TAKEDA R&D INVESTOR DAY 2019

NEW YORK, NY

November 14, 2019

Better Health, Brighter Future

R&D DAY AGENDA – NEW YORK, NOVEMBER 14, 2019

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

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Financial information

Takeda's financial statements are prepared in accordance with International Financial Reporting Standards ("IFRS").

The revenue of Shire plc ("Shire"), which were presently, presented in accordance with accounting principles generally accepted in the United States ("U.S. GAAP"), have been conformed to IFRS, without material difference.

The Shire acquisition closed on January 8, 2019, and our consolidated results for the fiscal year ended March 31, 2019 include Shire's results from January 8, 2019 to March 31, 2019. References to "Legacy Takeda" businesses are to our businesses held prior to our acquisition of Shire. References to "Legacy Shire" businesses are to those businesses acquired through the Shire acquisition.

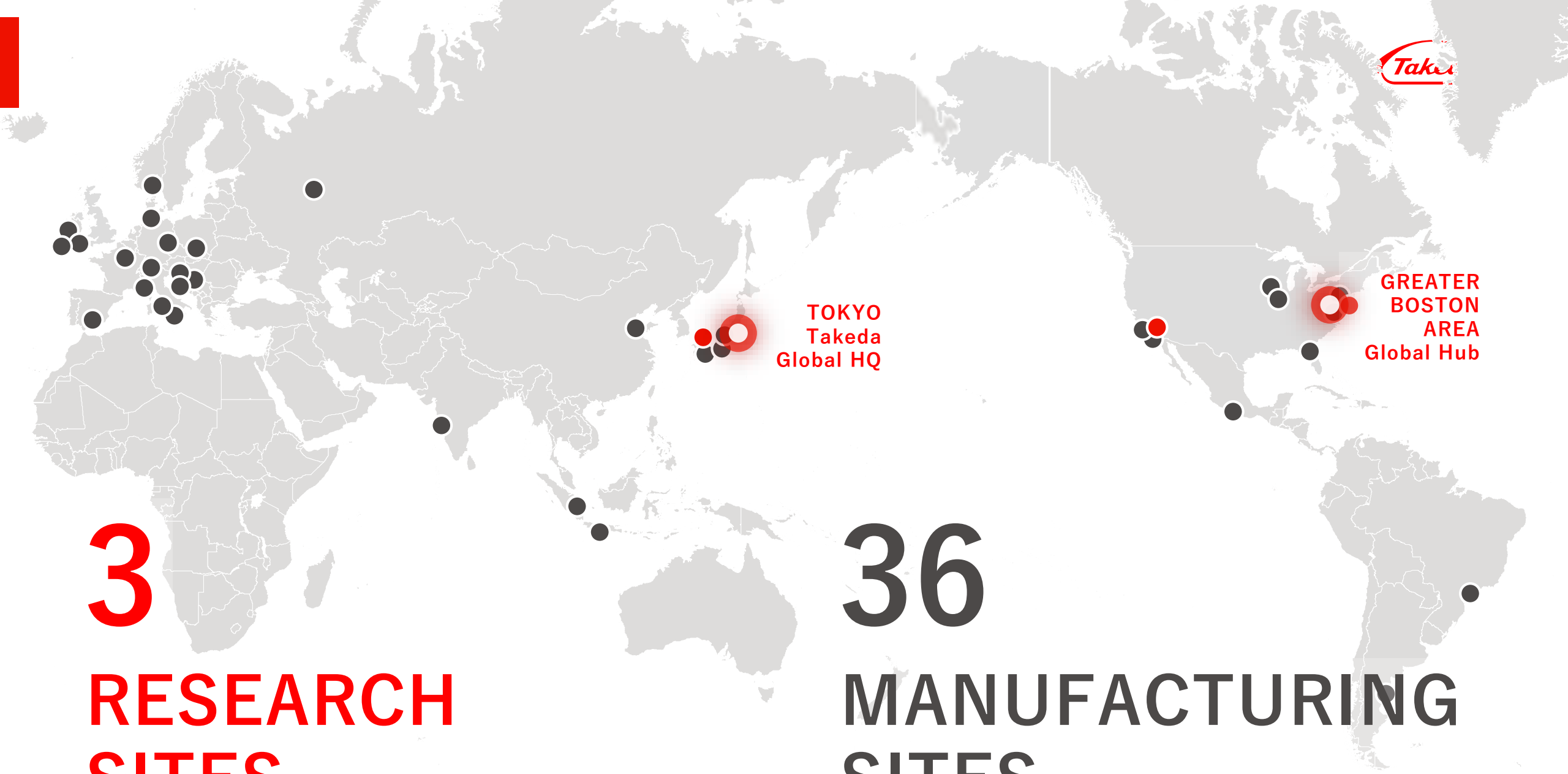
This presentation includes certain pro forma information giving effect to the Shire acquisition as if it had occurred on April 1, 2018. This pro forma information has not been prepared in accordance with Article 11 of Regulation S-X. This pro forma information is presented for illustrative purposes and is based on certain assumptions and judgments based on information available to us as of the date hereof, which may not necessarily have been applicable if the Shire acquisition had actually happened as of April 1, 2018. Moreover, this pro forma information gives effect to certain transactions and other events which are not directly attributable to the Shire acquisition and/or which happened subsequently to the Shire acquisition, such as divestitures and the effects of the purchase price allocation for the Shire acquisition, and therefore may not accurately reflect the effect on our financial condition and results of operations if the Shire acquisition had actually been completed on April 1, 2018. Therefore, undue reliance should not be placed on the pro forma information included herein.

Our mission is to strive towards Better Health and a Brighter Future for people worldwide through leading innovation in medicine

~50,000

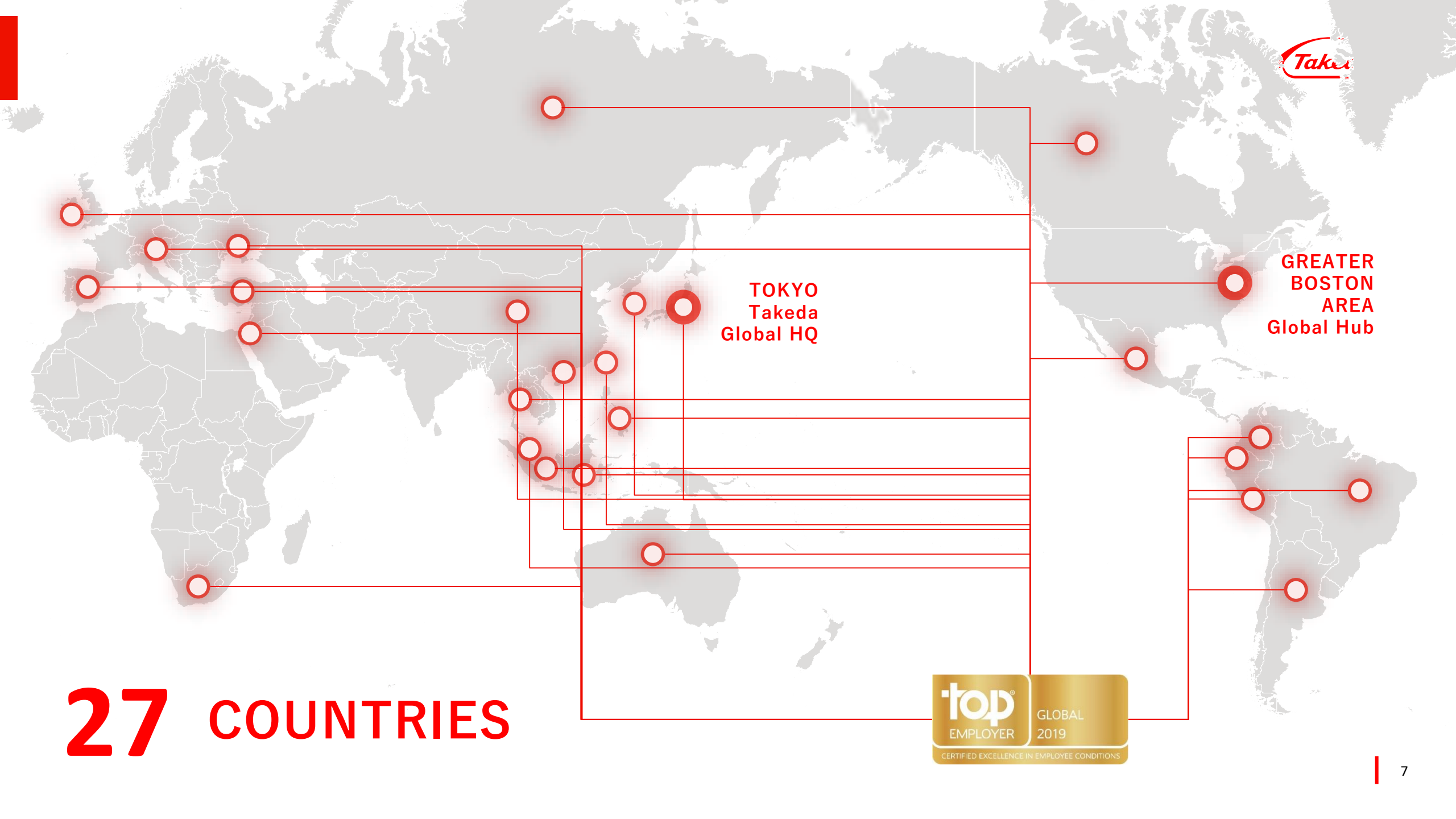
PEOPLE DEDICATED TO BRINGING BETTER HEALTH TO PATIENTS


ZURICH
TOKYO
Takeda
Global HQ
GREATER
BOSTON
AREA
Global Hub
SINGAPORE



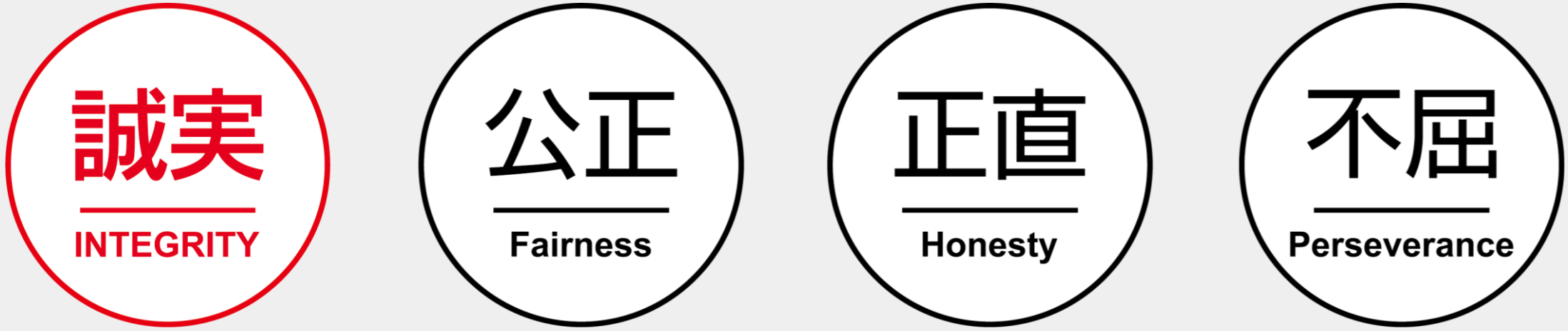
3
RESEARCH SITES

36
MANUFACTURING SITES

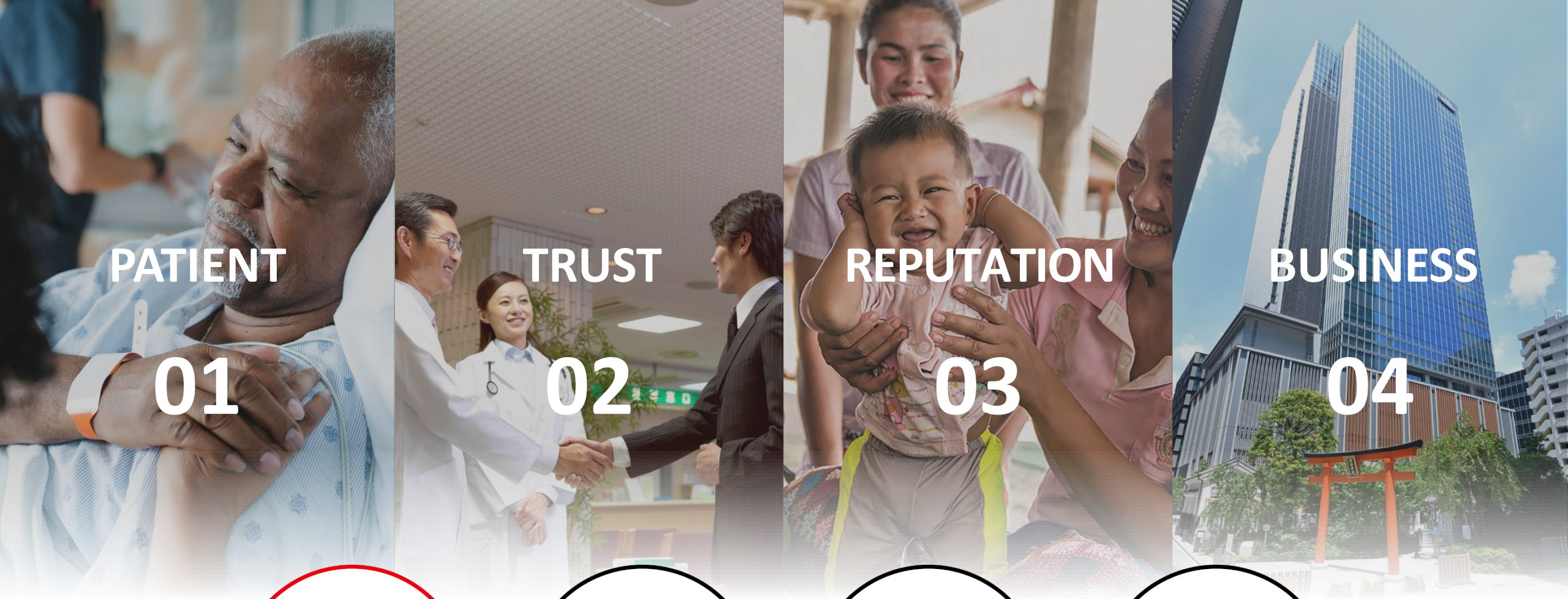


27 COUNTRIES

top EMPLOYER GLOBAL 2019
CERTIFIED EXCELLENCE IN EMPLOYEE CONDITIONS



TAKEDA-ISM



誠実
INTEGRITY

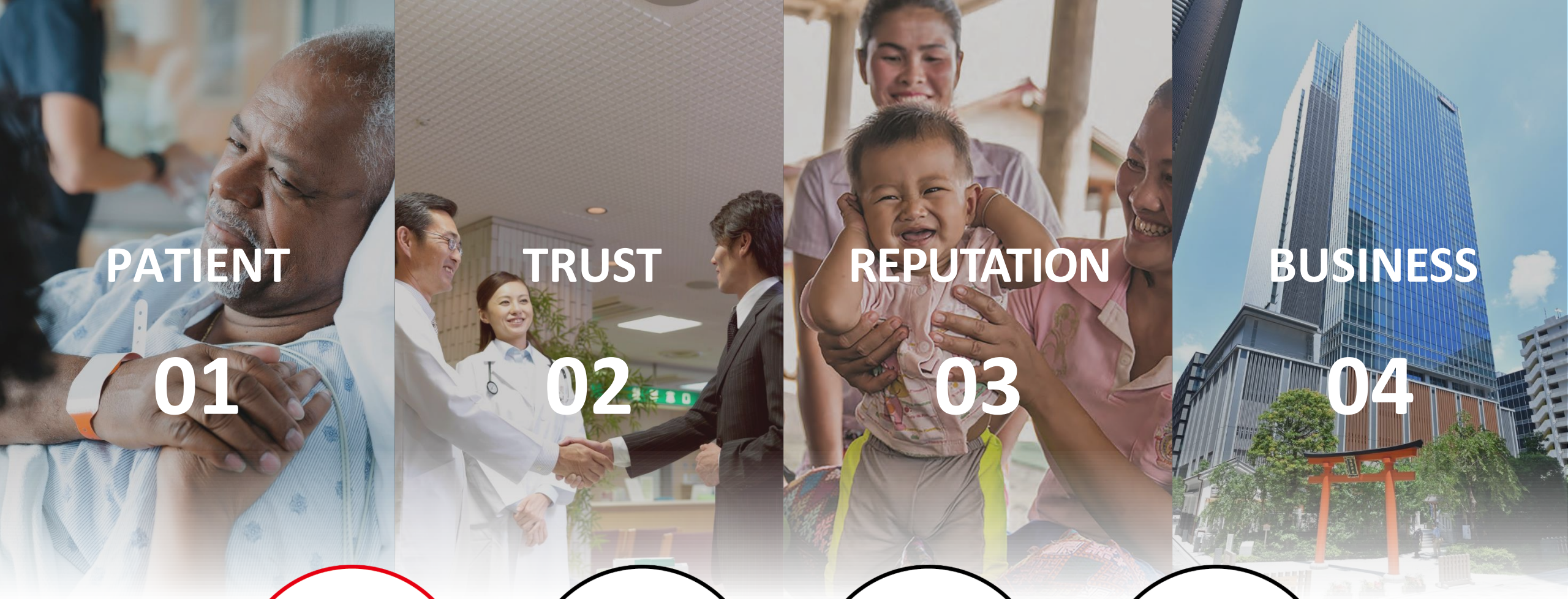
公正
Fairness

正直
Honesty

不屈
Perseverance

TAKEDA-ISM


01
PATIENT



誠実
INTEGRITY

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TAKEDA-ISM

HCPs

PATIENTS

SOCIETY

GOVERNMENT AGENCIES

02

TRUST

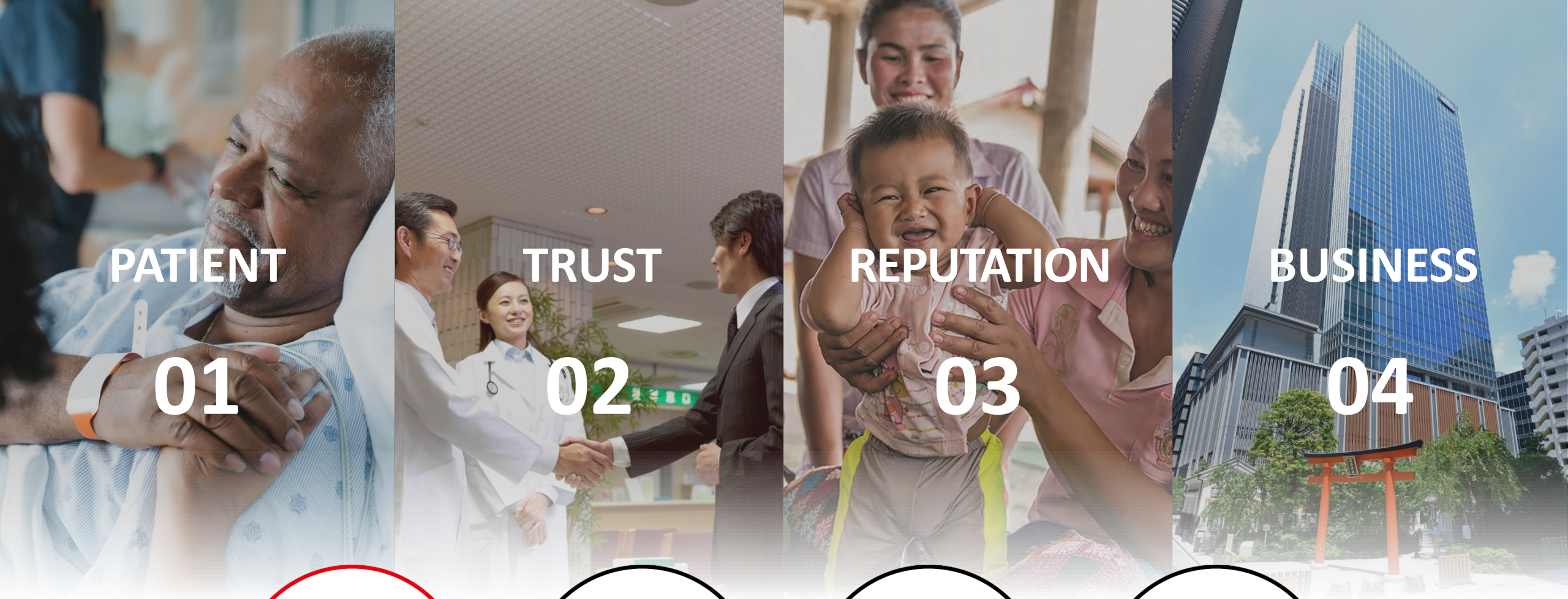
03

REPUTATION

INNOVATION

ACCESS TO MEDICINE

CORPORATE SOCIAL RESPONSIBILITY



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TAKEDA-ISM

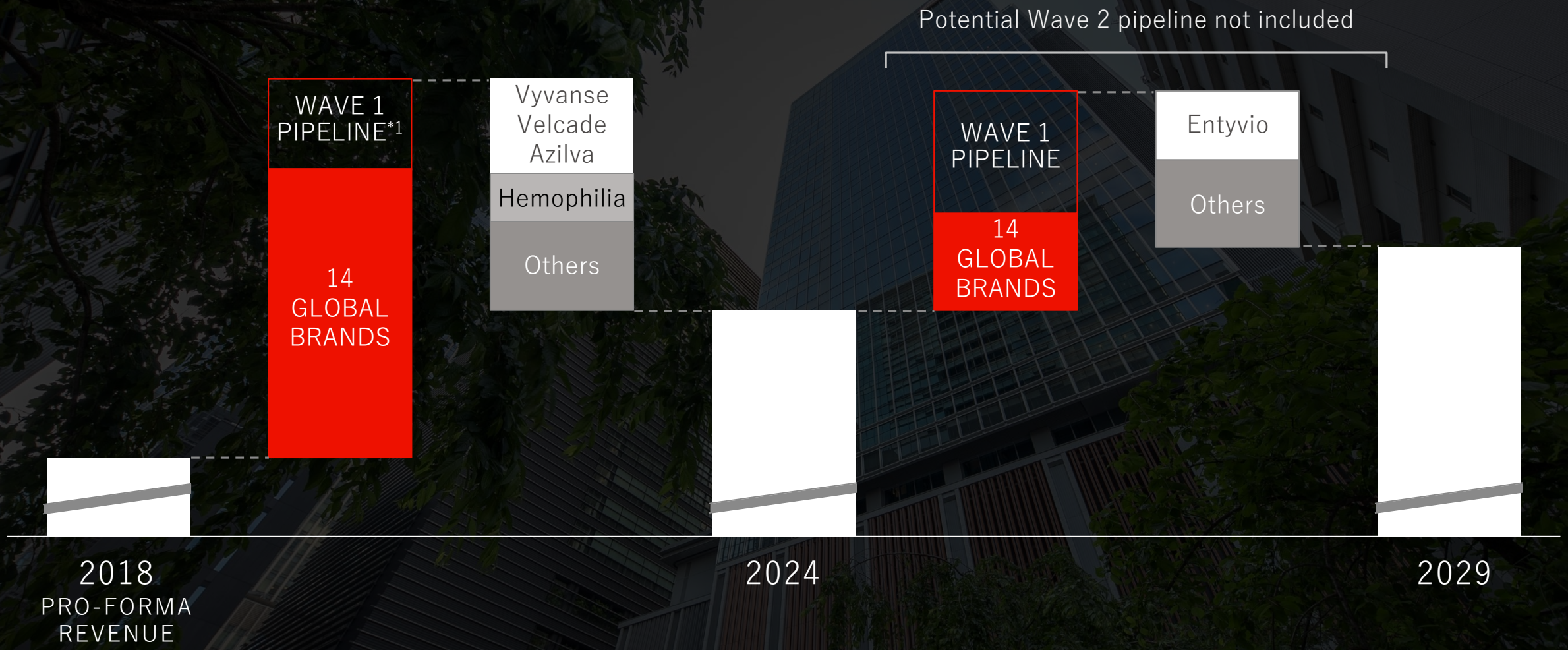
04

BUSINESS

LONG-TERM VALUE FOR PATIENTS, SOCIETY AND INVESTORS

SCIENCE DRIVEN COMPANY WITH A FOCUSED MIND

Positioned for **Sustainable Revenue Growth**



Note: The above chart represents conceptual changes in revenue through 2024 and 2029 demonstrating growth over time offsetting loss of exclusivities and achieving a single digit growth as compared to 2018 pro forma revenue which represents the sum of Takeda revenue for FY2018 plus Shire revenue for the same period (not including the Legacy Shire oncology business, which was sold in August 2018), converted to JPY at the rate of $1 = 111 JPY, and converted from US GAAP to IFRS. Actual future net sales achieved by our commercialized products and pipelines will be different, perhaps materially so, as there is a range of possible outcomes from clinical development, driven by a number of variables, including safety, efficacy and product labelling. In addition, if a product is approved, the effect of commercial factors including the patient population, the competitive environment, pricing and reimbursement is also uncertain. Sales estimate in Wave 1 Pipeline is non-risk adjusted.


