

A photograph of two scientists in a laboratory. A woman on the left and a man on the right are both wearing white lab coats and safety glasses. They are smiling and looking at each other. The man is also wearing blue gloves. In the background, there are shelves with various bottles and lab equipment. A semi-transparent white box is overlaid on the bottom left of the image, containing text.

TAKEDA ONCOLOGY

WE ASPIRE TO CURE CANCER

PHILIP ROWLANDS, PHD
Head, Oncology Therapeutic Area

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

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

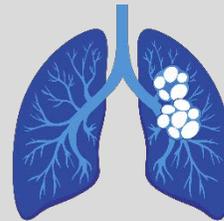
WE ASPIRE TO CURE CANCER

OUR MISSION

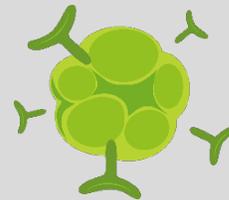
We endeavor to deliver novel medicines to patients with cancer worldwide through our commitment to science, breakthrough innovation, and passion for improving the lives of patients.



HEMATOLOGIC
MALIGNANCIES



LUNG CANCER



IMMUNO-ONCOLOGY (I/O)

BUILDING ON THE TAKEDA ONCOLOGY FOUNDATION IN HEMATOLOGIC MALIGNANCIES



GROWING
LEADERSHIP
POSITION IN
HEMATOLOGIC
MALIGNANCIES

Next Generation I/O



TAK-573



TAK-981

MDS	AML
Phase 3	Phase 3
pevonedistat	alisertib

Lymphoma	Chronic Myeloid Leukemia
 brentuximab vedotin I for injection	 (ponatinib) tablets

Improving Patient Outcomes
in Multiple Myeloma



(bortezomib)



(ixazomib) capsules



Current Status

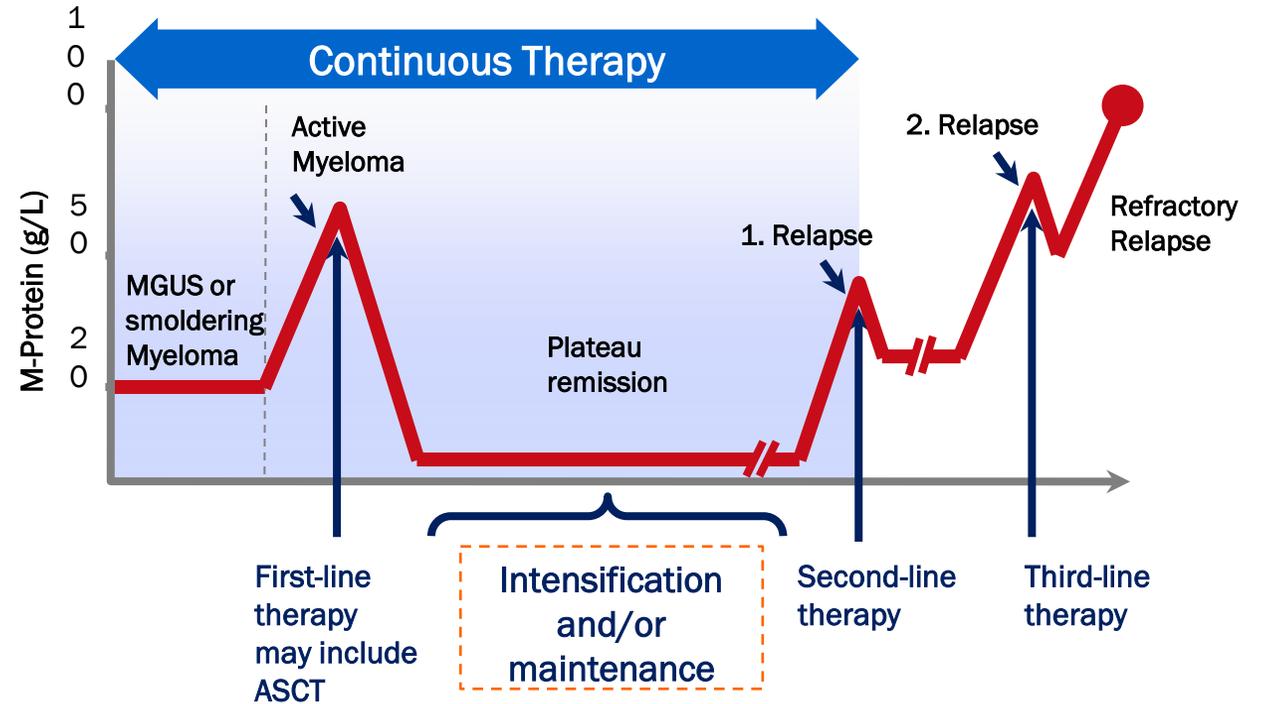
Approved in 59 countries for Relapsed/Refractory Multiple Myeloma
First Phase 3 maintenance readout (post-transplant)

Looking Forward

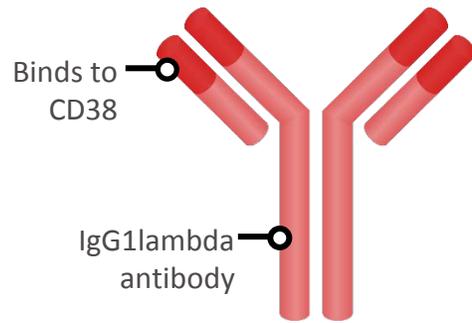
2019 Data Inflections:
MM2 (newly diagnosed)
MM4 (non-transplant maintenance)
AL1 (amyloidosis)
Evolution of real world evidence

Ideal Maintenance Therapies in Multiple Myeloma:

- ✓ Easy to administer
- ✓ Minimal toxicity
- ✓ Maintain response

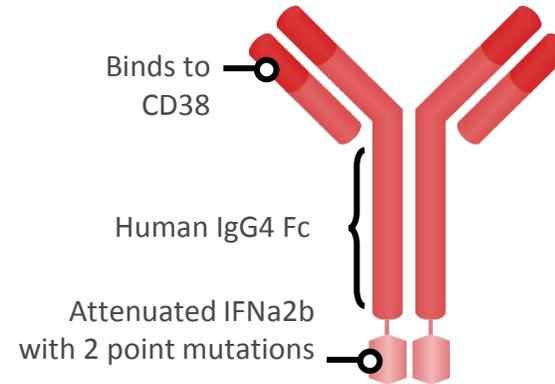


ADVANCE CD38 BIOLOGY FOR REFRACTORY MULTIPLE MYELOMA



TAK-079

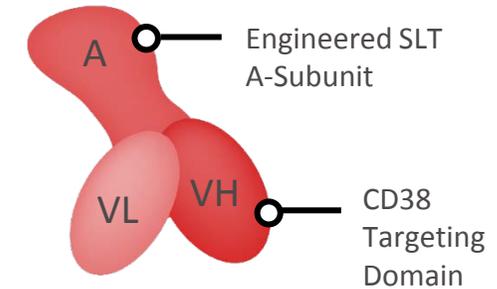
- A fully human, anti-CD38 cytolytic IgG1lambda antibody
- Potent and selective reduction of plasmablasts and NK cells
- Potential for convenient subcutaneous delivery
- Currently in Phase 1 for refractory multiple myeloma



