TAKEDA R&D INVESTOR DAY 2018

CAMBRIDGE, MASSACHUSETTS

October 11, 2018

Better Health, Brighter Future

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

DELIVERING ON OUR R&D VISION

CAMBRIDGE, MASSACHUSETTS

ANDY PLUMP MD, PHD
Chief Medical and Scientific Officer
October 11, 2018

Better Health, Brighter Future

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OUTLINE FOR TODAY

- **Overview of Takeda, our R&D transformation and progress to date**
- **Deep dive by Therapeutic Area (Oncology, Gastroenterology, Neuroscience plus Vaccines) and how each is contributing to unlock innovation and deliver meaningful value**
- **Recurring themes:**
  - Focus
  - Robust research engine and capabilities
  - New modalities
  - Differentiated, global partnership approach
  - High-performing teams
- **Review Shire acquisition and how it accelerates our R&D momentum**

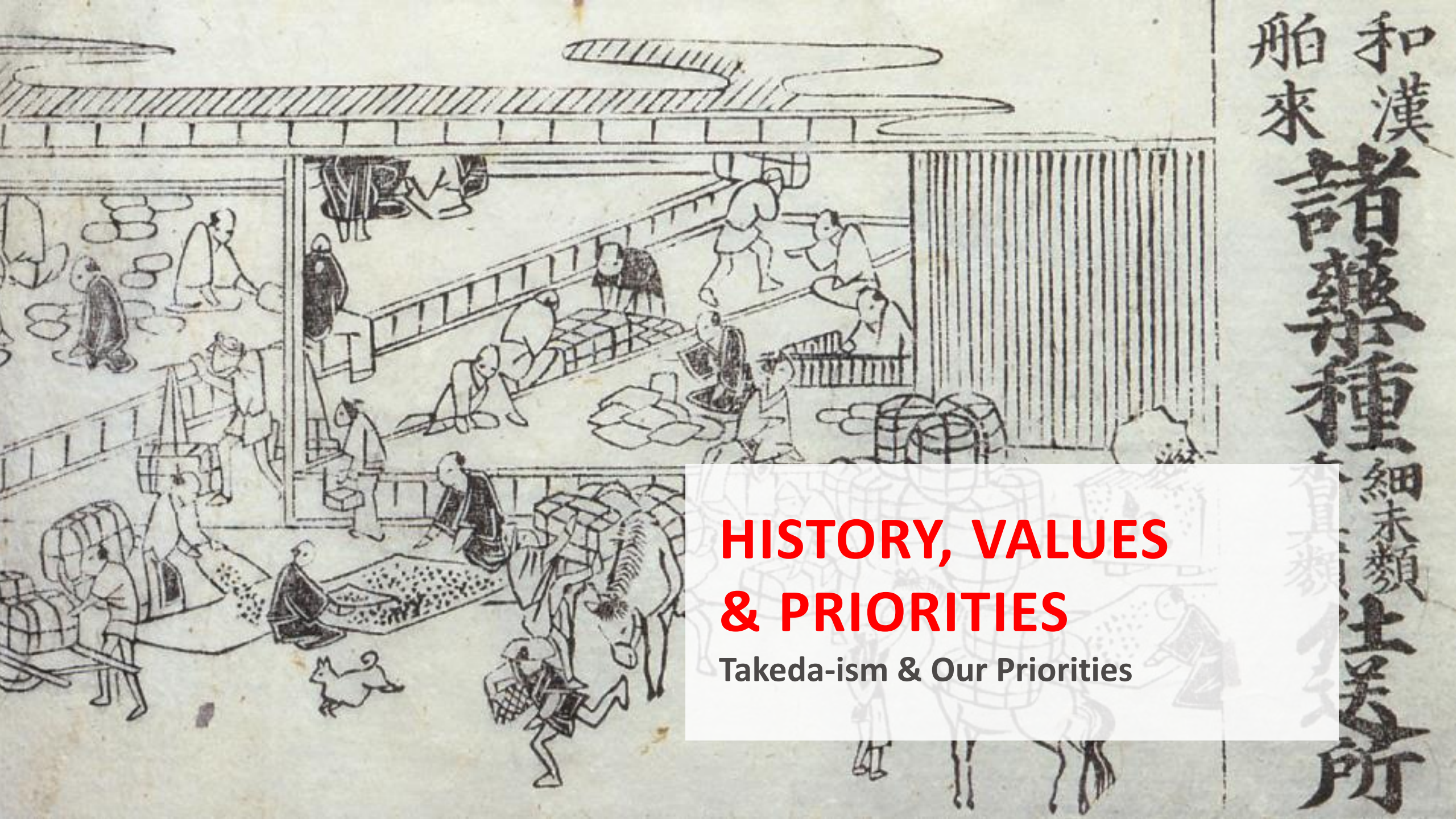
HISTORY, VALUES & PRIORITIES

R&D TRANSFORMATION

DOING MORE FOR OUR PATIENTS

WHAT WE'VE DELIVERED

WHAT'S NEXT



HISTORY, VALUES & PRIORITIES

Takeda-ism & Our Priorities

WHO WE ARE

PUTTING PATIENTS FIRST FOR OVER TWO CENTURIES

Takeda is a patient-centric, innovation-driven global pharmaceutical company that builds on a distinguished 237-year history, aspiring to bring **better health and a brighter future** for people worldwide.

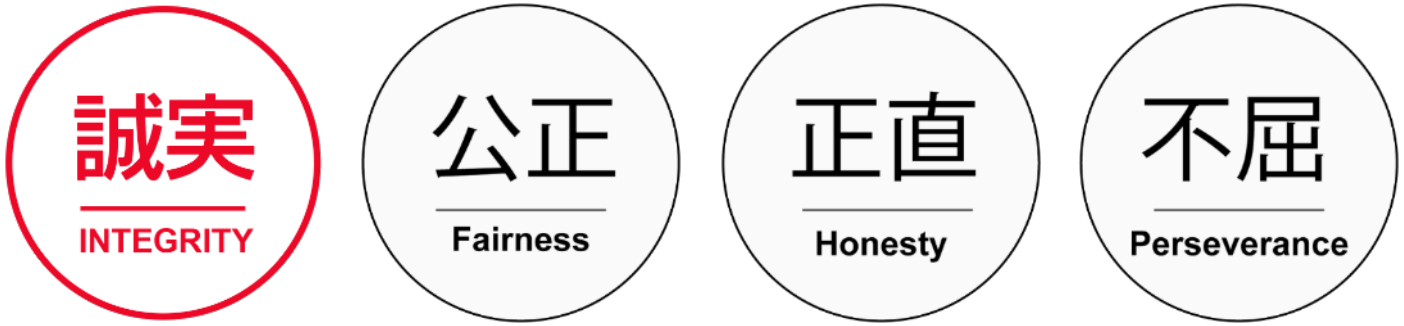
YEARS

Better Health, Brighter Future

TAKEDA-ISM & OUR PRIORITIES

Established by our founding spirit and integral to every part of our business, Takeda-ism and our priorities guide us in our efforts to achieve our Vision 2025.

TAKEDA-ISM



OUR PRIORITIES

We make decisions and take actions by focusing on our four priorities in this order:

1. Putting the patient at the center
2. Building trust with society
3. Reinforcing our reputation
4. Developing the business

R&D LEGACY: THE CASE FOR CHANGE WAS ABSOLUTE

Period of poor productivity following approval of pioglitazone in 1999

- Fragmented R&D footprint
- Lack of therapeutic area focus
- Inwardly facing
- Regional teams, regional mindset
- Pipeline >85% small molecule

PRODUCT LAUNCHES BY DISCOVERY SOURCE (FY2005 – 2015)

Internal (4)	Acquisition (8)	Licensed (10)
DEXILANT	NESINA	ADCETRIS
EDARBI / AZILVA[1]	COLCRYS[2]	AMITIZA
ROZEREM	DAXAS[3]	AZILECT
TAKECAB	ENTYVIO	BRINTELLIX / TRINTELLIX
	NINLARO	CONTRAVE[3,4]
	REVESTIVE[3]	COPAXONE
	ZAFATEK	REMINYL
	MEPACT	VECTIBIX
		XELJANZ[3]
		ULORIC

● Global ○ Regional

1. For purposes of NME counts, Edarbi and Azilva are combined.
2. Colcrys is counted as an NME, although the product was on-market in generic form.
3. Daxas, Revestive, Contrave, and Xeljanz have since been divested or returned to partner.
4. Contrave counts as an NME, although it is composed of two on-market compounds.

WHAT WE COMMITTED TO

Reinventing R&D

BUILDING AN AGILE R&D ORGANIZATION DRIVEN BY INNOVATIVE SCIENCE

THERAPEUTIC AREA FOCUS
Oncology, Gastroenterology, Neuroscience plus Vaccines

PARTNERSHIPS & CAPABILITIES

TRANSFORM OUR CULTURE

R&D TRANSFORMATION KEY IMPERATIVES

- Agile and lean
- Dynamic and sustainable research and early development engine
- Transformative advances via reciprocally advantageous partnerships
- Laser-focused on purposeful execution

WHAT R&D TRANSFORMATION MEANT…

A STRATEGIC, TECHNICAL, SKILL-SET, STRUCTURAL, GEOGRAPHIC AND CULTURAL CHANGE THAT IMPACTED NEARLY ALL R&D EMPLOYEES.

STRONG LEADERSHIP DRIVING CHANGE

ANDY PLUMP
CMSO

ASIT PARIKH
Gastroenterology TAU

STEVE HITCHCOCK
Research

DAN CURRAN
Center for External Innovation

PHIL ROWLANDS
Oncology TAU

EMILIANGELO RATTI
Neuroscience TAU

RAJEEV VENKAYYA
Vaccines Business Unit

NENAD GRMUSA
R&D Portfolio Strategy & Investment Mgmt

HIRED IN THE LAST 12 MONTHS

STEFAN WILDT
Pharmaceutical Sciences

GEORGIA KERESTY
Medical Sciences & Development Operations

COLLEEN BEAUREGARD
R&D Communications

TOSHIO FUJIMOTO
iPark

CHRIS MORABITO
R&D Shire Integration

ERIKA MARDER
R&D Human Resources

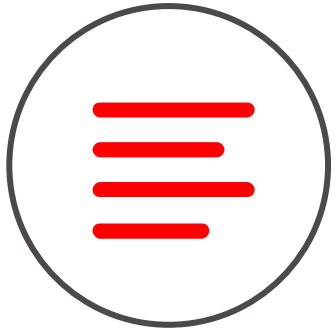
TAU: Therapeutic Area Unit

WHAT WE'VE DELIVERED

Our innovations are transforming our business and the lives of patients

TWO YEARS INTO A FIVE-YEAR R&D TRANSFORMATION JOURNEY

Focused (3+1) therapeutic area strategy and lean operating model



A pipeline that's delivering

- Fueled by a robust research engine and a rich, global partner ecosystem

Culture: engaged and empowered teams

WE'VE FOCUSED OUR THERAPEUTIC AREAS

ALL IN: 3+1

ONCOLOGY

GASTROENTEROLOGY

VACCINES

NEUROSCIENCE

RESEARCH, DIVERSE MODALITIES AND PARTNERSHIPS

WE'VE STREAMLINED OUR GLOBAL FOOTPRINT

BOSTON, MA

R&D Center
Oncology, GI Research

SHONAN, JAPAN

Neuroscience Research,
T-CiRA, iPark

SAN DIEGO, CA

Specialized drug
discovery technologies,
GI and Neuroscience

WE'VE REDIRECTED RESOURCES TO HIGHLY INNOVATIVE MEDICINES

FOCUS AND PRIORITIZATION

- Reduced Drug Discovery Units from 6 to 3

- Changed research from "pipe" to "funnel" along stage-gates*
- Aggressive resourcing of focused portfolio

FOCUS ON EXECUTION

Established a research KPI in FY18 to achieve industry leading cycle-times for candidate selection

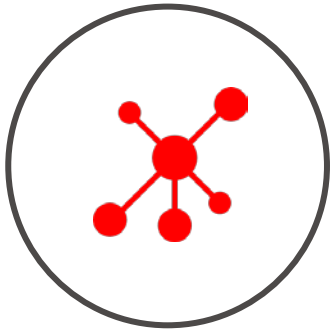
On track to achieve 11 planned candidate selections in FY18 of which 5 are non small molecules

* Beginning June 2016

RESEARCH & EARLY CLINICAL ENGINE: KEY CAPABILITIES

THE RIGHT TARGET

- Leveraging human-derived data
- Potential for game-changing patient impact
- Testable translational hypotheses
- First-in-class or best-in-class



THE RIGHT MODALITY

- Patient -> Biology -> Modality
- Embrace innovative platforms
- Expand internal capabilities through partnerships
- Invest in innovative biologics and cell therapies

FLAWLESS EXECUTION

- Human early POC is a key performance indicator
- Optimized partnership model
- Operational effectiveness incentives
- Specialized Pharmaceutical Sciences capabilities

SELECT PARTNERSHIPS

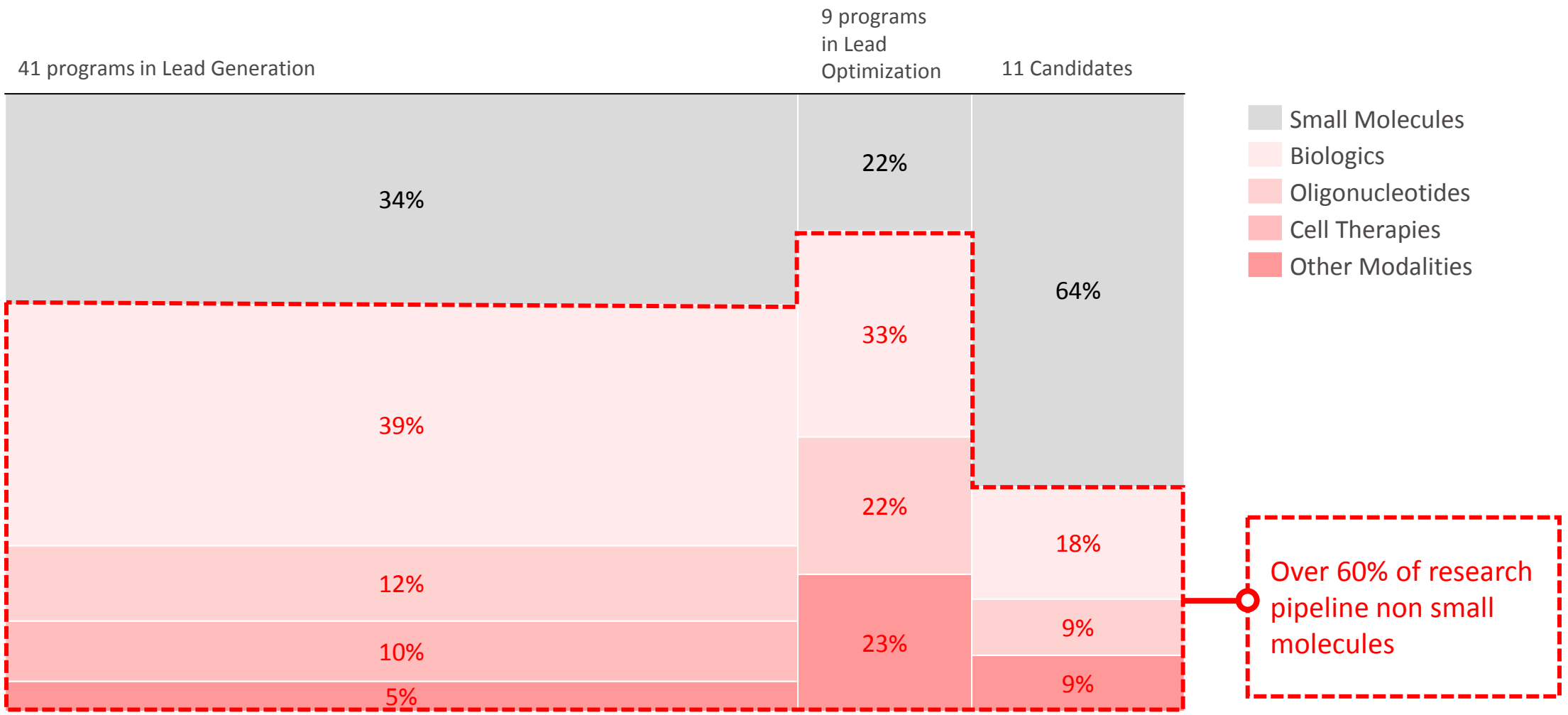
	STRATEGIC FOCUS AREA	DISCOVERY/ PRECLINICAL	PHASE 1	PH2, PH3, FILED, LCM
ONCOLOGY	Hematologic Malignancies	Molecular Templates, Adimab, Heidelberg, HaemaLogiX, HiFiBio	Nektar	Seattle Genetics
	Lung Cancer	Crescendo Biologics, Shattuck Labs		
	Next-gen IO / Cell Therapy	Discovery and development of next generation CAR-T assets (Key Academic Collaborations)	teva: Anti-CD38 Attenukine asset currently in MM trial. Multiple active discovery stage programs.	
		Gamma Delta Therapeutics, Noile-Immune Biotech, Shattuck Labs, Maverick Therapeutics, Ciml Immunology, Crescendo Biologics		
	Solid Tumor	NBE Therapeutics, Mersana	ImmunoGen	Exelixis, Tesaro
GASTRO-ENTEROLOGY	IBD	Beacon Discovery, Finch Therapeutics, Emulate, Enterome, EnGene	Nubiyota	Portal Instruments
	Motility	Beacon Discovery, Enterome, HiFiBio Therapeutics		Theravance Biopharma
	Celiac		PVP BIOLOGICS: Development agreement for KumaMax glutenase and option to acquire company	
			Cour	
	Liver	Ambys MEDICINES: Liver regeneration using cell therapy, gene therapy, small molecules for advanced liver disease/cirrhosis, acute liver failure, genetic disease		
		Arcturus, Hemoshear Therapeutics		
NEURO-SCIENCE	Depression *			Lundbeck
	Parkinson's		AstraZeneca	
	Alzheimer's	DENALI THERAPEUTICS: Novel platform for increasing transport of biotherapeutic products into the brain for neurodegenerative disorders (Alzheimer's, other)		
	Rare Disease	Wave Lifesciences	WAVE LIFE SCIENCES: Innovative anti-sense oligonucleotide platform for unmet needs in Neurology (Huntington's)	

Not inclusive of all partnerships

* Depression – Focus on MDD (major depressive disorder) and TRD (treatment-resistant depression)

WITH OUR PARTNERS, WE'RE AT THE FOREFRONT OF INNOVATION

Diversity of modalities in the research pipeline*



* As of August 28, 2018, Biologics include proteins, enzymes, antibodies, peptides. Other Modalities include microbiome, drug delivery systems, vaccine.

INVESTING IN THE TRANSFORMATIVE POTENTIAL OF CELL THERAPIES

RESEARCH

T-CiRA

NOILE-IMMUNE BIOTECH

GAMMADELTA THERAPEUTICS

Key Academic Collaborations in CAR-T

2019: Differentiated CAR-Ts in Phase I

2020+: Other Hematologic/Solid Tumor CAR-Ts

APPROVED*

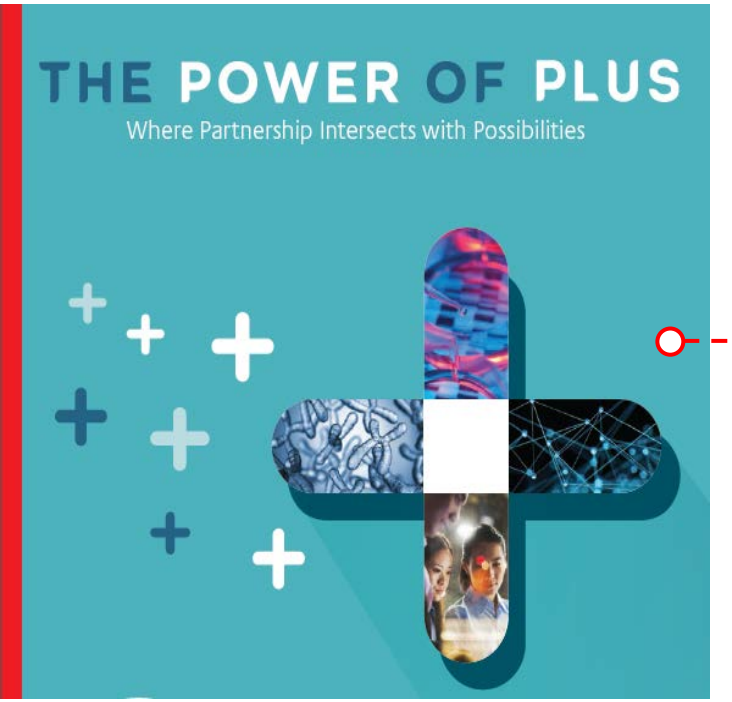
ALOFISEL

* EU launch 2018

"We're at a key point when it comes to cell and gene therapy…for a long time, they were largely theoretical constructs. Now they are a therapeutic reality."