Takeda

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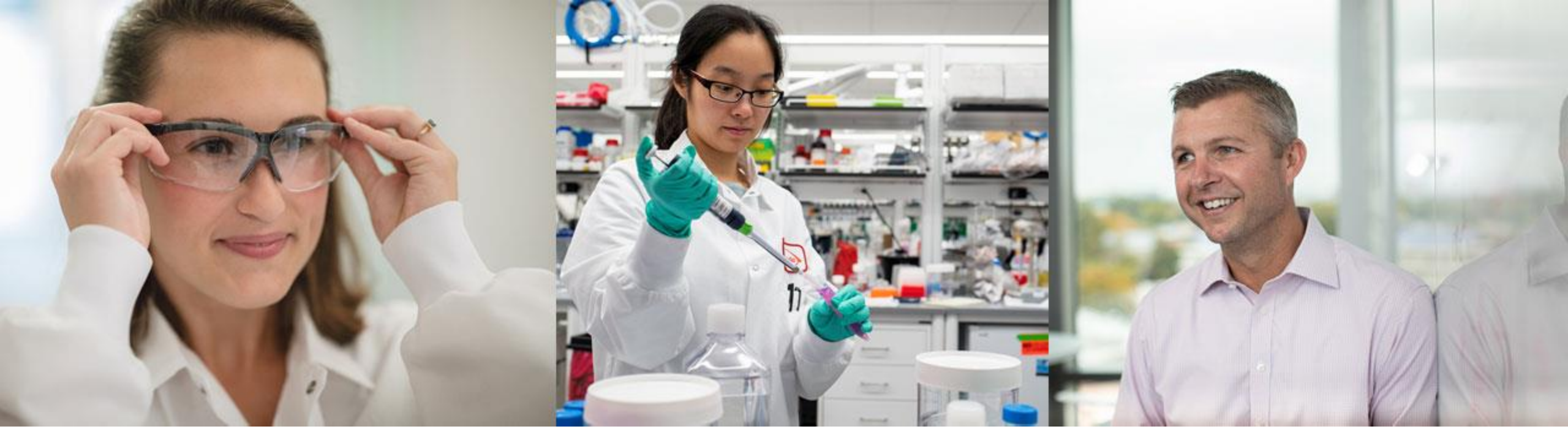


TRANSLATING SCIENCE INTO HIGHLY INNOVATIVE LIFE-CHANGING MEDICINES

Andy Plump MD, PhD

President R&D

Takeda Pharmaceutical Company Limited

New York, NY

November 14, 2019

Better Health, Brighter Future

WHAT YOU WILL HEAR TODAY

1

Our portfolio and pipeline will drive growth and offset key patent expirations

2

We are investing in novel mechanisms and capabilities for a sustainable future

3

We have cultivated an environment of empowerment, accountability and agility

WE ARE POSITIONED TO DELIVER NEAR-TERM & SUSTAINED GROWTH

TARGET APPROVAL →	WAVE 1[1] CLINICAL-STAGE NMEs					WAVE 2[2] CLINICAL-STAGE NMEs					PLATFORMS
	FY20	FY21	FY22	FY23	FY24	FY25 AND BEYOND					
ONCOLOGY		**TAK-788**[3] *2L NSCLC*		**TAK-007** *Hematologic malignancies*	**TAK-924** *AML*	**TAK-164** *GI malignancies*	**TAK-252** *Solid tumors*				CELL THERAPY AND IMMUNE ENGAGERS; TARGETED INNATE IMMUNE MODULATION; NEXT-GEN CHECKPOINT MODULATORS
		TAK-924[3] *HR-MDS*		**TAK-788** *1L NSCLC*		**TAK-573** *R/R MM*	**TAK-981** *Multiple cancers*				
RARE DISEASES *Immunology Hematology Metabolic*		**TAK-620** *CMV infect. in transplant*		**TAK-611** *MLD (IT)*	**TAK-607** *Complications of prematurity*	**TAK-079**[4] *MG, ITP*	**TAK-754** *HemA*	**TAK-755** *iTTP, SCD*			GENE THERAPY
		TAK-609 *Hunter CNS (IT)*		**TAK-755** *cTTP*		**TAK-531** *Hunter CNS*					
NEUROSCIENCE				**TAK-935** *DEE*	**Orexin2R-ag** *(TAK-925/994) Narcolepsy T1*	**TAK-341** *Parkinson's Disease*	**Orexin2R-ag** *Sleep Disorders*	**TAK-041** *CIAS NS*			GENE THERAPY; OTHER PLATFORMS *RNA Modulation Antibody Transport Vehicle*
						TAK-418 *Kabuki Syndrome*	**TAK-653** *TRD*	**TAK-831** *CIAS NS*			
						WVE-120101 *Huntington's Disease*	**WVE-120102** *Huntington's Disease*				
GASTRO-ENTEROLOGY	**TAK-721** *EoE*					**Kuma062** *Celiac Disease*	**TAK-101** *Celiac Disease*	**TAK-018** *Crohn's Disease (post-op and ileitis)*	**TAK-671** *Acute Pancreatitis*		GENE THERAPY; MICROBIOME; CELL THERAPY
						TAK-954 *POGD*	**TAK-906** *Gastroparesis*	**TAK-951** *Nausea & vomiting*			
VACCINES		**TAK-003** *Dengue Vaccine*				**TAK-214** *Norovirus Vaccine*	**TAK-426** *Zika Vaccine*	**TAK-021** *EV71 vaccine*			

1. Projected timing of approvals depending on data read-outs; some of these Wave 1 target approval dates assume accelerated approval
2. Some Wave 2 assets could be accelerated into Wave 1 if they have breakthrough data
3. Projected approval date assumes filing on Phase 2 data
4. TAK-079 to be developed in Rare Diseases indications myasthenia gravis (MG) and immune thrombocytopenic purpura (ITP) (FPI projected in each indication in 2H FY19)

Orphan potential in at least one indication
Estimated dates as of November 14, 2019

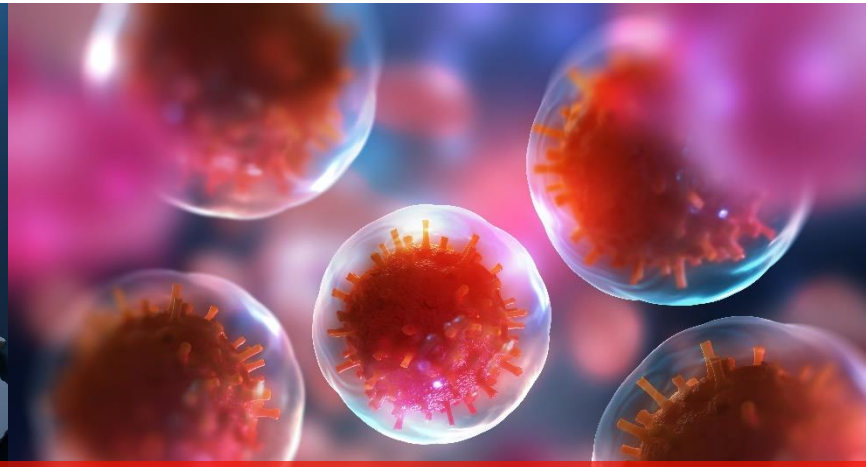
2019: A WATERSHED YEAR FOR TAKEDA

INTEGRATION OF SHIRE

- 18 assets added to the clinical pipeline*
- Creation of a Rare Diseases Therapeutic Area
- Access to world-class Gene Therapy capabilities

EXPANSION OF OUR GLOBAL BRANDS

- VARSITY study demonstrated head-to-head superiority of Entyvio vs Humira and published in New England Journal of Medicine
- TAKHZYRO indication expansions in bradykinin mediated angioedema
- Expecting >15 approvals in China over the next 5 years



UNPRECEDENTED NMEs

- 17 NMEs in Phase 2 and Phase 3
- Potentially curative novel mechanisms (e.g. TAK-101, Orexin2R-ag, CAR-NK)
- Momentum in Cell Therapies, including new partnership with MD Anderson

* Including approved products with ongoing R&D investment

PATIENT-DRIVEN AND SCIENCE-FIRST IN 3 CORE AREAS

INNOVATIVE BIOPHARMA

- ONCOLOGY
- RARE DISEASES
- NEUROSCIENCE
- GASTROENTEROLOGY

PLASMA DERIVED THERAPIES

Complementing our rare disease focus

VACCINES BUSINESS UNIT

Differentiated Dengue vaccine

WE ARE DOING MORE FOR OUR PATIENTS

8

POTENTIAL BIC/FIC NMEs IN PIVOTAL STUDIES[1]

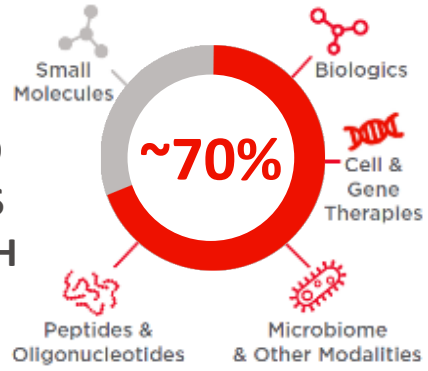
~40

NEW MOLECULAR ENTITY CLINICAL STAGE ASSETS

~4,500

R&D EMPLOYEES GLOBALLY

DIVERSIFIED MODALITIES IN RESEARCH



PIPELINE WITH ORPHAN DRUG DESIGNATION[2]

200+

ACTIVE PARTNERSHIPS

1. BIC/FIC Best-In-Class/First-In-Class (incl. relugolix). Three NMEs in pivotal studies in 2018
2. 31 Orphan Drug Designations in at least one indication for assets in Phase 1 through LCM in 2019 versus 15 in 2018

WE ARE TAKING COURAGEOUS RISKS TO MAKE A CRITICAL DIFFERENCE

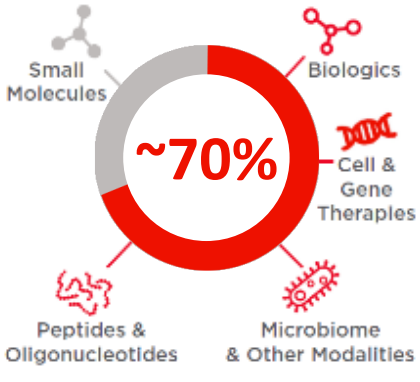
"There is a considerable need for improved treatments for individuals with NT1, which is caused by the loss of orexin-producing neurons in the brain"

Dr. Makoto Honda, Sleep Disorders Project Leader, Tokyo Metropolitan Institute of Medical Science

Data presented at World Sleep conference

NOVEL TARGET MECHANISMS WITH HUMAN VALIDATION

- Cell Tx
- Gene Tx
- Biologics
- Peptides
- Oligonucleotide
- Microbiome
- Small Molecule



MODALITY DIVERSIFICATION

5 Accelerated programs

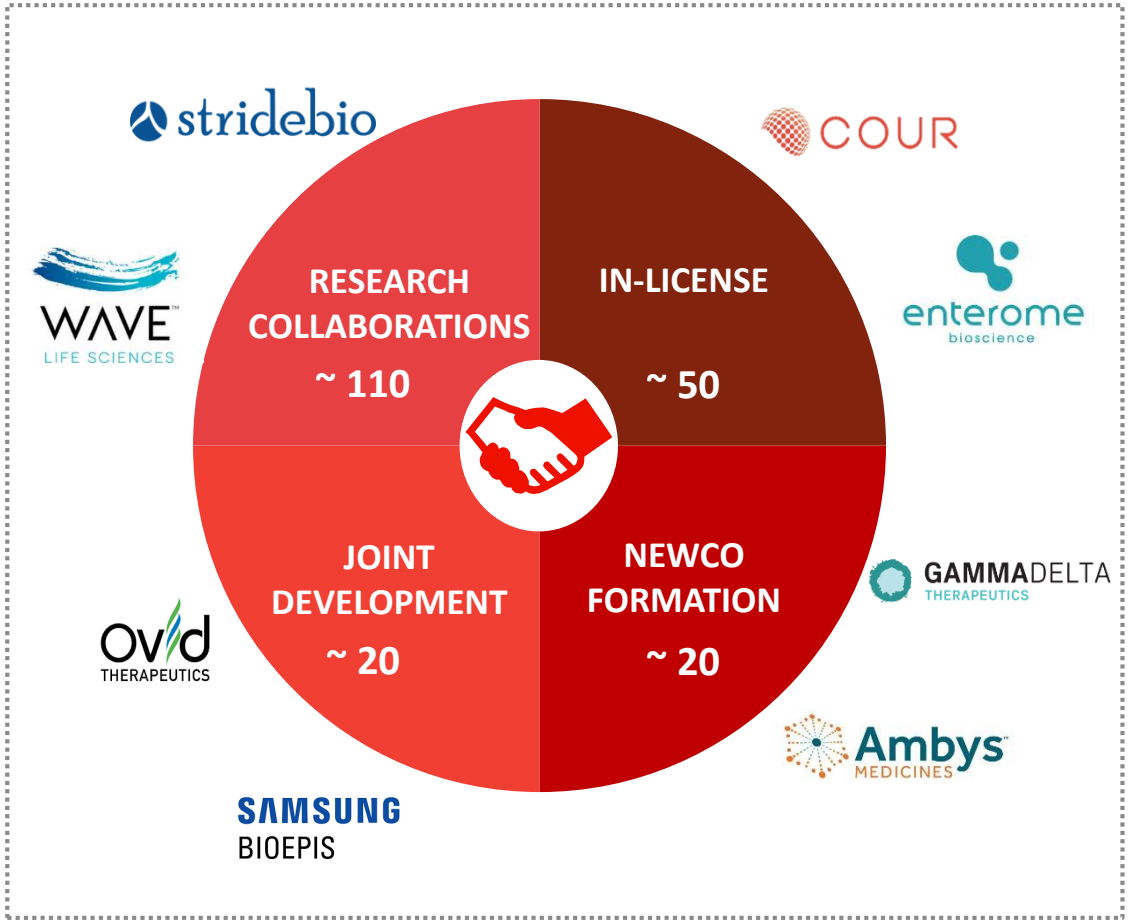
20 NME stage-ups since FY18

19 Indications terminated or externalized since FY18

FAST GO / NO-GO DECISION MAKING

WE ARE CULTIVATING THE BEST SCIENCE THROUGH DIFFERENTIATED PARTNERSHIPS…

*Select partnerships**



* Externalizations and venture investments are not included

- Access to Innovation
- Risk-Sharing
- Expanding Capacity

Total Value in Public & Private Equity

>$1B

WE ARE NURTURING INNOVATION WHEREVER IT OCCURS

CHARACTERISTICS	TAKEDA	PARTNER-SOURCED
TAKEDA DEVELOPS & COMMERCIALIZES	TAK-925, TAK-994 Narcolepsy	teva TAK-573 Multiple Myeloma
GREATER VALIDATION AND / OR LOWER DEVELOPMENT COST	TAK-951 Vomiting Syndromes	Memorial Sloan Kettering Cancer Center CD19 1XX (CAR-T)
	TAK-924 Myelodysplastic Syndrome	PVP BIOLOGICS Kuma-062 Celiac
TAKEDA/PARTNER SHARE DEVELOPMENT & COMMERCIALIZATION	Psychiatry Assets	DENALI THERAPEUTICS Alzheimer Disease
UNCERTAIN SCIENCE AND / OR HIGH DEVELOPMENT COST		

Representative examples only

TO DRIVE HIGHER RETURN ON OUR $4.5B ANNUAL R&D INVESTMENT

PRIORITIZED R&D PORTFOLIO

FLEXIBLE R&D FUNDING MODEL

BALANCED SPEND

Minimize internal spend and infrastructure

TARGETED POPULATIONS

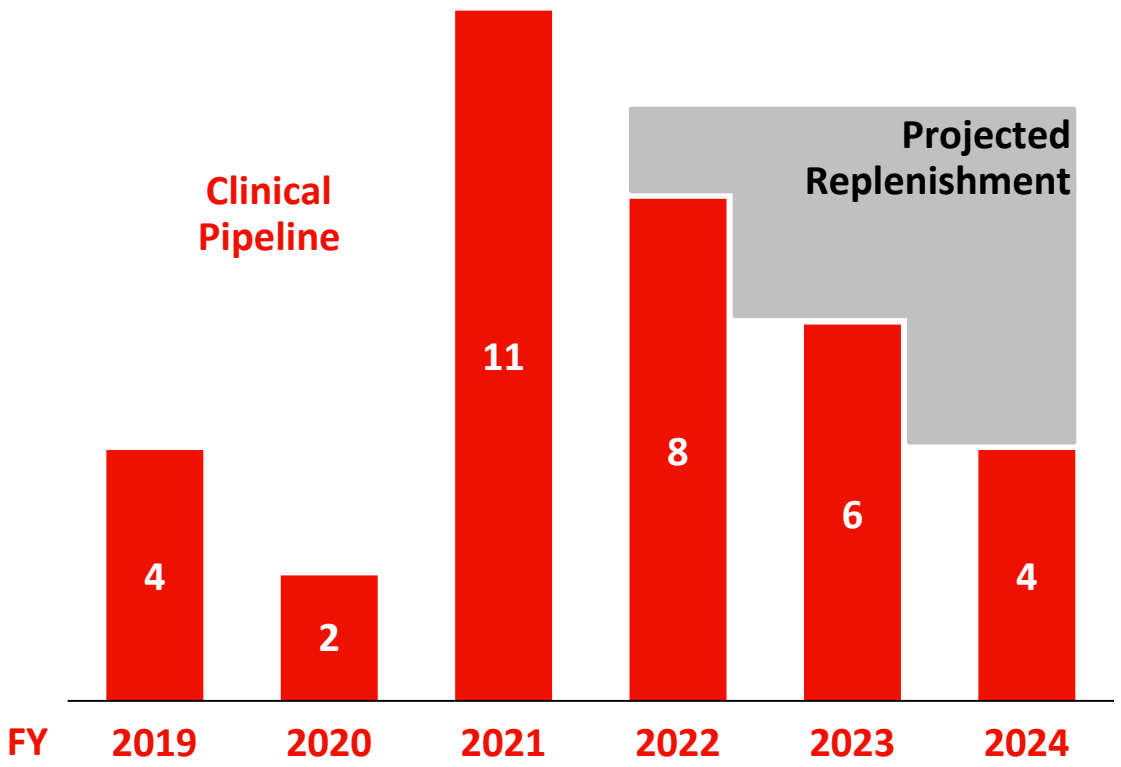
Smaller trials, lower costs, potential longer exclusivity

PARTNERSHIP MODEL

Success driven milestone payments

A RESEARCH ENGINE FUELING A SUSTAINABLE PIPELINE

POTENTIAL NME PIVOTAL STUDY STARTS BY YEAR

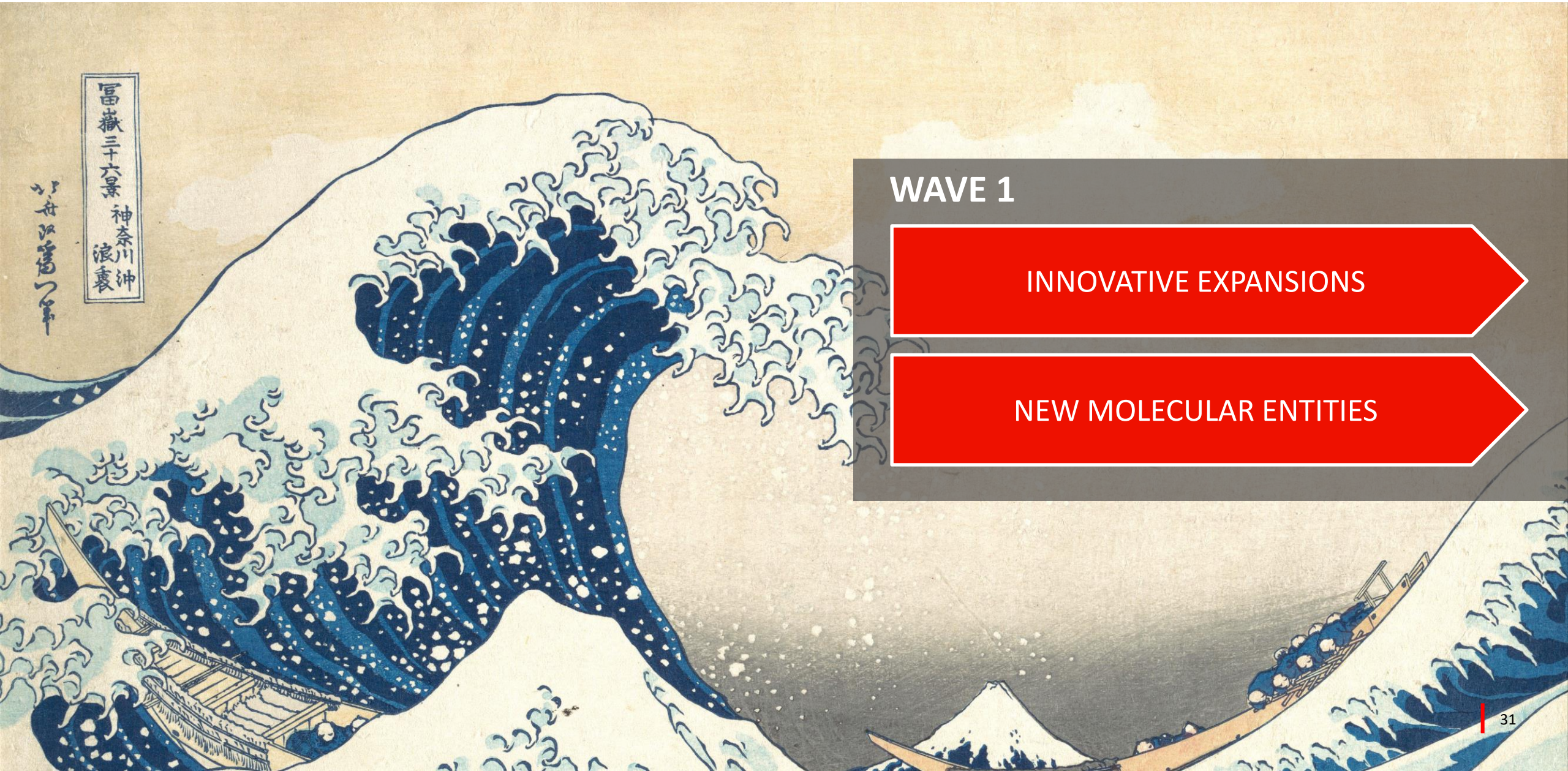


Note: Projections assume successful data readouts

IMPROVED PRODUCTIVITY

- Research momentum building with a projected ~18 portfolio entries in FY19
- Productivity likely to increase with expansion of cell and gene therapy capabilities
- Leveraging partnerships to access the best clinical or preclinical innovation

PIPELINE INVESTMENTS SUPPORTING NEAR-TERM GROWTH



WAVE 1

- INNOVATIVE EXPANSIONS
- NEW MOLECULAR ENTITIES

WE ARE DRIVING EXPANSION OF OUR GLOBAL BRANDS

SELECT GLOBAL GROWTH BRANDS

TAU	Therapies	New Indications / Geographic Expansions	Target (FY)
ONC	ALUNBRIG® BRIGATINIB	1L Non Small Cell Lung Cancer	2020
	NINLARO® (ixazomib) capsules	ND MM Maintenance (non-SCT and post-SCT)	2020 / 2022
Rare	TAKHZYRO® (lanadelumab-flyo) injection	Bradykinin Mediated Angioedema	2024
	vonvendi® *	Prophylactic Treatment of von Willebrand Disease	2021
GI	Entyvio® vedolizumab	Ulcerative Colitis, Crohn's Disease (subcutaneous formulation)	2019 / 2020
		Graft versus Host Disease (prophylaxis)	2022
	ALOFISEL	Complex Perianal Fistulas	2021

SELECT REGIONAL EXPANSIONS

Region	Therapies
China	Entyvio® vedolizumab, ALUNBRIG® BRIGATINIB, TAKHZYRO® (lanadelumab-flyo) injection, VPRIV® velaglucerase alfa for injection, ADYNOVATE® [Antihemophilic Factor (Recombinant), PEGylated]

Region	Therapies
Japan	Takecab® relugolix, cabozantinib, niraparib

ND MM: newly diagnosed multiple myeloma
SCT: stem cell transplant

* VONVENDI is emerging as a global brand
Estimated dates as of November 14, 2019

WAVE 1 NEW MOLECULAR ENTITIES HAVE POTENTIAL TO DELIVER >$10B AGGREGATE PEAK SALES…

Takeda

TARGET APPROVAL[1] →	FY20	FY21	FY22	FY23	FY24
ONCOLOGY		**TAK-788[2]** *2L NSCLC* 🧬		**TAK-007** *Hematologic malignancies* 🧬	**TAK-924** *AML* 🧬
		TAK-924[2] *HR-MDS* 🧬		**TAK-788** *1L NSCLC* 🧬	
RARE DISEASES (*Immunology, Hematology, Metabolic*)		**TAK-620** *CMV infect. in transplant* 🧬		**TAK-611** *MLD (IT)* 🧬	**TAK-607** *Complications of prematurity* 🧬
		TAK-609 *Hunter CNS (IT)* 🧬		**TAK-755** *cTTP* 🧬	
NEUROSCIENCE				**TAK-935** *DEE* 🧬	**Orexin2R-ag** *(TAK-925/994) Narcolepsy T1* 🧬
GASTRO-ENTEROLOGY	**TAK-721** *EoE* 🧬				
VACCINES		**TAK-003** *Dengue Vaccine*			