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

Engineered Toxin Bodies



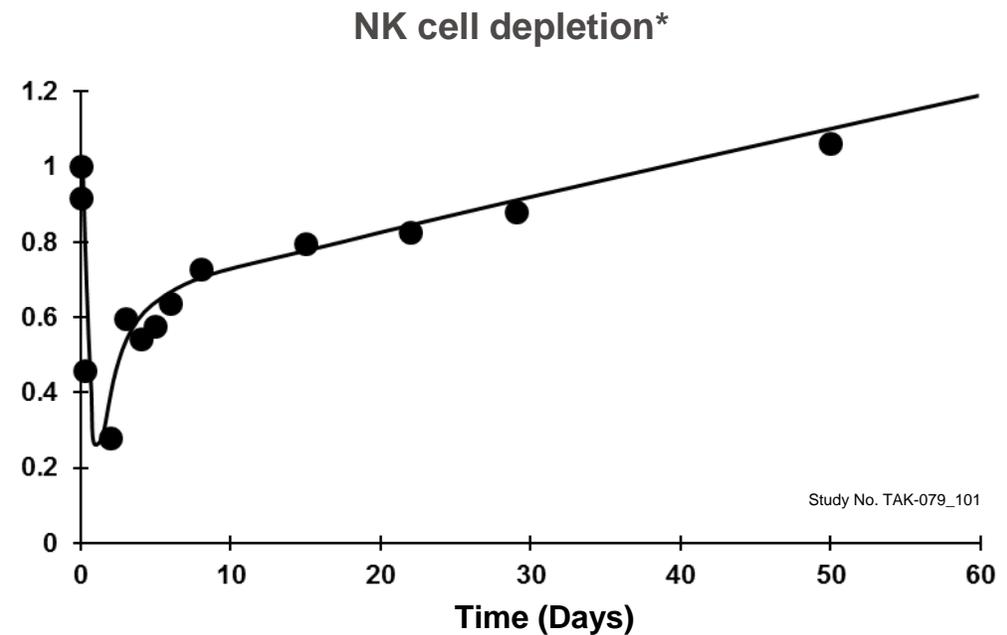
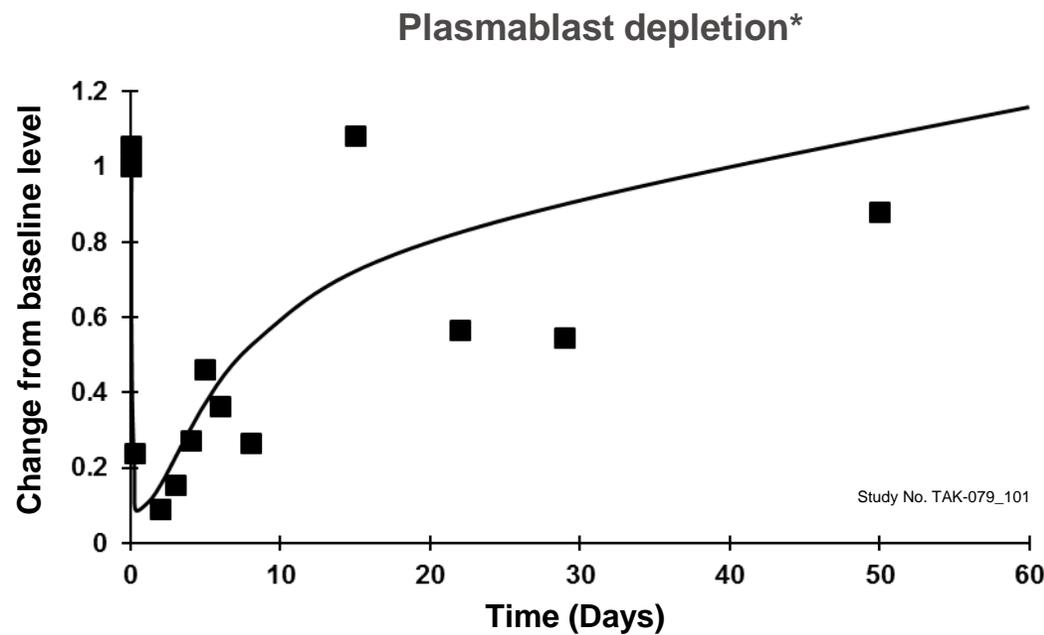
TAK-169

- 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



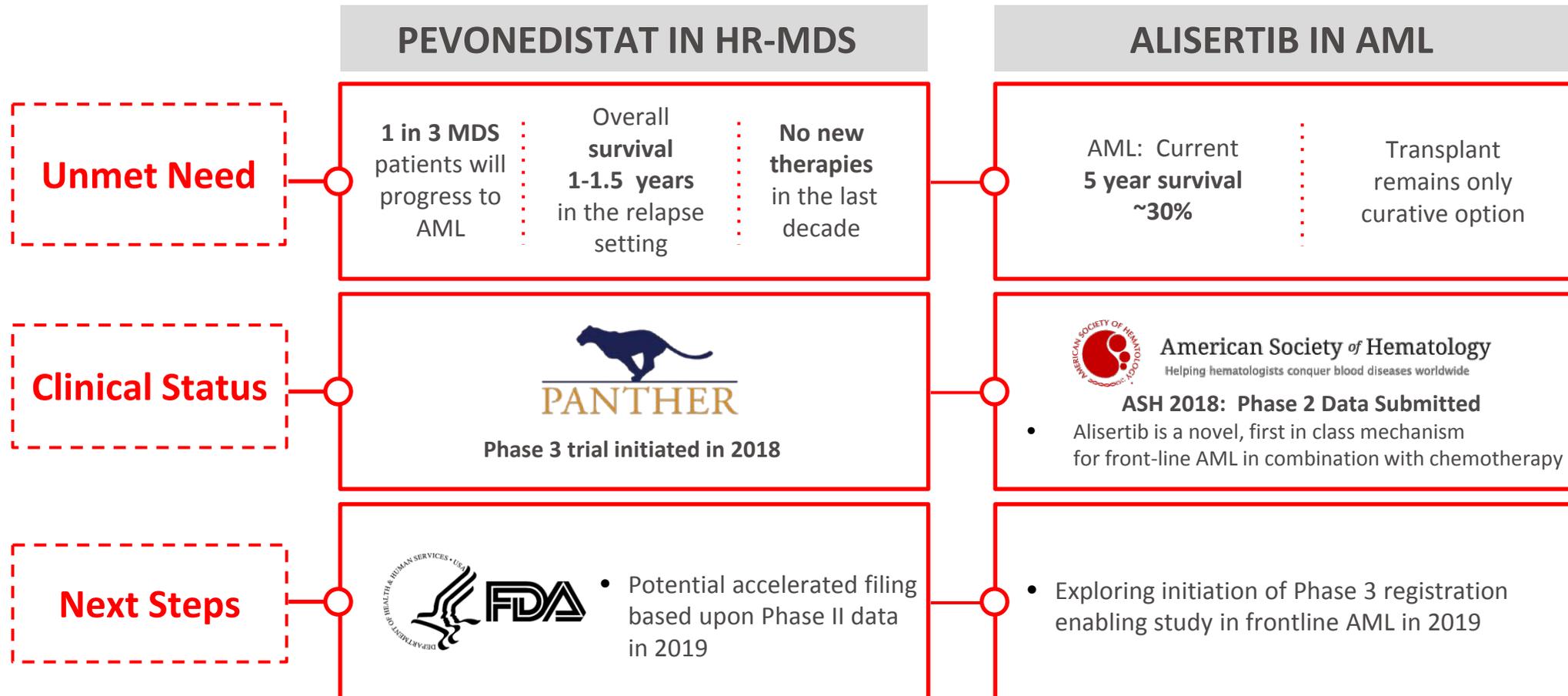
A potent anti-CD38 mAb administered as a low volume subcutaneous (SC) injection