SCOTT GOTTLIEB, M.D.
Alliance for Regenerative Medicine Annual Meeting | May 22, 2018

WE'VE BUILT A COMPREHENSIVE, DIFFERENTIATED PARTNERSHIP MODEL



CENTER FOR EXTERNAL INNOVATION (CEI)

- Integrated into the innovation system; access to promising, potentially revolutionary platforms prior to validation
- Close alignment of interests/incentives with many engagement mechanisms including: co-creation, in-licensing, out-licensing, Takeda financing, capabilities support, etc.
- Flexibility and optionality in partnership structure with clear two-way accountability

WE EXECUTED 56 PARTNERSHIPS IN FY17

THERAPEUTIC AREA FOCUSED

ONCOLOGY

GammaDelta Therapeutics · NEKTAR · Shattuck Labs · NOILE-IMMUNE BIOTECH · Heidelberg PHARMA · tem · TESARO

GASTROENTEROLOGY

BEACON DISCOVERY · BioSurfaces · HEMOSHEAR THERAPEUTICS · The University of Vermont · TiGENIX · Karolinska Institutet · Portal Instruments · HiFiBiO · NUBIYOTA

NEUROSCIENCE

AstraZeneca · DENALI THERAPEUTICS · mindstrong · WAVE

Takeda

NOVEL PLATFORMS, NEW CAPABILITIES

External Value Creation

CARDURION PHARMA · IZANA BIOSCIENCE · SCOHIA · SAMSUNG BIOEPIS · rhythm

Companies Created

Aikomi · ChromaJean Co. · Chordia Therapeutics · FIMECS · GenAhead Bio · GEXVal · SEEDSUPPLY · RebioRNA

New Capabilities

FUJIFILM Value from Innovation · HITGEN 先导药物 · isogenica · Numerate · SELEXIS · SCHRÖDINGER

Rare Disease Initiatives

Harrington Discovery Institute University Hospitals | Cleveland Ohio · RECURSION pharmaceuticals

Strategic Academic Alliances

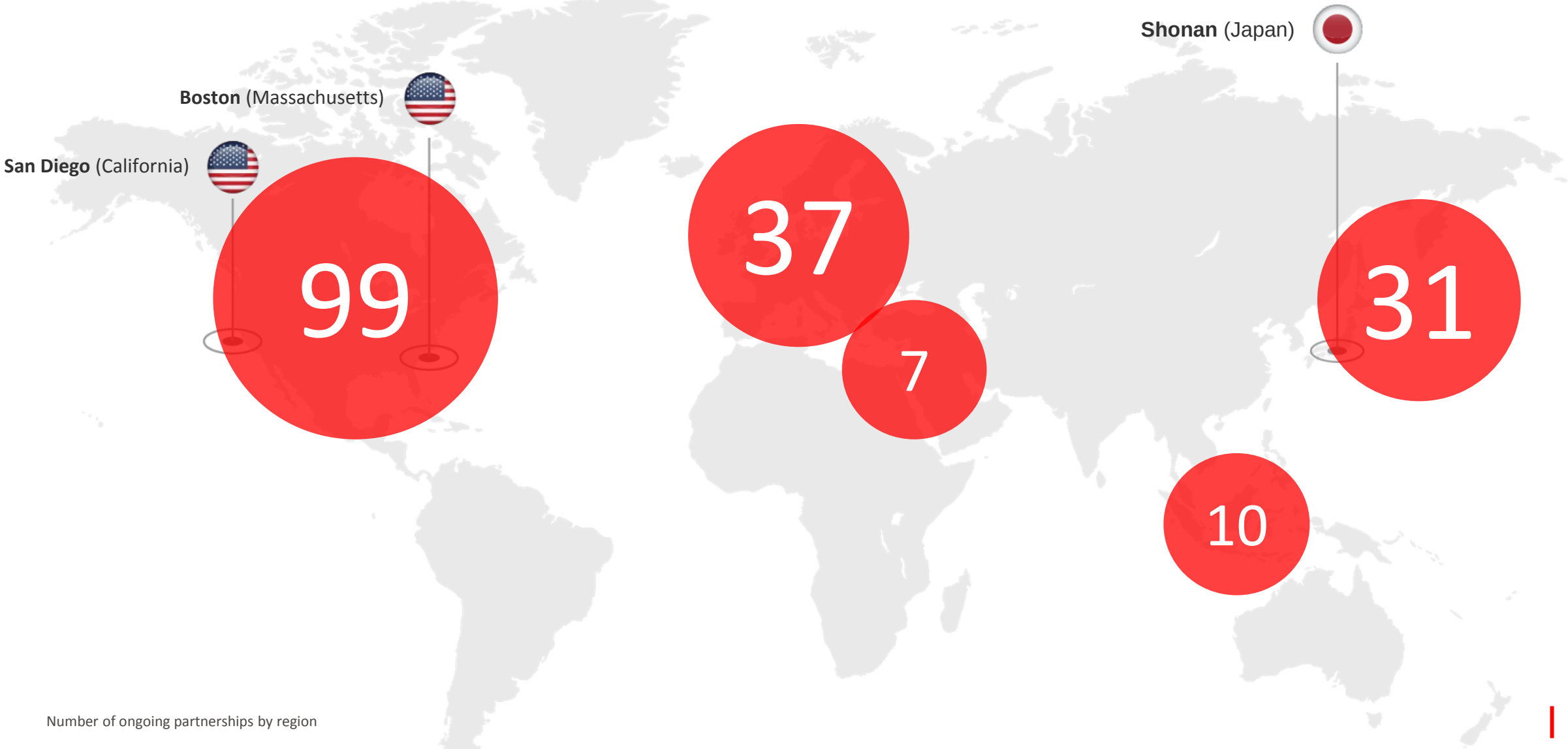
FRED HUTCH · UNIVERSITY of WASHINGTON · Leland Stanford Jr. University

Takeda Ventures

OBSIDIAN

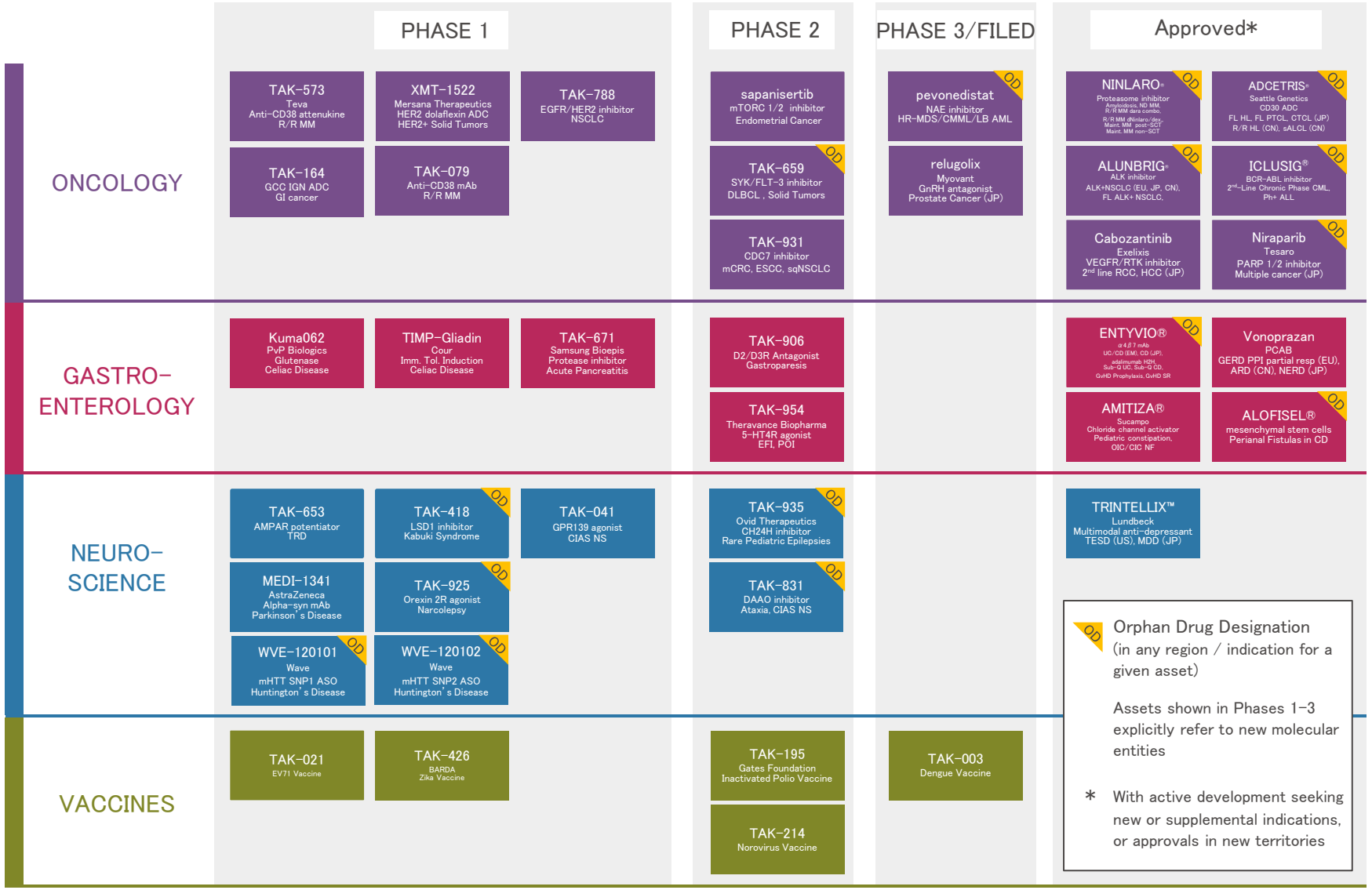
Slide is not all-inclusive of 56 deals: Only includes disclosed partnerships / collaborations

AND OUR APPROACH TO EXTERNAL INNOVATION IS GLOBAL



Number of ongoing partnerships by region

…RESULTING IN A DYNAMIC AND RE-INVIGORATED PIPELINE



30 pipeline assets progressed since the start of FY2016

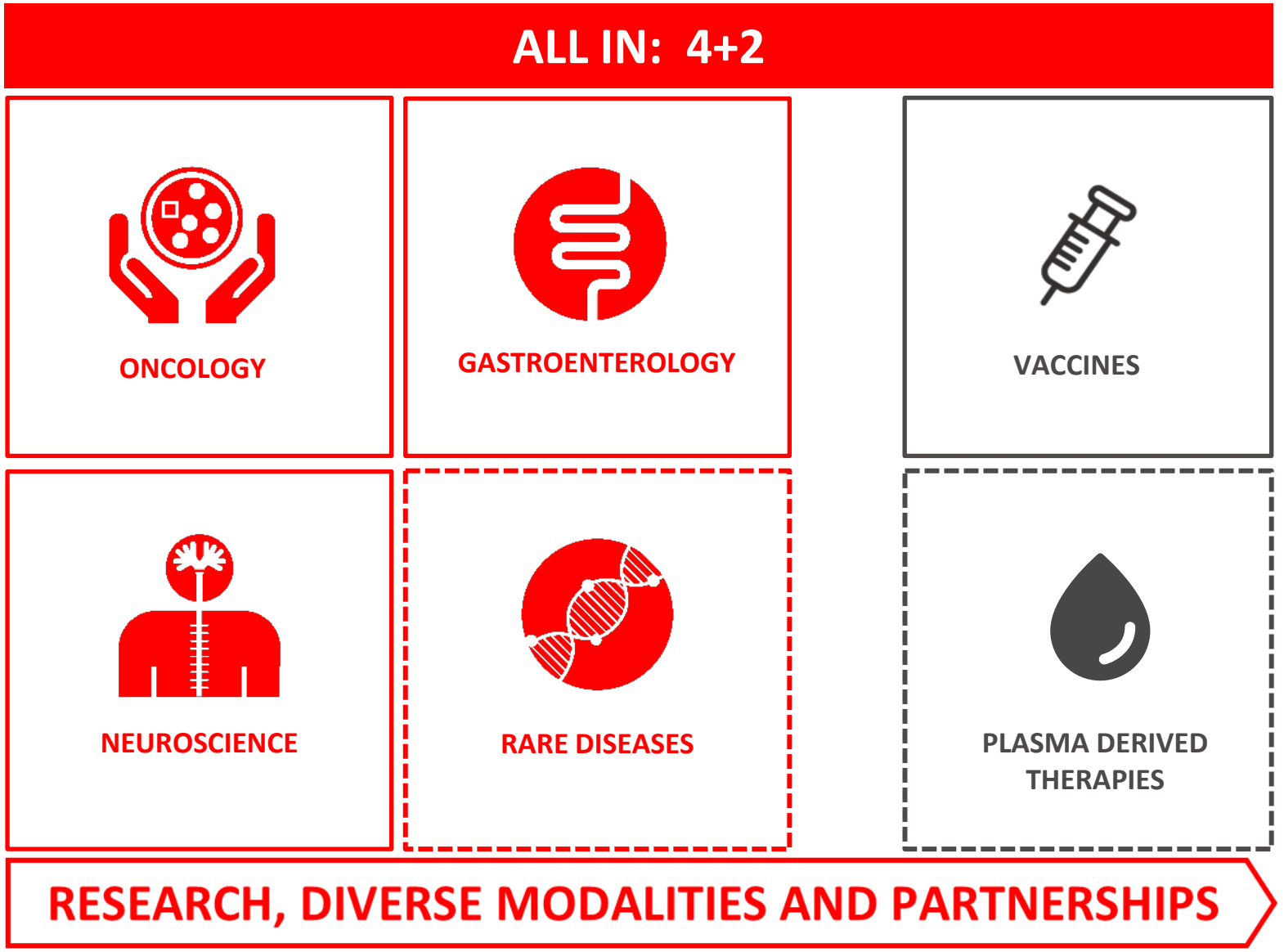
45% of pipeline is partnered

80% of pipeline with global development plans/rights

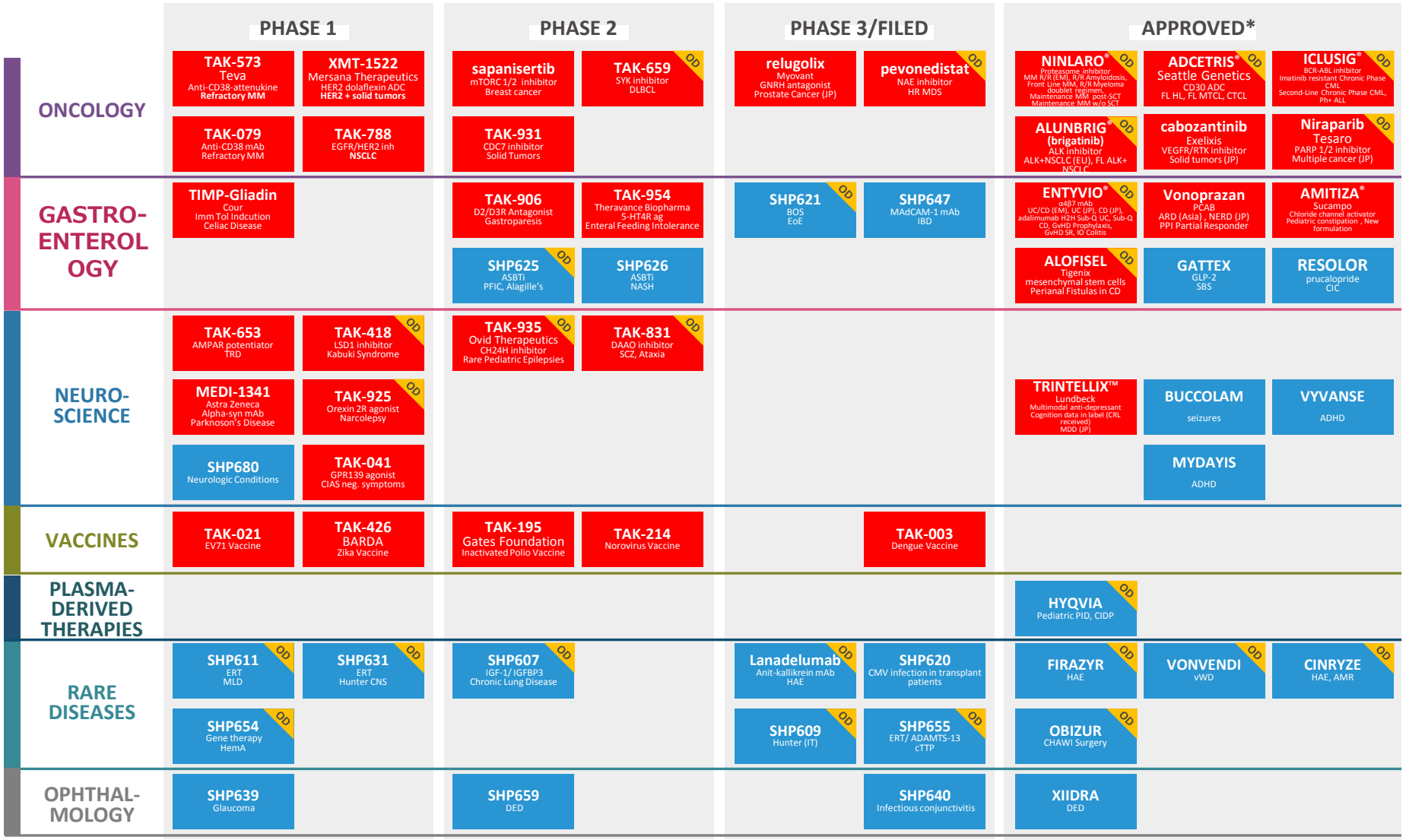
38% of pipeline has orphan drug designation

Pipeline as of September 23, 2018. Please refer to glossary for disease abbreviations

WE'LL CONTINUE TO FOCUS ON CORE THERAPEUTIC AREAS



WITH THE POTENTIAL TO DELIVER MORE VALUE IN THE FUTURE



Takeda

Shire

OD Orphan Drug Designation

Note: SHP652 and Natpara classified as "other" and not shown here | *With ongoing clinical development activities. Pipeline as of February 1, 2018

CENTRAL TO EVERYTHING, WE'VE EVOLVED OUR CULTURE AND THE WAY WE WORK

SELECT INITIATIVES

Co-location

Patient-centric activities and touchpoints

Transparency and engagement around Key Performance Indicators (KPIs)

METRICS

R&D Voluntary Turnover

0.9% vs. **3.4%** Pharma industry benchmark*

Engagement

84% ** vs. **74% in 2017** **

Alignment

83% ** of Takeda R&D employees understand how their work contributes to Takeda's success

* Q1 2018, Source: CEB/ Gartner. ** Takeda Best-in-Class pulse U.S. survey data, 2017 and 2018 survey.