14 potential NME launches which represent best-in-class or first-in-class therapies to advance patient standard of care

Peak sale estimate of >$10B is non-risk adjusted

1. Projected timing of approvals depending on data read-outs; some of these Wave 1 target approval dates assume accelerated approval
2. Projected approval date assumes filing on Phase 2 data

🧬 Orphan potential in at least one indication

Estimated dates as of November 14, 2019

…AND ARE EXPECTED TO DELIVER LIFE-CHANGING MEDICINES

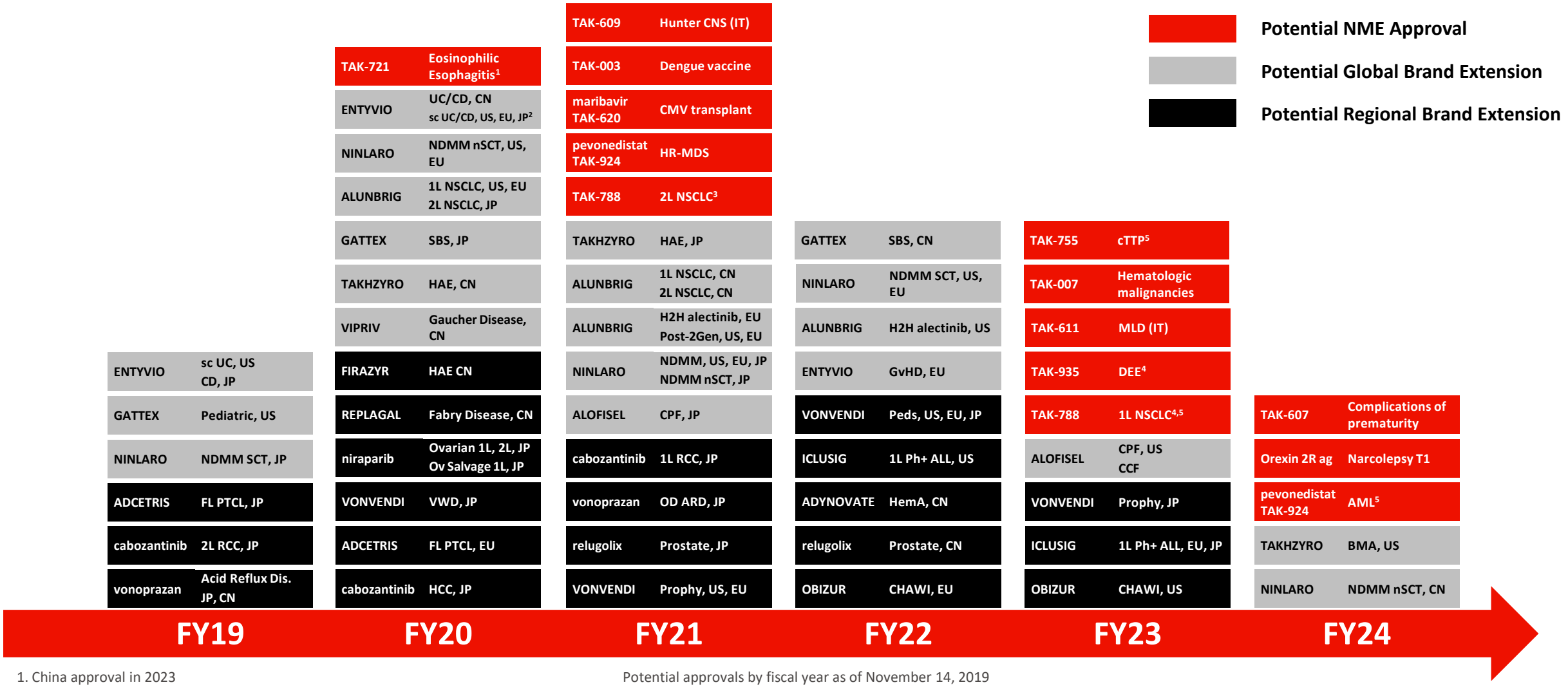
POTENTIAL FIRST-IN-CLASS OR BEST-IN-CLASS NMEs

	PRODUCT	MECHANISM	INDICATION	TARGET APPROVAL DATE (FY)[1]	ADDRESSABLE POPULATION (IN US)[2]	ADDRESSABLE POPULATION (WW)[2,3]
ONCOLOGY	● **TAK-788**	EGFR inhibitor (exon 20)	NSCLC – 2L / 1L	2021[4] / 2023	~2k	~20 - 30k
	● **pevonedistat (TAK-924)**	NAE inhibitor	HR-MDS / AML	2021[4] / 2024	~7k / ~12k	15 - 20k / 20 - 25k
	TAK-007	CD19 CAR-NK	Hematologic malignancies	2023	~9k	~15 - 25k
RARE DISEASES *Immunology Hematology Metabolic*	● **TAK-609**	ERT / I2S replacement	Hunter CNS (IT)	2021	~250	~1 - 1.5k
	● **maribavir (TAK-620)**	UL97 kinase inh	CMV infect. in transpl.	2021	~7 - 15k	~25 - 45k
	TAK-607	IGF-1/ IGFBP3	Complications of prematurity	2024[5]	~25k	~80 - 90k
	TAK-611	ERT / arylsulfatase A	MLD (IT)	2023	~350	~1 - 2k
	● **TAK-755**	ERT/ ADAMTS-13	cTTP / iTTP	2023 / 2025	~500 / ~2k	2 - 6k / 5 - 18k
NEUROSCIENCE	**Orexin programs**	Orexin 2R agonist	Narcolepsy Type 1	2024	70 - 140k	300k - 1.2M
	TAK-935	CH24H inhibitor	Developmental and Epileptic Encephalopathies (DEE)	2023	~50k	~70 - 90k
GASTRO-ENTEROLOGY	● **TAK-721**	Oral anti-inflammatory	Eosinophilic Esophagitis	2020	~150k	*Under evaluation*
VACCINES	● **TAK-003**	Vaccine	Dengue	2021	~32M	~1.8B

1. Projected timing of approvals depending on data read-outs; some of these target approval dates assume accelerated approval
2. Estimated number of patients projected to be eligible for treatment in markets where the product is anticipated to be commercialized, subject to regulatory approval
3. For TAK-788, TAK-924, TAK-007, TAK-607 and TAK-620 the addressable population represent annual incidence
4. Projected approval date assumes filing on Phase 2 data
5. Currently in a non-pivotal Ph 2; interim stage gates may advance program into pivotal trial for target approval by 2024

● Currently in pivotal study or potential for registration enabling Ph-2 study (note: table excludes relugolix)

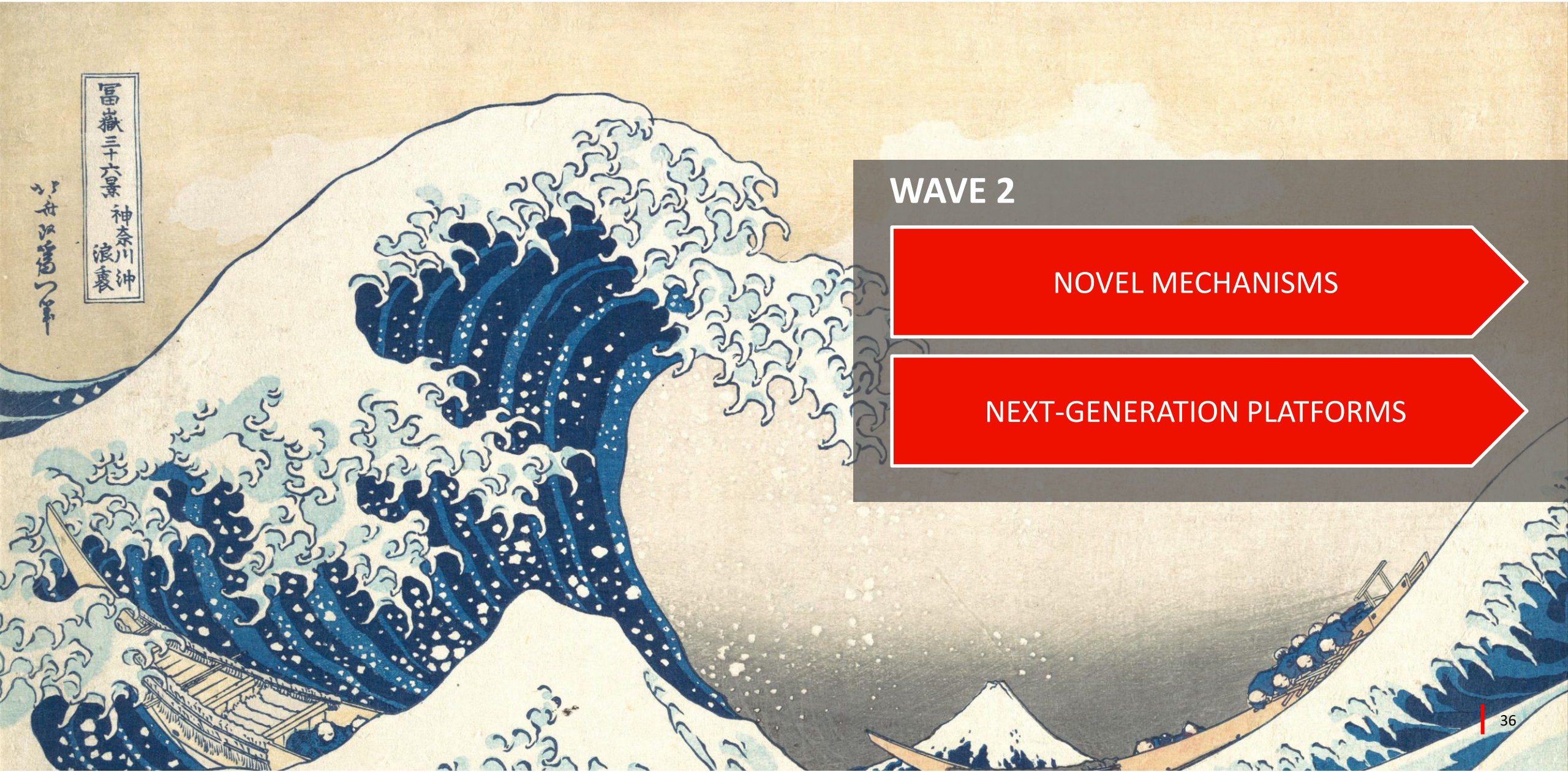
IN SUMMARY: ROBUST NEAR-TERM GROWTH



1. China approval in 2023
2. US approval for sc CD, EU approval for sc UC & CD, Japan approval for sc CD
3. Includes approval in China
4. China approval in 2024
5. New indication for currently unapproved asset

Potential approvals by fiscal year as of November 14, 2019
The target dates are estimates based on current data and subject to change

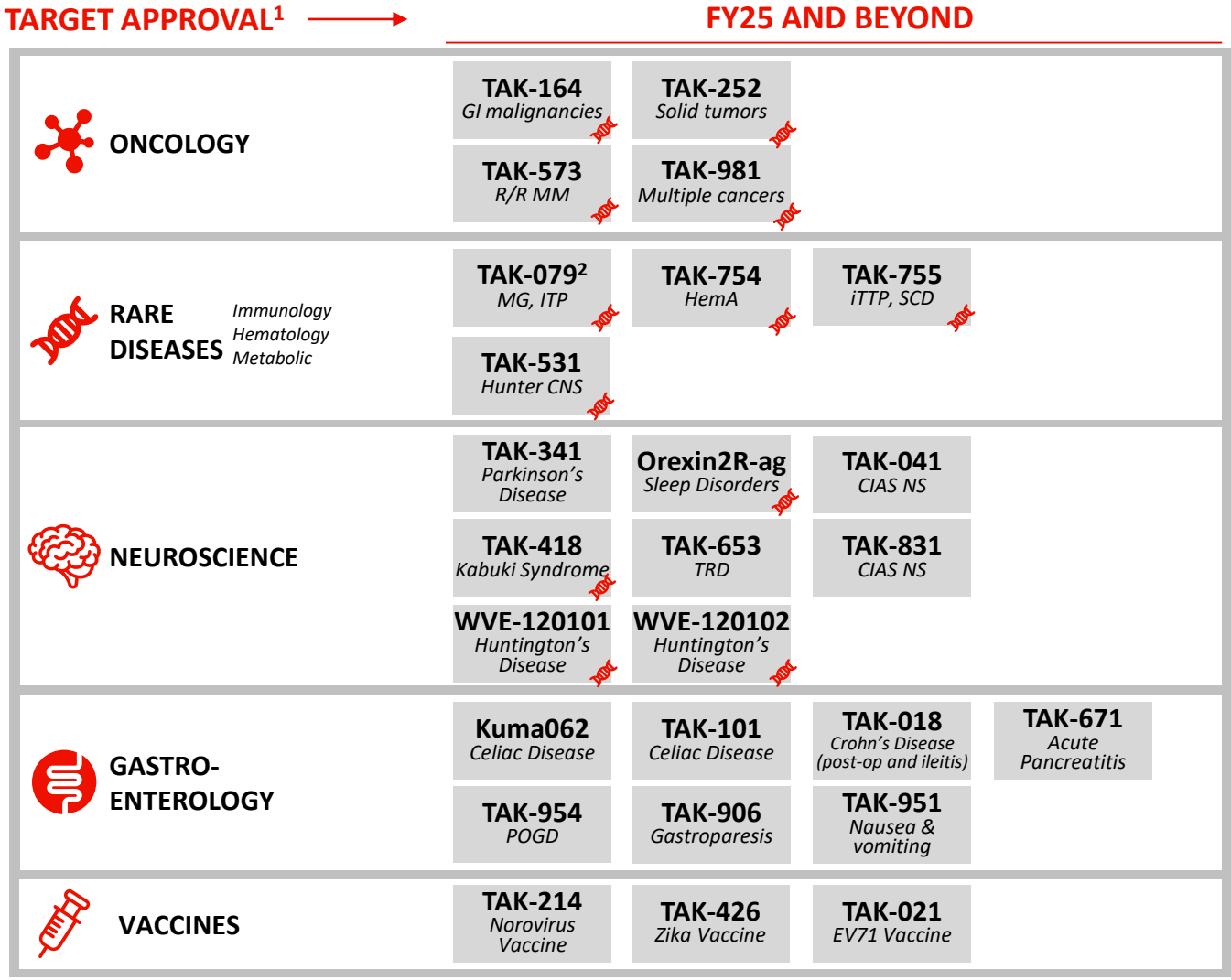
SUSTAINED GROWTH BEYOND FY25



WAVE 2

- NOVEL MECHANISMS
- NEXT-GENERATION PLATFORMS

DRIVEN BY A CLINICAL PIPELINE OF NOVEL MECHANISMS…



Rich early clinical pipeline of potentially transformative and curative NMEs

1. Some Wave 2 assets could be accelerated into Wave 1 if they have breakthrough data
2. TAK-079 to be developed in Rare Diseases indications myasthenia gravis (MG) and immune thrombocytopenic purpura (ITP) (FPI projected for 2H FY19)

Orphan potential in at least one indication

Estimated dates as of November 14, 2019

…AND WITH OUR NEXT-GENERATION PLATFORMS

TARGET APPROVAL → **FY25 AND BEYOND**

ONCOLOGY	**CELL THERAPIES AND IMMUNE ENGAGERS** **CAR-T** *MSKCC, Noile-Immune T-CiRA, Takeda* **CAR-NK** *MD Anderson* **GammaDelta CAR-T** *GammaDelta Tx* **Conditional T cell engagers** *Maverick*	**TARGETED INNATE IMMUNE MODULATION** **Attenukine** *Teva* **STING** *CuraDev, Takeda* **SUMOylation** *Takeda*	**NEXT-GEN CHECKPOINT MODULATORS** **Agonist-redirected checkpoints** *Shattuck* **Humabodies** *Crescendo*	
RARE DISEASES *Immunology* *Hematology* *Metabolic*	**GENE THERAPY** **Hemophilia** **Lysosomal Storage Diseases**			
NEUROSCIENCE	**GENE THERAPY** **Neurodegenerative Diseases** *StrideBio*	**OTHER PLATFORMS** **RNA Modulation** *Wave, Skyhawk* **Antibody Transport Vehicle** *Denali*		
GASTRO-ENTEROLOGY	**GENE THERAPY** **Liver** *Ambys*	**MICROBIOME** **FIN-524** *FInch* **Microbial Consortia** *NuBiyota*	**CELL THERAPY** *Ambys*	

Harnessing the potential of cell and gene therapies and other diverse modalities

Some Wave 2 assets could be accelerated into Wave 1 if they have breakthrough data

Estimated dates as of November 14, 2019

INVESTING IN CAPABILITIES TO POSITION US FOR SUCCESS

Cell Therapy	• 5 clinical programs by end of FY20 • Disruptive platforms, including off-the-shelf cell-therapies
Gene Therapy	• World-class gene therapy manufacturing • Accessing innovation through partnerships (e.g. Stridebio, Ambys)
Data Sciences	• Accelerate clinical development with real world data (e.g. TAK-788) • Use machine learning to identify rare disease patients

COMMITTED TO OUR PEOPLE

LIVING OUR VALUES THROUGHOUT THE INTEGRATION PROCESS

誠実 INTEGRITY

公正 Fairness

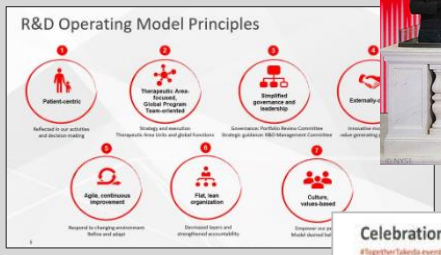
正直 Honesty

不屈 Perseverance

December 2018
Leadership Team and Proposed R&D Operating Model Announced

April 2019
Prioritization of Combined Pipeline and Portfolio

August 2019
R&D Employees Informed of Employment Status*



* Where legally cleared

STRONG LEADERSHIP EXECUTING ON OUR VISION

ASIT PARIKH
Head, Gastroenterology Therapeutic Area Unit

PHIL ROWLANDS
Head, Oncology Therapeutic Area Unit

DAN CURRAN
Head, Rare Diseases Therapeutic Area Unit

EMILIANGELO RATTI
Head, Neuroscience Therapeutic Area Unit

SARAH SHEIKH
Head, Neuroscience Therapeutic Area Unit*

STEVE HITCHCOCK
Head, Research

NENAD GRMUSA
Head, Center for External Innovation

GEORGIA KERESTY
R&D Chief Operating Officer

ANNE HEATHERINGTON
Head, Data Sciences Institute

WOLFRAM NOTHAFT
Chief Medical Officer

STEFAN WILDT
Head, Pharmaceutical Sciences and Translational Engine, Cell Therapies

JEREMY CHADWICK
Head, Global Development Office†

WOLFGANG HACKEL
Head, Global R&D Finance

ERIKA MARDER
Head, Global R&D Human Resources

COLLEEN BEAUREGARD
Head, Global R&D Communications

TOSHIO FUJIMOTO
General Manager, Shonan Health Innovation Park (iPark)

New hire

*Sarah Sheik to succeed Emiliangelo Ratti upon his retirement beginning November 25

†includes Regulatory, Global Patient Safety Evaluation, Development Operations, and Clinical Supply Chain

OUR COMMITMENT TO OUR PEOPLE IS BEING RECOGNIZED

BOSTON BUSINESS JOURNAL

BPtW

2019 BEST PLACES TO WORK

WORKING MOTHER

100 BEST COMPANIES 2019

SAN DIEGO BUSINESS JOURNAL

BEST PLACES TO WORK 2019

The Boston Globe

TOP PLACES TO WORK 2018

CEO CANCER GOLD STANDARD

Best Workplaces™ in Health Care & Biopharma

Great Place To Work.

USA 2019

HUMAN RIGHTS CAMPAIGN FOUNDATION

BEST PLACES TO WORK for LGBTQ Equality

2019

100% CORPORATE EQUALITY INDEX

WE ARE POSITIONED TO DELIVER NEAR-TERM & SUSTAINED GROWTH

TARGET APPROVAL →	WAVE 1[1]					WAVE 2[2]				
	CLINICAL-STAGE NMEs									PLATFORMS
	FY20	FY21	FY22	FY23	FY24	FY25 AND BEYOND				
ONCOLOGY		**TAK-788**[3] *2L NSCLC*		**TAK-007** *Hematologic malignancies*	**TAK-924** *AML*	**TAK-164** *GI malignancies*	**TAK-252** *Solid tumors*			CELL THERAPY AND IMMUNE ENGAGERS; TARGETED INNATE IMMUNE MODULATION; NEXT-GEN CHECKPOINT MODULATORS
		TAK-924[3] *HR-MDS*		**TAK-788** *1L NSCLC*		**TAK-573** *R/R MM*	**TAK-981** *Multiple cancers*			
RARE DISEASES *Immunology Hematology Metabolic*		**TAK-620** *CMV infect. in transplant*		**TAK-611** *MLD (IT)*	**TAK-607** *Complications of prematurity*	**TAK-079**[4] *MG, ITP*	**TAK-754** *HemA*	**TAK-755** *iTTP, SCD*		GENE THERAPY
		TAK-609 *Hunter CNS (IT)*		**TAK-755** *cTTP*		**TAK-531** *Hunter CNS*				
NEUROSCIENCE				**TAK-935** *DEE*	**Orexin2R-ag** *(TAK-925/994) Narcolepsy T1*	**TAK-341** *Parkinson's Disease*	**Orexin2R-ag** *Sleep Disorders*	**TAK-041** *CIAS NS*		GENE THERAPY; OTHER PLATFORMS *RNA Modulation Antibody Transport Vehicle*
						TAK-418 *Kabuki Syndrome*	**TAK-653** *TRD*	**TAK-831** *CIAS NS*		
						WVE-120101 *Huntington's Disease*	**WVE-120102** *Huntington's Disease*			
GASTRO-ENTEROLOGY	**TAK-721** *EoE*					**Kuma062** *Celiac Disease*	**TAK-101** *Celiac Disease*	**TAK-018** *Crohn's Disease (post-op and ileitis)*	**TAK-671** *Acute Pancreatitis*	GENE THERAPY; MICROBIOME; CELL THERAPY
						TAK-954 *POGD*	**TAK-906** *Gastroparesis*	**TAK-951** *Nausea & vomiting*		
VACCINES		**TAK-003** *Dengue Vaccine*				**TAK-214** *Norovirus Vaccine*	**TAK-426** *Zika Vaccine*	**TAK-021** *EV71 vaccine*		

1. Projected timing of approvals depending on data read-outs; some of these Wave 1 target approval dates assume accelerated approval
2. Some Wave 2 assets could be accelerated into Wave 1 if they have breakthrough data
3. Projected approval date assumes filing on Phase 2 data
4. TAK-079 to be developed in Rare Diseases indications myasthenia gravis (MG) and immune thrombocytopenic purpura (ITP) (FPI projected in each indication in 2H FY19)

Orphan potential in at least one indication
Estimated dates as of November 14, 2019