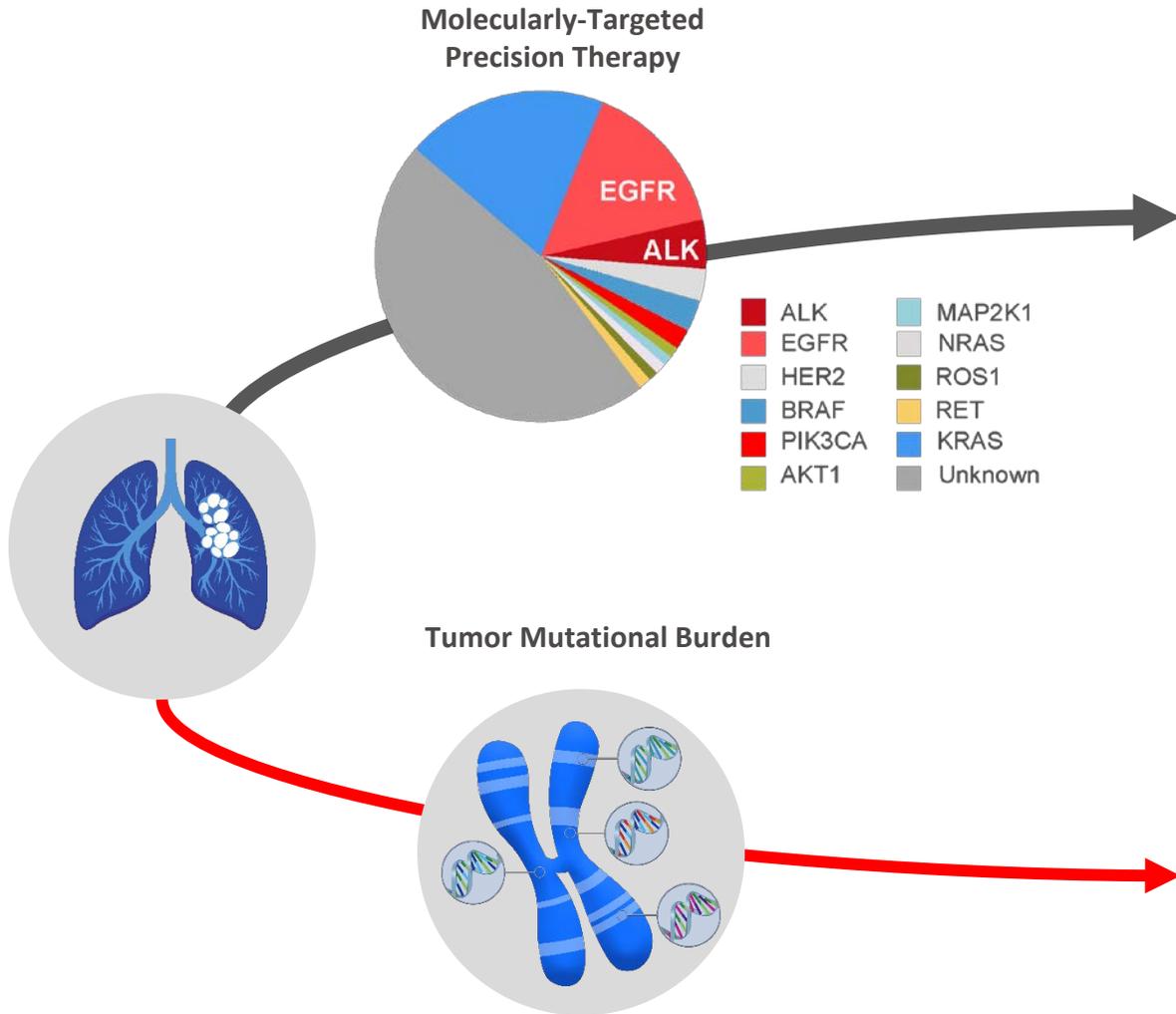
* After a single SC injection of 0.6 mg/kg into healthy volunteers (n=6)

Novel pharmacokinetic properties enhance potency and enable convenient administration

BRINGING NOVEL THERAPIES TO MDS AND AML



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

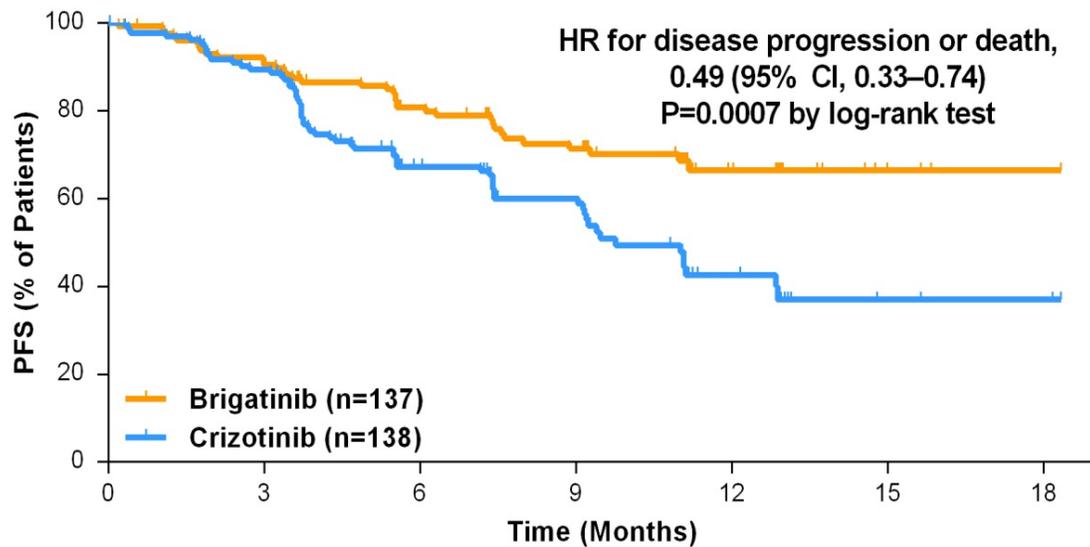


CURRENT PORTFOLIO	EMERGING ASSETS
<p>TAK-788</p>	<p>Sapanisertib (TAK-228)</p> <p>Next-generation kinase inhibitors</p>