R&D ALIGNMENT AROUND BIG IMPORTANT VALUE INFLECTIONS (BIVIs) FOR R&D FY18

1

Trintellix:
Approval of processing speed (important aspect of cognitive function) in U.S. label

2

Alunbrig:
a) ALTA-1L interim analysis
b) EU approval for 2nd line in ALK+ non-small cell lung cancer

3

Ninlaro:
a) Interim analysis
b) Submission for both newly diagnosed multiple myeloma and maintenance post-transplant

4

Entyvio:
Ulcerative colitis subcutaneous submission

5

Dengue vaccine:
Successful primary endpoint of Ph3 trial

6

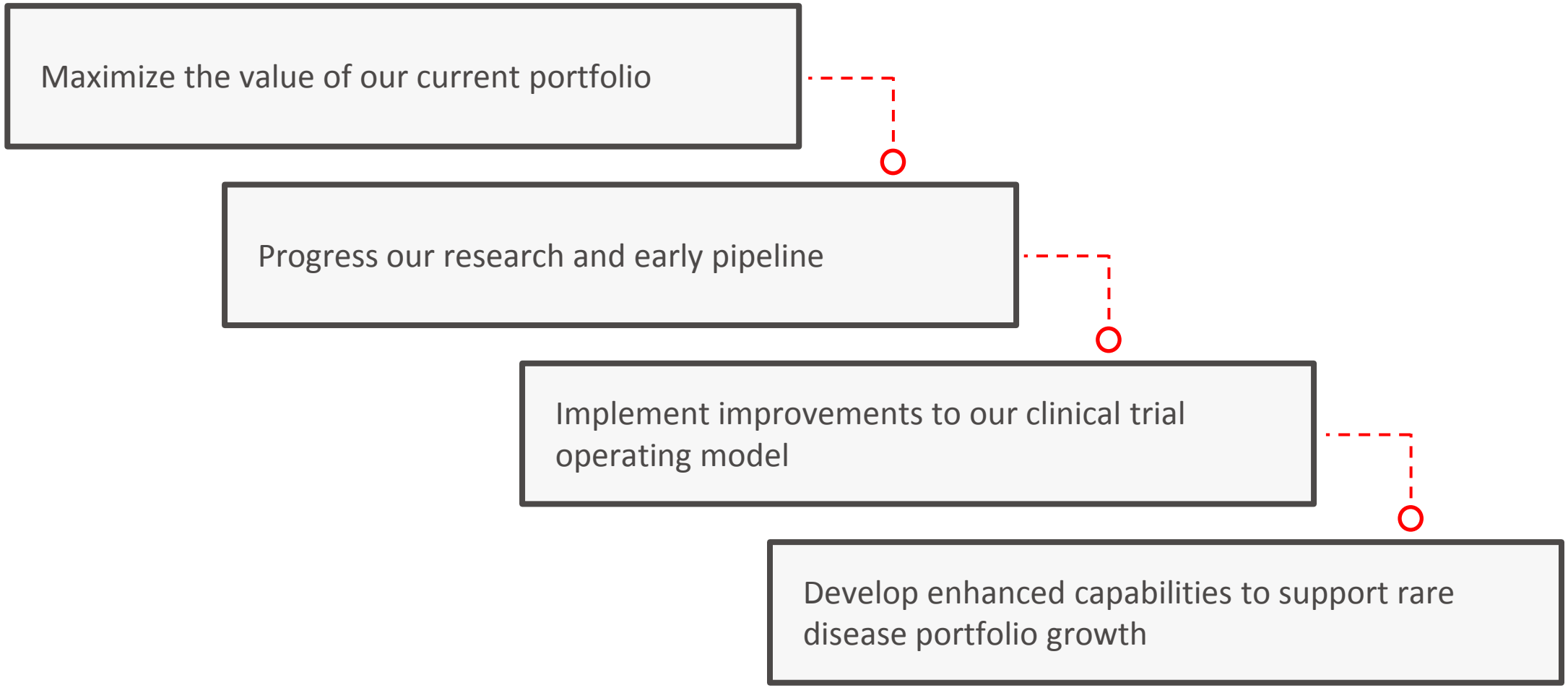
STING agonists:
Achieve in vivo POC for a drug delivery system

Internal R&D KPIs established in April 2018

WHAT'S NEXT

Looking Ahead

WHAT WE STILL NEED TO DELIVER

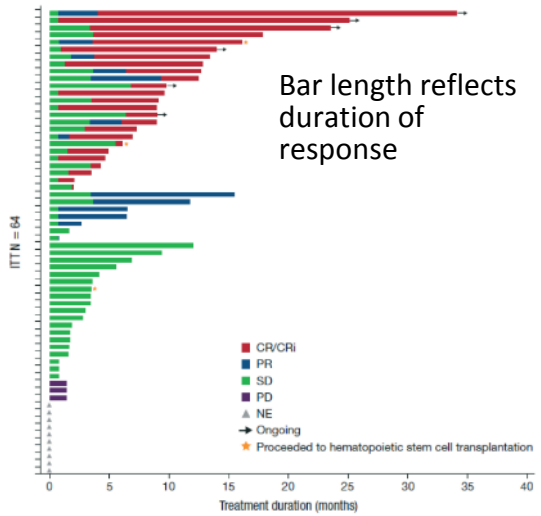


PROMISING PIVOTAL PROGRAMS

NEAR-TERM PIVOTAL RESULTS

Pevonedistat NAE inhibitor

Phase 1b study of pevonedistat with azacytidine[1]

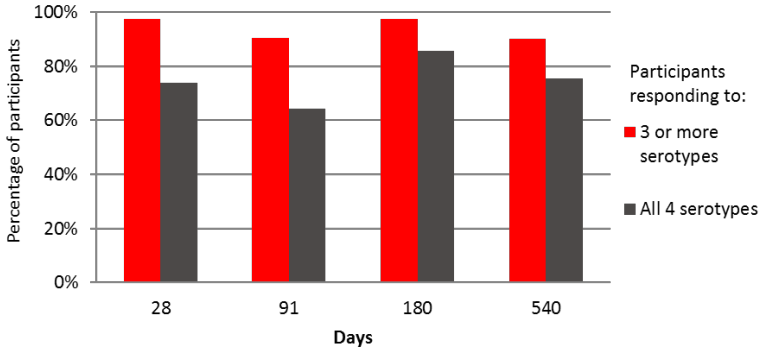


[1] Blood. 2018;131(13):1415-1424

Registration-enabling results expected in FY19

TAK-003 Dengue vaccine

Antibody-mediated immune response in dengue naïve popoulation[2]



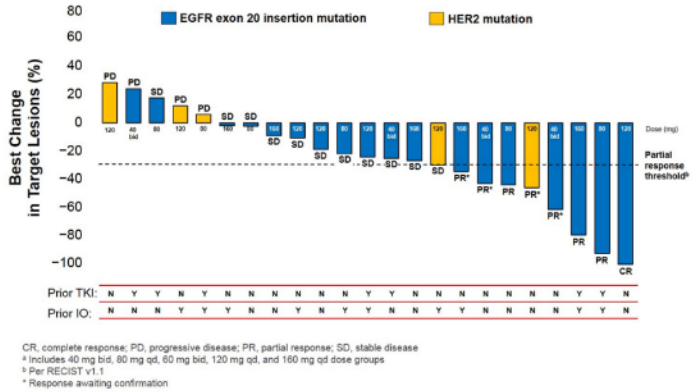
[2] Lancet Infect Dis 2018; 18: 162–70 Published Online November 6, 2017 http://dx.doi.org/10.1016/ S1473-3099(17)30632-1

Phase 3 results expected in FY18

NEXT PIVOTAL INITIATION

TAK-788 EGFR/HER2 inhibitor

Antitumor activity in all patients treated with TAK-788 at a total daily dose of ≥80–160 mg

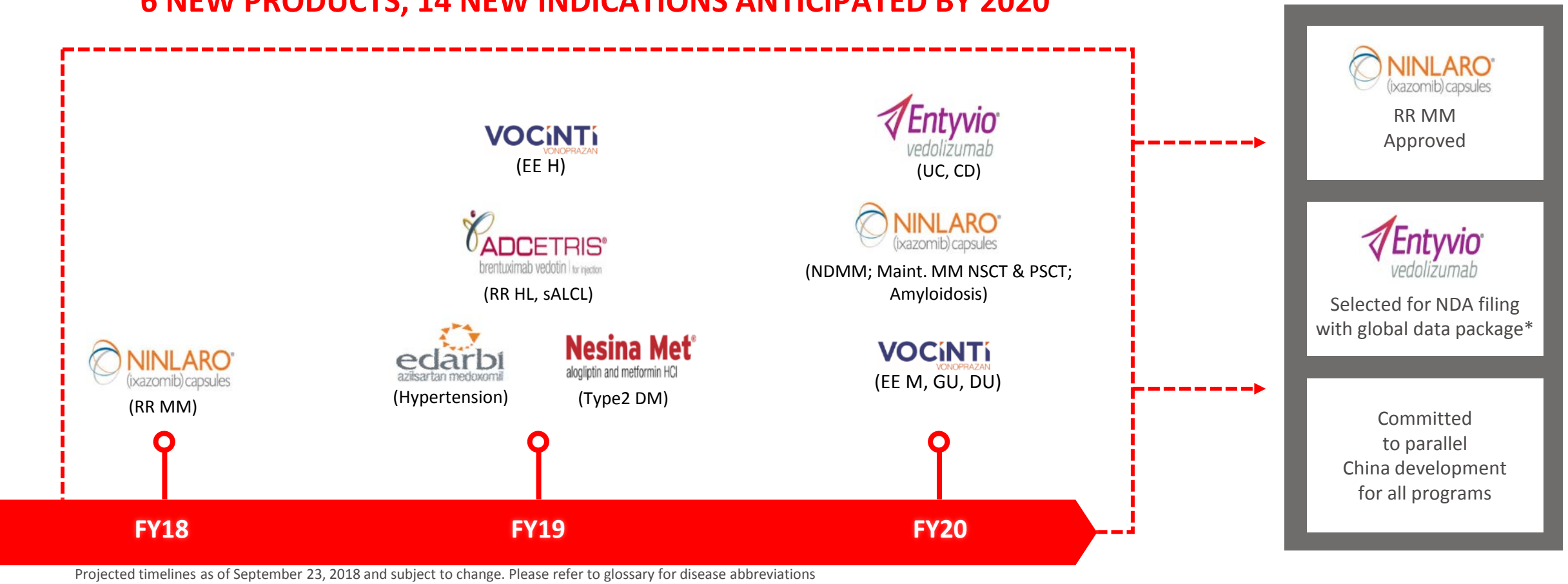


Neal et al., WCLC 2018

Registration-enabling trial start expected in FY18

CHINA IS AN IMPORTANT PART OF OUR GLOBAL GROWTH STRATEGY

6 NEW PRODUCTS, 14 NEW INDICATIONS ANTICIPATED BY 2020



Projected timelines as of September 23, 2018 and subject to change. Please refer to glossary for disease abbreviations

* On Aug 8th 2018, a total of 48 products marketed outside of China were selected by the Center Drug Evaluation 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.

SUSTAINED VALUE CREATION

FY 2018

- ONC ALUNBRIG, 2L ALK+ NSCLC post crizotinib (EU)
- NS TRINTELLIX, TESD (US)
- ONC ADCETRIS, 1L HL (EU, JP)
- GI Entyvio, UC H2H vs. adalimumab
- VBU TAK-003 Dengue Vaccine
- ONC ADCETRIS, PTCL
- ONC ALUNBRIG, 2L H2H vs. alectinib
- ONC ICLUSIG, Ph+ ALL
- ONC TAK-788, NSCLC Phase 2
- GI Entyvio, GvHD prophylaxis
- ONC ALUNBRIG, 2L post-2nd Gen
- VBU TAK-214 Norovirus Ph2b results

FY 2019

- ONC NINLARO MM maint. post-SCT (US, EU, JP, CN)
- ONC ALUNBRIG, 1L ALK+ NSCLC (US, EU)
- GI Entyvio, CD (JP)
- NS TRINTELLIX, MDD (JP)
- ONC ADCETRIS, PTCL (EU)
- Entyvio, SC UC (US)
- ONC NINLARO, ND MM
- ONC NINLARO, MM maint. non-SCT
- ONC Pevonedistat, HR-MDS
- GI Entyvio SC CD
- ONC ICLUSIG, Ph+ ALL 1st interim analysis
- GI Alofisel, fistulizing CD
- ONC TAK-079 R/R MM EPOC results
- GI TIMP-Gliadin Celiac EPOC results
- ONC TAK-659 Lymphoma EPOC results
- GI TAK-954 EFI Ph2b results
- ONC TAK-573 MM EPOC results
- GI Kuma062 Celiac EPOC results
- ONC TAK-931 GI Cancers EPOC results
- NS Wave, Huntington's Ph1b/2a results
- NS TAK-925 preliminary NT1 efficacy data
- NS TAK-831, Friedreich Ataxia Ph2 results

FY 2020

- ONC NINLARO, ND MM (US, JP, CN)
- ONC NINLARO, MM maint. non-SCT (US, EU, JP, CN)
- GI Entyvio, SC UC (EU, JP)
- ONC Pevonedistat, HR-MDS (US)
- ONC ADCETRIS, sALCL (CN)
- ONC ADCETRIS, R/R HL (CN)
- VBU TAK-003, Dengue Vaccine (EM)
- GI Entyvio, SC CD (US, EU)
- ONC ALUNBRIG, 2L H2H vs. alectinib
- GI Alofisel, fistulizing CD (JP)
- ONC TAK-788, NSCLC
- ONC ALUNBRIG, 2L post-2nd Gen

Future pivotal starts based on EPOC

- ONC TAK-164, GI Cancers EPOC results
- GI TAK-906, gastroparesis Ph2b results

MAJOR APPROVALS | PIVOTAL STUDY RESULTS | PIVOTAL STUDY STARTS | EARLY STAGE RESULTS

Projected timelines as of September 23, 2018, subject to change
EPOC: early proof-of-concept
Please refer to glossary for disease abbreviations

CONCLUSION:

1 Distinct R&D strategy based on TA focus, sustainable research and partnership engine

2 Delivering an innovative and compelling pipeline with near-term, data-driven inflections across each therapeutic area

3 With the successful execution of R&D transformation complete, we're now ready to effectively integrate Shire

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

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

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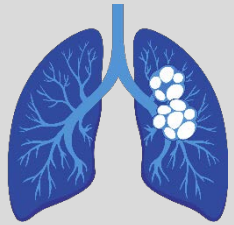
WE ASPIRE TO CURE CANCER

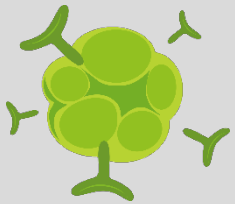
OUR MISSION

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.

HEMATOLOGIC MALIGNANCIES



LUNG CANCER

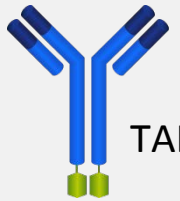


IMMUNO-ONCOLOGY (I/O)

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

ADCETRIS® brentuximab vedotin | for injection

Chronic Myeloid Leukemia

ICLUSIG® (ponatinib) tablets

Improving Patient Outcomes in Multiple Myeloma

VELCADE® (bortezomib)

NINLARO® (ixazomib) capsules

RECENT PROGRESS AND NEXT STEPS

Current Status

Approved in 59 countries for Relapsed/Refractory Multiple Myeloma

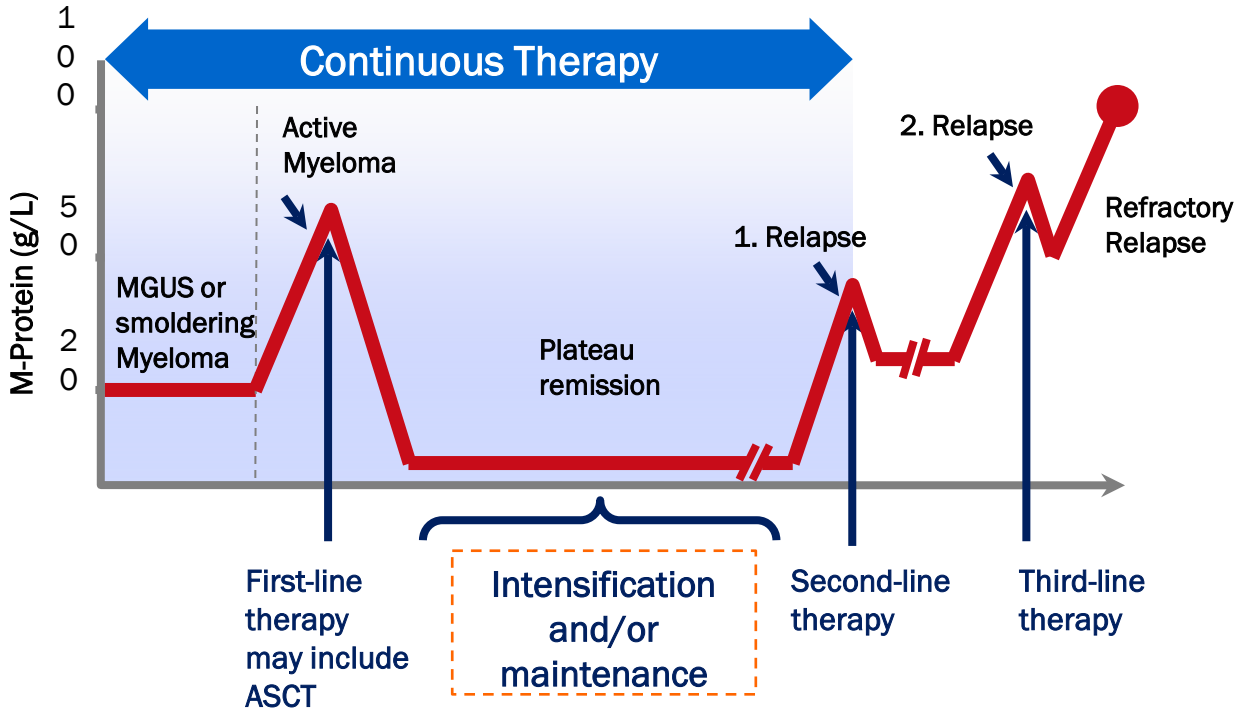
First Phase 3 maintenance readout (post-transplant)

Looking Forward

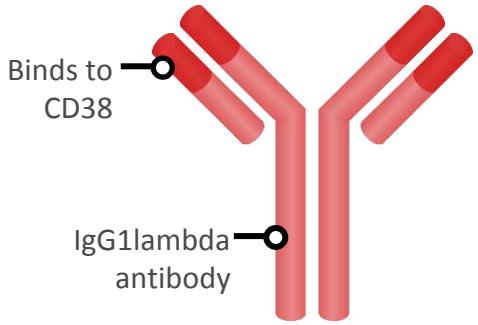
2019 Data Inflections:
MM2 (newly diagnosed)
MM4 (non-transplant maintenance)
AL1 (amyloidosis)
Evolution of real world evidence

Ideal Maintenance Therapies in Multiple Myeloma:

✓Easy to administer ✓Minimal toxicity ✓Maintain response

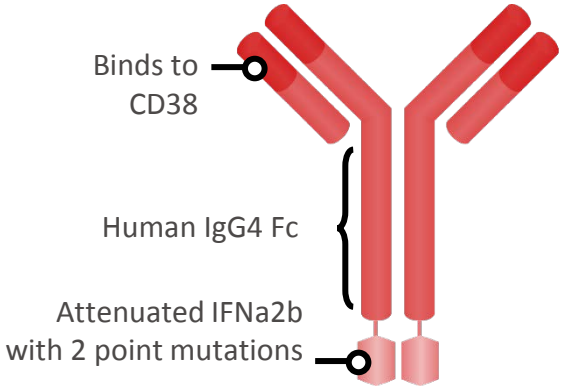


ADVANCE CD38 BIOLOGY FOR REFRACTORY MULTIPLE MYELOMA



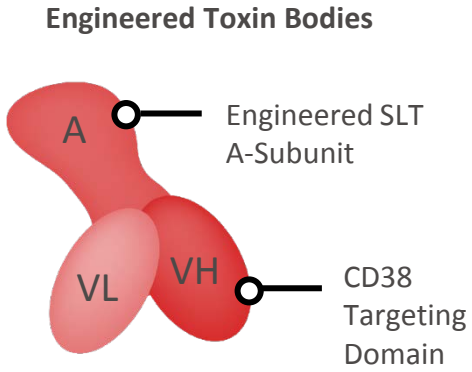
TAK-079

- 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

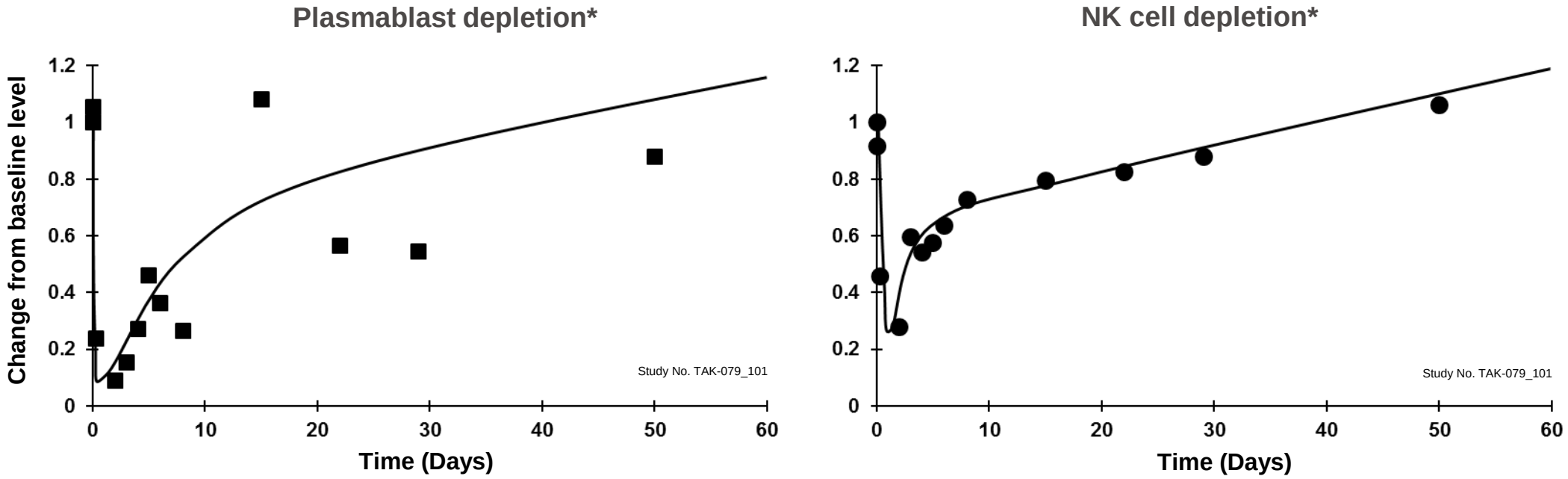


TAK-169

- 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

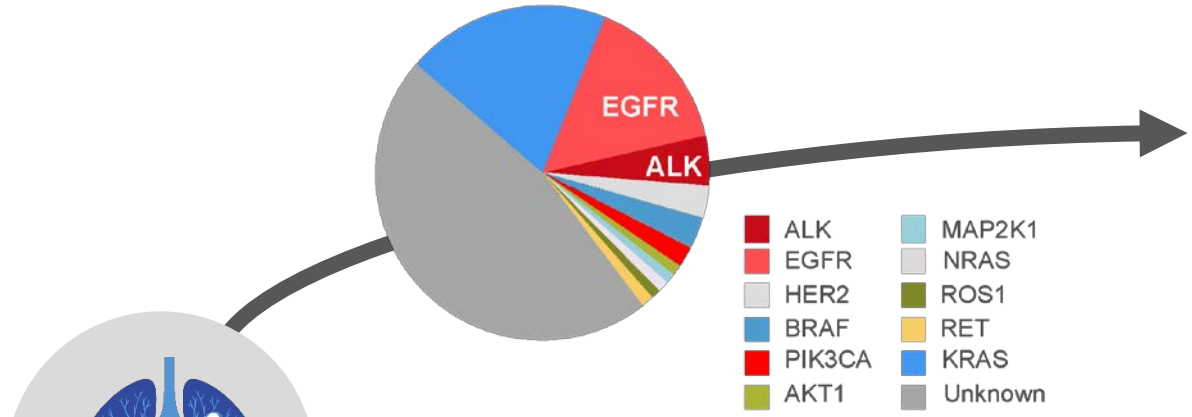
BRINGING NOVEL THERAPIES TO MDS AND AML

	PEVONEDISTAT IN HR-MDS	ALISERTIB IN AML
Unmet Need	**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	AML: Current **5 year survival ~30%** Transplant remains only curative option
Clinical Status	PANTHER **Phase 3 trial initiated in 2018**	American Society of Hematology Helping hematologists conquer blood diseases worldwide **ASH 2018: Phase 2 Data Submitted** • Alisertib is a novel, first in class mechanism for front-line AML in combination with chemotherapy
Next Steps	FDA • Potential accelerated filing based upon Phase II data in 2019	• Exploring initiation of Phase 3 registration enabling study in frontline AML in 2019

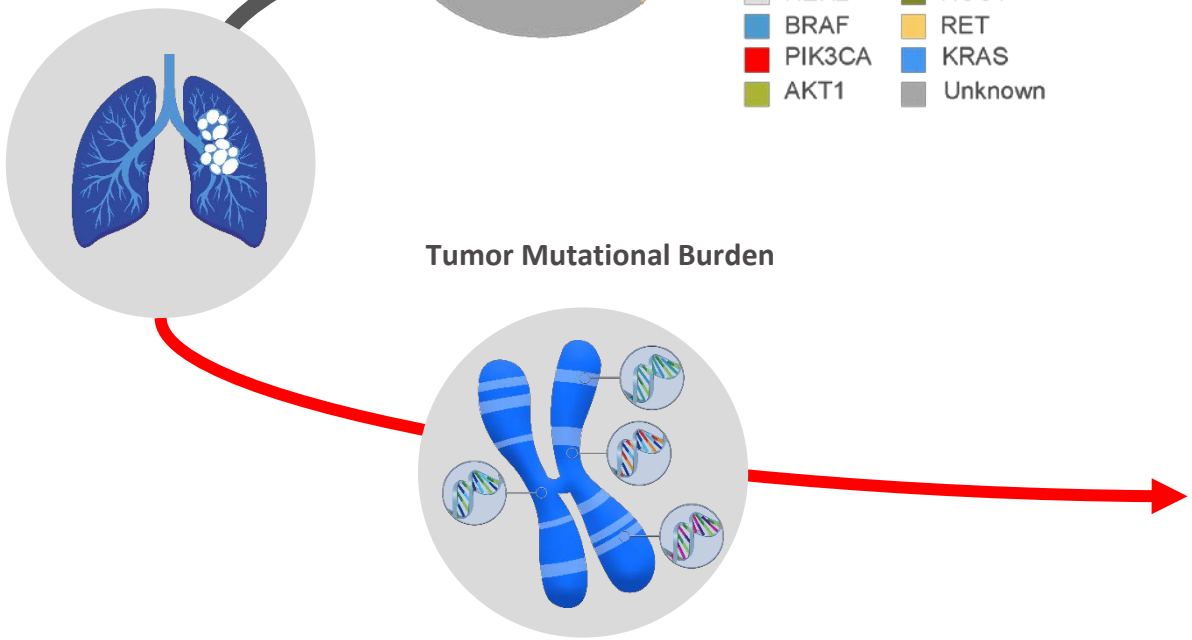
American Cancer Society – Survival Statistics for Myelodysplastic Syndromes, Tamamyan et al. *Critical Reviews in Oncology/Hematology* 2017, Yeung et al. *Biology of Blood and Marrow Transplantation* 2015, Courville et al. *BMC* Clinical *Pathology* 2017.

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

Molecularly-Targeted Precision Therapy



Tumor Mutational Burden



CURRENT PORTFOLIO

ALUNBRIG™ BRIGATINIB 30 mg TABLETS

TAK-788

EMERGING ASSETS

Sapanisertib (TAK-228)

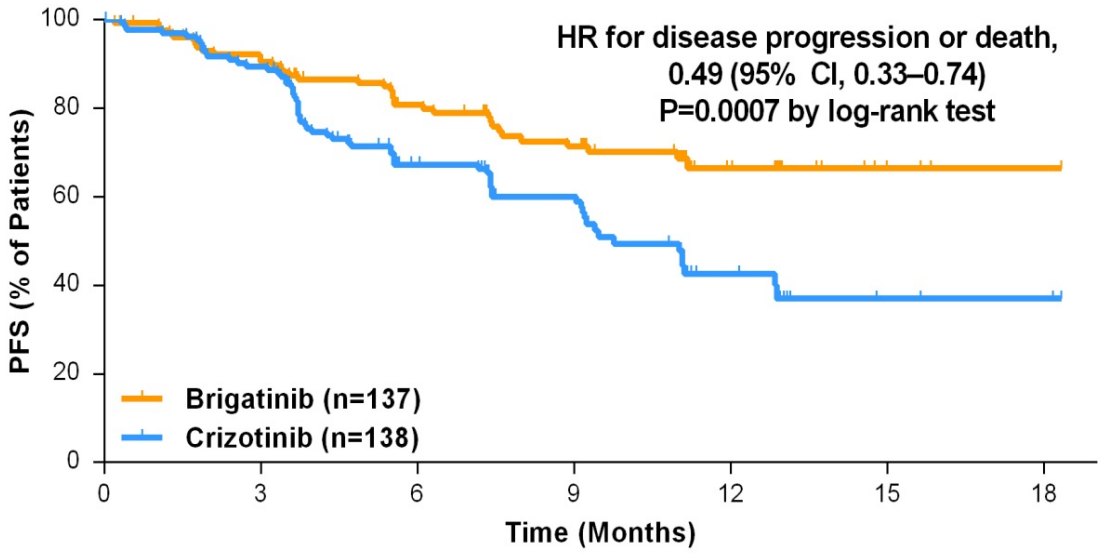
Next-generation kinase inhibitors

NEXT GENERATION TARGETS AND PLATFORM

SHATTUCK LABS

Crescendo® biologics

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

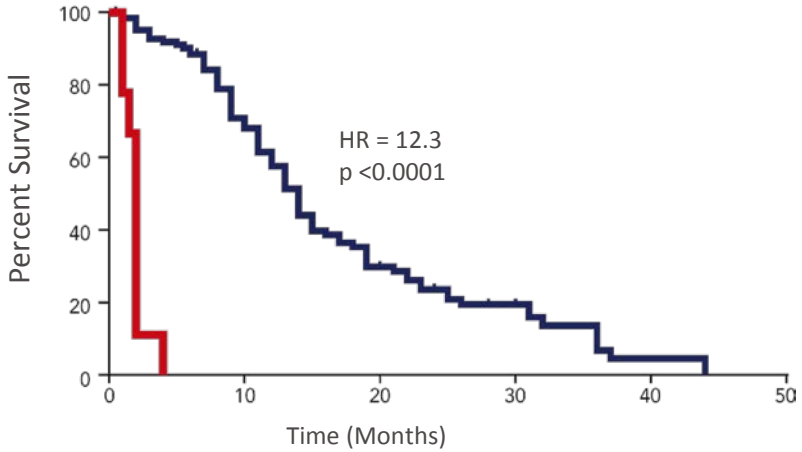


- Clear superiority to crizotinib and early separation in PFS curve
- Primary endpoint (PFS) hazard ratio is 0.49
- Risk/benefit profile consistent with the expectations of a best-in-class therapy

Camidge R., WCLC 2018

TAK-788: ADDRESSING UNMET NEED IN EGFR EXON20 MUTATIONS

RESPONSE TO CURRENT EGFR TKIs in EXON 20 INSERTIONS



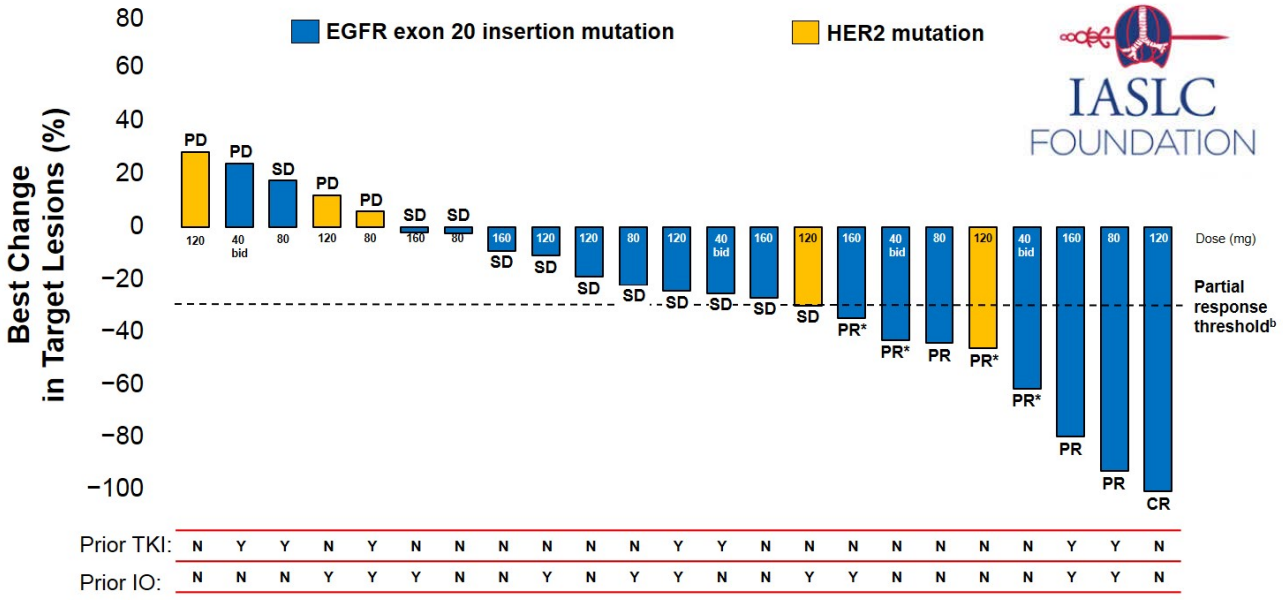
	Median PFS
EGFR Ex20 insertion (N=9)	2 months
Classical EGFR mut (N=129)	14 months

Overall survival <6 months for exon 20 insertions

Current therapies ineffective for these mutations

Robichaux et al. WCLC 2016

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

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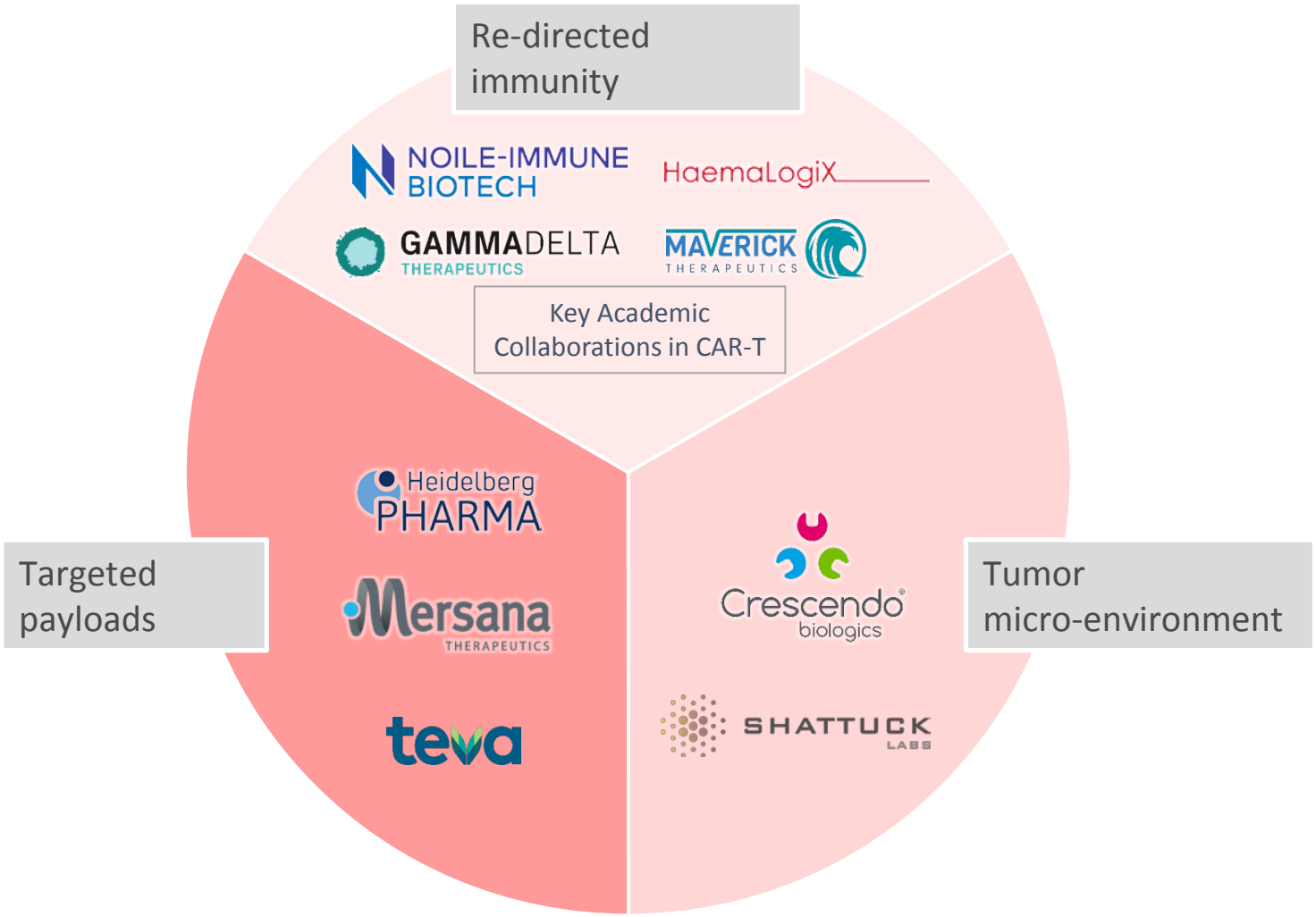
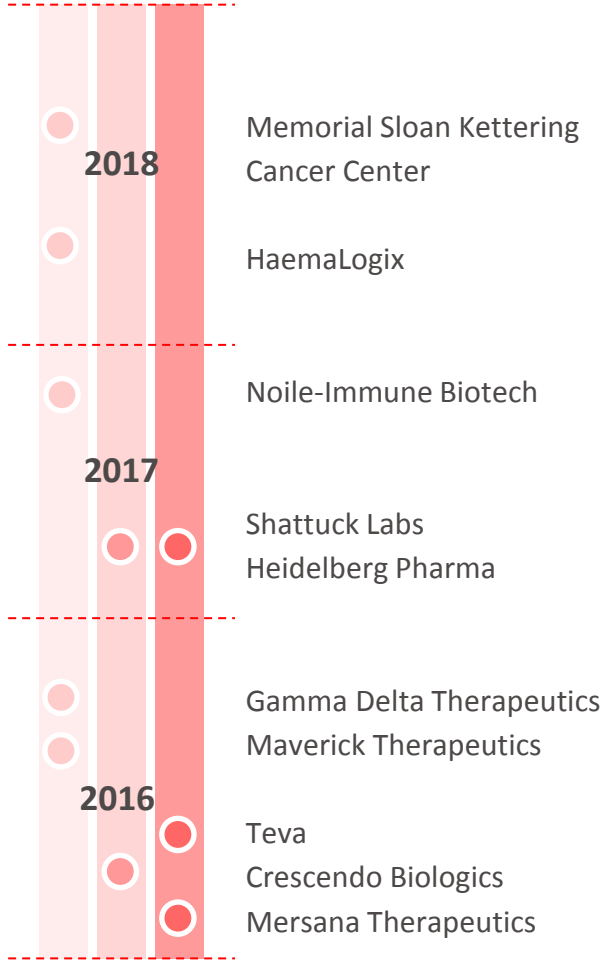
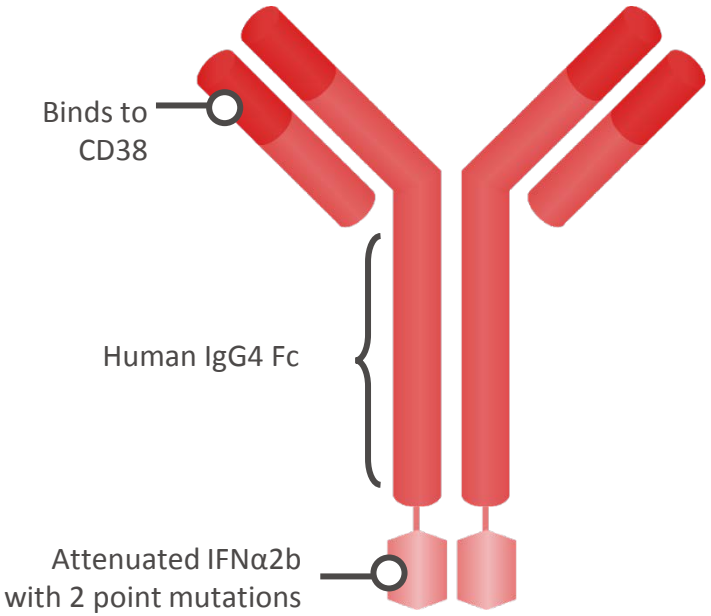
WORLD CLASS PARTNERS FUELING THE I/O PIPELINE