R&D DAY AGENDA – NEW YORK, NOVEMBER 14, 2019

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

TAKEDA ONCOLOGY: INNOVATIVE CELL THERAPIES & NEW FRONTIERS IN IMMUNO-ONCOLOGY

Chris Arendt, PhD

Head of Oncology Drug Discovery Unit

Takeda Pharmaceutical Company Limited

New York, NY

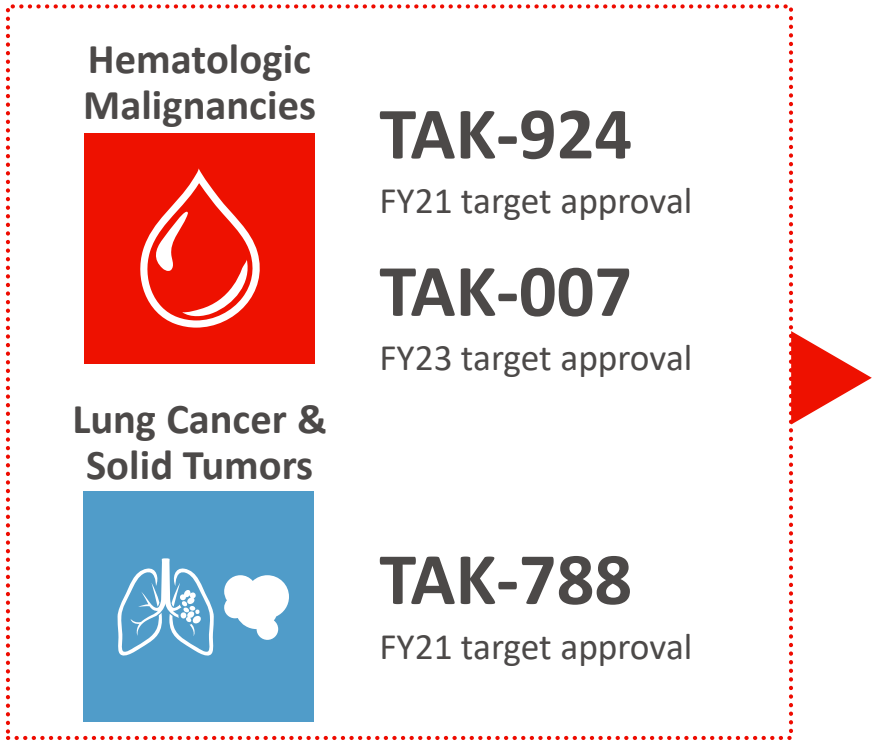
November 14, 2019

Better Health, Brighter Future

A CURATIVE-INTENT IMMUNO-ONCOLOGY PIPELINE IS TAKING SHAPE

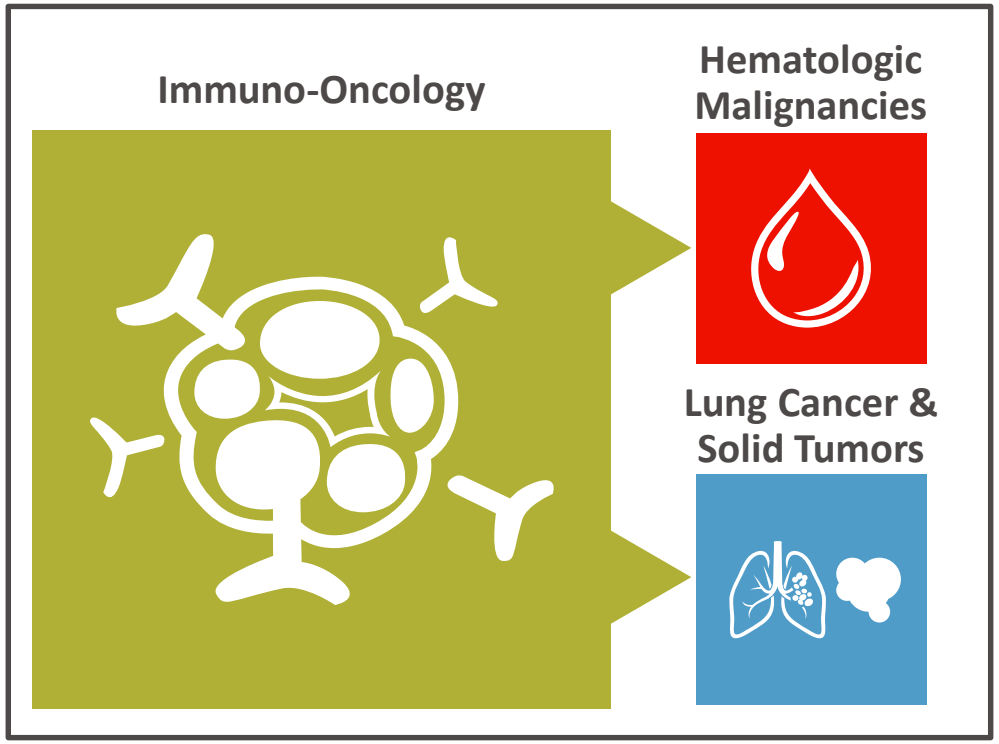
WAVE 1

NMEs that complement our global brands



WAVE 2

Leading platforms in immuno-oncology and cell therapies

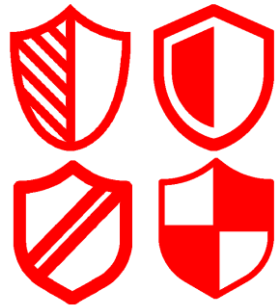


PARTNERSHIPS DRIVE OUR DIFFERENTIATED EARLY CLINICAL PIPELINE

Unique Partnership Model

- Innovative, disruptive platforms
- Agility in ‘open lab’ model

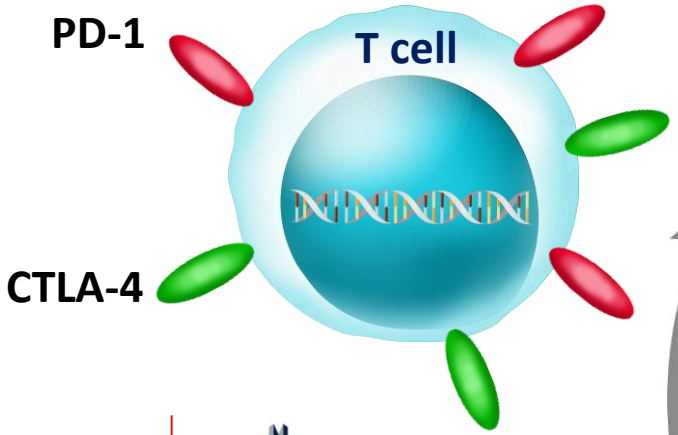
Differentiated Portfolio



- Harness innate immunity
- Eye towards solid tumors

THE FIRST BREAKTHROUGHS IN CANCER IMMUNOTHERAPY TARGET T CELLS

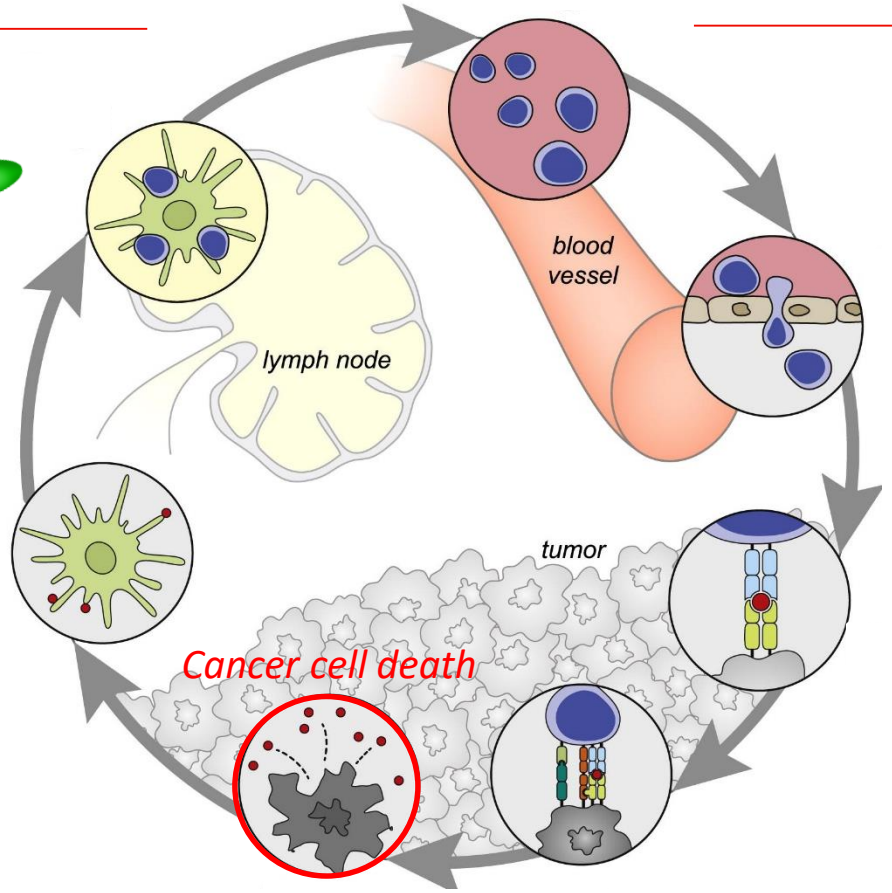
T CELL CHECKPOINT INHIBITORS



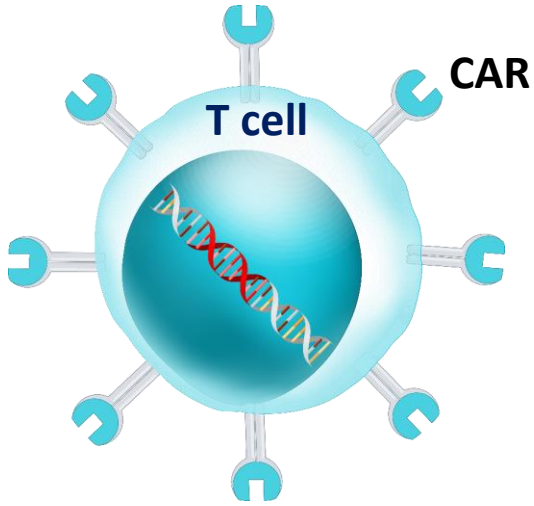
KEYTRUDA

OPDIVO (nivolumab)

YERVOY (ipilimumab) Injection for intravenous use 5 mg/mL



FIRST-GEN CAR-Ts



YESCARTA® (axicabtagene ciloleucel) Suspension for IV infusion

KYMRIAH™ (tisagenlecleucel) Suspension for IV infusion

Adapted from Chen & Mellman, *Immunity 2013*

OUR FOCUS IS ON NOVEL MECHANISMS IN THE CANCER-IMMUNITY CYCLE

2 **Novel-scaffold immune checkpoint platforms**

SHATTUCK LABS

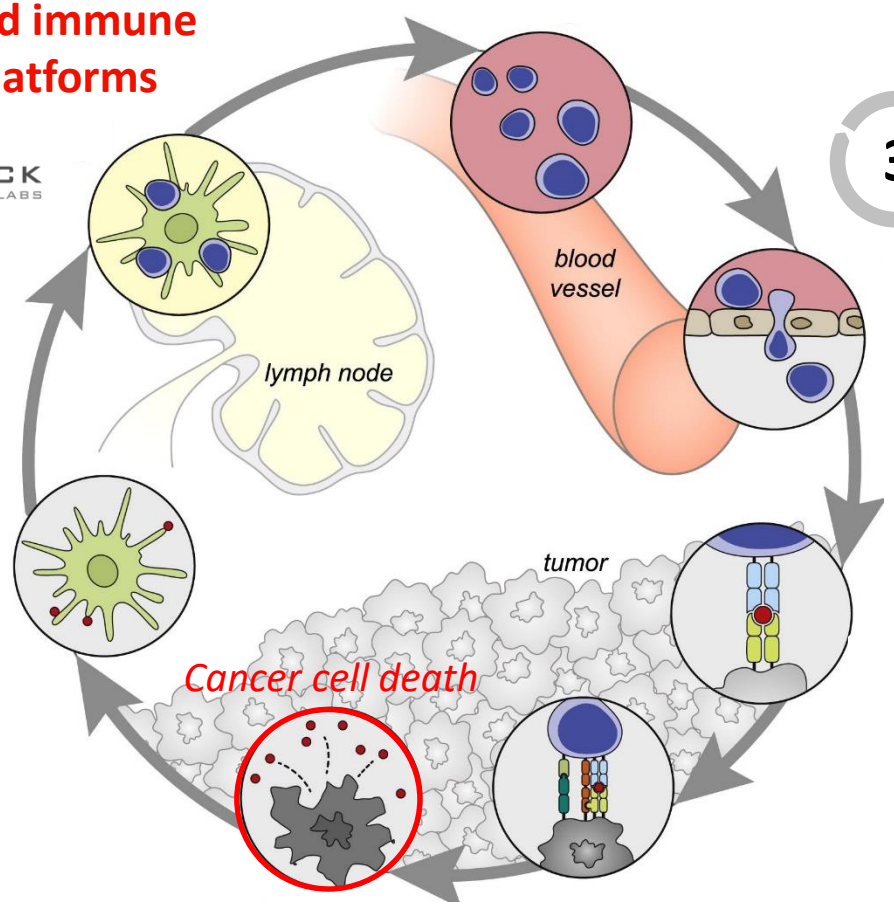
Crescendo biologics

1 **Innate immuno-modulation**

CURADEV
Let science do the talking

teva

Takeda



3 **Next-gen cell therapy & immune engager platforms**

MAVERICK THERAPEUTICS

T-CiRA

NOILE-IMMUNE BIOTECH

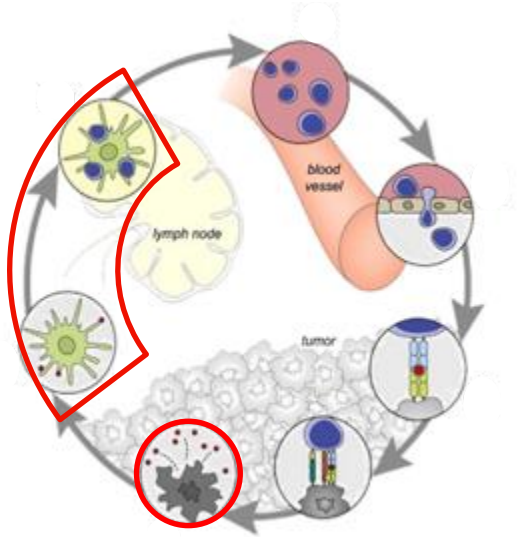
GAMMADELTA THERAPEUTICS

MD Anderson Cancer Center

Memorial Sloan Kettering Cancer Center

Adapted from Chen & Mellman, *Immunity 2013*

1 EMERGING STRENGTH IN TARGETED INNATE IMMUNE MODULATION



Cancer cell death

HIGH UNMET NEED	**Patients refractory/ unresponsive to current immunotherapies**
OUR DIFFERENTIATED APPROACH	**Systemic therapies leveraging innate immunity to enhance response breadth, depth & durability**

PLATFORM	PARTNER	MECHANISM-OF-ACTION	PROGRAMS	PRE-CLINICAL	PH 1
STING agonism	CURADEV *Let science do the talking*	• Innate-to-adaptive priming	**TAK-676** (STING agonist) Targeted STING agonist		
SUMOylation		• Innate immune enhancer	**TAK-981** **TAK-981** (ADCC combo)		
Attenukine™	teva	• Targeted attenuated IFN-α	**TAK-573** (CD38-Attenukine™) Next-gen Attenukine™		

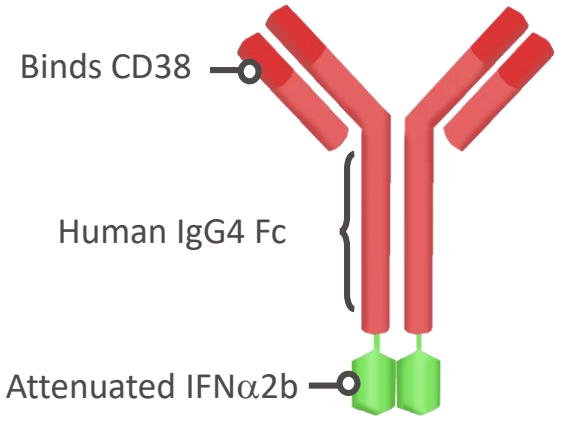
ADCC = Antibody-dependent cellular cytotoxicity

= first-in-class

1 ATTENUKINE™ PLATFORM ELICITS BOTH DIRECT TUMOR KILL AND IMMUNE ACTIVATION

TARGETED ATTENUATED TYPE I IFN PAYLOAD

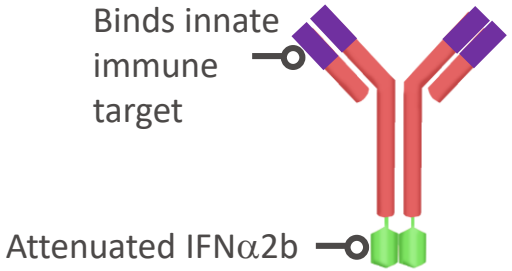
TAK-573



Immunomodulation in preclinical models

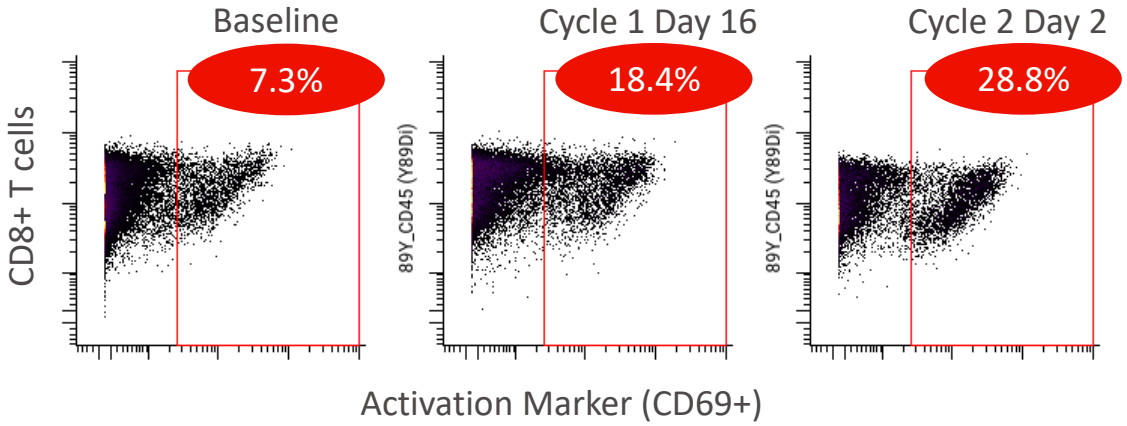
Includes CD8+ T cell migration / activation

NEXT-GEN ATTENUKINE™



TAK-573 POM IN ONGOING PHASE 1 R/R MM STUDY

Activation of CD8+ T cells in bone marrow

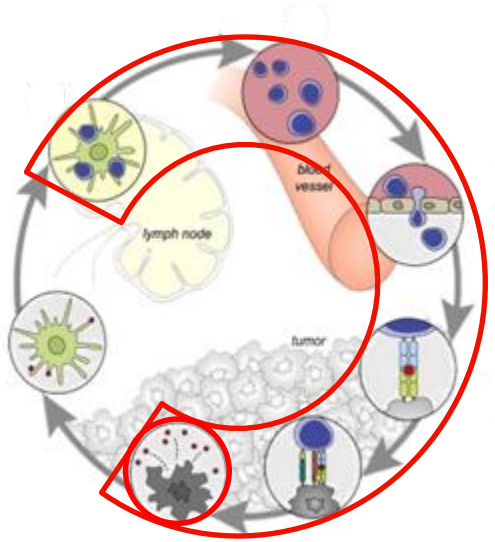


EXPECTED MILESTONES (FY)

2019	2020
Ph1 FPI in solid tumors	Ph1b MM (incl. combinations)

FPI = first patient in R/R MM = Relapsed / refractory multiple myeloma POM = proof-of-mechanism

1 NOVEL SCAFFOLD NEXT-GENERATION CHECKPOINT MODULATORS



Cancer cell death

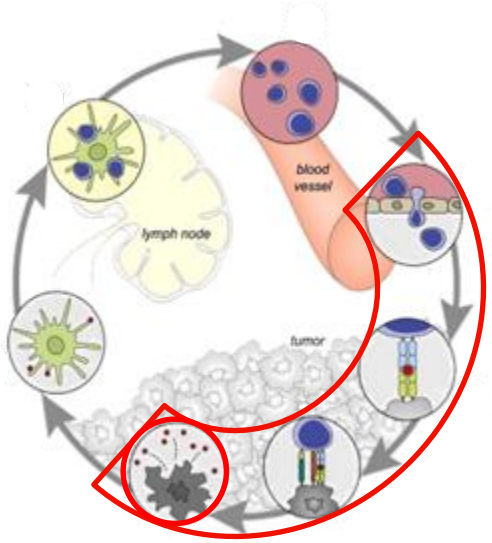
HIGH UNMET NEED	**Current checkpoint modulators fail to improve overall survival in majority of patients**
OUR DIFFERENTIATED APPROACH	**New classes of checkpoint inhibitors designed to increase breadth and depth of responses**

PLATFORM	PARTNER	MECHANISM-OF-ACTION	PROGRAMS	PRE-CLINICAL	PH 1
Humabody Vh	Crescendo biologics	• Unique pharmacology	**Concept 1** **Concept 2**		
Agonist-redirected checkpoints	SHATTUCK LABS	• Co-inhibition & co-stimulation	**TAK-252** / SL-279352 (PD1-Fc-OX40L) **TAK-254** / SL-115154 (CSF1R-Fc-CD40L)		

Vh = Variable heavy domain

= first-in-class

1 BRINGING 5 NOVEL CELL THERAPY PLATFORMS TO THE CLINIC BY THE END OF FY20

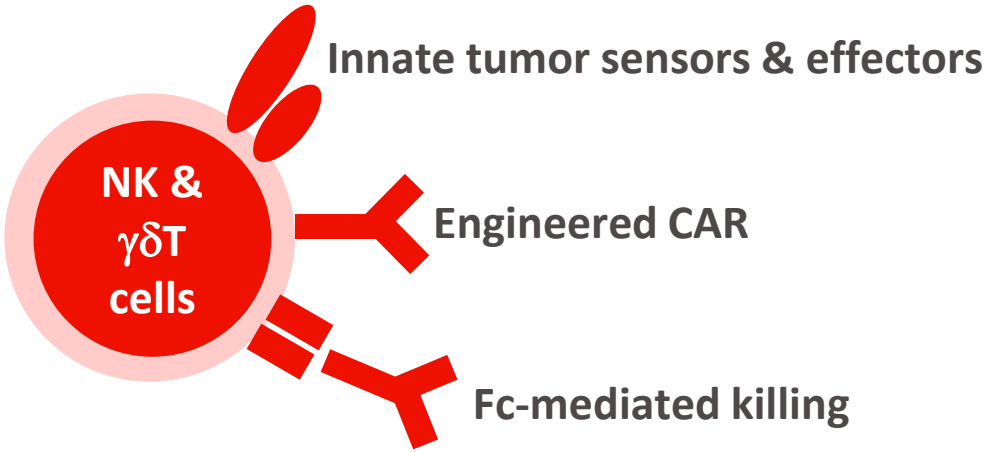


Cancer cell death

HIGH UNMET NEED	**Current CAR-T therapies have significant challenges & fail to address solid tumors**
OUR DIFFERENTIATED APPROACH	**Leverage novel cell platforms & engineering to address shortcomings in liquid & solid tumors**

INNATE IMMUNE PLATFORMS

- **Multiple mechanisms of tumor killing**
- **'Off-the-shelf'**
- **Utility in solid tumors**



NK = Natural killer

A NETWORK OF TOP INNOVATORS IS FUELING TAKEDA'S CELL THERAPY ENGINE

CUTTING-EDGE ENGINEERING & CELL PLATFORMS

IPSC expertise	γδT cell platform	Armored CAR-Ts	Next-gen CARs	IPSC CAR-Ts	CAR-NK platform
T-CiRA	GAMMADELTA THERAPEUTICS	NOILE-IMMUNE BIOTECH	Memorial Sloan Kettering Cancer Center	T-CiRA	MD Anderson Cancer Center
					
Shinya Yamanaka	Adrian Hayday	Koji Tamada	Michel Sadelain	Shin Kaneko	Katy Rezvani
Dec 2015	May 2017	Sept 2017	July 2018	April 2019	Nov 2019
			Takeda Cell Therapy Translational Engine		First Development-Stage Partnership

2016 2017 2018 2019

IPSC = Induced pluripotent stem cell NK = Natural killer

Dr. Sadelain is a co-inventor on patents relative to next-gen CARs, intellectual property that MSK has licensed to Takeda. As a result of these licensing arrangements, Dr. Sadelain and MSK have financial interests related to these research efforts.