NEXT GENERATION TARGETS AND PLATFORM

--	--

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



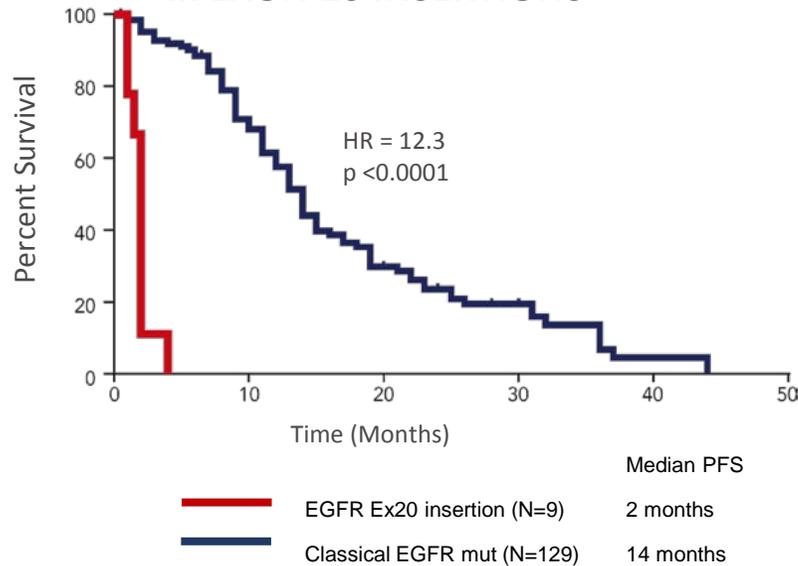
Camidge R., WCLC 2018

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

TAK-788: ADDRESSING UNMET NEED IN EGFR EXON20 MUTATIONS



RESPONSE TO CURRENT EGFR TKIs in EXON 20 INSERTIONS



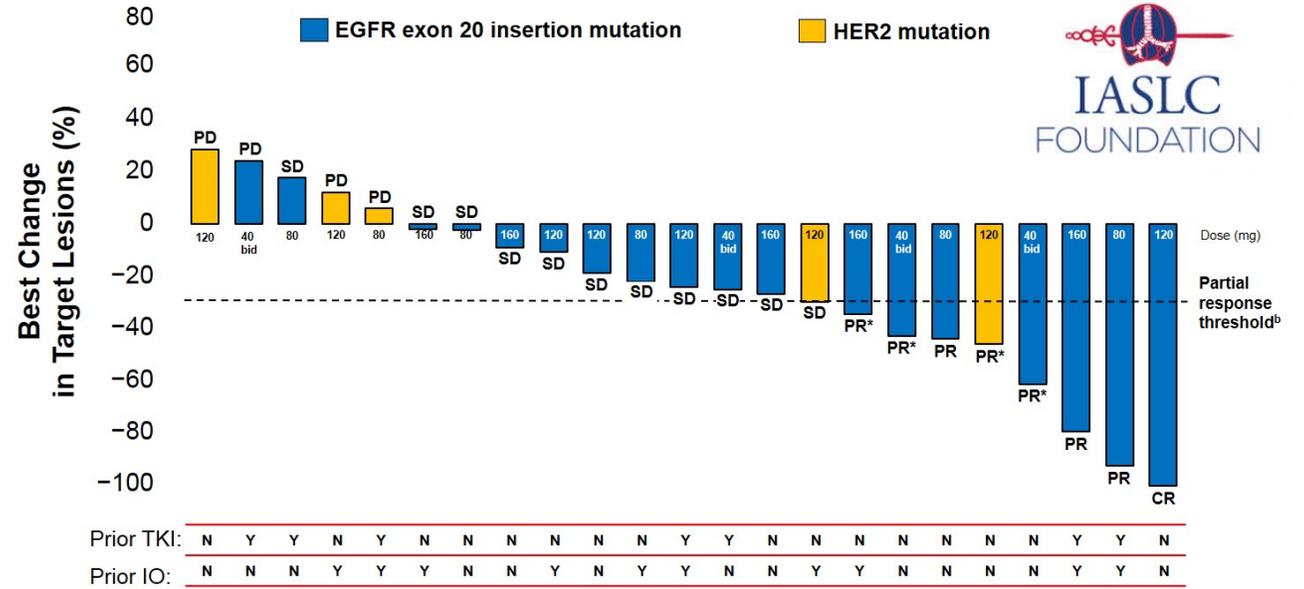
Overall survival <6 months for exon 20 insertions



Current therapies ineffective for these mutations



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



CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease
^a Includes 40 mg bid, 80 mg qd, 60 mg bid, 120 mg qd, and 160 mg qd dose groups
^b Per RECIST v1.1
 * Response awaiting confirmation