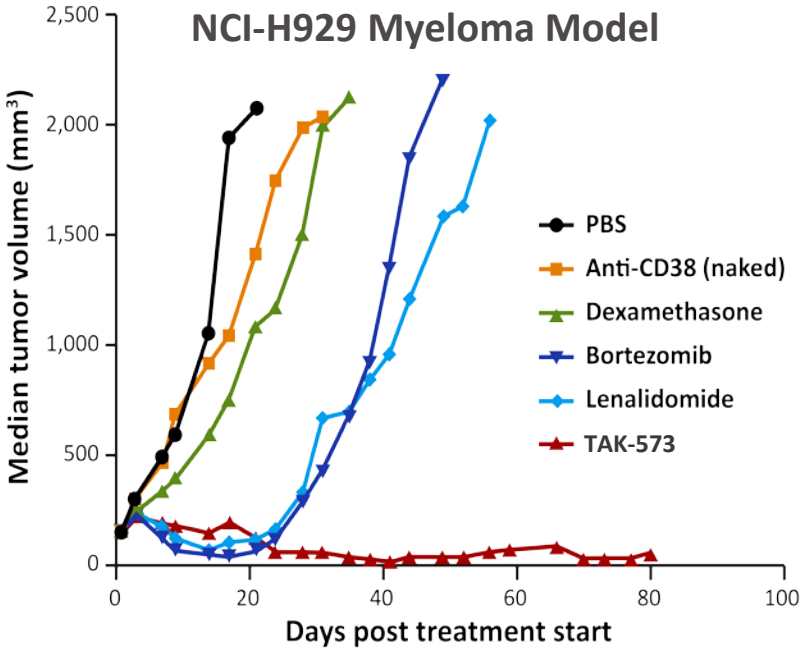




TAK-573: BRINGING A NOVEL IMMUNO-CYTOKINE APPROACH TO MULTIPLE MYELOMA

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

Pogue et al. PLOS ONE 2016

TAKEDA ONCOLOGY AIMS TO BECOME A LEADER IN CELL THERAPIES

TRANSFORMATIVE POTENTIAL UTILIZING NEXT GENERATION CELL THERAPY PLATFORMS

GAMMADELTA THERAPEUTICS

NOILE-IMMUNE BIOTECH

T-CiRA

(Takeda-CiRA) Joint Program Framework

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

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AN INNOVATIVE PIPELINE ENHANCED WITH EXTERNAL PARTNERSHIPS

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

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*

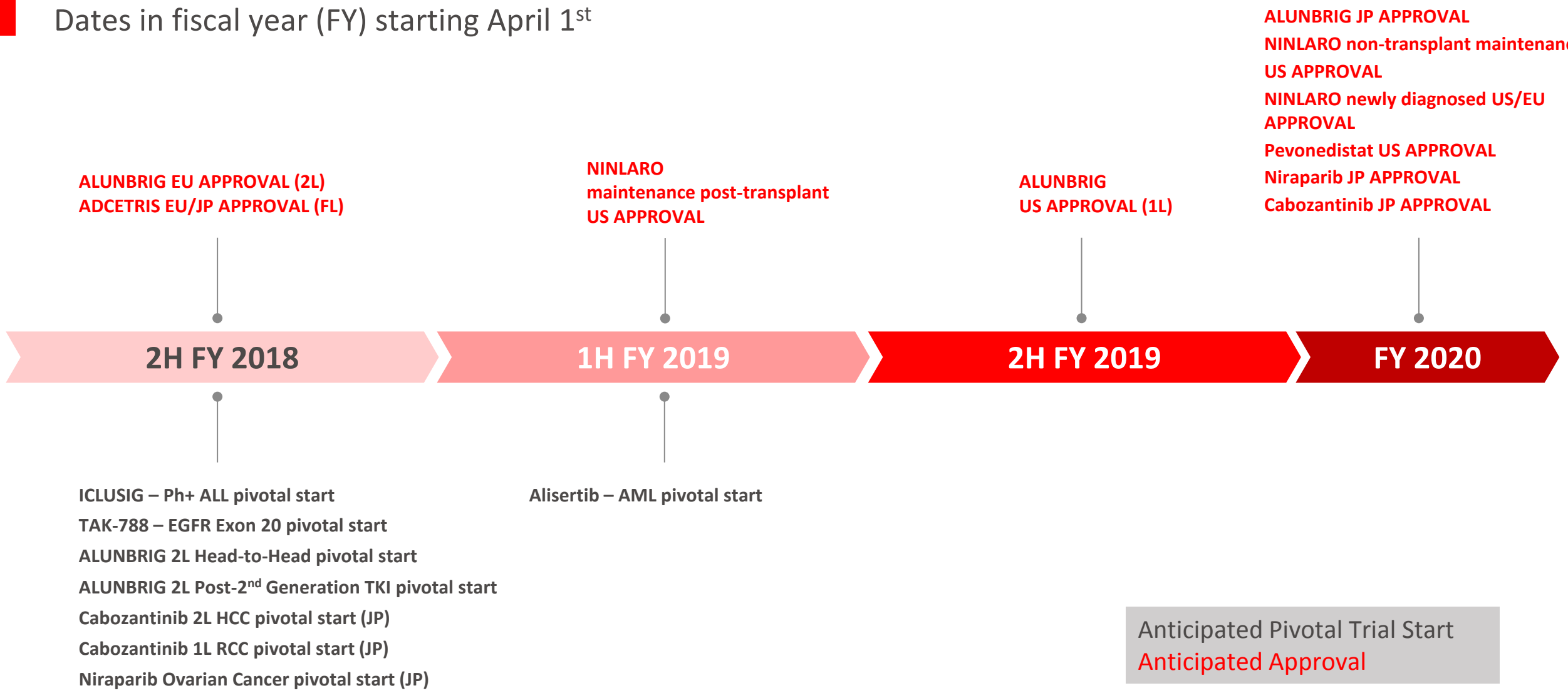
**** In pivotal trial for Japan approval*

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



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

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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

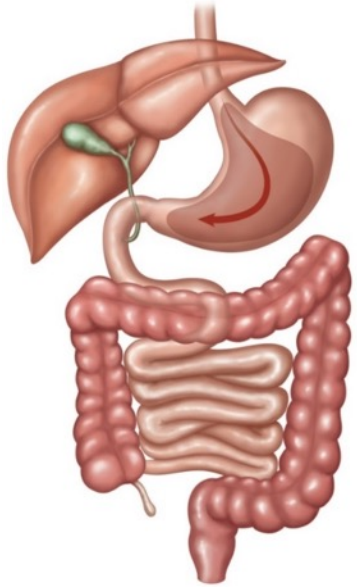
OUR STRATEGY EXPANDS THE PORTFOLIO ACROSS CORE DISEASE AREAS SUPPORTED BY PLATFORM TECHNOLOGIES

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

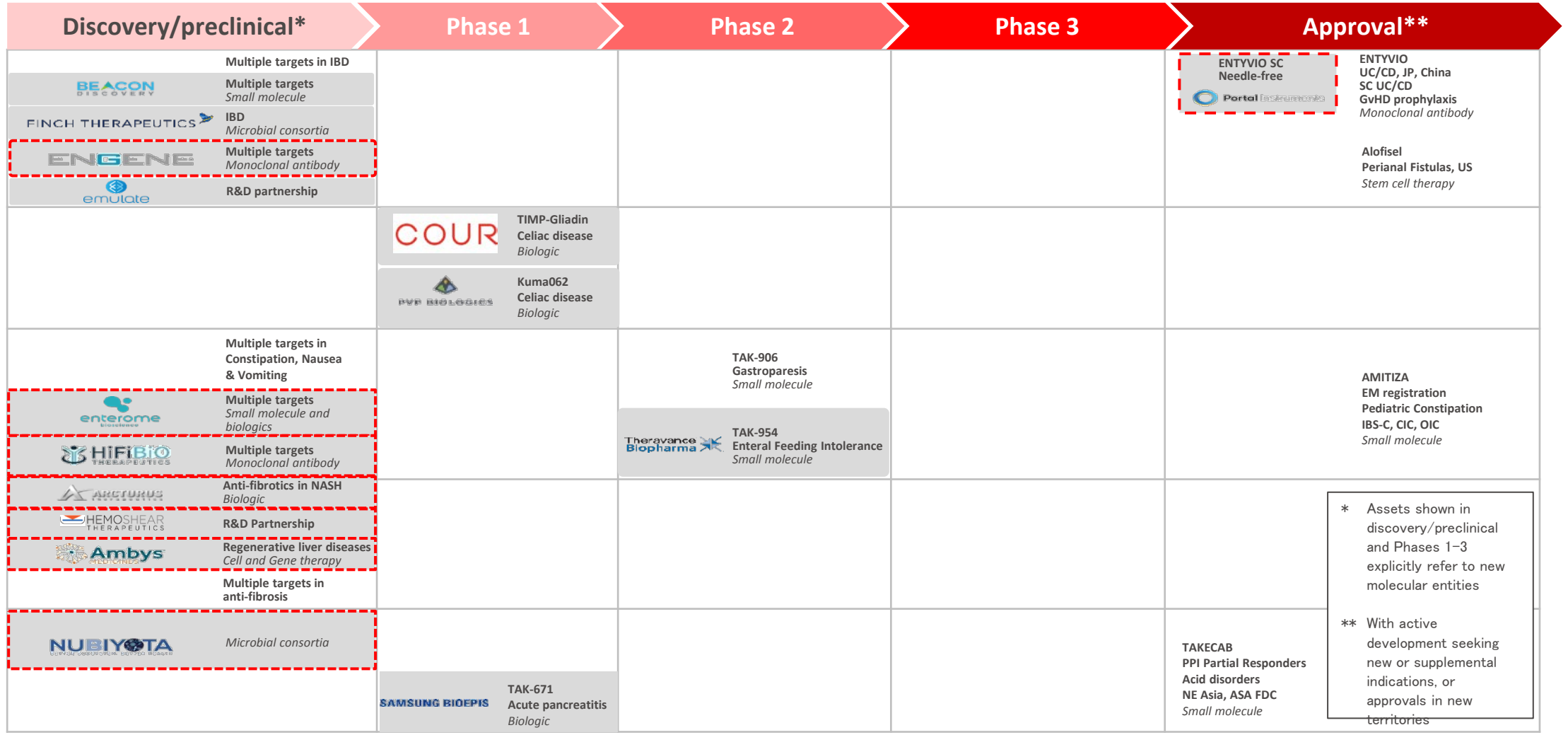
Luminal platforms

- 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.

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



External collaboration *Platform*

Pipeline as of September 23, 2018

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

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

Entyvio® vedolizumab — ***First and only*** biologic specifically targeting gut inflammation

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

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

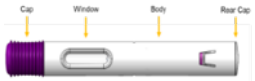
* On Aug 8th 2018, a total of 48 products marketed outside of China were selected by the CDE based on urgent medical needs, companies are encouraged to apply for NDA with overseas data including data demonstrating lack of ethnic differences. Priority review/approval process will be applied.
** As of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

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

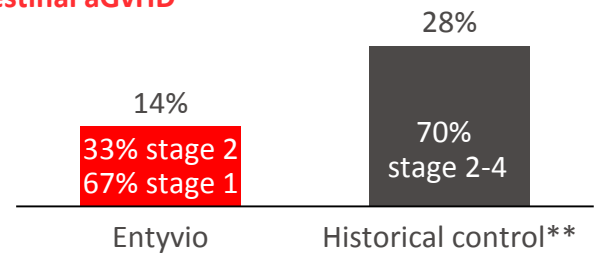
Prefilled syringe *Autoinjector pen* *Portal needle-free*



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

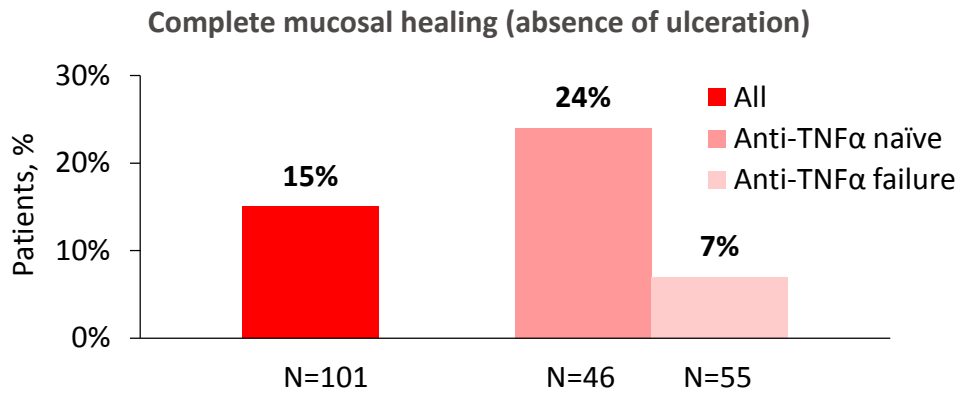
** Adjusted for patient population including allogenic stem cell transplant characteristics with similar conditioning regimen

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 treatment[1] 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 Gut[2]
- Real world propensity score matched analyses by the VICTORY Consortium[3] 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)

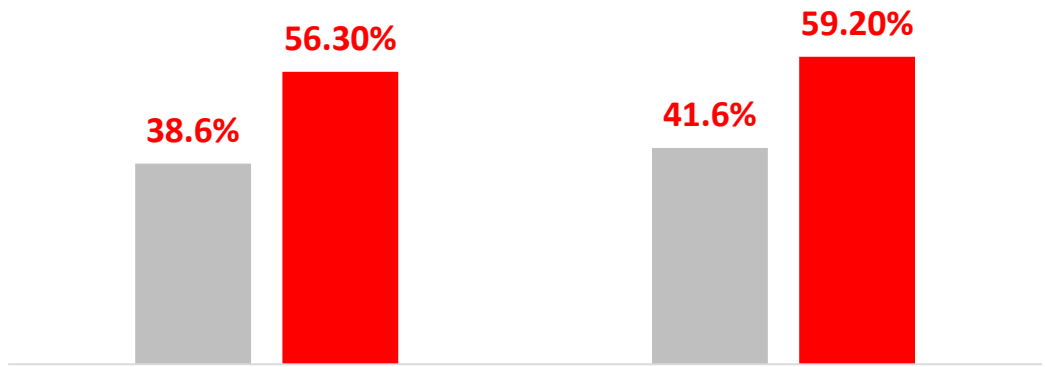
Abbreviations: SES-CD, Simple Endoscopic Score for CD; TNFα, tumor necrosis factor alpha.

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)*



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

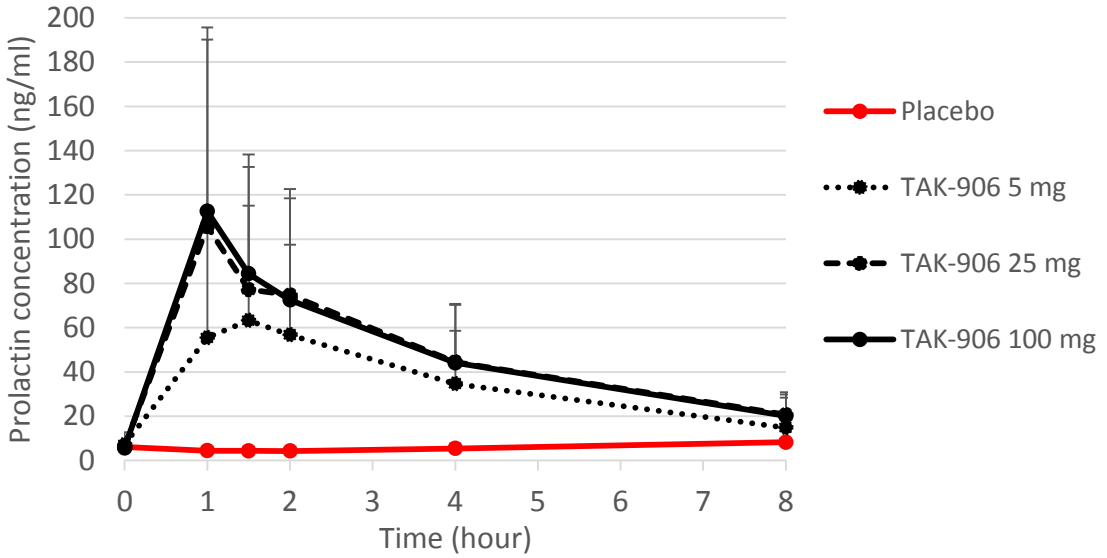
Abbreviations: SOC, Standard of care

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.

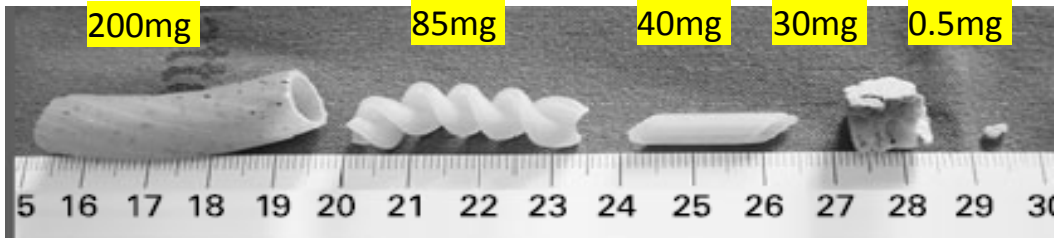
Abbreviations: AE, Adverse event; HV, healthy volunteer; GP, Gastroparesis