1 TAKEDA IS EMBARKING ON A TRANSFORMATIVE CAR-NK PARTNERSHIP THAT COULD ENTER PIVOTAL TRIALS IN 2021

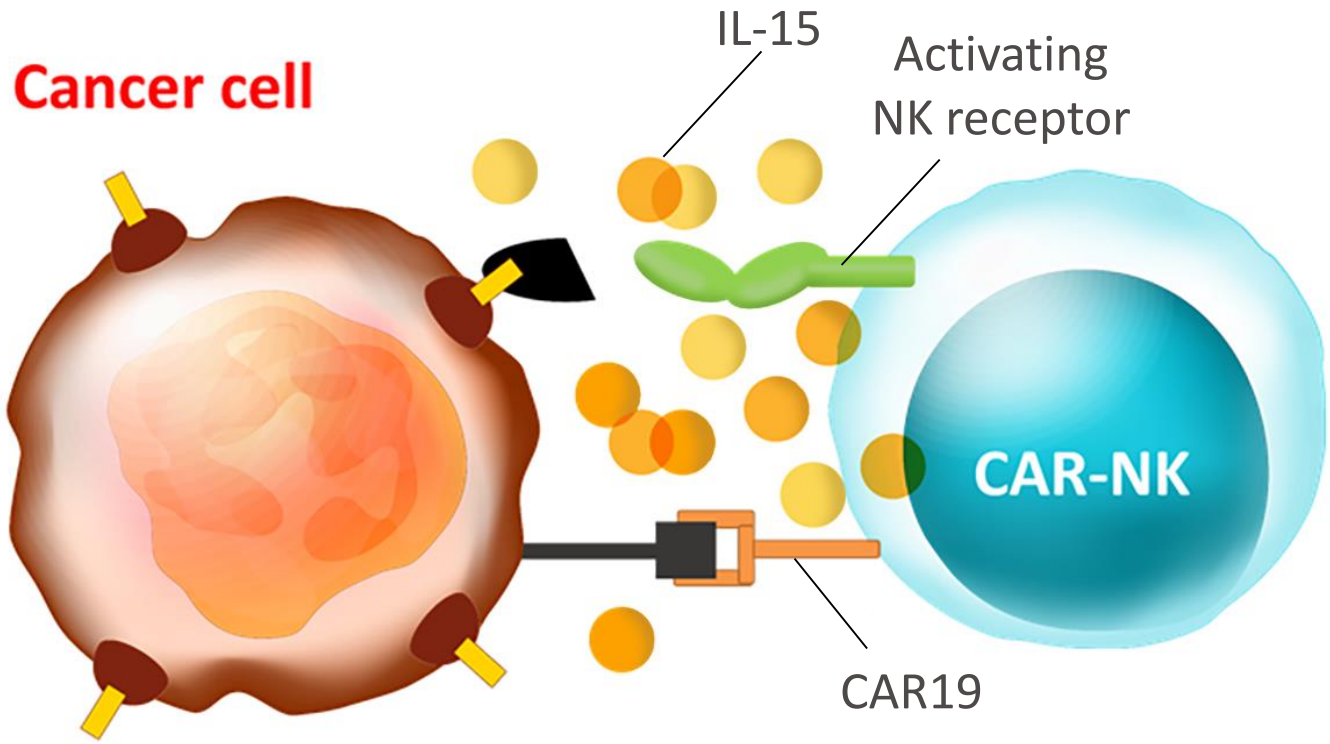
Takeda

MD Anderson Cancer Center

NK CAR Platform

Multiple mechanisms of tumor killing

Potentiation of innate & adaptive immunity



1 FOUR NOVEL, OFF-THE-SHELF CAR-NK THERAPIES IN DEVELOPMENT

PATIENT VALUE PROPOSITION

Rapid and deep responses with a short-time-to-treatment, safe, off-the-shelf CAR-NK available in outpatient & community settings

Initial opportunity in G7 countries (CD19)*	
3L+ DLBCL	~8,000
3L+ CLL	~5,000
3L+ iNHL	~6,000

Potential to move into earlier lines of therapy

PLATFORM VALUE INFLECTIONS

Ongoing maturation of clinical data: Efficacious dose, durability, partial vs. full allo, cryopreserved product

Manufacturing process complete

Pivotal trials in r/r DLBCL / CLL / Indolent NHL

BLA filing

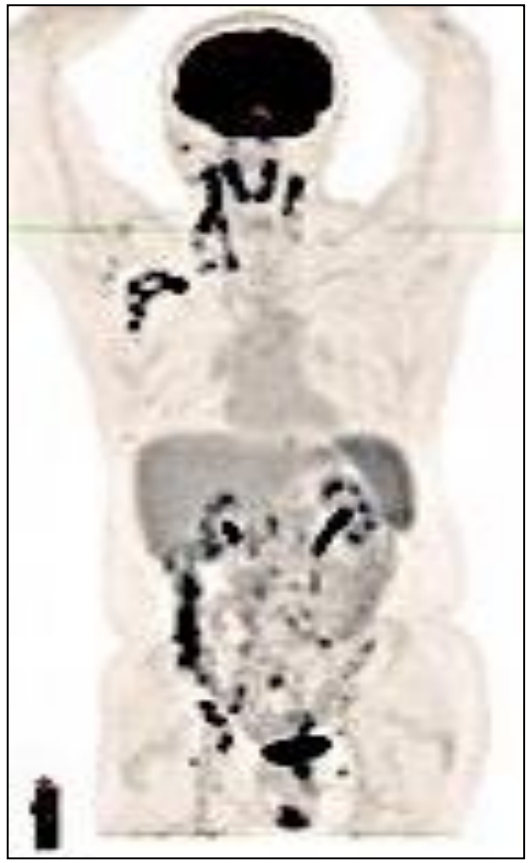
PLATFORM	PARTNER	MECHANISM-OF-ACTION	PROGRAMS	PRECLINICAL	PH 1
CAR-NK (allo cord blood)	MD Anderson Cancer Center – Dr. Katy Rezvani	• Non-autologous NK cell therapy	**TAK-007** (CD19 CAR-NK)		
			BCMA CAR-NK		
			Platform expansion		

= first-in-class

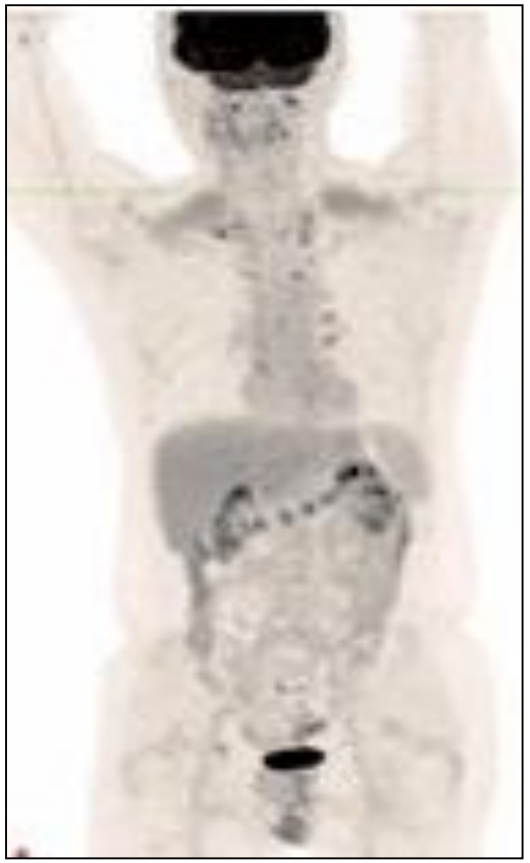
CLL = Chronic lymphocytic leukemia DLBCL = Diffuse large B-cell lymphoma iNHL = Indolent non-Hodgkin's lymphoma
*Estimated number of patients projected to be initially eligible for treatment in G7 markets, subject to regulatory approval

1 DRAMATIC COMPLETE RESPONSE IN FIRST PATIENT TREATED

47-YEAR OLD MALE WITH RELAPSED TRANSFORMED DOUBLE-HIT (C-MYC / BCL-2) DLBCL

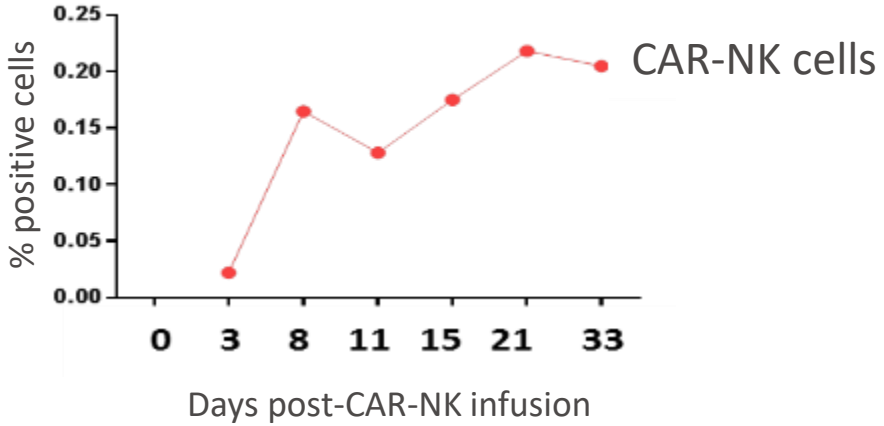


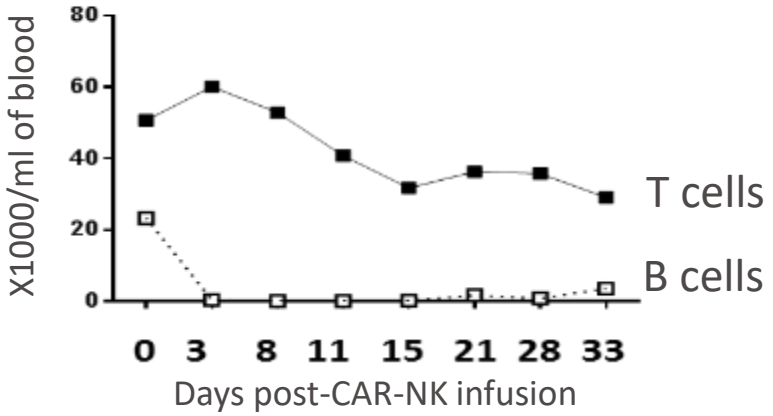
Baseline scan



Day 30 post CAR19-NK

KINETICS OF CAR-NK VERSUS ENDOGENOUS T AND B CELLS IN PERIPHERAL BLOOD

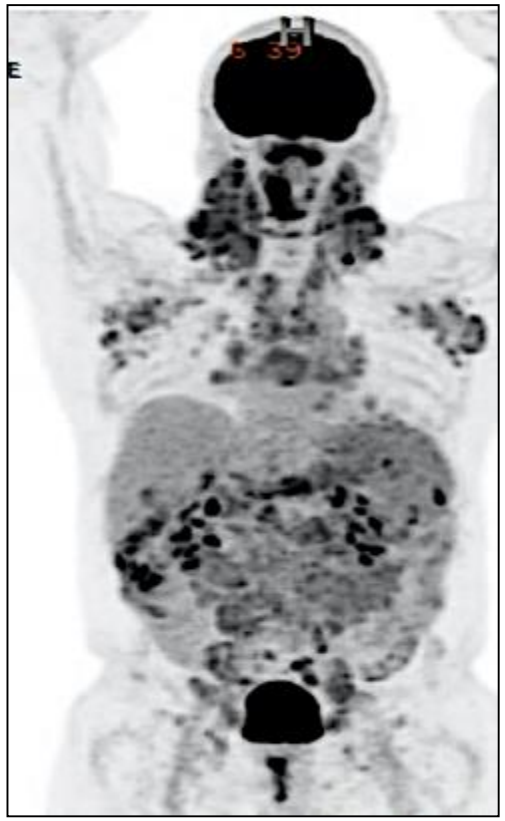




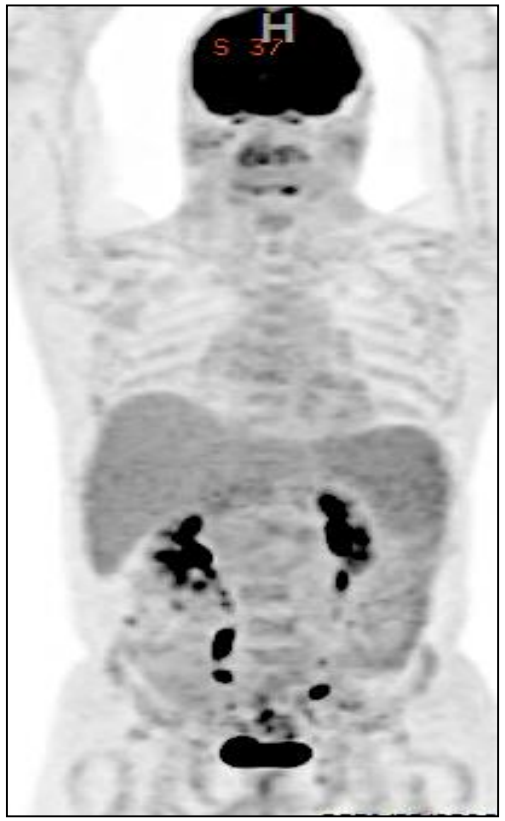
Data from Dr. Katy Rezvani, MD Anderson Cancer Center

1 IMPRESSIVE RESPONSES IN OTHER HEAVILY PRETREATED PATIENTS

61-YEAR OLD MALE CLL/RICHTER'S TRANSFORMATION (5 PRIOR LINES OF THERAPY)



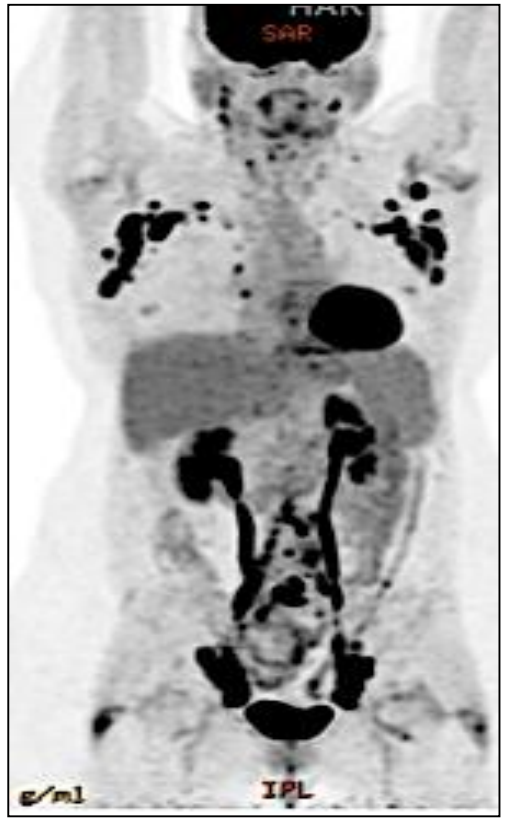
Baseline scan



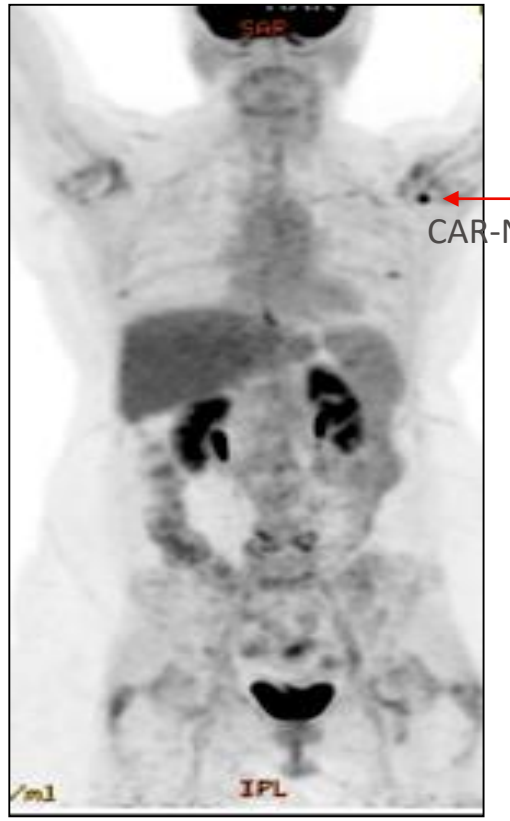
Day 30 post CAR19-NK

CR in Richter's; SD in CLL

60-YEAR OLD FEMALE WITH CLL / ACCELERATED CLL (5 PRIOR LINES OF THERAPY)



Baseline scan

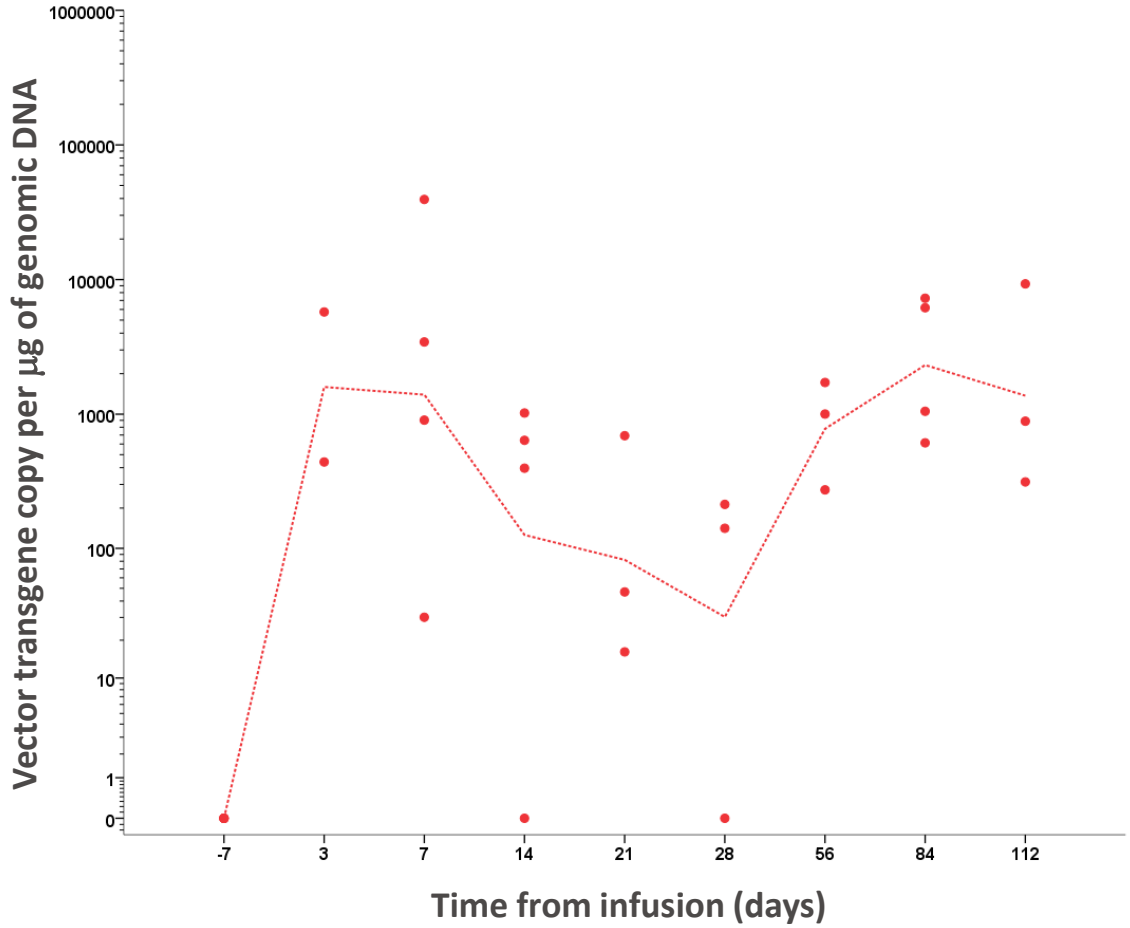


Day 30 post CAR19-NK

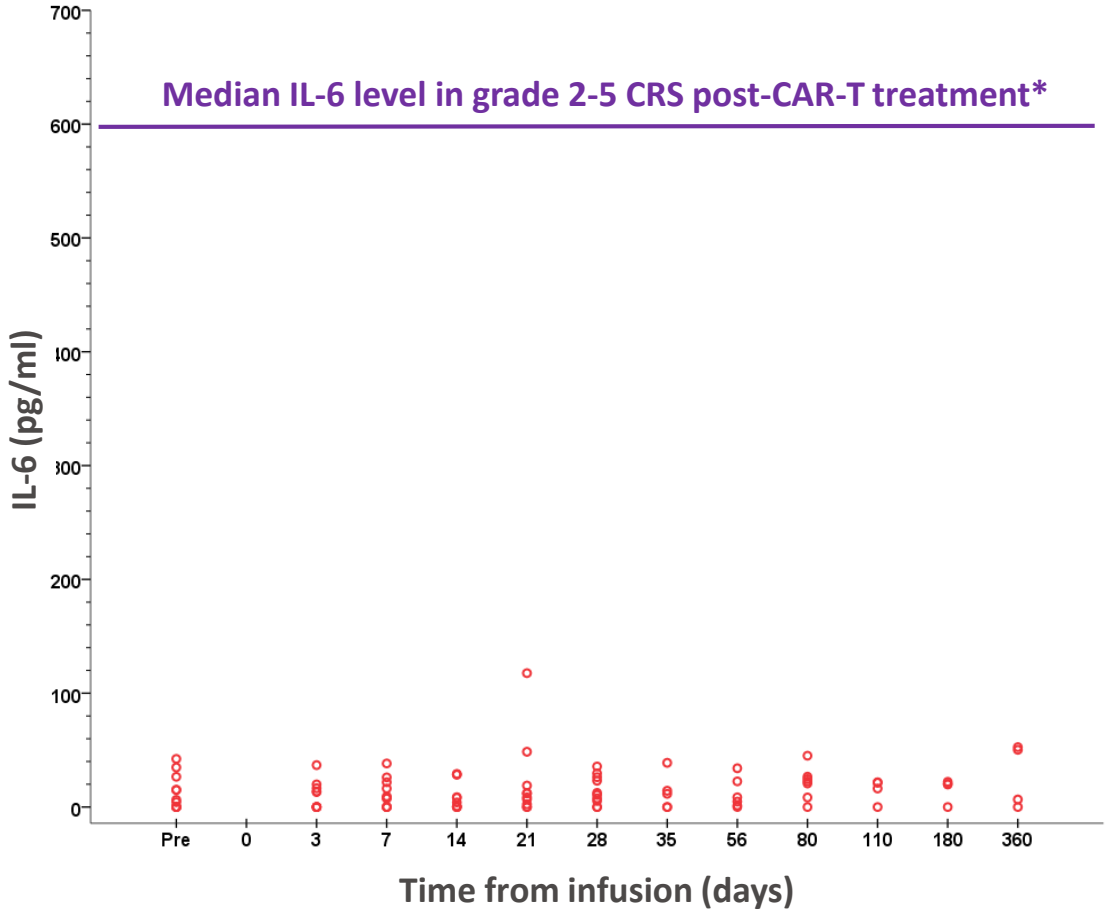
CLL = Chronic lymphocytic leukemia CR = Complete response SD = Stable disease
Data from Dr. Katy Rezvani, MD Anderson Cancer Center

1 CAR-NK CELLS PERSIST IN PATIENTS AND DO NOT TRIGGER CYTOKINE RELEASE SYNDROME (CRS)

CAR-NK CELLS PERSIST UP TO 4 MONTHS POST INFUSION



IL-6 LEVLS POST CAR-NK INFUSION DO NOT INDICATE CRS



CRS = Cytokine Release Syndrome

*Turtle et al. 2017

Data from Dr. Katy Rezvani, MD Anderson Cancer Center

1 CAR-NK EFFICACY & TOXICITY TREATING MULTPLE DIAGNOSES

	Diagnosis	Lines of Treatment	HLA Match	CRS / Neurotox	Complete Response
Dose Level 1	DLBCL - Relapsed transformed double-hit	**3** Incl. ASCT	Partial match	None	✓
	DLBCL - Refractory	**7**	Partial match	None	PD
	CLL	**4** Incl. ibrutinib & venetoclax	Partial match	None	✓
Dose Level 2	CLL	**4** Incl. ibrutinib	Partial match	None	PD
	CLL/Richter's transformation	**5** Incl. ibrutinib	Partial match	None	✓* Richter's
	CLL/Accelerated CLL	**5** Incl. ibrutinib & venetoclax	Partial match	None	✓
	CLL	**4** Incl. ibrutinib	Partial match	None	✓
Dose Level 3	DLBCL - Refractory	**11** Incl. ASCT	Partial match	None	✓
	DLBCL - Relapsed transformed double-hit	**4** Incl. ASCT	Partial match	None	✓
	Follicular lymphoma - Relapsed	**4** Incl. ASCT	Mismatch	None	PD
	Follicular lymphoma - Relapsed	**4**	Mismatch	None	✓

CLL = Chronic lymphocytic leukemia

CRS = Cytokine release syndrome

DLBCL = Diffuse large B-cell lymphoma

ASCT = Autologous stem cell transplant

HLA = Human leukocyte antigen

PD = Progressive disease

*Complete response for Richter's

Data from Dr. Katy Rezvani, MD Anderson Cancer Center

1 FAST-TO-CLINIC CELL THERAPY ENGINE WILL MAXIMIZE LEARNINGS ON MULTIPLE 'DISRUPTIVE' PLATFORMS

5 CLINICAL-STAGE PROGRAMS EXPECTED BY END OF FY20

FY19 → **FY20**

TAK-007
MD Anderson Cancer Center
Off-the-shelf CAR-NK product

TAK-102
NOILE-IMMUNE BIOTECH
Cytokine + chemokine armed CAR-T

CD19 1XX-CAR-T
Memorial Sloan Kettering Cancer Center
Next-gen CART signaling domain

GDX012
GAMMADELTA THERAPEUTICS
Gamma-delta T cells

GCC CAR-T
Takeda
Colorectal Cancer

Hematology
Solid tumors

FY21+: Other cell therapy candidates

1 A RICH AND POTENTIALLY TRANSFORMATIVE EARLY CLINICAL ONCOLOGY PIPELINE

PLATFORM	PARTNER(S)	MECHANISM-OF-ACTION	PROGRAMS
STING agonism	CURADEV	• Innate-to-adaptive priming	**TAK-676** (STING agonist) Targeted STING agonist
SUMOylation		• Innate immune enhancer	**TAK-981** **TAK-981** (ADCC combo)
Attenukine™	teva	• Targeted attenuated IFN-α	**TAK-573** (CD38-Attenukine™)
Agonist-redirected checkpoints	SHATTUCK LABS	• Co-inhibition & co-stimulation	**TAK-252** / SL-279353 **TAK-254** / SL-115154
Shiga-like toxin A	tem	• Novel cytotoxic payload	**TAK-169** (CD38-SLTA)
IGN toxin	immunogen	• Solid tumor-targeted ADC	**TAK-164** (GCC-ADC)
Conditional T cell engagers	MAVERICK THERAPEUTICS	• Novel solid tumor platform	**MVC-101** (EGFR COBRA™)
Cell therapy platforms	Memorial Sloan Kettering Cancer Center, 7-CiRA, NOILE-IMMUNE BIOTECH, MD Anderson Cancer Center, GAMMADELTA THERAPEUTICS	• Off-the-shelf cell therapies	**TAK-007** (CD19 CAR-NK) **5 cell therapies expected in clinic by end of FY20**

PRECLINICAL PH1

= first-in-class

UNDISCLOSED TARGETS

Crescendo biologics
MAVERICK THERAPEUTICS
Memorial Sloan Kettering Cancer Center
NOILE-IMMUNE BIOTECH
7-CiRA
MD Anderson Cancer Center
tem
teva

Hematology Solid tumors

NME MILESTONES ACHIEVED IN FY19 AND LOOKING AHEAD TO OTHER POTENTIAL MILESTONES[1] THROUGH FY20

PIVOTAL STUDY STARTS, APPROVALS

1H FY 2019

- ☑ TAK-611 — MLD — Ph 2 start[2]
- ☑ TAK-755 — cTTP — Ph 3 start
- ☑ TAK-925 — Narcolepsy — POC
- ☑ TAK-721 — EoE — Ph 3 data (induction)
- ☑ TAK-101 — Celiac Disease — POC

2H FY 2019

- ☑ PEVONEDISTAT TAK-924 — AML — Ph 3 start
- TAK-788 — 1L NSCLC — Ph 3 start
- ☑ PEVONEDISTAT TAK-924 — HR-MDS — Ph 2 Overall Survival
- ☑ TAK-007 — Hem. Malignancies — POC
- TAK-609 — Hunter (IT) — Ph 3 data 2yr extension
- mHTT ASO — Huntington's Disease — POC
- TAK-721 — EoE — Ph 3 data (maintenance)

1H FY 2020

- TAK-788 — 2L NSCLC — Ph 2 Pivotal
- TAK-573 — R/R MM, Solid Tumor — POC

2H FY 2020

- TAK-721 — EoE — Approval
- mHTT ASO — Huntington's Disease — Pivotal start
- TAK-620 — R/R CMV SOT & HSCT — Ph 3 data
- TAK-755 — iTTP — POC
- TAK-935 — DEE — POC
- TAK-906 — Gastroparesis — POC
- TAK-951 — Nausea & Vomiting — POC

Oncology

Rare Disease

Neuroscience

Gastroenterology

☑ Denotes milestones that have been achieved.

