**

Note: Takeda holds the right to develop and commercialize Adcetris in ex-US/Canada. For Niraparib and Cabozantinib, Takeda holds the right to develop and commercialize in Japan and selected Emerging Markets.
EXPECTED KEY ONCOLOGY PORTFOLIO INFLECTION AND MILESTONES

Dates in fiscal year (FY) starting April 1st

ALUNBRIG EU APPROVAL (2L)
ADCETRIS EU/JP APPROVAL (FL)

2H FY 2018

ICLUSIG – Ph+ ALL pivotal start
TAK-788 – EGFR Exon 20 pivotal start
ALUNBRIG 2L Head-to-Head pivotal start
ALUNBRIG 2L Post-2nd Generation TKI pivotal start
Cabozantinib 2L HCC pivotal start (JP)
Cabozantinib 1L RCC pivotal start (JP)
Niraparib Ovarian Cancer pivotal start (JP)

1H FY 2019

ALUNBRIG maintenance post-transplant
US APPROVAL
NINLARO non-transplant maintenance
US APPROVAL
NINLARO newly diagnosed US/EU APPROVAL
Pevonedistat US APPROVAL

ALUNBRIG JP APPROVAL
Niraparib JP APPROVAL
Cabozantinib JP APPROVAL

2H FY 2019

Alisertib – AML pivotal start

FY 2020

Anticipated Pivotal Trial Start
Anticipated Approval

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

<table>
<thead>
<tr>
<th></th>
<th>Focused on delivering the next approvals for NINLARO, ALUNBRIG, and pevonedistat</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Expanding transformative treatment options in our focus areas of hematologic malignancies and lung cancer with alisertib, TAK-788 and novel CD38 targeted mechanisms</td>
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<tr>
<td>3</td>
<td>Harnessing the power of external innovation with a diverse set of world-class partnerships, accelerating novel therapies into the clinic</td>
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<td>Time</td>
<td>Agenda</td>
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<tr>
<td>12:00 – 12:30</td>
<td>Registration and Lunch</td>
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<td>12:30 – 13:10</td>
<td>R&amp;D Transformation, Progress To Date, Future Outlook</td>
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<tr>
<td></td>
<td>Andy Plump</td>
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<td>13:10 – 13:45</td>
<td>Oncology</td>
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<td>Phil Rowlands</td>
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<td>13:45 – 14:05</td>
<td>Gastroenterology</td>
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<td>Asit Parikh</td>
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<td>14:05 – 14:20</td>
<td>Break</td>
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<td>14:20 – 14:40</td>
<td>Neuroscience</td>
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<td>Emiliangelo Ratti</td>
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<td>14:40 – 15:00</td>
<td>Vaccines</td>
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<td>Rajeev Venkayya</td>
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<td>15:00 – 16:05</td>
<td>Looking Ahead</td>
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<td>Andy Plump</td>
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<td>Panel Q&amp;A Session</td>
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<td>16:10 – 17:30</td>
<td>Reception</td>
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</table>
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

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

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

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>
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<th>Phase 2</th>
<th>Phase 3</th>
<th>Approval**</th>
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<td>IBD</td>
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<td>ENTYVIO SC</td>
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<td>UC/CD, JP, China</td>
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<td>SC UC/CD</td>
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<td>GvHD prophylaxis</td>
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<td>Monoclonal antibody</td>
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<td>Alofasol</td>
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<td>Perianal Fistulas, US</td>
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<td>Stem cell therapy</td>
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<td>** With active development seeking new or supplemental indications, or approvals in new territories</td>
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<td>Celiac</td>
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<td>AMITIZA</td>
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<td>EM registration</td>
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<td>Pediatric Constipation</td>
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<td>IBS-C, CIC, OIC</td>
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<td>Small molecule</td>
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<td>Pipeline as of September 23, 2018</td>
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<td>GI Motility</td>
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<td>Liver</td>
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<tr>
<td>Acid disease/Other</td>
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<tr>
<td>Abbreviations: IBD, Inflammatory Bowel Disease e.g., Ulcerative Colitis (UC), Crohn's disease (CD); SC, Subcutaneous; PPI, Proton pump inhibitor</td>
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</table>
WE ARE BUILDING ON THE SUCCESS OF ENTYVIO TO ADDRESS CONTINUED UNMET NEED IN IBD PATIENTS