Neal et al., WCLC 2018

Expected to begin registration-enabling Phase 2 trial in FY2018

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

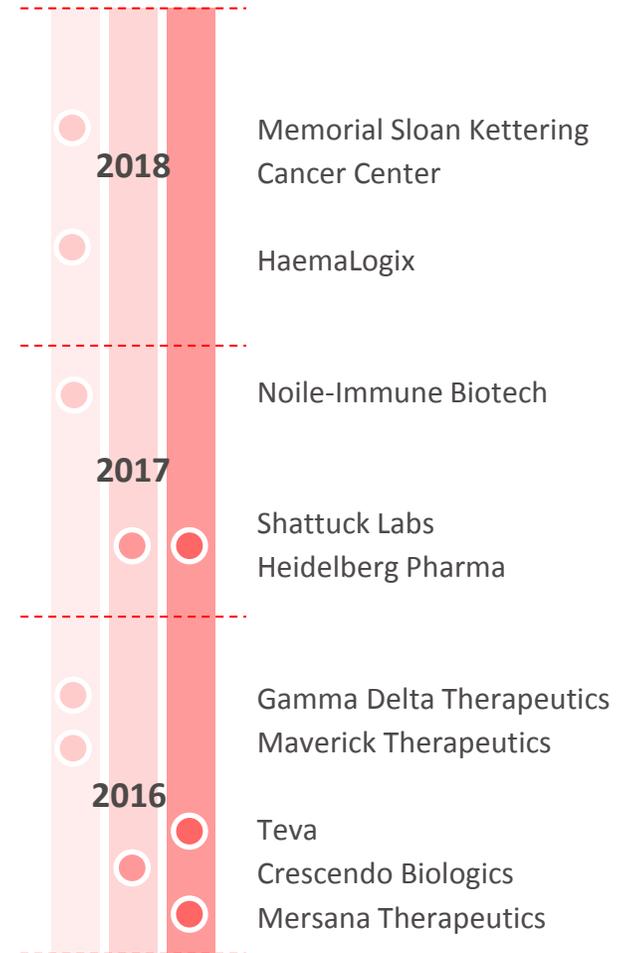
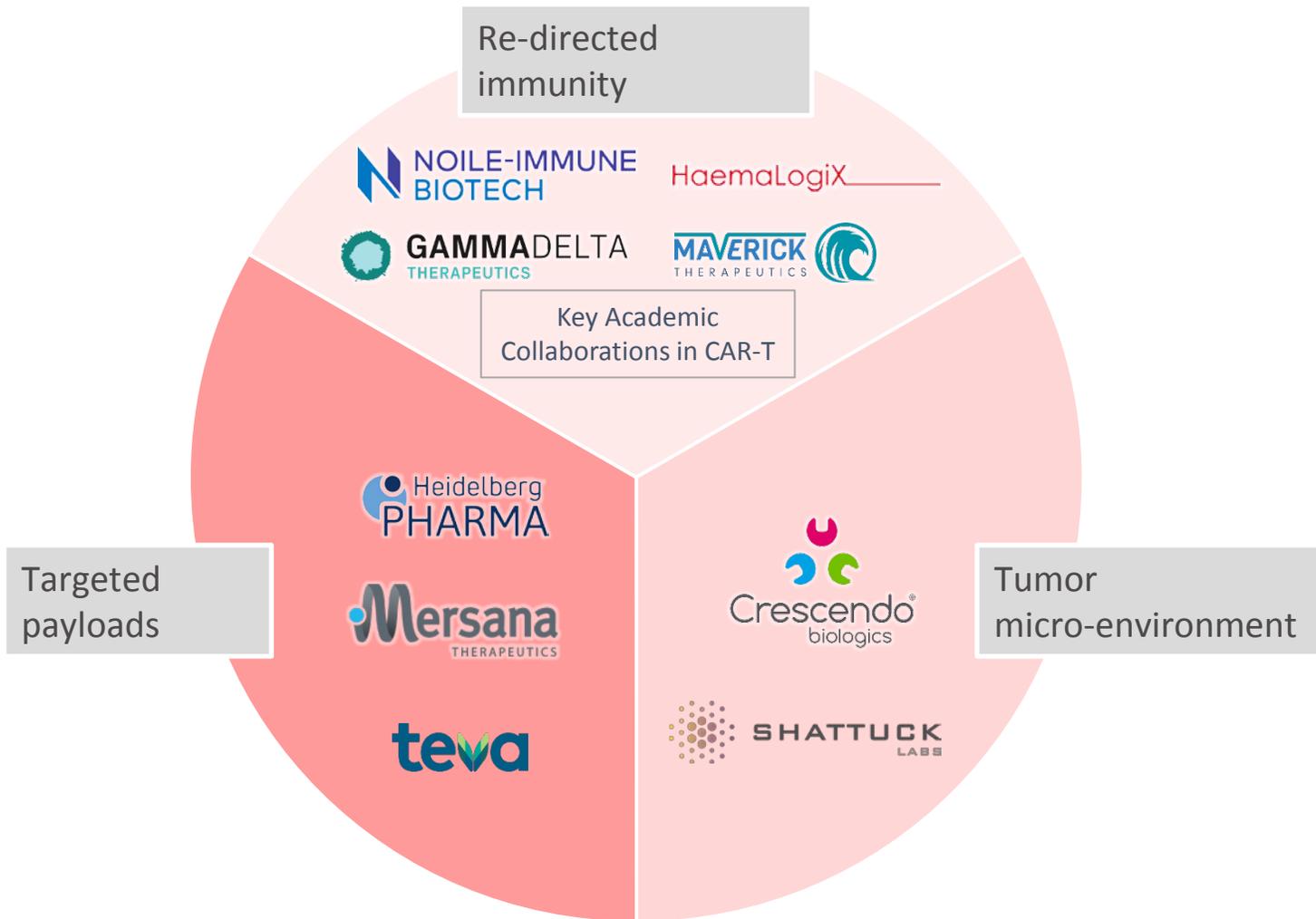
Novel Discovery Strategy in Immuno-Oncology (I/O) and Advance in Cell Therapies

- 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

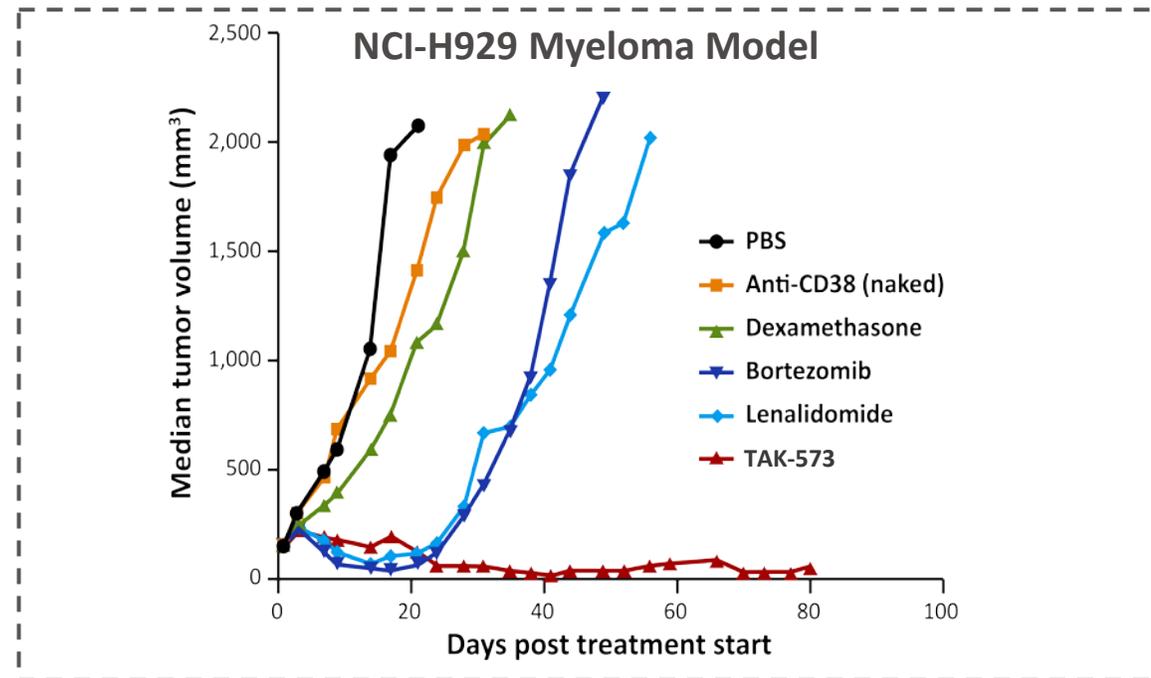
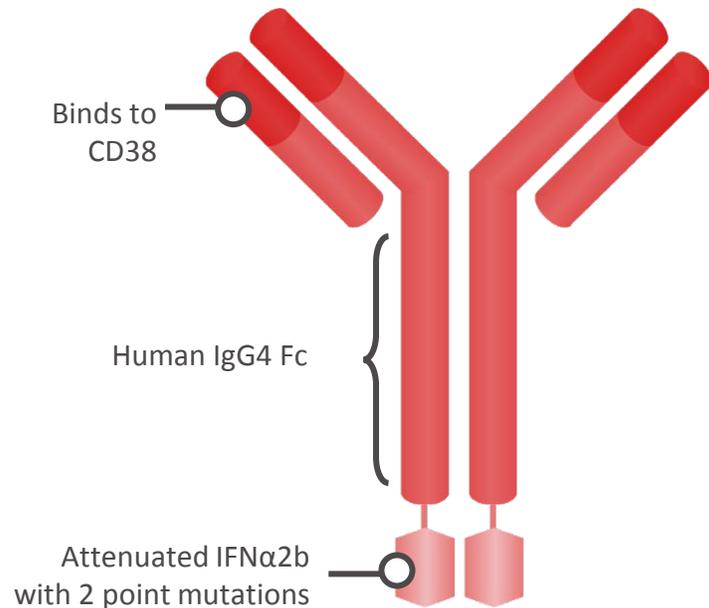
WORLD CLASS PARTNERS FUELING THE I/O PIPELINE