KEY DATA READOUTS

1. Potential key milestone dates as of November 14, 2019. The dates included herein are estimates based on current data and are subject to change
2. Potentially registration enabling

SUMMARY

1

Total transformation of preclinical & early clinical pipeline

2

Differentiated opportunities in IO leveraging innate immunity & cell therapies

3

Multiple near-term catalysts informing momentum towards solid tumors

R&D DAY AGENDA – NEW YORK, NOVEMBER 14, 2019

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

TAK-788: PURSUING A FAST-TO-PATIENT STRATEGY FOR NSCLC PATIENTS WITH EGFR EXON 20 INSERTIONS

Rachael L Brake, PhD

Global Program Leader, Oncology

Takeda Pharmaceutical Company Limited

New York, NY

November 14, 2019

THE SIZE OF THE LUNG CANCER CHALLENGE IS VAST

228,000[1]

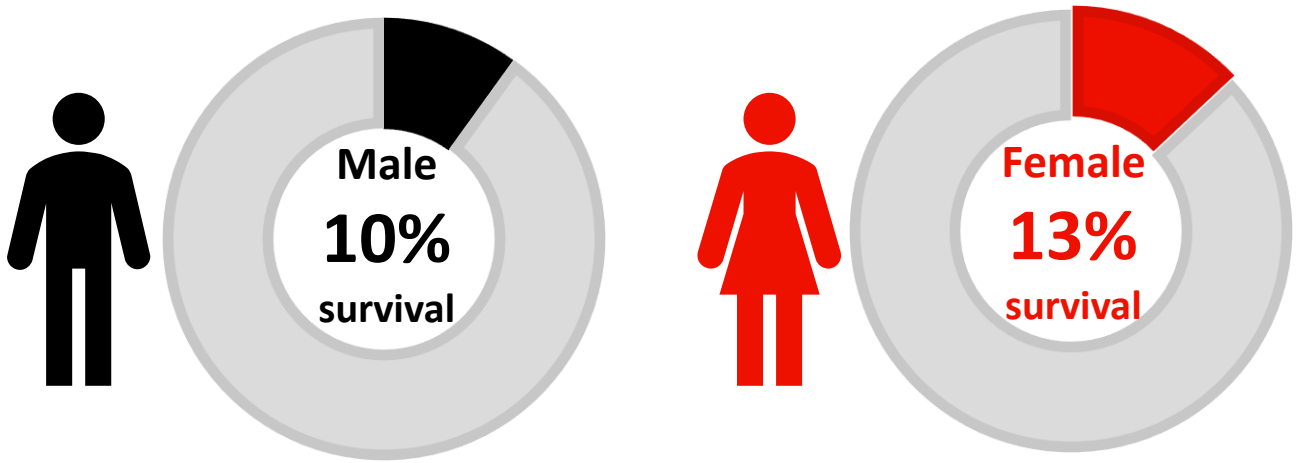
New Lung cancer cases / year

143,000[1]

Lung cancer deaths/ yr

More than breast, colon, and prostate cancer combined

Survival of Lung cancer is amongst the lowest of all cancers

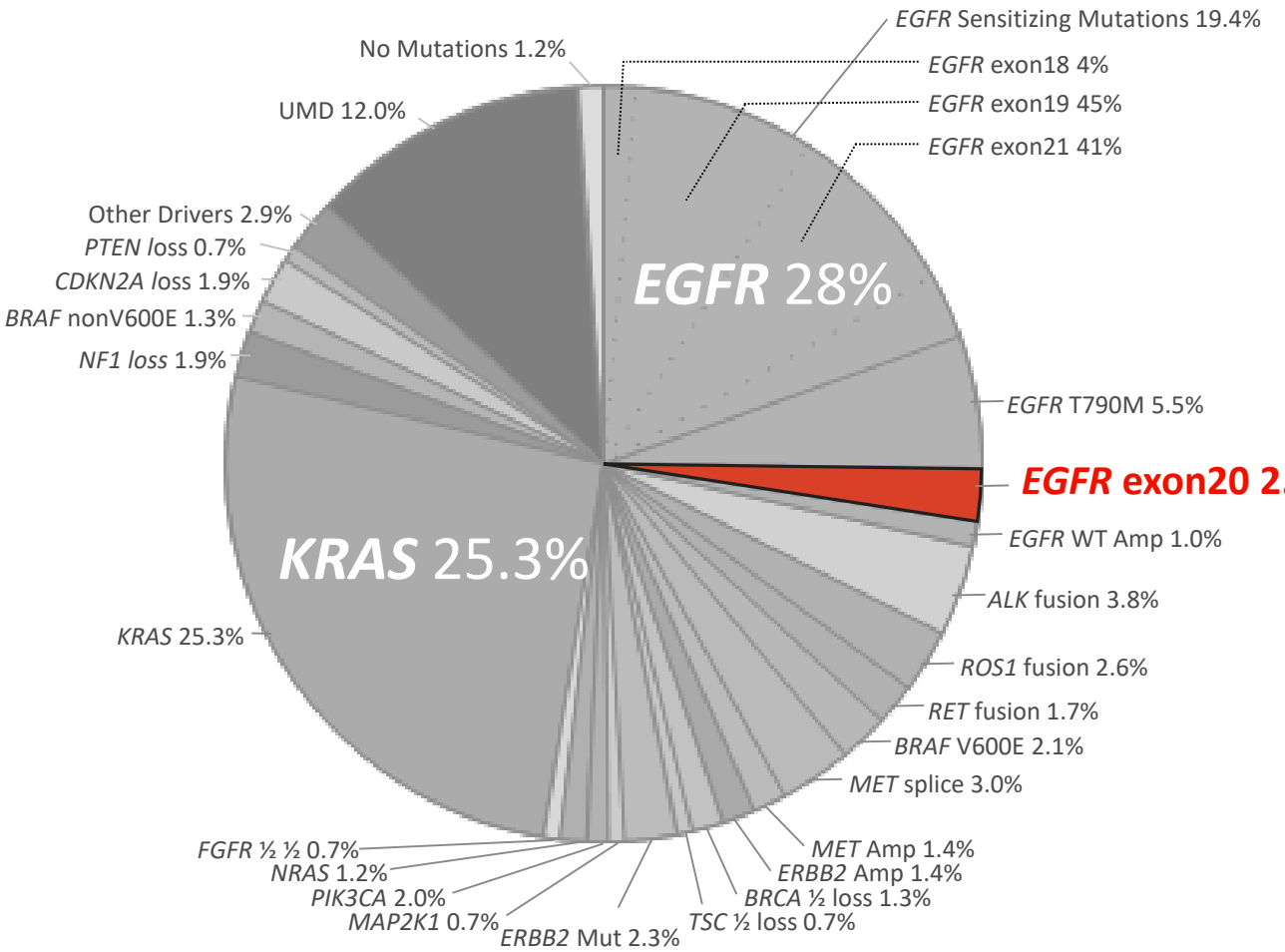


5 yr survival estimates among adults diagnosed with lung cancer between 2007-2011[2]

1. American Cancer Society; Cancer facts and figures 2019
2. Office for National Statistics UK (www.ons.gov.uk)

EXON 20 INSERTIONS ARE A RARE SUBSET OF EGFR MUTANT NSCLC

Non-Sq NSCLC 200,000 pts/yr[1]



EGFR Exon 20 insertions 2,000 pts/yr[2]

Insertion variants		
1.	V769_D770insASV	(≈20%)
2.	D770_N771insSVD	(≈19%)
3.	H773_V774insH	(≈8%)
4.	A763_Y764insFQEA	(≈7%)
5.	H773_v774insPH	(≈5%)
6.	H773_V774insNPH	(≈4%)
7.	N771_P772insN	(≈3%)
8.	H773_V774insAH	(≈3%)
9.	Other	(≈31%)

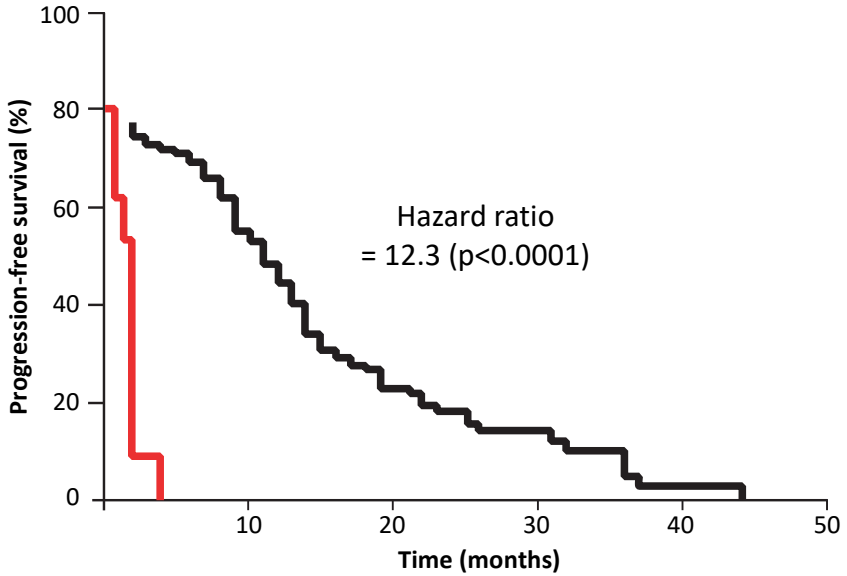
Sources: Leduc C et al., Ann Oncol 2017; Jorge S et al. Braz J Med Biol Res 2014; Kobayashi Y & Mitsudomi T. Cancer Sci 2016; Arcila M et al. Mol Cancer Ther 2013; Oxnard G et al. J Thorac Oncol 2013

1. Estimated US annual incidence of non-squamous NSCLC
2. Represents annual incidence of the US addressable patient population

PATIENTS WITH EGFR EXON 20 INSERTIONS HAVE NO EFFECTIVE THERAPY

POOR RESPONSE TO EXISTING TKIs [1]

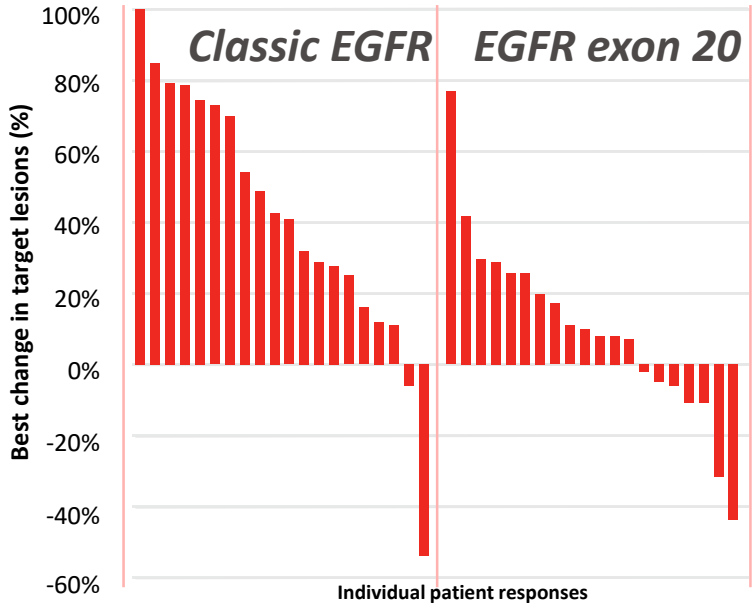
EGFR exon 20 insertions do not demonstrate significant PFS benefit with 1st and 2nd gen EGFR TKIs



Group	Median PFS (months)
EGFR exon 20 ins (n=9)	2.0
Classical EGFR mut (n=129)	12.0

POOR RESPONSE TO ANTI PD-1/PDL-1 THERAPY [2]

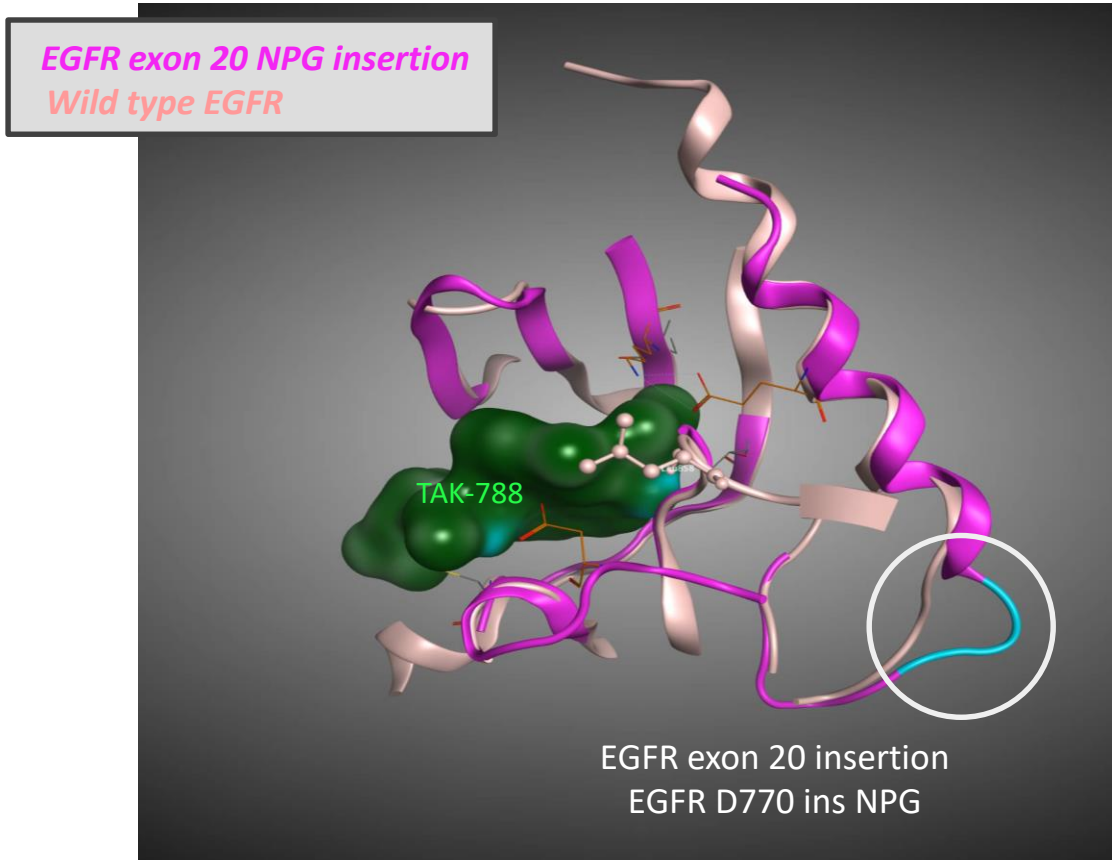
EGFR exon 20 ins patients demonstrate limited benefit to anti PD-1 directed therapy



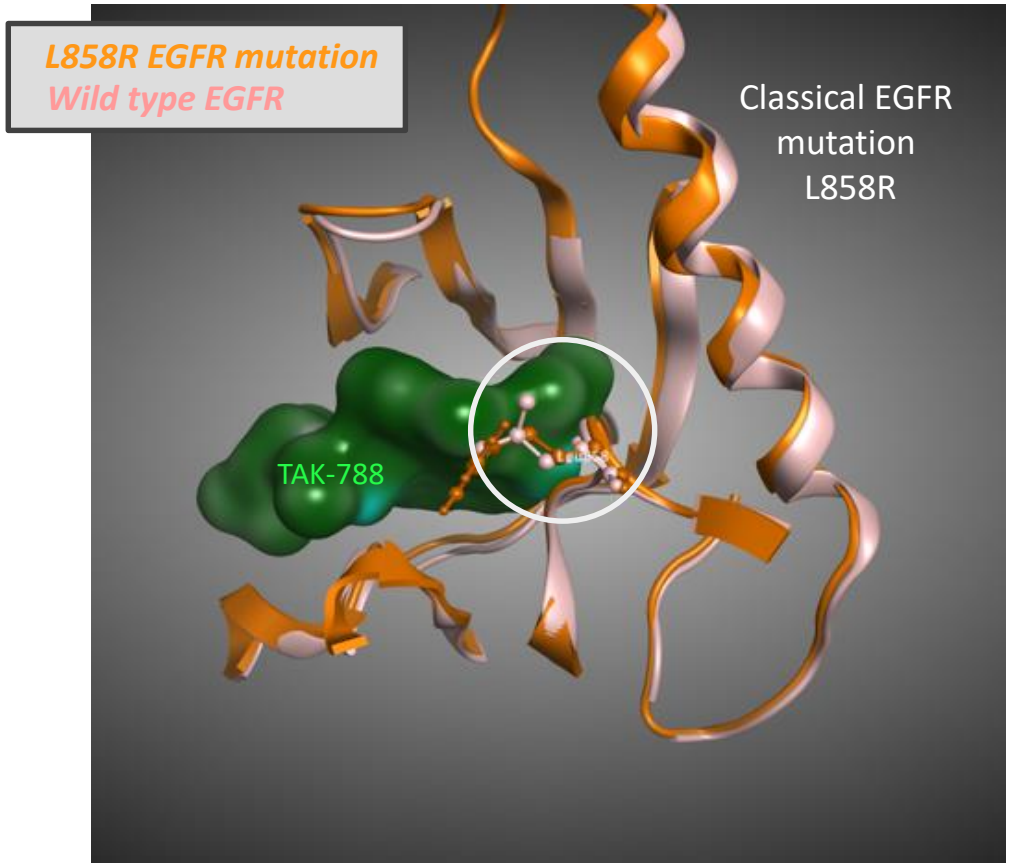
Group	Median PFS (months)	PDL-1 expression ≥1%
EGFR exon 20 ins (n=20)	2.7 (1.7-3.8)	40%
Classical EGFR mut (n=22)	1.8 (1.2-2.4)	25%

1. Robichaux et al., WCLC 2016.
2. Adapted from Negrao et al., WCLC 2019

OVERCOMING THE DRUG DEVELOPMENT CHALLENGE IN EXON 20 INSERTIONS



EGFR exon 20 insertion mutations have a similar structure and similar affinity for ATP to wild type EGFR



Classical EGFR mutations Significantly alter both structure and affinity for ATP compared to wild type EGFR

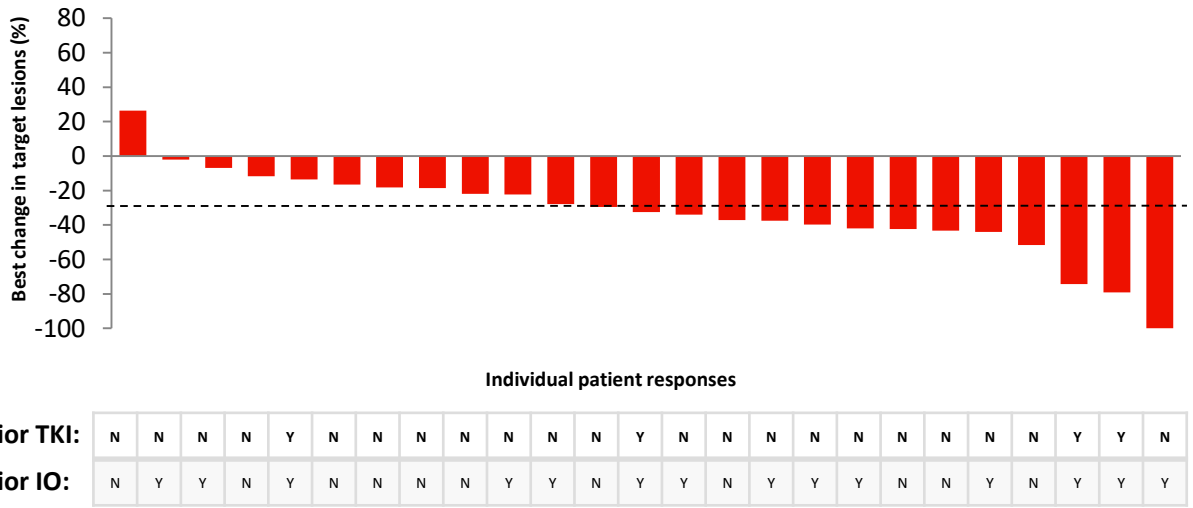
Source. TAK-788 bound to EGFR kinase domain containing D770 ins NPG, crystal structure (data on file)

TAK-788 PROOF OF CONCEPT DATA IN EGFR EXON 20 INSERTIONS

2019 ASCO ANNUAL MEETING

• Confirmed ORR: 12/28 patients: 43% (24.5-62.8%) • Median PFS: 7.3 months (4.4 mo - NR)

ANTITUMOR ACTIVITY IN EGFR EXON 20 INS AT 160 MG DAILY



SAFETY SUMMARY IN PATIENTS TREATED WITH TAK-788

N (%)	All Patients 160 mg qd (n=72)
Treatment-related AE	
Any grade	68 (94)
Grade ≥3	29 (40)
Dose reduction due to AE	18 (25)
Dose interruption due to AE	36 (50)
Discontinuation due to treatment-related AE	10 (14)

TAK-788 has not been approved for the use or indications under investigation in the clinical trials (and there is no guarantee it will be approved for such use or indication). Claims of safety and effectiveness can only be made after regulatory review of the data and approval of the labeled claims.
Adapted from Riley et al. ASCO. 2019

ENCOURAGING EFFICACY AND SAFETY HAS BEEN OBSERVED WITH TAK-788

Select signs of efficacy				
Clinical feature	**TAK-788 [1] n=28**	**Poziotinib [2] n=50**	**Afatinib [3] n=23**	**Osimertinib [4] n=15**
ITT confirmed ORR (%)	43%	NR	8.7%	0%
Evaluable confirmed ORR (%)	NR	43%	NR	NR
ITT median PFS (months)	7.3	5.5	2.7	3.5
Select treatment related adverse events attributable to wild type EGFR inhibition				
Grade ≥ 3 Adverse event	**TAK-788 [1] n=72**	**Poziotinib [2] n=63**	**Afatinib [5] n=229**	**Osimertinib [6] n=279**
Diarrhea ≥ Gr3	18%	17.5%	14%	1%
Rash ≥ Gr3	1%	35%	16%	1%
Paronychia ≥ Gr3	0%	9.5%	11%	0%
Total dose reduction rates				
AE related dose reductions (%)	25%	60%	52%	2.9%

Direct cross-trial comparison can not be made between TAK-788 and other treatments due to different studies with different designs
ITT = Intention to treat, ORR = Overall response rate, PFS = progression free survival, NR = Not reported.
Sources: 1. Riley et al. ASCO. 2019; 2. Haymach et al. WCLC 2018; 3. Yang et al., Lancet. 2016.; 4. Kim et al., ESMO 2019; 5. Yang et al., Lancet. 2012; 6. Mok et at., NEJM 2017

STRONGER DIARRHEA MANAGEMENT SHOULD = ENHANCED EFFICACY

June 2016
FIRST IN HUMAN
Diarrhea management very late - medicate when at Grade 2

Average time on TAK-788 7.9 months

Diarrhea	Time on Treatment (Mo)
Grade 3	4.6
Grade 2	9.8
Grade 1	12.7
No diarrhea	12.1

Feb 2019 new trial
Exclaim

Comprehensive diarrhea management guidelines implemented earlier

WE HAVE MODIFIED OUR APPROACH TO GI ADVERSE EVENT MANAGEMENT WITH THE AIM TO IMPROVE EFFICACY

Source. TAK-788 Clinical trial database (data on file)

2021: EXPECTED FIRST APPROVAL IN EGFR EXON 20 INSERTIONS

· Single arm Phase 2 trial
· Refractory EGFR Exon 20 insertion patients

- Previously treated, ≤2 systemic anticancer chemotherapy
- Locally advanced or metastatic
- NSCLC harboring *EGFR* exon 20 insertion

Exclaim

TAK-788 at 160 mg qd

1. Overall Response Rate
2. Duration of Response
3. Median Progression Free Survival
4. Overall survival

· ACTIVELY ENROLLING US, EU, AND ASIA
· POTENTIAL APPROVAL MID 2021

· Supporting data generation
· Real world evidence (RWE) data collection

RWE will be used to assess the benefit of conventional standard of care (SOC) agents in patients with EGFR Exon 20 insertions