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

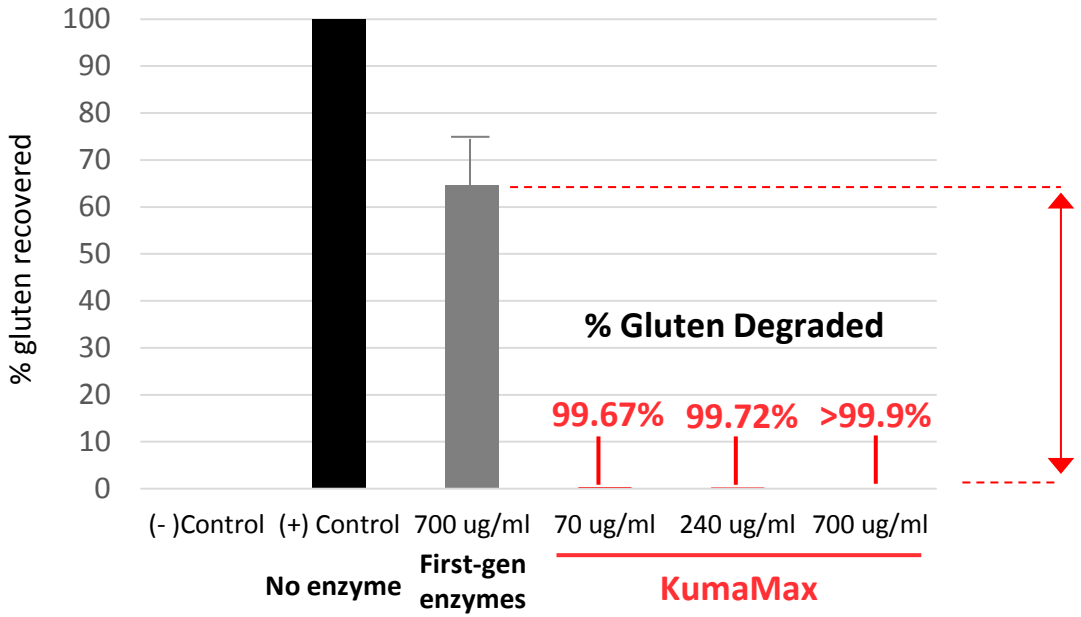
CELIAC DISEASE

- 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



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

HEMOSHEAR THERAPEUTICS

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

ARCTURUS therapeutics

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

Ambys MEDICINES

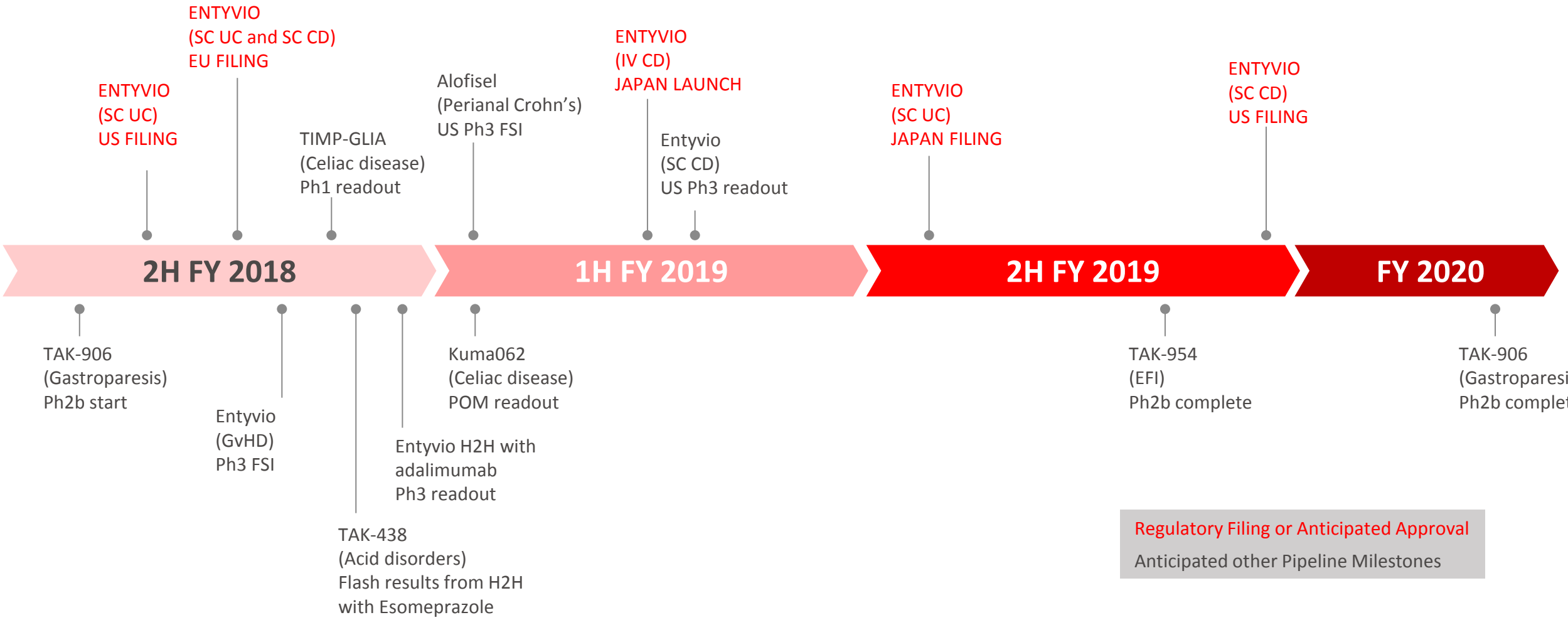
Takeda co-founded with Third Rock Ventures to focus on cell and gene therapy for end-stage liver diseases

Series A announced August 2018

Abbreviations: MOA, Mechanism of action

EXPECTED KEY GI PORTFOLIO INFLECTIONS AND MILESTONES

Dates in fiscal year (FY) starting April 1st



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

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

TAKEDA NEUROSCIENCE

BRINGING INNOVATIVE MEDICINES TO PATIENTS FOR WHOM THERE ARE NO TREATMENTS AVAILABLE

EMILIANGELO RATTI, PHD
Head, Neuroscience Therapeutic Area

WE HAVE TAKEN ON THE CHALLENGE TO ALLEVIATE THE IMMENSE PATIENT NEED IN NEUROSCIENCE

MISSION

To bring innovative medicines to patients suffering from neurologic and psychiatric diseases for **whom there are no treatments available**

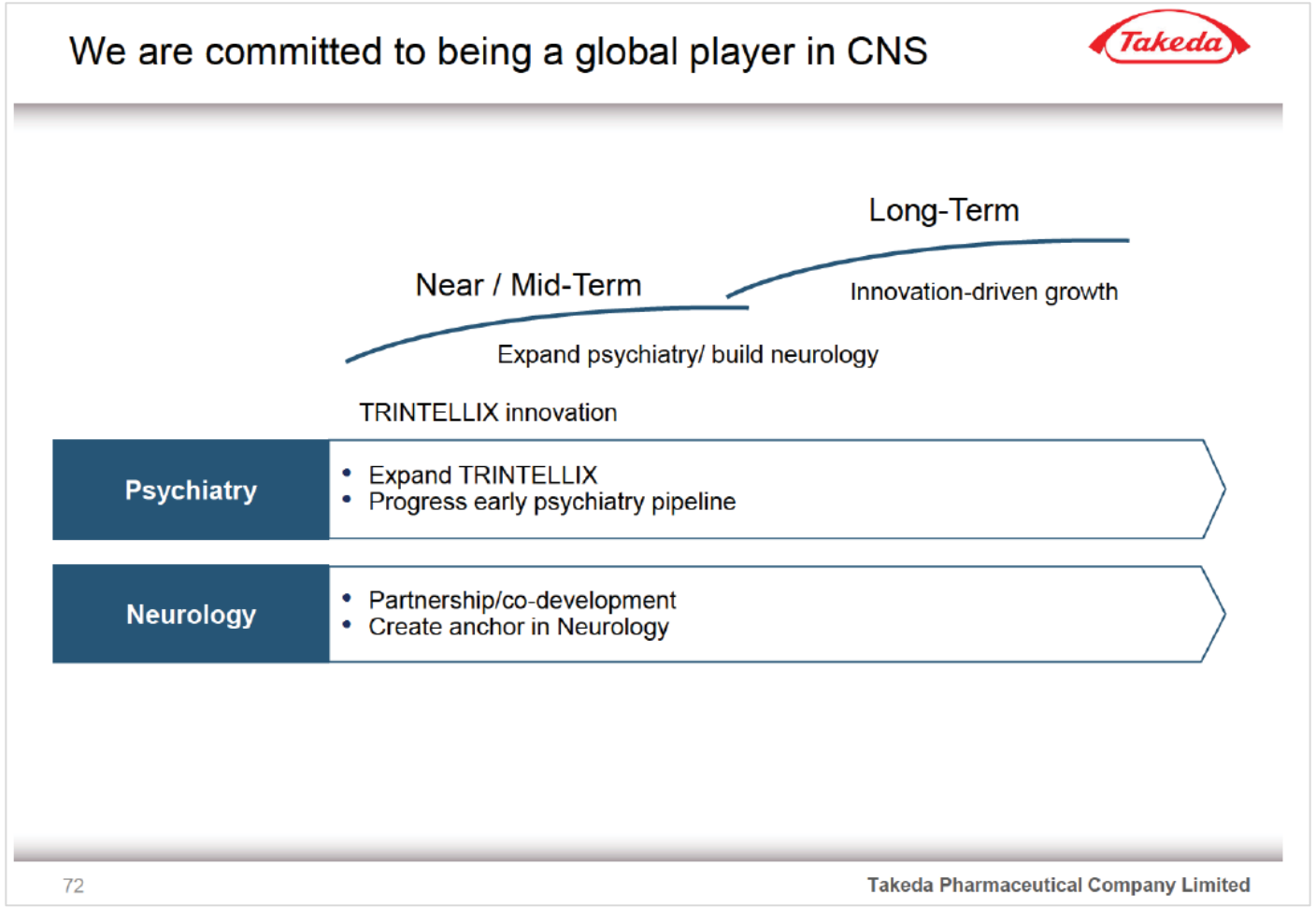
FOCUS

- Treatment Resistant Depression
- Schizophrenia Negative Symptoms & CIAS
- ***Selected rare CNS diseases***
- Alzheimer's Disease
- Parkinson's Disease

CIAS: Cognitive Impairment Associated with Schizophrenia

WE HAVE EXECUTED ON THE ROADMAP DESCRIBED IN 2016

FROM 2016 R&D DAY



KEY COMPONENTS OF ROADMAP

- Differentiate TRINTELLIX
- Advance early pipeline towards POC
- Further expand in neurology and rare CNS diseases through partnerships

BUILDING AN INNOVATIVE PIPELINE ENHANCED WITH EXTERNAL PARTNERSHIPS

	Discovery/Preclinical[1]	Phase 1*	Phase 2	Phase 3	Approved**
Depression		**TAK-653** **AMPA PAM** **Treatment Resistant Depression** *Small Molecule*			**TRINTELLIX** ***Processing Speed sNDA Approved 2018*** **TESD sNDA (US) Submitted** **MDD (JP) Submitted**
Schizophrenia		**TAK-041** **GPR139 Agonist, 2xFT** *Small Molecule*	**TAK-831** **DAAO Inhibitor, 2xFT** *Small Molecule*		
Parkinson's Disease		AstraZeneca **MEDI1341** **α-synuclein mAb** *Monoclonal Antibody*			teva **AZILECT** **PD (JP) Launched 2018**
Alzheimer's Disease	DENALI THERAPEUTICS **BACE1/TAU, TREM2, Undisclosed** *Antibody Transport Vehicle Monoclonal Antibody*				
Rare CNS Diseases	WAVE LIFE SCIENCES **C9orf72, ATXN3, Multiple targets** *Stereopure Antisense Oligonucleotide*	**TAK-925, Narcolepsy, OD** **OX2R Agonist** *Small Molecule* **TAK-418, Kabuki Syndrome, OD** **LSD1 Inhibitor** *Small Molecule* WAVE LIFE SCIENCES **WVE-120101; WVE-120102** **Huntington's Disease, OD** *Stereopure Antisense Oligonucleotide*	Ovid THERAPEUTICS INC **TAK-935** **Epileptic Encephalopathy, OD** **CH24H Inhibitor** *Small Molecule* **TAK-831** **Friedreich's Ataxia, OD, FT** **DAAO Inhibitor** *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

External collaboration *FT = Fast Track* *OD = Orphan Designation* *New partnerships since June 2016* *Progress since June 2016 shown in red*

Pipeline as of September 23, 2018

[1] Discovery/preclinical phase: Only external collaborations shown, does not include internal programs

WE HAVE BUILT OUR PORTFOLIO THROUGH THREE MAIN LEVERS

EXECUTED ON OPPORTUNITIES WITH LATE-STAGE ASSETS

- **Successful differentiation of TRINTELLIX**
- Launched AZILECT in Japan

ADVANCED EARLY STAGE PIPELINE TOWARDS POC

- TAK-925 Narcolepsy
- TAK-831 Schizophrenia, Friedreich's Ataxia
- TAK-935 Epileptic Encephalopathy

EXPANDED IN NEURODEGENERATION AND RARE DISEASE WITH WORLD CLASS PARTNERS

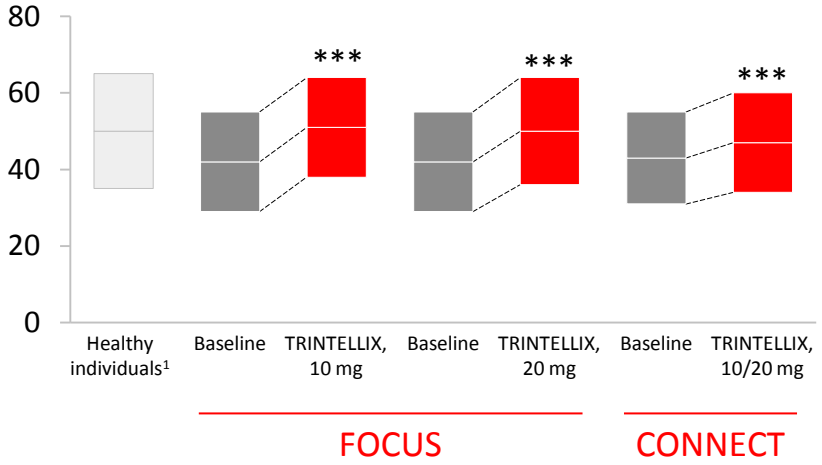
- Denali Therapeutics partnership to address extracellular targets with highly brain penetrant monoclonal antibodies
- Wave Life Sciences partnership to address intracellular targets with stereopure oligonucleotides
- AstraZeneca partnership to treat Parkinson's Disease

TRINTELLIX SHOWS BENEFITS IN PROCESSING SPEED, AN IMPORTANT ASPECT OF COGNITION, AND TREATMENT EMERGENT SEXUAL DYSFUNCTION FOR PATIENTS WITH MDD

COGNITIVE FUNCTION (PROCESSING SPEED)

Digit Symbol Substitution Test (DSST) after 8 weeks of treatment

Total number of correct symbols; mean score with standard deviation



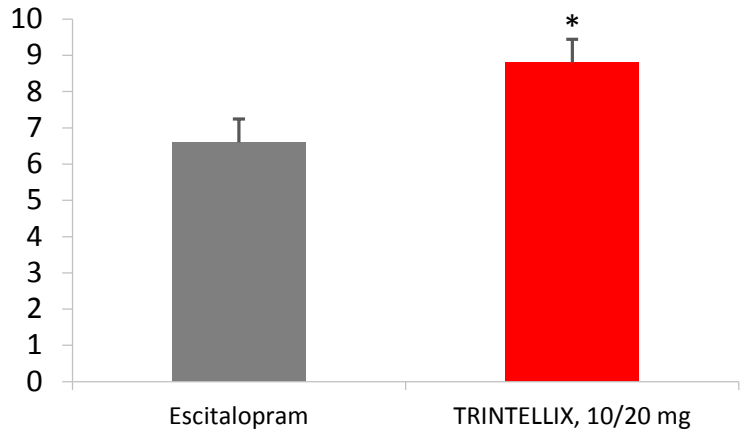
- **In May 2018, FDA approved sNDA that includes DSST, which most specifically measures processing speed, an important aspect of cognition**
- TRINTELLIX® is the first MDD treatment labelled for improvement of processing speed, an important aspect of cognitive function

[1] Normative data from healthy individuals
***p<0.001 vs baseline
Change from baseline was also significant vs placebo in both FOCUS and CONNECT studies
CONNECT study: Mahableshwarkar AR, et al. Neuropsychopharmacology. 2015
FOCUS study: McIntyre RS, et al. Int J Neuropsychopharmacol. 2014
MDD = Major Depressive Disorder

TREATMENT EMERGENT SEXUAL DYSFUNCTION

Changes in Sexual Functioning Questionnaire (CSFQ-14) after 8 weeks of treatment

Change from baseline in CSFQ-14 total score; least squares mean, standard error



- **TRINTELLIX showed statistical superiority to escitalopram in improving sexual dysfunction while maintaining efficacy** in MDD patients with SSRI-induced sexual dysfunction
- **Submitted sNDA to include TESD recovery data in label;** FDA decision expected in 4Q 2018
- Overall, the safety profile of vortioxetine in these studies was consistent with that in the approved vortioxetine label

* Statistically superior to escitalopram; p<0.05
Jacobsen et al. Journal of Sexual Medicine 2015

In collaboration with Lundbeck

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DESPITE CURRENT TREATMENTS, PATIENTS WITH NARCOLEPSY TYPE 1 (NT1) SUFFER FROM A RANGE OF DEBILITATING SYMPTOMS

NARCOLEPSY TYPE 1

- Affects ~100K patients in US (~400K in G-7), with typical disease onset from 7-25 years old[1]
- Symptoms characterized by:
  - Excessive daytime sleepiness
  - Sleep/wake fragmentation
  - Cataplexy
- Current treatments are only partially effective and only provide benefit for some disease symptoms

"We take our current meds to **survive.** We want new medications to help us **live.**"

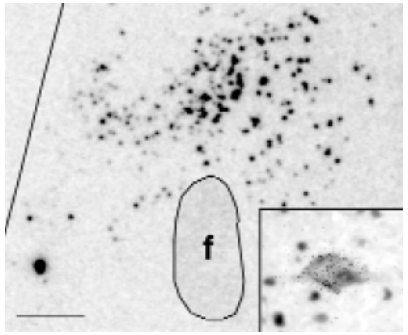
Narcolepsy patient advisor
Patient Advisory Board sponsored by Takeda

[1] Longstreth. Sleep. 2007;30(1):13

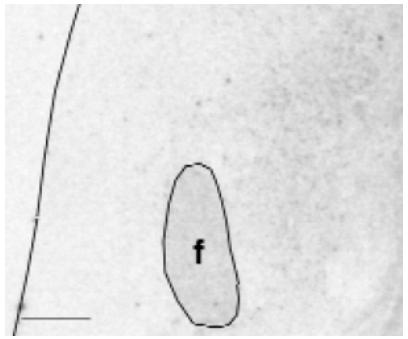
NARCOLEPSY TYPE 1 IS CAUSED BY LOSS OF OREXIN PRODUCING NEURONS

OREXIN mRNA LABELLING OF POSTMORTEM HYPOTHALAMIC SECTIONS[1]

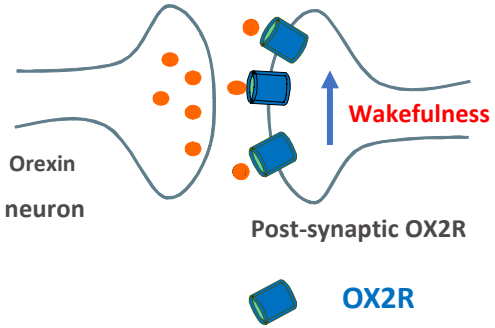
Healthy Control

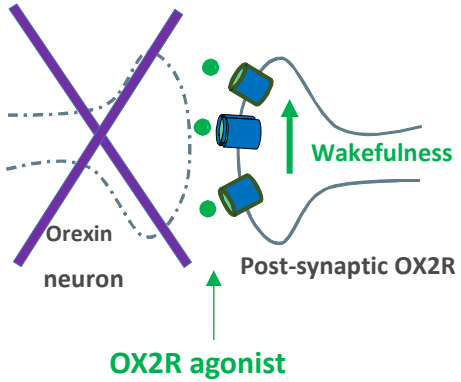


Narcolepsy Type 1 patient



- Orexin mRNA transcripts are detected in control but not in Narcolepsy Type 1 patients





- Orexin receptors may remain functional in Narcolepsy Type 1 patients

LEADING RESEARCH TO SUPPORT THE OREXIN HYPOTHESIS

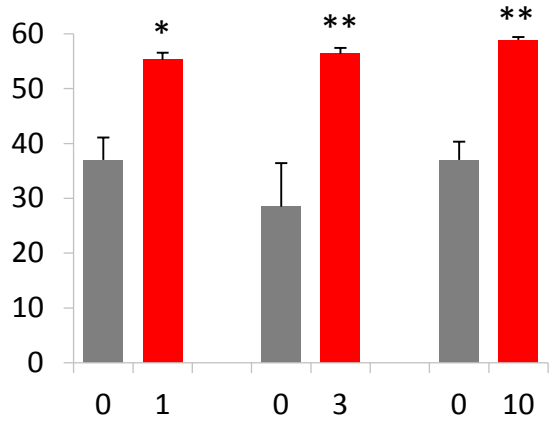
An orexin 2 receptor agonist may mimic the missing endogenous peptide (orexin) and address the neurotransmitter deficiency of Narcolepsy Type 1 leading to reduction in disease specific symptoms