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

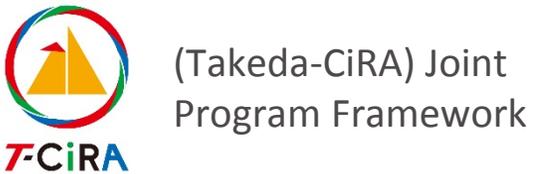


Highly compelling pre-clinical data with TAK-573 in a core area of our clinical development expertise in multiple myeloma
Ph 1 currently enrolling for patients with refractory multiple myeloma

TAKEDA ONCOLOGY AIMS TO BECOME A LEADER IN CELL THERAPIES



TRANSFORMATIVE POTENTIAL UTILIZING NEXT GENERATION CELL THERAPY PLATFORMS



Key Academic Collaborations in CAR-T



Cell therapy engine for Takeda R&D

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

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

AN INNOVATIVE PIPELINE ENHANCED WITH EXTERNAL PARTNERSHIPS

	Discovery/preclinical*	Phase 1	Phase 2	Phase 3	Approved**	
Hematologic Malignancies	 TAK-169 CD38 SLTA	TAK-079 RR MM, SLE CD38 mAB	TAK-659 Lymphoma SYK, FLT-3 <i>Small Molecule</i> Alisertib AML AURORA A <i>Small Molecule</i>	Pevonedistat HR-MDS/AML NEDD 8 <i>Small Molecule</i>	NINLARO Amyloidosis, ND MM, R/R MM dara combo, R/R MM Ninlaro/dex., Maint. MM post-SCT PROTEASOME <i>Small Molecule</i> ADCETRIS FL HL, FL PTCL, CTCL (JP) R/R HL (CN), sALCL (CN) CD30 mAB ADC	 ICLUSIG 2nd-Line Chronic Phase CML, Ph+ ALL BCR-ABL <i>Small Molecule</i> 
Lung Cancer		TAK-788 NSCLC Exon 20 EGFR/HER2 <i>Small Molecule</i>	Sapanisertib Endometrial Cancer Lung Cancer mTORC1/2 <i>Small Molecule</i>		ALUNBRIG 2L post-crizotinib ALK+NSCLC (EU, JP, CN), FL ALK+ NSCLC ALK <i>Small Molecule</i>	
Immuno-Oncology	 PD-1/OX40L	 TAK-573 RR MM CD38 Attenukine mAB Fusion Protein				
	TAK-676 STING	TAK-981 SUMOYLATION <i>Small Molecule</i>				
Solid Tumors		 TAK-522 Solid Tumors HER2 mAB ADC TAK-164 Solid Tumors GCC mAB ADC	TAK-931 Solid Tumors CDC7 <i>Small Molecule</i>	 relugolix Prostate Cancer (JP) GnRH antagonist <i>Small Molecule</i>	 niraparib*** Ovarian Cancer. PARP 1/2 <i>Small Molecule</i>  cabozantinib*** 1L/2L RCC, 2L HCC Multi-RTK <i>Small Molecule</i>	

Pipeline as of September 23, 2018 * 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

 External collaboration

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)

NINLARO
maintenance post-transplant
US APPROVAL

ALUNBRIG
US APPROVAL (1L)

ALUNBRIG JP APPROVAL
NINLARO non-transplant maintenance
US APPROVAL
NINLARO newly diagnosed US/EU
APPROVAL
Pevonedistat US APPROVAL
Niraparib JP APPROVAL
Cabozantinib JP APPROVAL

2H FY 2018

1H FY 2019

2H FY 2019

FY 2020

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)

Alisertib – AML pivotal start

Anticipated Pivotal Trial Start
Anticipated Approval

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

CONCLUSION

- 1** Focused on delivering the next approvals for **NINLARO, ALUNBRIG, and pevonedistat**
- 2** Expanding transformative treatment options in our focus areas of **hematologic malignancies and lung cancer with alisertib, TAK-788 and novel CD38 targeted mechanisms**
- 3** Harnessing the power of external innovation with a diverse set of world-class partnerships, accelerating novel therapies into the clinic

R&D DAY AGENDA – CAMBRIDGE, OCTOBER 11, 2018

Time	Agenda
12:00 – 12:30	Registration and Lunch
12:30 – 13:10	R&D Transformation, Progress To Date, Future Outlook Andy Plump
13:10 – 13:45	Oncology Phil Rowlands
13:45 – 14:05	Gastroenterology Asit Parikh
14:05 – 14:20	Break
14:20 – 14:40	Neuroscience Emiliangelo Ratti
14:40 – 15:00	Vaccines Rajeev Venkayya
15:00 – 16:05	Looking Ahead Andy Plump Panel Q&A Session
16:10 – 17:30	Reception

A close-up photograph of a man and a woman smiling and embracing each other. The man is on the left, and the woman is on the right. They are both looking at each other and smiling warmly. The background is a soft, out-of-focus green and white, suggesting an indoor setting with a window.

TAKEDA GASTROENTEROLOGY

A GLOBAL LEADER IN GASTROENTEROLOGY

ASIT PARIKH MD, PHD

Head, Gastrointestinal Therapeutic Area

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



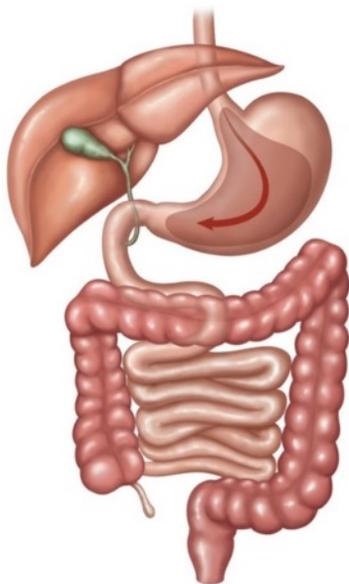
OUR STRATEGY EXPANDS THE PORTFOLIO ACROSS CORE DISEASE AREAS SUPPORTED BY PLATFORM TECHNOLOGIES

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



Celiac disease

- Advance approaches for the prevention of immune responses to gluten

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.

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

	Discovery/preclinical*	Phase 1	Phase 2	Phase 3	Approval**	
IBD	Multiple targets in IBD Multiple targets Small molecule IBD Microbial consortia Multiple targets Monoclonal antibody R&D partnership				ENTYVIO SC Needle-free Portal Therapeutics ENTYVIO UC/CD, JP, China SC UC/CD GvHD prophylaxis Monoclonal antibody Alofisel Perianal Fistulas, US Stem cell therapy	
		TIMP-Gliadin Celiac disease Biologic Kuma062 Celiac disease Biologic				
				TAK-906 Gastroparesis Small molecule TAK-954 Enteral Feeding Intolerance Small molecule		AMITIZA EM registration Pediatric Constipation IBS-C, CIC, OIC Small molecule
						* 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
GI Motility	Multiple targets in Constipation, Nausea & Vomiting Multiple targets Small molecule and biologics Multiple targets Monoclonal antibody Anti-fibrotics in NASH Biologic R&D Partnership Regenerative liver diseases Cell and Gene therapy					
Liver	Multiple targets in anti-fibrosis Microbial consortia					
Acid disease/ Other		TAK-671 Acute pancreatitis Biologic			TAKECAB PPI Partial Responders Acid disorders NE Asia, ASA FDC Small molecule	