EMR claims databases and Medical Chart Review

Chemo +/- VEGFR | **Immunotherapy** | **Other**

1. Overall Response Rate
2. Time to treatment failure
3. Median progression free survival
4. Duration of Response
5. Overall survival

· US (FLAT IRON HEALTH) · JP (SCRUM-JAPAN)
· EU AND CHINA CHART REVIEW

Source. https://clinicaltrials.gov/ct2/show/NCT02716116, https://www.exclaimstudy.com/

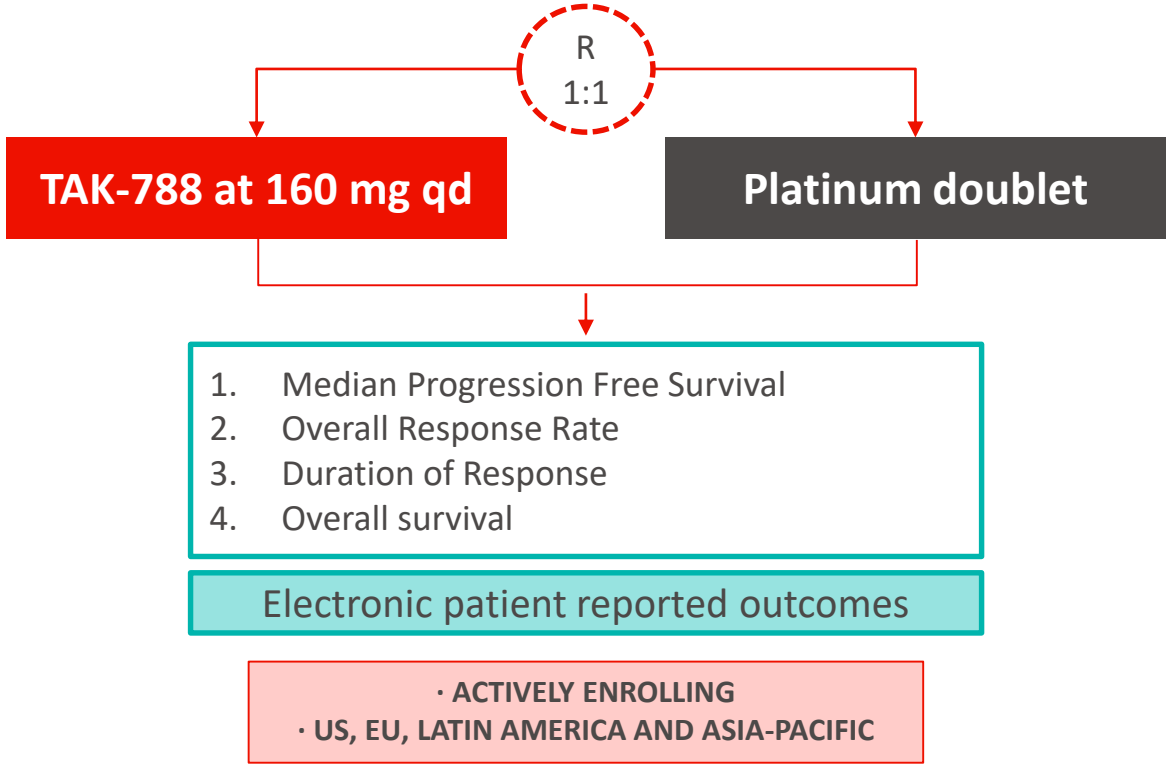
NEW ACTIVATION: A TRIAL FOR NEWLY DIAGNOSED PATIENTS

Exclaim -2

2 year enrollment
Anticipated approval 2023

· Randomized, controlled, Phase 3 trial
· Treatment-naïve EGFR exon 20 insertion patients

- Advanced or metastatic
- Treatment-naïve patients diagnosed with NSCLC harboring EGFR exon 20 insertion mutations



Source. https://clinicaltrials.gov/ct2/show/NCT04129502

SUMMARY

1

NSCLC patients with EGFR Exon 20 insertions are underserved with the current available therapies

2

TAK-788 is the first purposely designed inhibitor and clinical proof-of-concept has demonstrated efficacy

3

The EXCLAIM trial in refractory patients could lead to the first approval of TAK-788 by 2021

PEVONEDISTAT (TAK-924): A POTENTIAL NEW TREATMENT FOR HR-MDS AND AML

Phil Rowlands, PhD

Head Oncology Therapeutic Area Unit

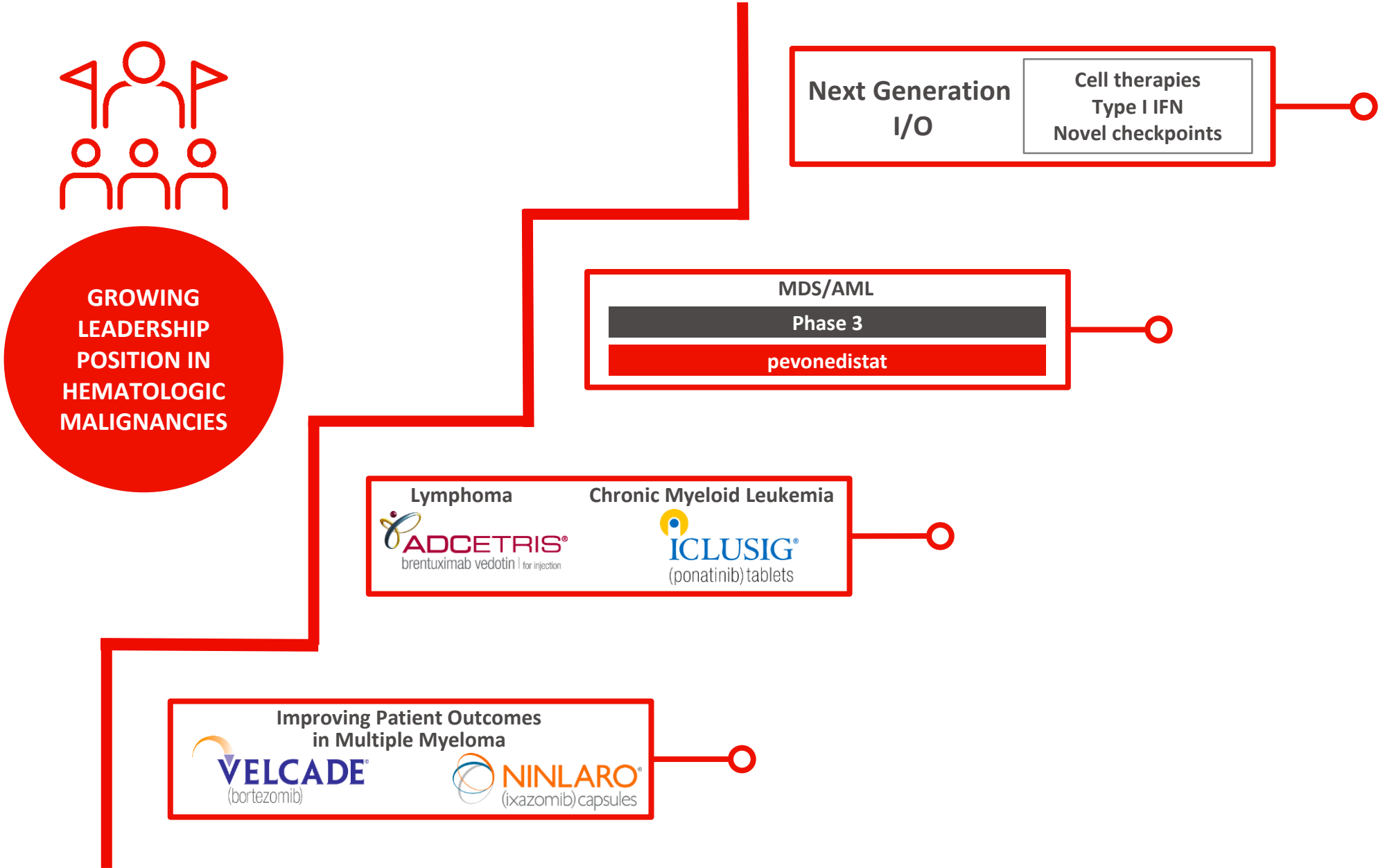
Takeda Pharmaceutical Company Limited

New York, NY

November 14, 2019

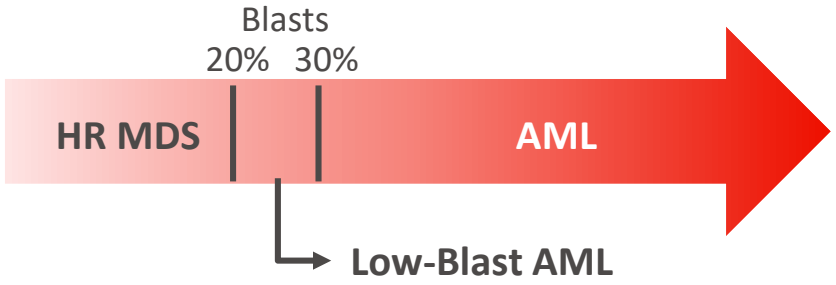
Better Health, Brighter Future

BUILDING ON THE TAKEDA ONCOLOGY FOUNDATION IN HEMATOLOGIC MALIGNANCIES



HIGH RISK MYELODYSPLASTIC SYNDROME (HR-MDS) AND ACUTE MYELOID LEUKEMIA (AML) HAVE LIMITED TREATMENT OPTIONS

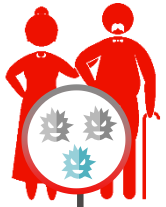
CONTINUUM OF HR-MDS AND AML



- HR-MDS and AML are both rare bone marrow-related cancers that share foundational biology, clinical features, and genetic mutations*
- Incidence highest in elderly (>70 years old)
- Overall survival several months to a few years, depending on risk category

CLINICAL TREATMENT

BM failure → cytopenias
- **Fatigue (anemia)**
- **Infection (neutropenia)**
- **Bleeding (thrombocytopenia)**



Clinical treatment goals:
Alleviate cytopenias
Improve patient quality of life
Improve survival

Fit Patients
Younger
Fewer co-morbidities
Better performance status

Intensive Chemotherapy

Stem Cell Transplant
(Only curative treatment)
≤ 10% HR-MDS, ~45% AML

Unfit Patients
Older
Unfit for intensive chemotherapy and/or stem cell transplant

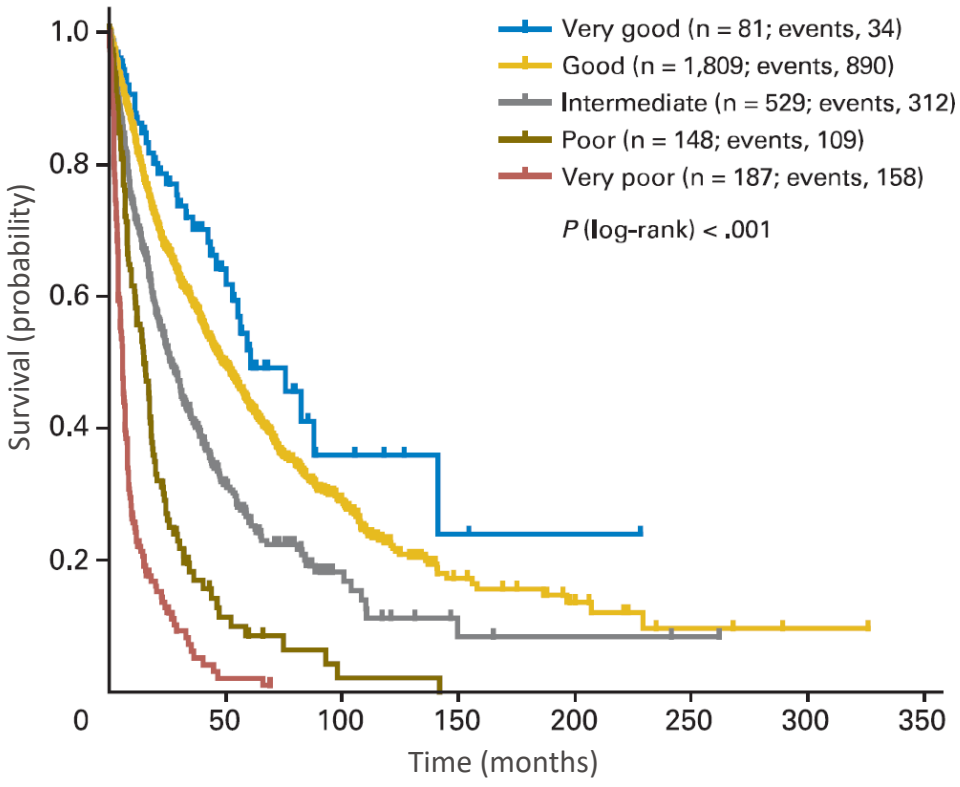
Chemotherapy
azacitidine
decitabine
Low dose ara-c

Targeted therapies
(AML only)
BCL2
IDH1/2
FLT3

* 30% of HR-MDS patients progress to AML

CURRENT STANDARD OF CARE IS INADEQUATE FOR HR-MDS PATIENTS

MDS SURVIVAL BY PROGNOSTIC RISK



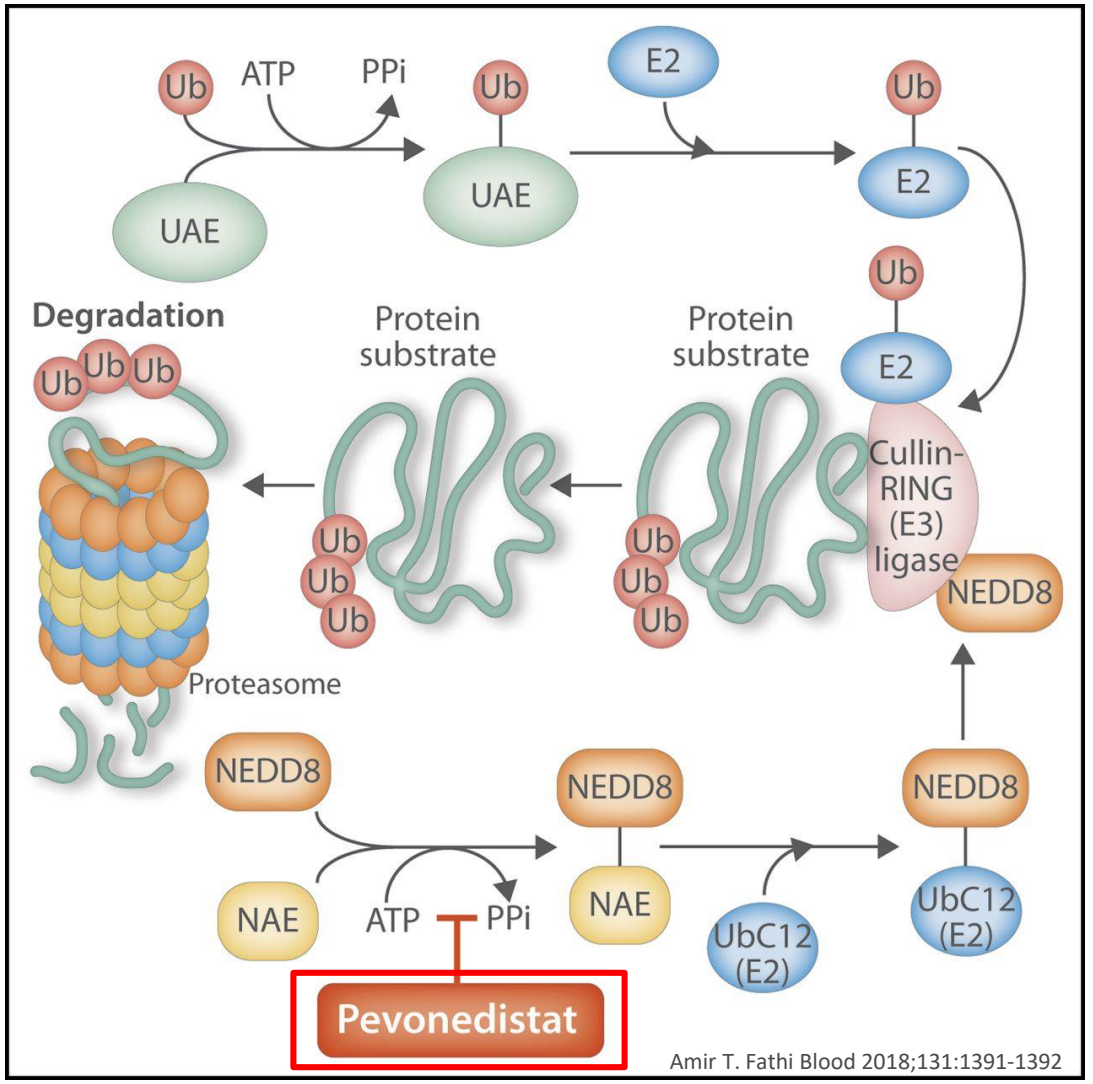
Schanz et al., *J Clin Oncol.* 2012, 30:820-829

Median survival ~6 months to 5 years

- No new treatments have been approved for MDS in over a decade
- Transplant ineligible patients treated with first line therapy: Median OS = 15mo; 2yr OS rate 35%
- Economic burden is substantial - hospitalizations are common among patients and many are transfusion dependent

PEVONEDISTAT: A UNIQUE FIRST-IN-CLASS NAE INHIBITOR

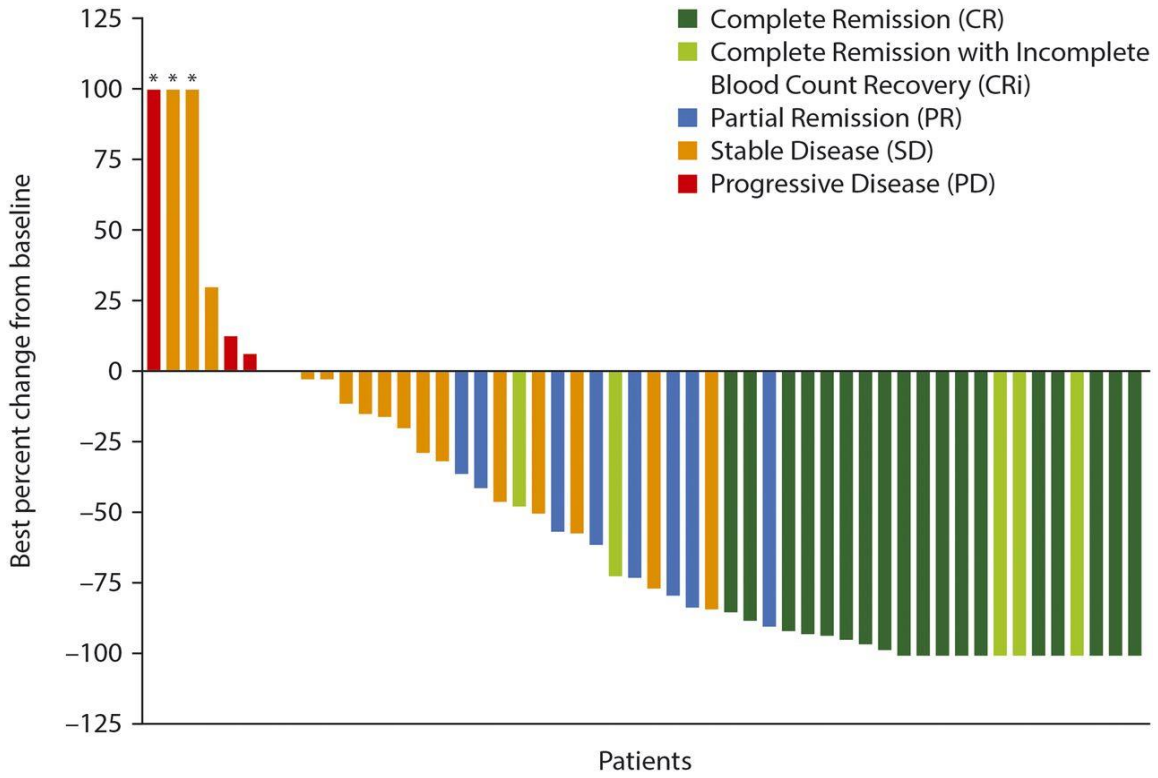
- Pevonedistat is a small molecule inhibitor of NAE (NEDD-8 activating enzyme), a protein involved in the ubiquitin-proteasome system
- NAE acts upstream of the proteasome and catalyzes the first step in the neddylation pathway



Amir T. Fathi Blood 2018;131:1391-1392

ENCOURAGING RESPONSES IN AML PATIENTS TREATED WITH PEOVNEDISTAT + AZACITIDINE

Figure 1: Waterfall plot of best percent change from baseline in marrow blasts for the response-evaluable pts who received pev 20 mg/m^2 (n=52). Responses are listed as best responses achieved on study



*Best percent change from baseline >100%.
SD represents those evaluations which did not qualify for response or PD.

Ronan T Swords et al. Blood 2016;128:98

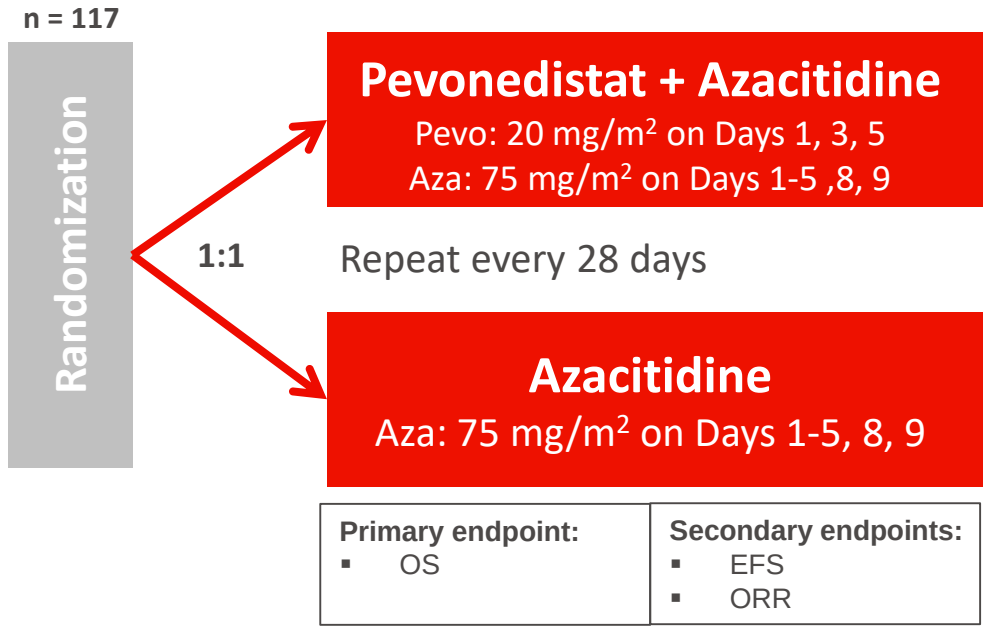
60% ORR with a trend towards improved survival in secondary AML

Response rates not influenced by AML genetic risk or leukemia burden

Initial data drove interest to move to registration

A PHASE 2 STUDY IN HR-MDS TO CONFIRM THE RISK / BENEFIT PROFILE OBSERVED IN AML

Phase 2, Randomized, Open-label, Global, Multicenter Study Comparing Pevonedistat Plus Azacitidine vs. Azacitidine in Patients with Higher-Risk MDS, CMML, or Low-Blast AML

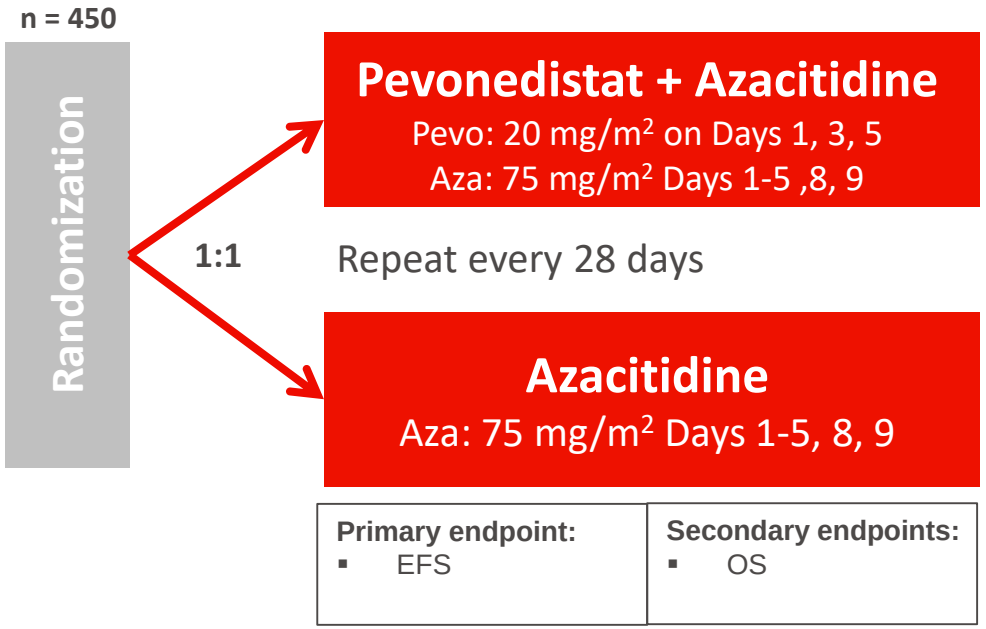


- Mature OS data will be available in November
- Data will be presented in upcoming congress
- Potential approval in FY21*