1. Geographic expansion
2. New formulations
3. Expanded patient populations
4. New evidence generation

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

First and only biologic specifically targeting gut inflammation

First-in-class mesenchymal stem cell therapy for fistulizing 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

NEW FORMULATIONS

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*

<table>
<thead>
<tr>
<th>Entyvio</th>
<th>Historical control**</th>
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<tbody>
<tr>
<td>14%</td>
<td>28%</td>
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<tr>
<td>33% stage 2</td>
<td>67% stage 1</td>
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<td>70% stage 2-4</td>
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* 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
*** For FY 2017

Abbreviations: IBD, Inflammatory Bowel Disease e.g., Ulcerative Colitis (UC), Crohn’s disease (CD); aGvHD, Acute Graft vs. Host Disease
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 treatment\(^1\) at levels comparable to other biologic therapies

<table>
<thead>
<tr>
<th>Patients, %</th>
<th>N=101</th>
<th>N=46</th>
<th>N=55</th>
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<tbody>
<tr>
<td>Complete mucosal healing (absence of ulceration)</td>
<td>15%</td>
<td>24%</td>
<td>7%</td>
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</table>

\(^1\) Head-to-head vs. adalimumab readout expected in H1 FY2019
\(^2\) Long-term safety data published in Gut
\(^3\) Real world propensity score matched analyses by the VICTORY Consortium trended favorable to superior profile for Entyvio vs. anti-TNFs

Abbreviations: SES-CD, Simple Endoscopic Score for CD; TNF\(\alpha\), tumor necrosis factor alpha.
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></th>
<th>COMBINED** REMISSION</th>
<th>CLINICAL REMISSION</th>
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<tbody>
<tr>
<td>Control group</td>
<td>38.6% (95% CI): 17.7% (4.2-31.2) p=0.010</td>
<td>41.6% (95% CI): 17.6% (4.1-31.1) p=0.013</td>
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<tr>
<td>Cx601 group</td>
<td>56.30%</td>
<td>59.20%</td>
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</tbody>
</table>

Control group (Placebo + SOC; n=101)  ■ Cx601 group (Cx601 + SOC; n=103)

20.4% of patients in the Cx601 group vs. 26.5% in the control group experienced treatment related adverse events

* Panés 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

* 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.

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

[Graph showing prolactin concentration over time for Placebo, TAK-906 5 mg, TAK-906 25 mg, and TAK-906 100 mg]
KUMA062: A HIGHLY POTENT ORAL GLUTENASE THAT COULD CHANGE THE STANDARD OF CARE IN CELIAC DISEASE

CELIAC DISEASE

- Affects ~1% of the population\(^1\), 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)

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

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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

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\(^1\) Pooled global prevalence; Clin Gastroenterol Hepatol. 2018 Jun;16(6):823-836
Abbreviations: POM, Proof of mechanism
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

- 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

Abbreviations: MOA, Mechanism of action

*Series A announced August 2018*
EXPECTED KEY GI PORTFOLIO INFLECTIONS AND MILESTONES

Dates in fiscal year (FY) starting April 1st

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.

ENTYVIO (SC UC) US FILING

TAK-906 (Gastroparesis) Ph2b start

TAK-954 (EFI) Ph2b complete

TIMP-GLIA (Celiac disease) Ph1 readout

ENTYVIO (SC UC and SC CD) EU FILING

Alofisel (Perianal Crohn’s) US Ph3 FSI

ENTYVIO (IV CD) JAPAN LAUNCH

Enthyvio (SC CD) US Ph3 readout

ENTYVIO (SC UC) JAPAN FILING

TIMP-GLIA (Celiac disease) Ph1 readout

ENTYVIO (SC UC) EU FILING

2H FY 2018

Kuma062 (Celiac disease) POM readout

Kuma062 (Celiac disease) Ph1 readout

2H FY 2019

Kuma062 (Celiac disease) Ph1 readout

Entyvio H2H with adalimumab Ph3 readout

1H FY 2019

TAK-438 (Acid disorders) Flash results from H2H with Esomeprazole

2H FY 2019

Entyvio (GvHD) Ph3 FSI

Entyvio (GvHD) Ph3 FSI

FY 2020

Entyvio H2H with adalimumab Ph3 readout

REGULATORY FILING OR ANTICIPATED APPROVAL

ANTICIPATED OTHER PIPELINE MILESTONES

Projected timelines as of September 23, 2018, subject to change

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.
**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