External collaboration Platform

Pipeline as of September 23, 2018

WE ARE BUILDING ON THE SUCCESS OF ENTYVIO TO ADDRESS CONTINUED UNMET NEED IN IBD PATIENTS

1
2
3
4

Geographic expansion

New formulations

Expanded patient populations

New evidence generation



First and only biologic specifically targeting gut inflammation

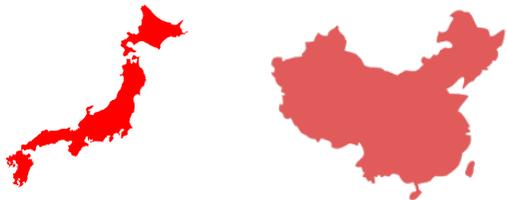


First-in-class mesenchymal stem cell therapy for fistulizing Crohn's disease

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



* 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 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

Prefilled syringe



Autoinjector pen



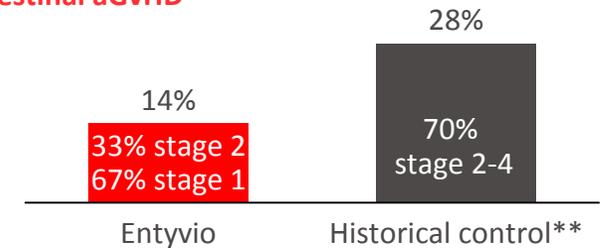
Portal needle-free



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*



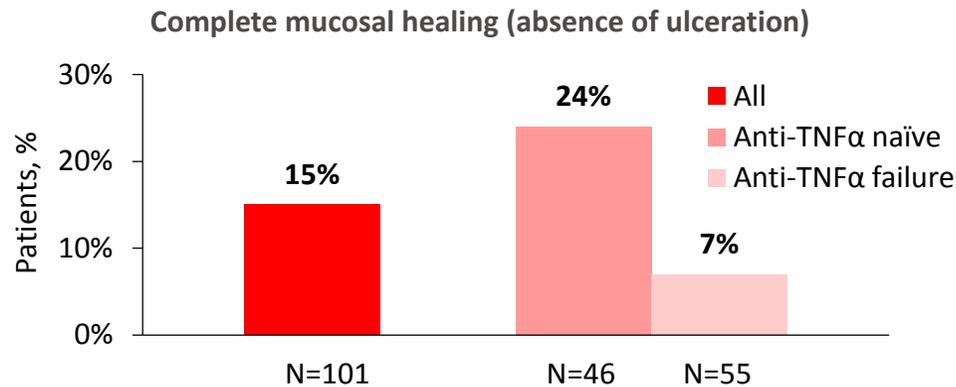
- * The safety profile of Entyvio in the GvHD patient population remains unchanged and is consistent with the approved US labelling
- ** Adjusted for patient population including allogeneic stem cell transplant characteristics with similar conditioning regimen

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

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 trended favorable to superior profile for Entyvio vs. anti-TNFs

¹ Danese S, et al. ECCO 2018. Oral presentation OP023.

² Colombel J, Sands BE, Rutgeerts P, et al. The safety of vedolizumab for ulcerative colitis and Crohn's disease. Gut 2017;66:839-851.

³ References for the Victory Consortium Studies:

Bohm et al—CD propensity; (https://academic.oup.com/ecco-jcc/article/12/supplement_1/S018/4807655)

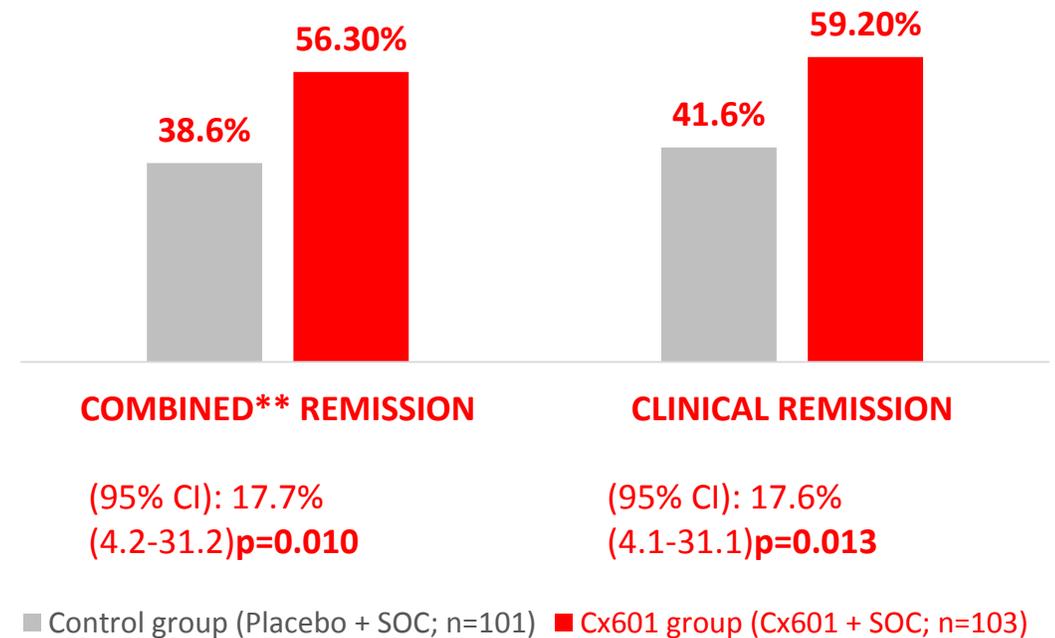
Faleck et al—UC propensity; (https://academic.oup.com/ecco-jcc/article/12/supplement_1/S019/4807661)