[1] Nature Medicine 2000 Vol 6 p 991-997

TAK-925 IS A SELECTIVE OX2R AGONIST SHOWING REDUCTION IN NARCOLEPSY-LIKE SYMPTOMS IN A MOUSE MODEL

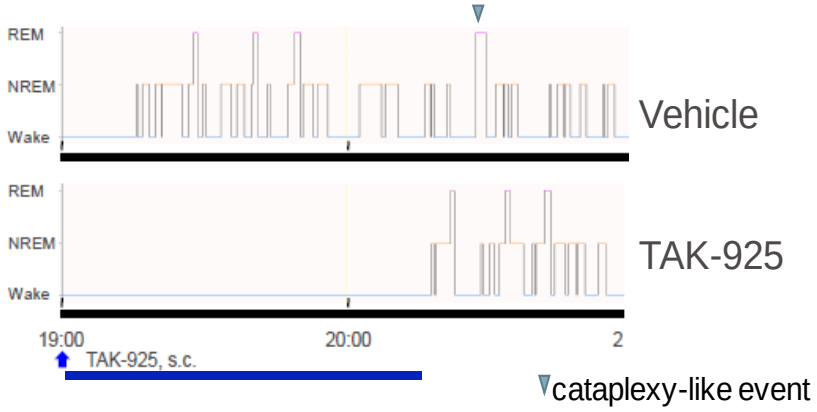
TAK-925 FULLY RESTORED WAKEFULNESS

Wakefulness time of NT1 mouse model in active phase for one hour
Minutes awake



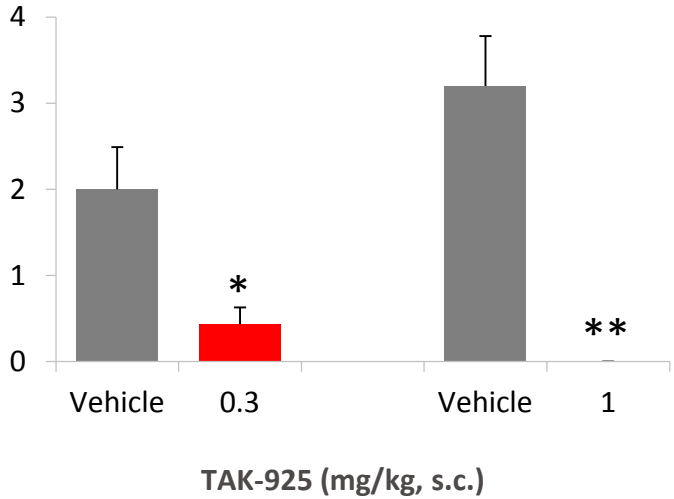
TAK-925 ELIMINATED SLEEP / WAKE TRANSITIONS

Hypnogram of sleep/wake transitions in NT1 mouse model
EEG recordings



TAK-925 ABOLISHED CATAPLEXY-LIKE EPISODES

Cataplexy-like episodes in NT1 mouse model for three hours after chocolate
Count



Phase I clinical studies are ongoing to evaluate safety and efficacy of TAK-925

*p<0.05, **p<0.01 vs placebo

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MANY NEURODEGENERATIVE DISEASES CAN BE ADDRESSED WITH ALTERNATIVE MODALITIES TARGETED TO PATHOGENIC PROTEINS

Antisense oligonucleotides can reduce *intracellular* expression of toxic proteins

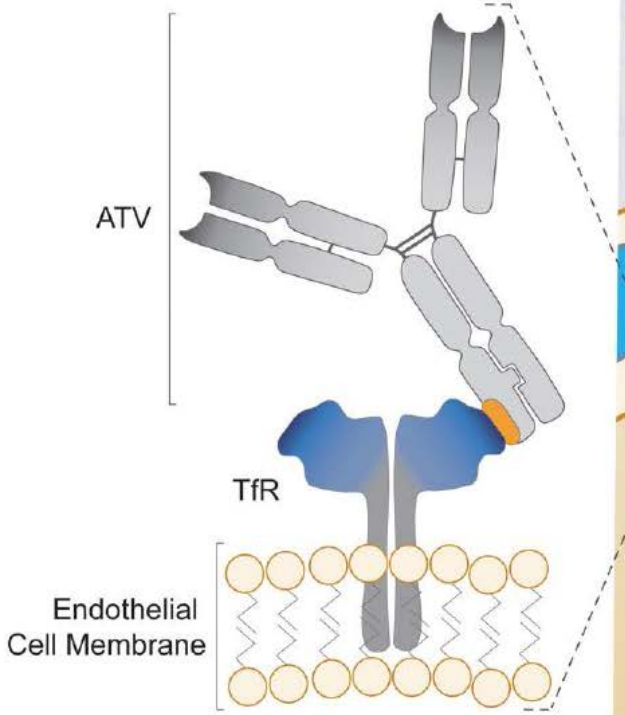
Monoclonal antibodies can clear pathogenic *extracellular* proteins

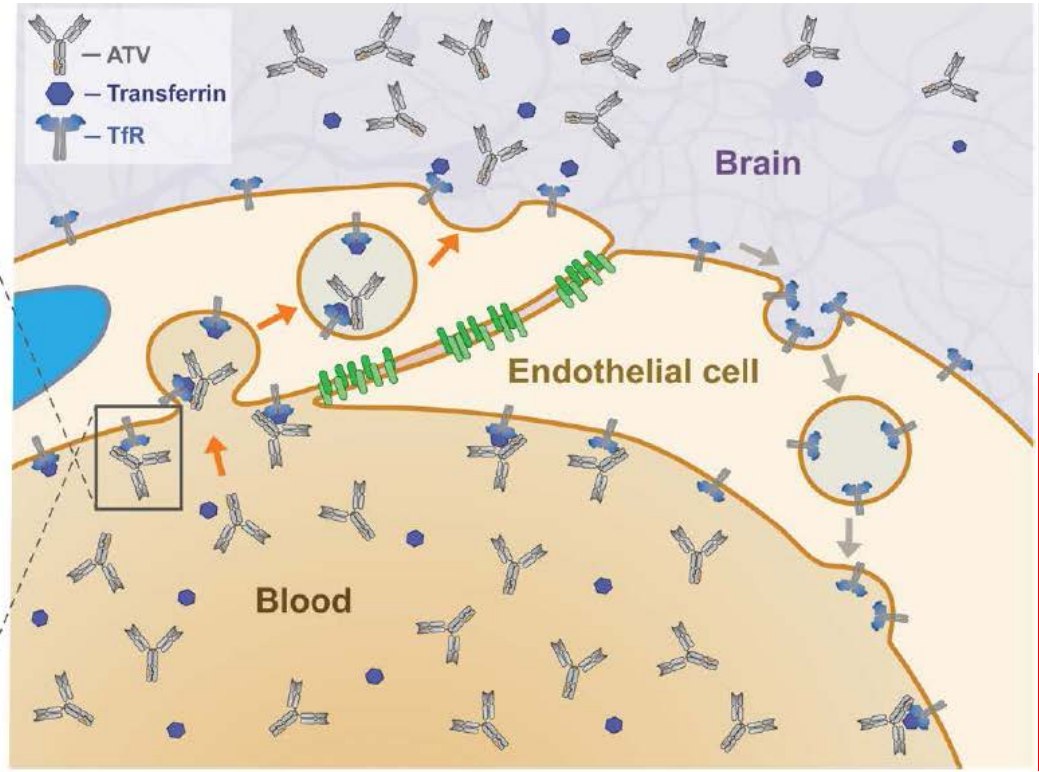
ASOs and mAbs could be combined for greater efficacy

Pathogenic protein monomers, oligomers, and fibrils can spread from neuron to neuron and propagate the disease

PARTNERSHIP WITH DENALI HAS REINFORCED OUR ALZHEIMER'S DISEASE PORTFOLIO WITH HIGHLY BRAIN PENETRANT MONOCLONAL ANTIBODIES

DENALI THERAPEUTICS





Antibody Transport Vehicles (ATVs) enable up to > 20X higher brain penetration of monoclonal antibodies than the same antibody without ATV[1]

Collaboration agreement to co-develop three named programs

- ATV: BACE1 / TAU
- ATV: TREM2
- Additional undisclosed program

[1] Denali Therapeutics S-1/A

PARTNERSHIP WITH WAVE LIFE SCIENCES ENABLES TARGETED THERAPIES TO RARE CNS DISEASES WITH STEREOPURE ANTISENSE OLIGONUCLEOTIDES

SYNTHESIS OF STEREOPURE OLIGONUCLEOTIDES: A SIGNIFICANT IMPROVEMENT IN THE FIELD

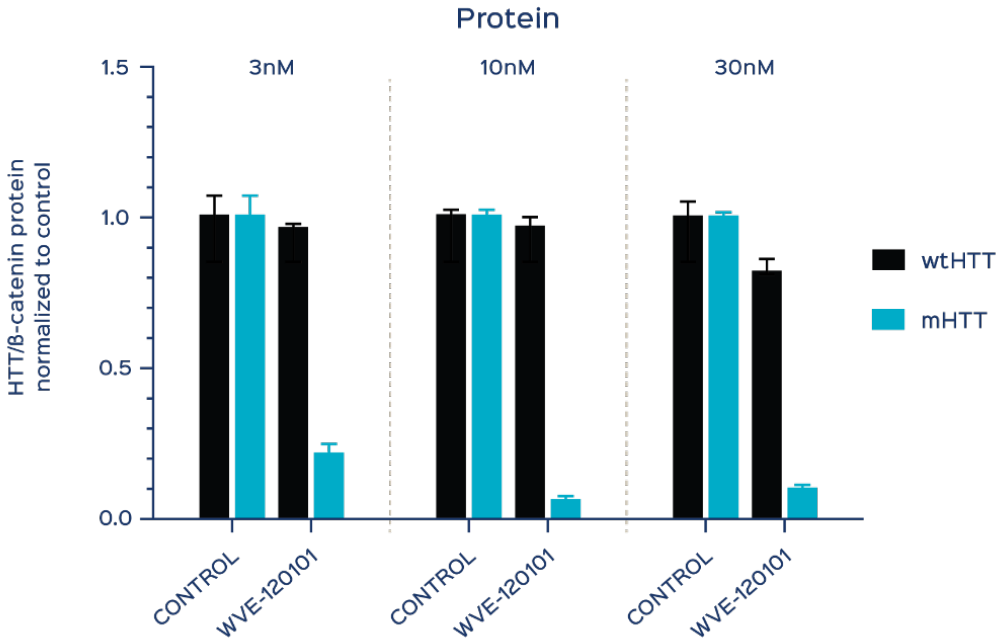
STANDARD OLIGONUCLEOTIDE APPROACHES

Racemic mixture up to >500,000 molecules per sequence

WAVE RATIONAL DESIGN

Selection of 1 stereopure molecule per sequence allows a proper optimization of desired drug properties

STEREOPURE APPROACH ENABLES ALLELE-SPECIFIC TARGETING OF DISEASE GENES



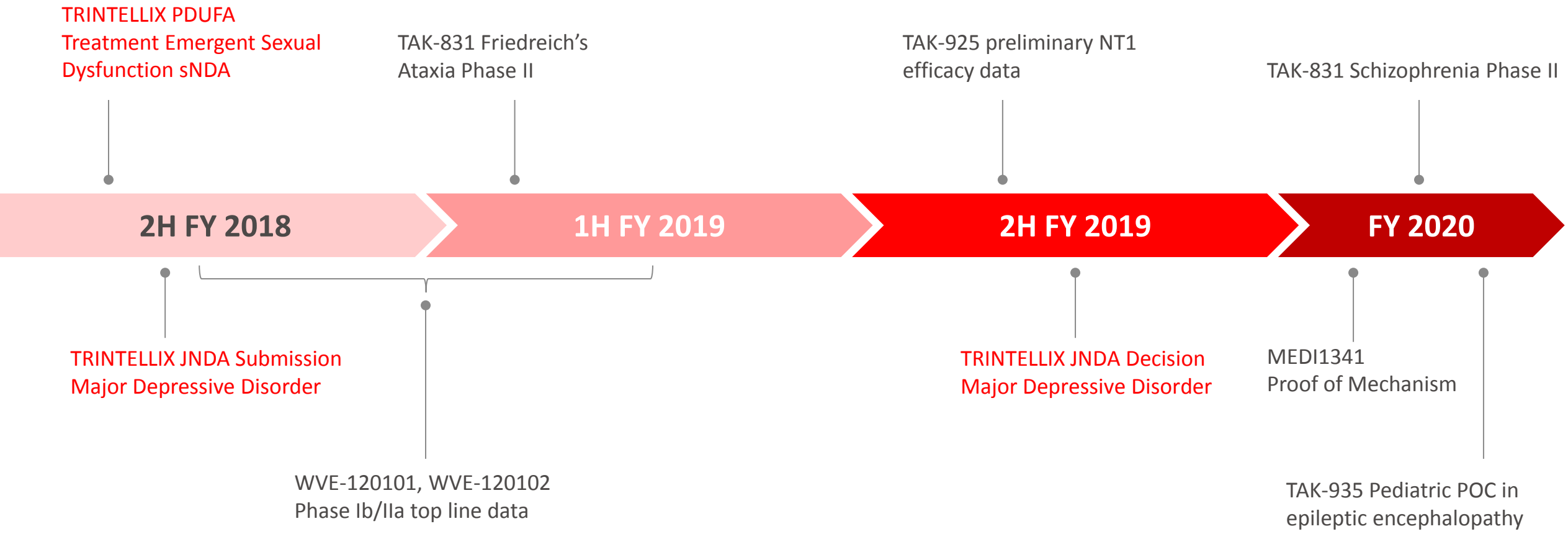
PARTNERSHIP PROVIDES:

- **Option to co-develop and co-commercialize programs for rare CNS diseases (Huntington's Disease, Amyotrophic Lateral Sclerosis, Frontotemporal Dementia and Spinocerebellar Ataxia Type 3)**
- **Exclusive license to research, develop, and commercialize multiple additional programs for CNS indications**

Courtesy of Wave Life Sciences

EXPECTED KEY NEUROSCIENCE PORTFOLIO INFLECTIONS AND MILESTONES

Dates in fiscal year (FY) starting April 1st



Regulatory Filing or Anticipated Approval

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

CONCLUSION

1. Successful differentiation of TRINTELLIX in processing speed, an important aspect of cognitive function, and treatment emergent sexual dysfunction in MDD

2. Progressed TAK-925, the first OX2R agonist, as potential transformative therapy for Narcolepsy Type 1

3. Expanded in neurodegeneration and CNS rare disease with world-class partners (exemplified by Wave and Denali partnerships)

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16:10 – 17:30	Reception

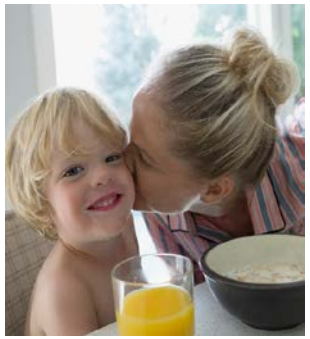
TAKEDA VACCINES

INNOVATION FOR GLOBAL IMPACT

RAJEEV VENKAYYA, MD
President, Global Vaccine Business Unit

OUR MISSION

Develop and deliver innovative vaccines that tackle the toughest problems in public health and improve the lives of people around the world



WE HAVE BUILT A GLOBAL VACCINE BUSINESS UPON A STRONG FOUNDATION IN JAPAN

1946

Japan vaccine business established

1947

1st Takeda manufactured vaccine

2010

Multiple vaccine products manufactured internally and marketed in Japan

2012

Global vaccine business established

2014

Partnered with Japan government to develop and supply pandemic influenza vaccines for people in Japan

ACQUISITIONS

inviragen — Dengue vaccine candidate

LIGOCYTE PHARMACEUTICALS, INC. — Norovirus vaccine candidate

2016

Global pivotal Phase 3 clinical trial of dengue vaccine candidate initiated: 20,100 participants in 8 countries in 2 regions

2018

Phase 3 clinical trial results of dengue vaccine candidate is expected in H2 FY18

PARTNERSHIPS

Bill & Melinda Gates Foundation — Polio vaccine candidate

U.S. Government- BARDA — Zika vaccine candidate

THE VACCINE MARKET IS AN ATTRACTIVE PLACE FOR INVESTMENT

Vaccine sales growth projected at 7.1% between 2017 and 2024, reaching $44.6 billions in 2024[1]

Durability in sales with limited impact of patent expiry

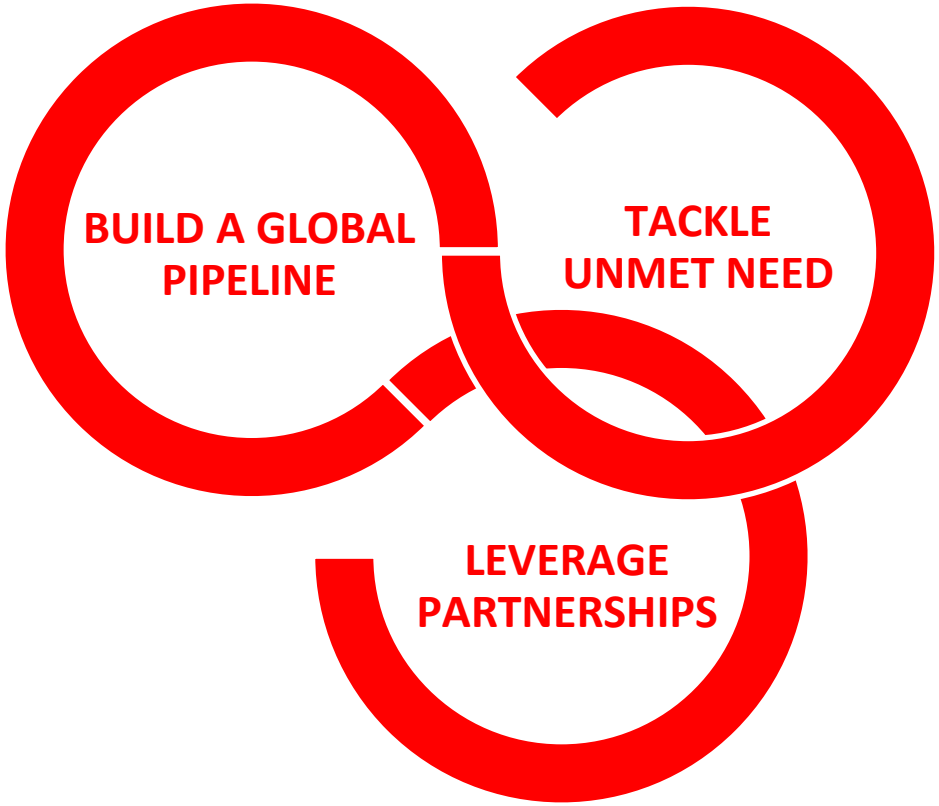
Blockbuster potential in newly launched vaccines

Threat of emerging and existing infectious diseases with epidemic potential

1 Evaluate Pharma report 2018

OUR STRATEGY

Develop vaccines with global relevance and business potential



Target the greatest opportunity in infectious diseases

Partner to de-risk and drive vaccine development

OUR PIPELINE

Discovery/preclinical	Phase 1	Phase 2	Phase 3	Japan Marketed Vaccines	
			DENGUE VACCINE (TAK-003)	H5N1 FLU (BLB-750)	EGG-BASED SEASONAL FLU *DENKA & KM BIOLOGICS*
		NOROVIRUS VACCINE (TAK-214)		MEASLES RUBELLA+	VARICELLA^ *BIKEN*
	BARDA ZIKA VACCINE (TAK-426)	SABIN INACTIVATED POLIOVIRUS VACCINE (TAK-195)		MUMPS	JAPANESE ENCEPHALITIS *BIKEN*
Zydus Cadila CHIKUNGUNYA VACCINE (TAK-507)	ENTEROVIRUS 71 VACCINE (TAK-021)			DIPHTHERIA TETANUS TOXOID‡	

Pipeline as of September 23, 2018

External collaboration

+ Takeda has a measles-rubella combined vaccine, a measles vaccine and a rubella vaccine on the Japanese market.
‡ Takeda has a diphtheria-tetanus combined toxoid vaccine and a tetanus-toxoid vaccine on the Japanese market.
^ Takeda's varicella vaccine has been approved for an additional indication preventing herpes-zoster.