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)*



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

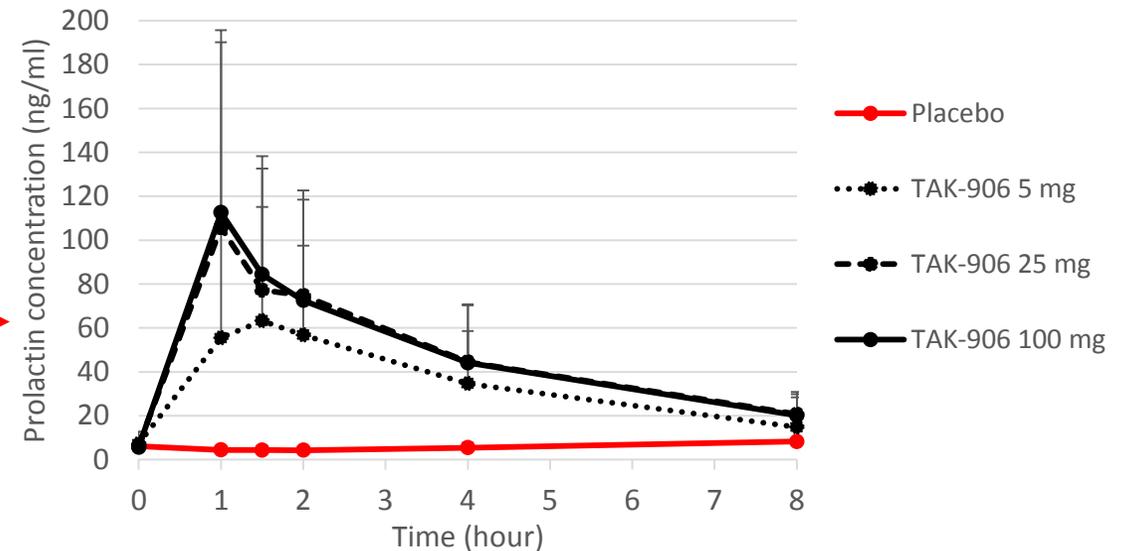
Abbreviations: SOC, Standard of care

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

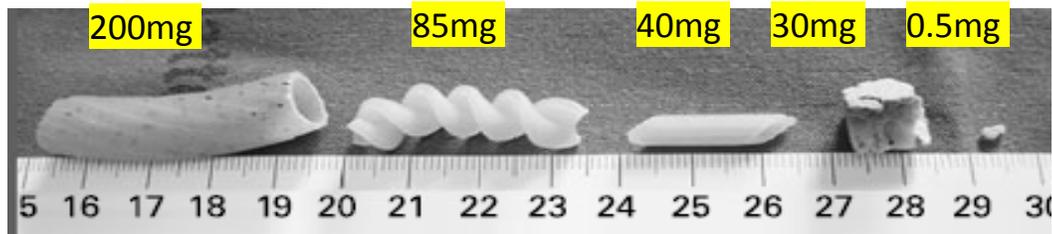
* Other AEs observed in Phase 2a study not related to TAK-906 administration included a case of tremor in a subject with history of depression, anxiety, T2DM and Neurontin use. Also, acute kidney insufficiency in a patient with urinary tract infection and in a patient with prior chronic renal failure.

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

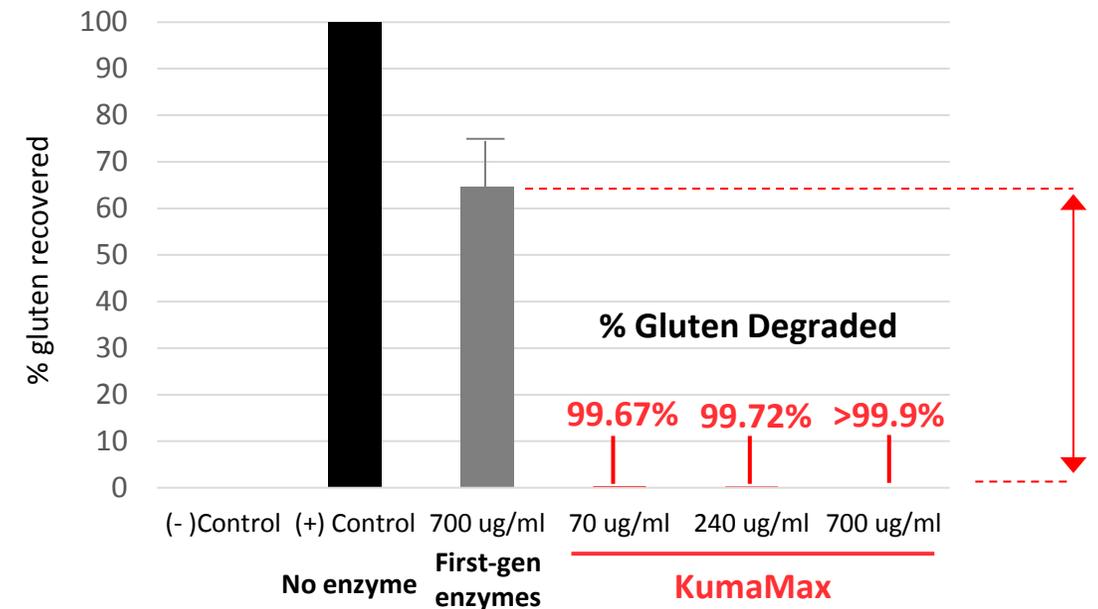
CELIAC DISEASE

- Affects ~1% of the population¹, 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



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**

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

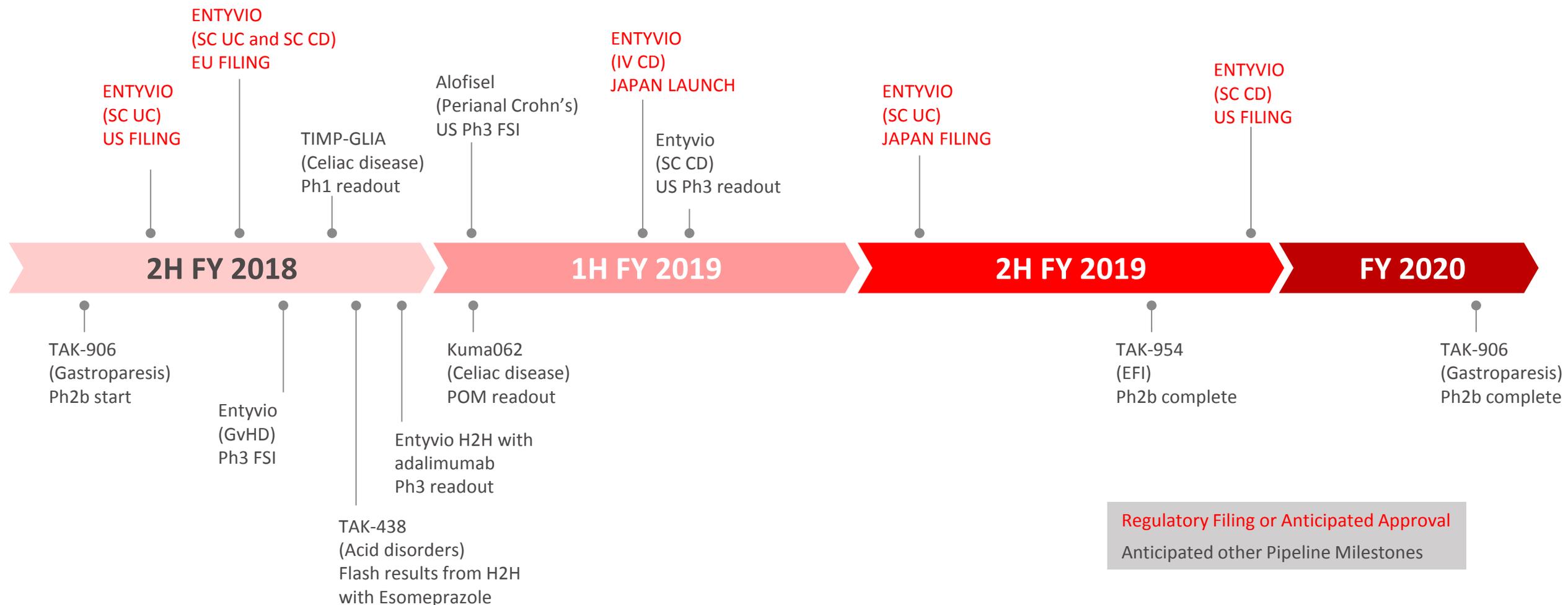


Takeda co-founded with Third Rock Ventures to focus on cell and gene therapy for end-stage liver diseases

Series A announced August 2018

EXPECTED KEY GI PORTFOLIO INFLECTIONS AND MILESTONES

Dates in fiscal year (FY) starting April 1st



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