DENGUE THREATENS HALF OF THE WORLD'S POPULATION

Endemic in more than

120

countries[1]

Causes an estimated

390M

infections[1]

Causes more than

20K

deaths each year[2]

In 2015,

>85M

US, Canada, and Japan travelers to endemic countries[3]

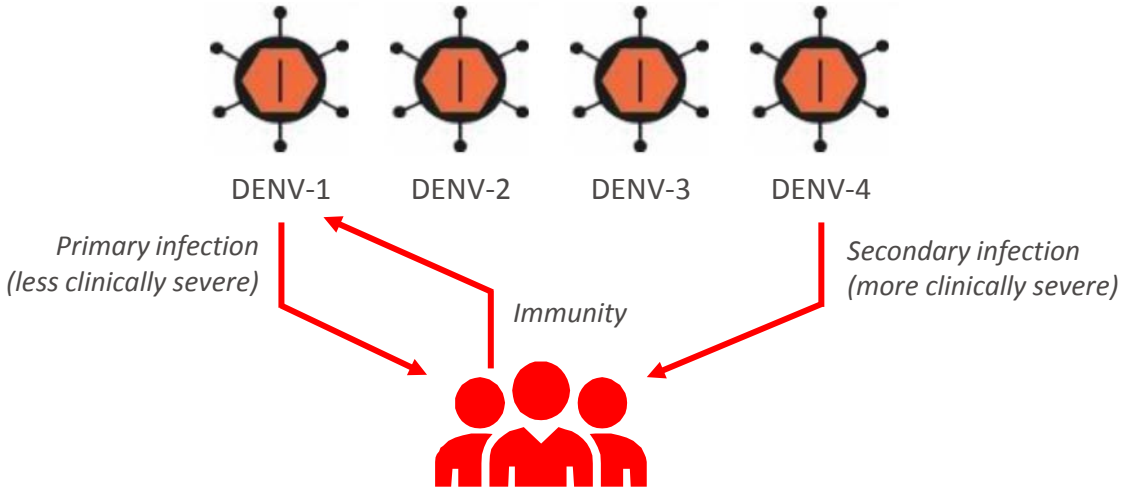
Without safe and effective dengue vaccine

>3.9 BILLION

people around the globe are at risk of dengue[1]

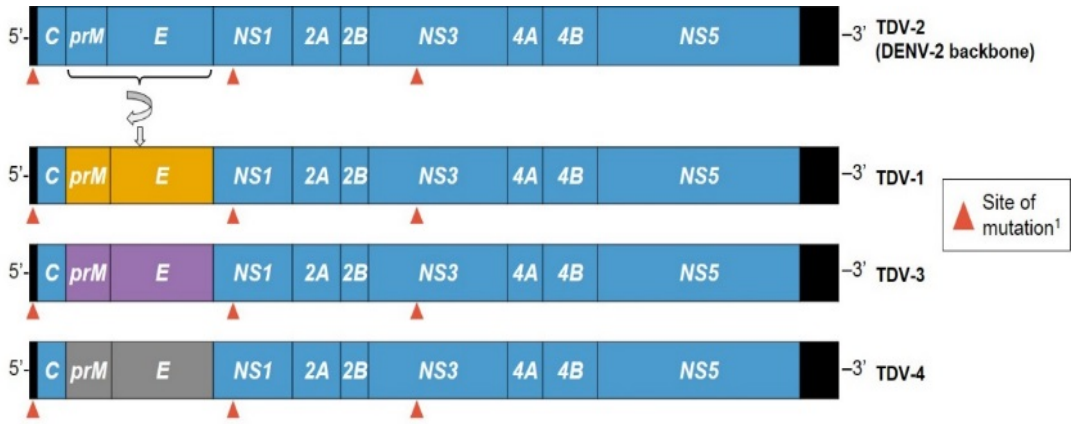
1 World Health Organization. Dengue and Severe Dengue. Retrieved August 2018. http://www.who.int/mediacentre/factsheets/fs117/en/
2 World Health Organization. Dengue. Retrieved August 2018. http://www.searo.who.int/entity/vector_borne_tropical_diseases/data/data_factsheet/en/
3 Travel data from: UNWTO. Yearbook of Tourism Statistics, Data 2011 – 2015 (2017 Edition)

A SAFE AND EFFECTIVE DENGUE VACCINE SHOULD BE DESIGNED TO PROTECT AGAINST ALL FOUR STRAINS OF THE VIRUS



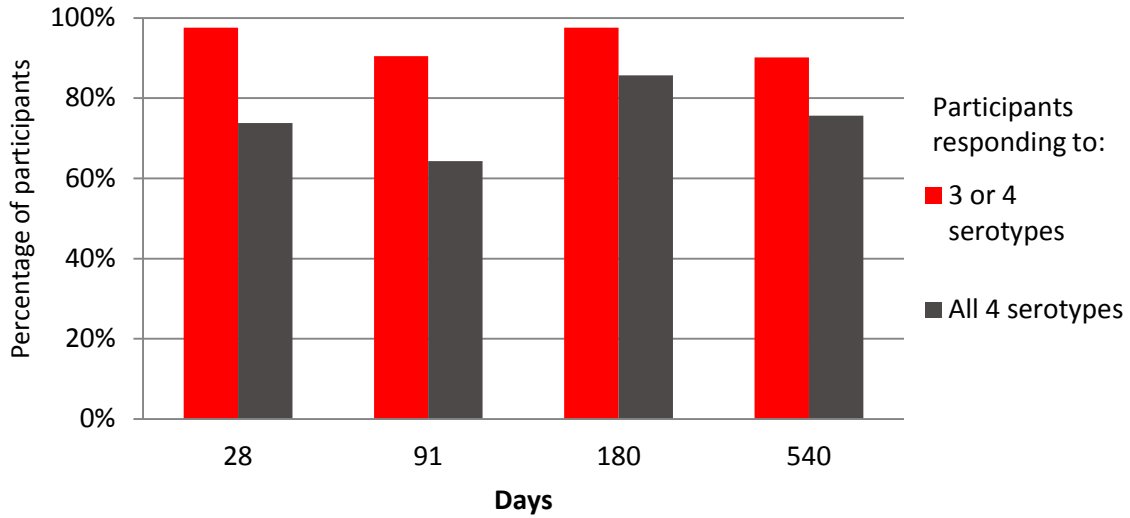
- Dengue is a mosquito-borne disease that can be caused by each of the four strains of the dengue virus (DENV) 1-4
- In people previously exposed to dengue, a subsequent infection with a different strain could lead to more severe disease
- A dengue vaccine must provide broad protection against all four strains of dengue, particularly in persons who have never been exposed to the virus (“naïve”)

TAK-003 IS MODELED ON THE COMPLETE DENGUE VIRUS AND ACTIVATES MULTIPLE ARMS OF THE IMMUNE SYSTEM



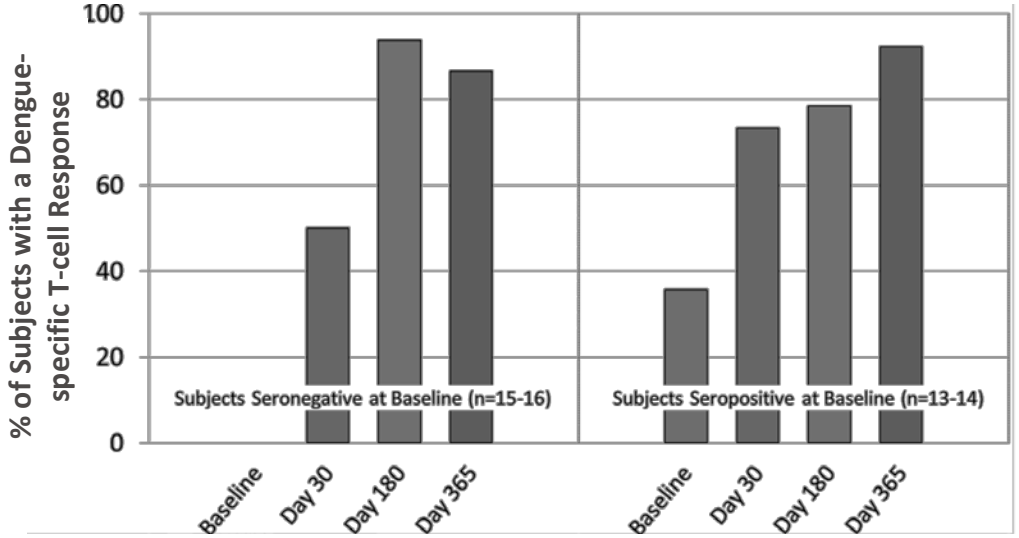
- Live attenuated dengue vaccine based on the complete DENV-2 genome
- Vaccine virus stimulates robust immune response without causing illness
- Components of immune response that are activated include:
  - Neutralizing antibodies
  - Cell-mediated immunity
  - Antibodies to the NS1 protein (NS1 is implicated in severe disease)

TAK-003 TRIGGERS BOTH ANTIBODY AND CELL-MEDIATED IMMUNE RESPONSES



Antibody-mediated immune response in dengue naïve population[1]

- High and sustained antibody response to multiple serotypes after 2 doses (0, 3 month), in participants without prior exposure to dengue



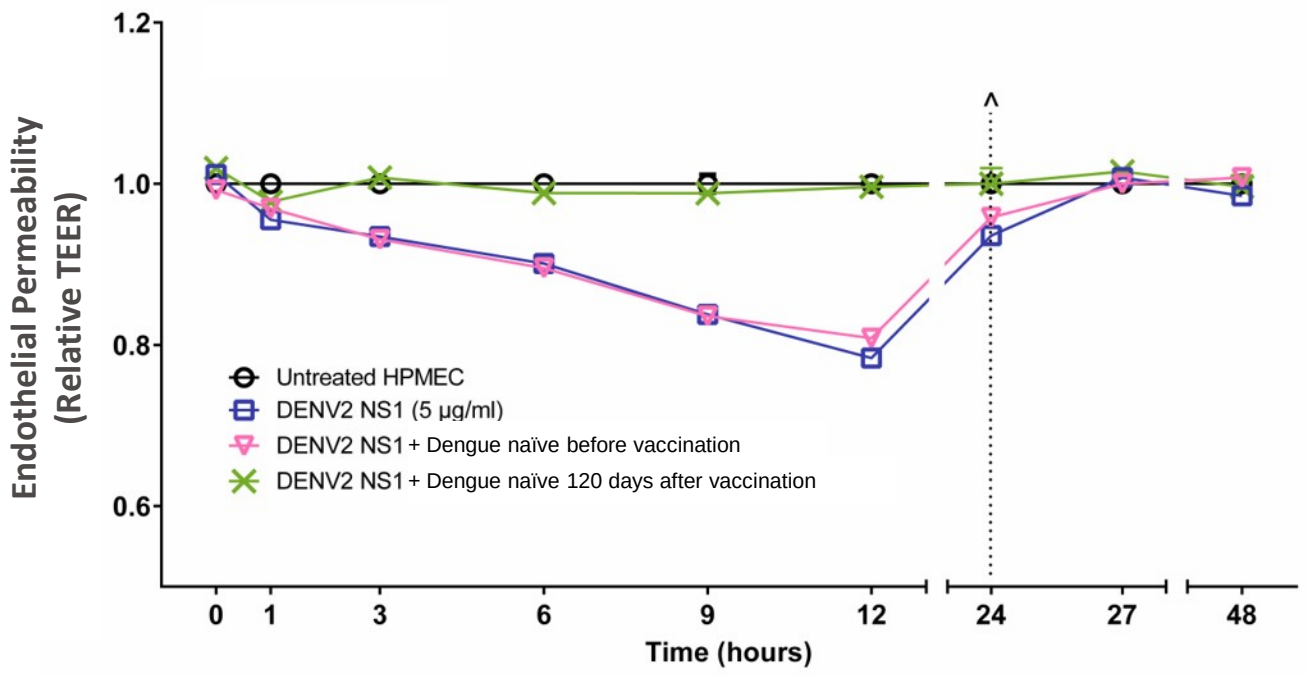
DENV-2 cell-mediated immune response [2]

- >90% of TAK-003 vaccinated participants demonstrate a Dengue-specific T-cell response
- Comparable response between seronegative and seropositive participants at baseline
- Demonstrated cross-reactivity to DENV-1, -3, and -4

1 Lancet Infect Dis 2018; 18: 162–70 Published Online November 6, 2017 http://dx.doi.org/10.1016/ S1473-3099(17)30632-1; results from DEN-204, a Phase 2 study in children living in 3 dengue endemic countries
2 6th Pan-American Dengue Research Network Meeting; results from DEN-205, a Phase 2 study

TAK-003 TRIGGERS NS1 ANTIBODIES THAT PREVENT VASCULAR LEAKAGE IN THE LABORATORY[1]

- Severe dengue is characterized by vascular leakage in the lungs and abdomen
- This vascular leakage is thought to be mediated by the dengue virus non-structural protein 1 (NS1)
- TAK-003-induced NS1 antibodies block NS1-induced vascular leakage in human pulmonary tissue models



[1] 6th Pan-American Dengue Research Network Meeting; results from DEN-203, a Phase 2 study
HPMEC = Human Pulmonary Microvascular Endothelial Cells

TAK-003 WAS GENERALLY SAFE AND REDUCED THE INCIDENCE OF DENGUE IN CHILDREN IN A RECENT PHASE 2 STUDY

STUDY FEATURES

- 1,800 participants received either TAK-003 (1 dose; 2 doses at 0, 3 months; or 2 doses at 0, 12 months) or placebo
- Mean age 7.3 years, range 2 – 17 years
- Approximately 45% of participants were dengue naïve

INCIDENCE OF SYMPTOMATIC DENGUE WAS SIGNIFICANTLY LOWER IN VACCINE RECIPIENTS OVER 18 MONTHS[1]

Dengue Incidence		Relative risk of dengue in vaccines (95% CI)
TAK-003 (%)	Placebo (%)	
1.3	4.5	0.29 (0.13–0.72)

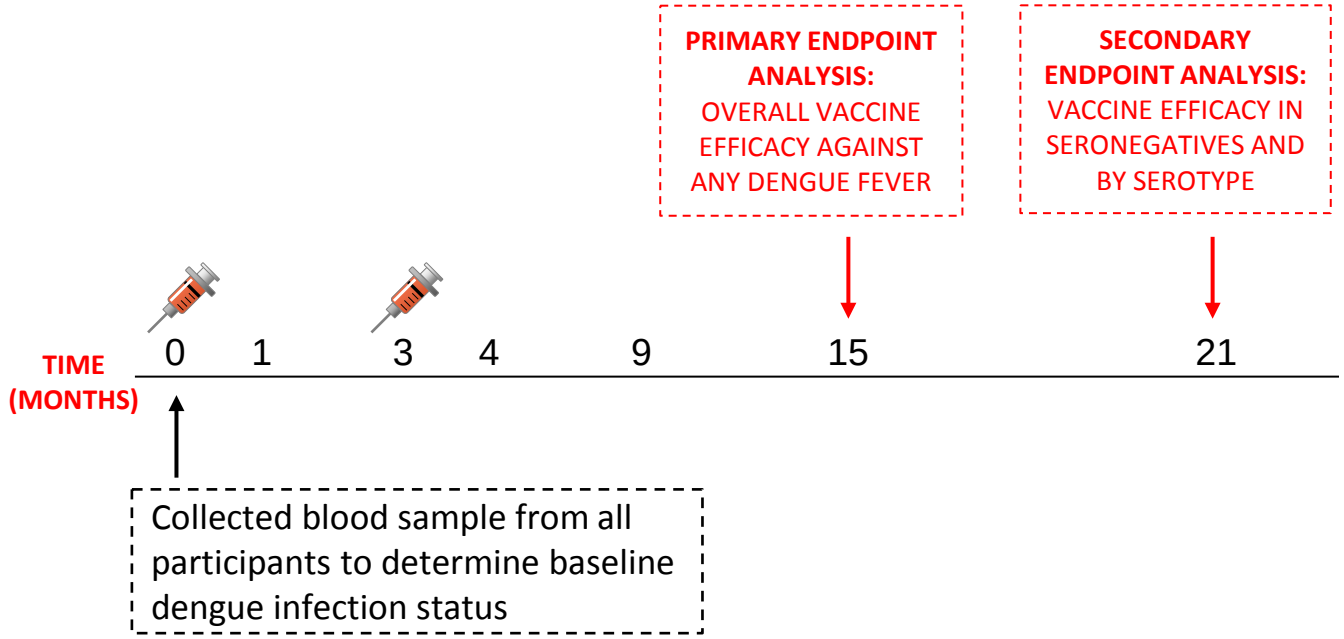
THESE PROOF-OF-CONCEPT FINDINGS REQUIRE CONFIRMATION IN OUR ONGOING PHASE 3 EFFICACY STUDY

[1] Lancet Infect Dis 2018; 18: 162–70 Published Online November 6, 2017 http://dx.doi.org/10.1016/ S1473-3099(17)30632-1; results from DEN-204, a Phase 2 study in children living in 3 dengue endemic countries

OUR PHASE 3 PIVOTAL TRIAL IS DESIGNED TO ANSWER THE MOST IMPORTANT QUESTIONS ABOUT SAFETY AND EFFICACY OF OUR DENGUE VACCINE CANDIDATE

STUDY DESIGN

- **20,100 participants, aged 4 – 16 years old**
  - Age range ensures a mix of dengue exposed and naïve participants
- **Blood sample in all participants at baseline**
  - Enables identification of seronegative subjects
- **8 countries in 2 regions**
  - Brazil, Colombia, Dominican Republic, Nicaragua, Panama, Philippines, Sri Lanka, Thailand
    - Assesses the safety and efficacy of TAK-003 in diverse populations and epidemiological scenarios



PRIMARY ENDPOINT RESULTS EXPECTED IN H2 FY18 FOLLOWED BY REGULATORY FILING IN FY19

TAKEDA HAS THE MOST ADVANCED NOROVIRUS VACCINE CANDIDATE (TAK-214) AND RECENTLY COMPLETED PHASE 2B STUDY

CHALLENGE

- Leading cause of acute gastroenteritis – 600M infections per year
- No vaccine available

OUR PATH

- Most advanced vaccine in development
- Completed Phase 2b study
- Phase 3 preparations underway

OUR GOAL

- Potential for first and best vaccine
- Impact in all markets

TAKEDA HAS PARTNERED WITH THE U.S. GOVERNMENT TO DEVELOP THE FIRST ZIKA VACCINE (TAK-426)

CHALLENGE

- Devastating impact on newborns
- Potential for recurrent outbreaks
- No vaccine available

OUR PATH

- Largest Zika investment by U.S. government
- Proven platform
- Fast track designation

OUR GOAL

- Deliver the first Zika vaccine to market

CONCLUSION

1 STRONG FOUNDATION AND TOP TALENT

- Over 70 years of vaccine manufacturing experience
- Top talent in vaccine development
- Built a high impact global pipeline

2 BEST-IN-CLASS AND FIRST-IN-CLASS POTENTIAL

- Dengue vaccine (TAK-003) in Phase 3
- Norovirus vaccine (TAK-214) in Phase 2b
- Zika vaccine (TAK-426) in Phase 1

3 A PARTNER OF CHOICE FOR VACCINES

- U.S. Government
- Japan Government
- Bill & Melinda Gates Foundation
- Industry Partners


“If you want to save and improve lives around the world, vaccines are a fantastic investment.”
- Bill Gates

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

LOOKING AHEAD

Shire

RECOMMENDED OFFER FOR SHIRE – TRANSACTION UPDATE

PROGRESS TO DATE

- $7.5 billion term loan agreed with leading global financial institutions
- Regulatory review process commenced
  - U.S. Federal Trade Commission (FTC) clearance received
  - Chinese State Administration for Market Regulation (SAMR) clearance received
  - Brazilian Administrative Council for Economic Defense (CADE) clearance received
- Integration planning underway

KEY NEXT STEPS

- Detailed functional integration planning kicked off; consistent with Takeda's core values, leveraging both companies' knowledge and expertise
- Remaining regulatory approvals pending (including EU and Japan)
- Expected to close in first half of calendar year 2019

PENDING ACQUISITION AND INTEGRATION OF SHIRE WILL ACCELERATE TAKEDA R&D

- Increase cash flow and strengthen R&D functions
- Continue our TA focus, partnership model
- Extend and elevate our rare disease expertise
- Deliver consistent, breakthrough innovation
- Reinforce patient-centric, science driven culture

Q&A PANEL CAMBRIDGE

ANDY PLUMP
CMSO

PHIL ROWLANDS
Oncology TAU

ASIT PARIKH
Gastroenterology TAU

EMILIANGELO RATTI
Neuroscience TAU

RAJEEV VENKAYYA
Vaccine Business Unit

CHRIS MORABITO
R&D Shire Integration

Takeda Pharmaceutical Company Limited