* Projected approval date assumes filing on Phase 2 data

THE PHASE 3 PANTHER STUDY WAS INITIATED AT RISK TO ACCELERATE DEVELOPMENT

Phase 3, Randomized controlled trial of Pevonedistat Plus Azacitidine Versus Single-Agent Azacitidine as First-Line Treatment for Patients with Higher risk-MDS/CMML, or Low-blast AML



PANTHER

- Completed global enrollment 10 months earlier than originally projected*
- Indicative of demand for new innovative therapies

* Closed to global enrollment; Open for extended enrollment in China

EXPANDING PATIENT-CENTRIC DEVELOPMENT OF PEVONEDISTAT

Continuum of disease

HR-MDS

Ph2 (P2001)

*Potential approval in FY21**

Ph3 (P3001)

PANTHER

NEW STUDIES IN UNFIT AML

Ph3 PEVOLAM

pevo + aza vs. aza
Currently enrolling patients

Utilizing partnership (PETHEMA) for efficient development

Ph2 (P2002) Combo

pevo + venetoclax + aza vs. venetoclax + aza
Study will open in 2020

Unique MOA and biologic hypothesis to support combination

* Projected approval date assumes filing on Phase 2 data

SUMMARY

1

Unmet need in High-risk MDS and AML remain high with few treatment options

2

Pevonedistat is a selective first-in-class inhibitor with potential to be first new therapy in over a decade for HR-MDS

3

The Ph2 HR-MDS trial has reached the updated OS endpoint data readout and the PANTHER Ph3 trial has completed global enrollment

R&D DAY AGENDA – NEW YORK, NOVEMBER 14, 2019

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



RARE DISEASES & GENE THERAPY

Dan Curran, MD

Head Rare Diseases Therapeutic Area Unit

Takeda Pharmaceutical Company Limited

New York, NY

November 14, 2019

Better Health, Brighter Future

RARE DISEASES: AN OPPORTUNITY TO TRANSFORM TREATMENT

HIGH UNMET NEED

7,000	Distinct rare diseases[1]
350 million	Patients worldwide
95%	Diseases have no FDA-approved treatment

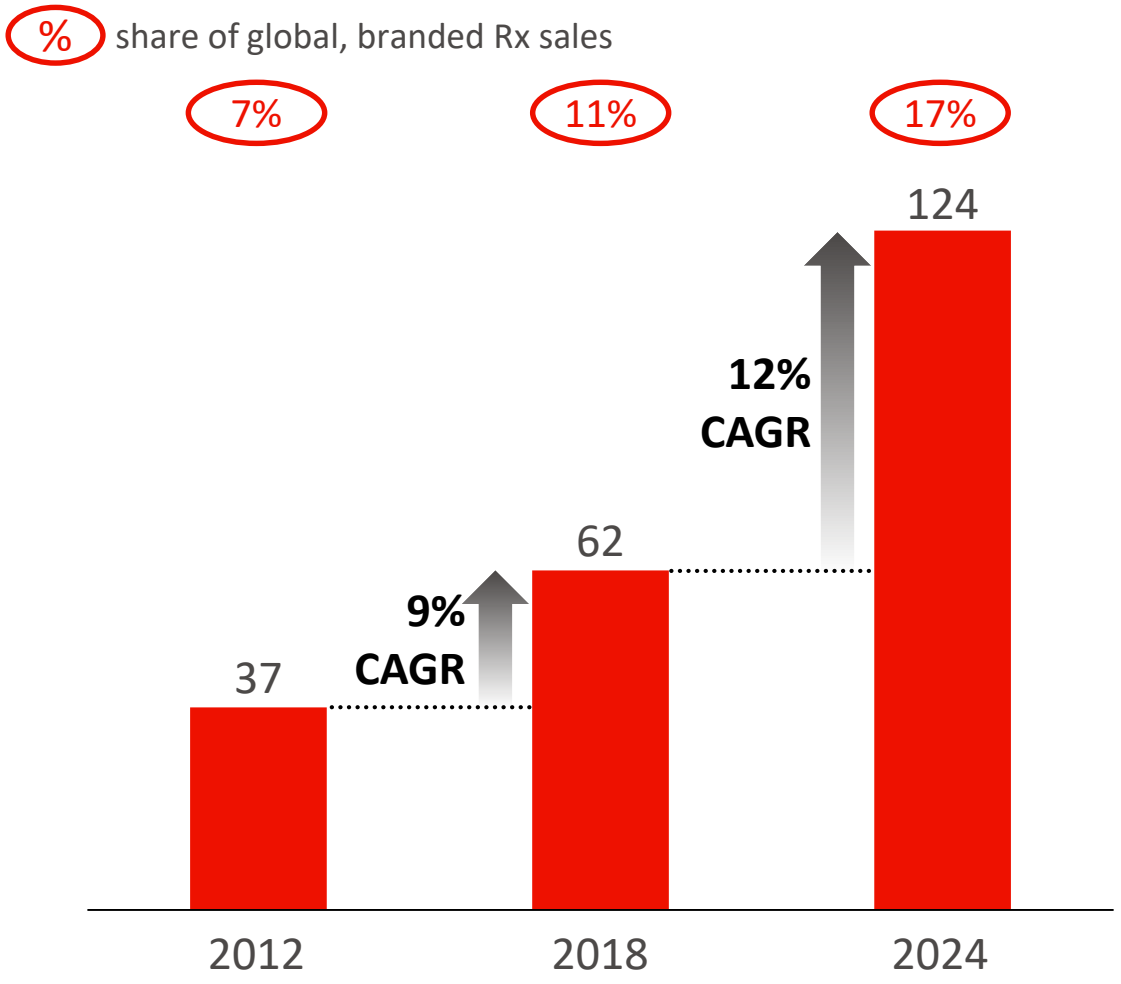
SCIENTIFIC AND REGULATORY ADVANCES

80%	Diseases are genetic in origin
Transformative therapies	Recombinant engineering & delivery of proteins and nucleic acids
~90%[2] 	Orphan drug approvals benefited from expedited review
100%[3] 	

1. Rare diseases defined by prevalence in line with regulatory agencies (US: <7 in 10,000, EU: < 5 in 10,000 and JPN: <4 in 10,000), Global Genes, NIH National Human Genome Research Institute; 2. Comprises four pathways in US: Accelerated approval, breakthrough therapy designation, fast track designation, priority review designation; 3. Three pathways in JPN: Priority review, Sakigake designation and conditional approval, CIRS R&D Briefing 70, New drug approvals in six major authorities 2009-2018

RARE DISEASE MARKET IS EXPECTED TO DOUBLE IN SIZE

GLOBAL ORPHAN DRUG[1] SALES EXCLUDING ONCOLOGY[2], USD BN



- Orphan drugs expected to make up ~17% of global branded Rx sales by 2024
- Growth driven by advances in new modalities and new indications
- Orphan cell and gene therapies estimated at ~$20 bn by 2024, up from ~$2bn in 2018

1. Orphan drugs generally used as synonym for rare disease due to lack of uniform definition, including also non-rare, but neglected diseases lacking therapy (e.g., tropical infectious diseases); 2. EvaluatePharma (03 June 2019)

TAKEDA IS THE LEADER IN RARE DISEASES

PATIENT IMPACT

- **Foundation of >30 year history of leadership in rare diseases**
- Leading portfolio of rare disease therapies: 11 out of 14 global brands spanning Hematology, Metabolic, GI and Immunology

SCIENCE & INNOVATION

- Multiple opportunities for transformational therapies across therapeutic areas
- **Emerging, cutting edge platforms to drive high-impact pipeline**
- Investments in technologies to accelerate diagnosis

CAPABILITIES AND SCALE

- Engagement with key stakeholders within the ecosystem e.g. patient groups, regulators
- Pioneering regulatory pathways
- **Global footprint**

OUR STRATEGY IS TO TRANSFORM AND CURE RARE DISEASES

As the global leader in Rare Diseases, we aspire to provide transformative and curative treatments to our patients

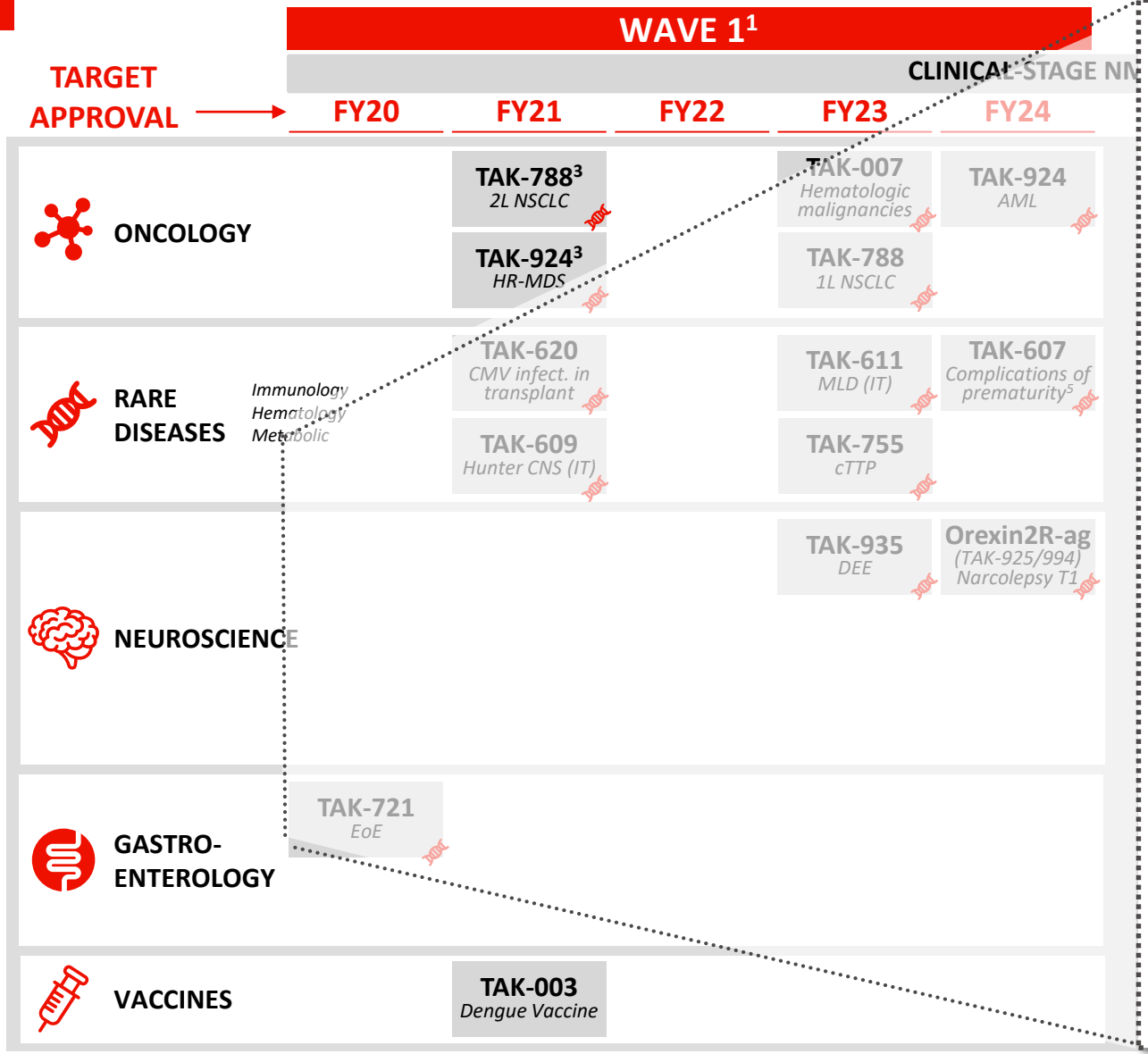
Transformative

Programs with transformative potential in devastating disorders with limited or no treatment options today

Curative

Emerging early pipeline of AAV gene therapies to redefine treatment paradigm in monogenic rare diseases

WE ARE POSITIONED TO DELIVER NEAR-TERM & SUSTAINED GROWTH



TAK-620
CMV infect. in transplant

TAK-607
Complications of prematurity[5]

TAK-755
cTTP

Orexin2R-ag
(TAK-925/994) Narcolepsy T1

TAK-721
EoE

1. Projected timing of approvals depending on data read-outs; some of these Wave 1 target approval dates assume accelerated approval; 2. Some Wave 2 assets could be accelerated into Wave 1 if they have breakthrough data; 3. Projected approval date assumes filing on Phase 2 data; 4. TAK-079 to be developed in Rare Diseases indications myasthenia gravis (MG) and immune thrombocytopenic purpura (ITP) (FPI projected in each indication in 2H FY19); 5. Currently in a non-pivotal Phase 2 study; planning underway to include interim stage gates that can advance the program into a pivotal trial

Orphan potential in at least one indication
Estimated dates as of November 14, 2019

POTENTIAL APPROVALS OF TRANSFORMATIVE THERAPIES

WAVE 1[1]

Phase 3	Phase 3	Phase 3	Phase 2	Phase 2	Phase 1/2	Phase 2b
TAK-721 Eosinophilic Esophagitis (EoE)	**TAK-620** Cytomegalovirus (CMV) infection in transplant	**TAK-755** Congenital Thrombotic Thrombocytopenic Purpura (cTTP)	**TAK-611** Metachromatic Leukodystrophy (MLD)	**TAK-935** Developmental and Epileptic Encephalopathies (DEE)	**Orexin** Narcolepsy Type 1 (NT1)	**TAK-607** Complications of Prematurity[2]
TARGET APPROVAL						**POSSIBLE WAVE 1 APPROVAL[2]**
FY 2020	**FY 2021**	**FY 2023**	**FY 2023**	**FY 2023**	**FY 2024**	
ADDRESSABLE POPULATION IN US/WW[3,4]						
~150k/Under evaluation	**~7 - 15k/ ~25 - 45k**	**~500/ 2 - 6k**	**~350/ ~1 - 2k**	**~50k/ ~70 - 90k**	**70 - 140k/ 300k – 1.2M**	**~25k/ ~80 - 90k**

1. Projected timing of approvals depending on data read-outs; some Wave 1 target approval dates assume accelerated approval
2. Currently in a non-pivotal Phase 2 study; planning underway to include interim stage gates that can advance the program into a pivotal trial
3. Estimated number of patients projected to be eligible for treatment, in markets where the product is anticipated to be commercialized, subject to regulatory approval
4. For TAK-620 and TAK-607, the addressable population represents annual incidence

SELECTED TRANSFORMATIVE PROGRAMS

TAK-620	Potential first treatment of CMV infection in transplant patients in over 10 years. Inhibitor of protein kinase UL97.
TAK-755	Potential best-in-class therapy for Thrombotic Thrombocytopenic Purpura (TTP). Recombinant ADAMTS13.
TAK-607	Potential first pharmacologic therapy in >20 years to prevent complications of prematurity. Recombinant IGF-1 growth factor.

TAK-620: POTENTIAL BEST IN CLASS TREATMENT FOR POST-TRANSPLANT CMV INFECTION

BURDEN OF CMV INFECTION IN TRANSPLANT RECIPIENTS

CMV infection is the most common post-transplant viral infection[1]

Affects >25% of transplants

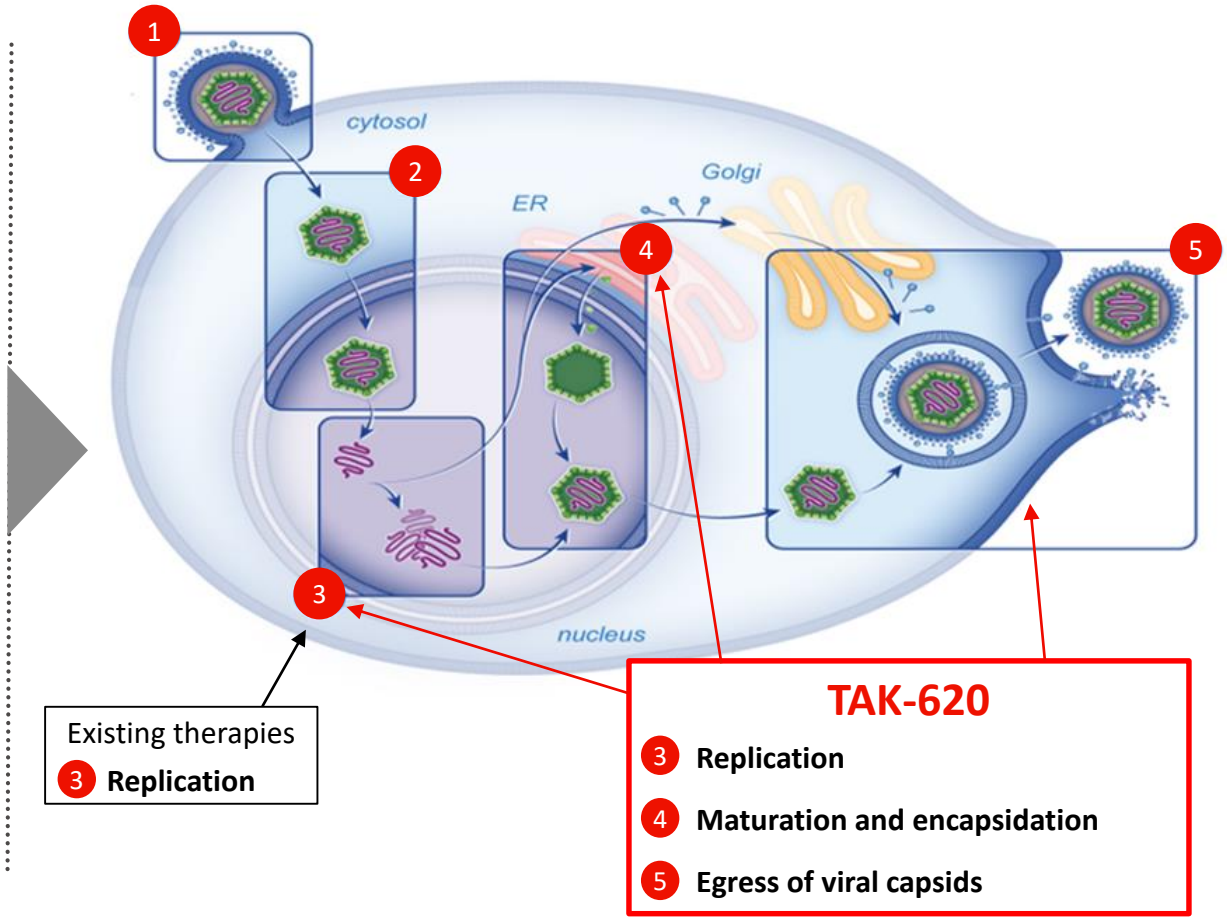
CMV infection can be fatal[2,3]

Higher rates of graft failure: 2.3X and mortality: 2.6X

Current therapies have significant toxicities and resistance[4,5,6,7]

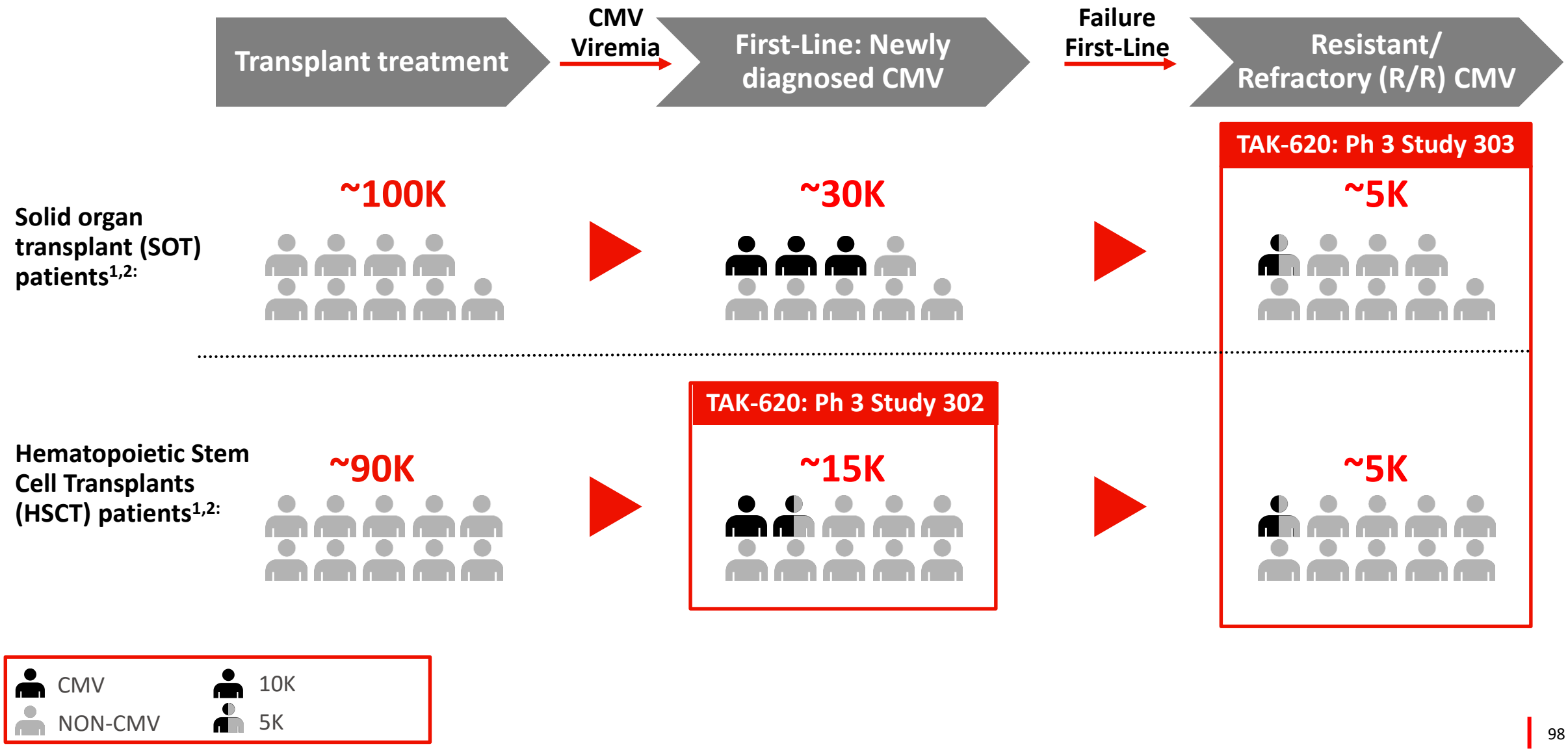
Incidence of neutropenia >20% and renal toxicity >50%

TAK-620: NOVEL MOA TARGETING PROTEIN KINASE UL97



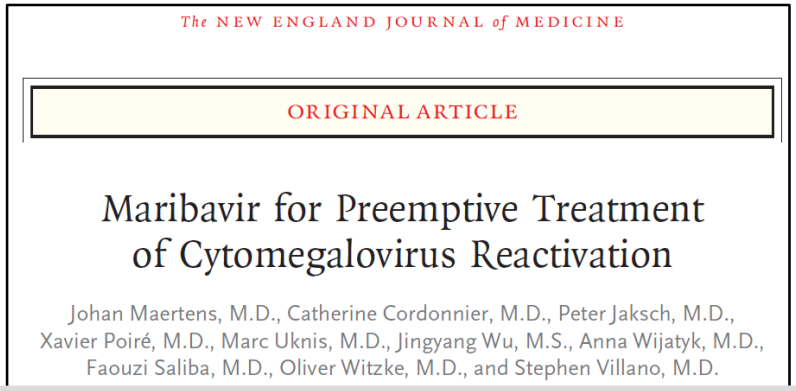
1. Minerva Med. 2009 Dec; 100(6): 479-501; 2. Blood. 2016 May 19;127(20):2427-38; 3. Infect Chemother. 2013 Sep; 45(3): 260–271; 4. Antimicrob Agents Chemother. 2014 Jan; 58(1): 128–135;
5. Transplantation. 2016 Oct;100(10):e74-80;. 6. Clin Microbiol Infect. 2015 Dec;21(12):1121.e9-15; 7. Clin Transplant 2009: 23: 295–304

TAK-620: ADDRESSES UNMET NEED IN BOTH FIRST-LINE AND RESISTANT / REFRACTORY SETTING



1. Solid organ and allogeneic HSCT transplants in global major markets: US, Europe, Canada, Japan, China , Australia and Korea 2. UNOS Data 2018; CIBMR2017IRODaT Registry 2017, EBMT activity survey 2019 , Shire CMV Epi Study, Feb. 2018

TAK-620 DEMONSTRATED SIMILAR EFFICACY AND BETTER SAFETY VERSUS SOC IN A PHASE 2 STUDY IN FIRST-LINE PATIENTS



DEMONSTRATED SIMILAR ANTI-VIRAL ACTIVITY TO VALGANCICLOVIR (VGV) ACROSS ALL DOSES[1]

	TAK-620: Dose 400, 800 or 1200 mg BID[2] All Doses (N=119)	VGV (N=40)
Confirmed undetectable plasma CMV DNA within 6 weeks	79%	67%

NEUTROPENIA WAS TREATED WITH GROWTH FACTORS MORE OFTEN IN THE VGV ARM (15%) VS. TAK-620 ARM (7%)[2]

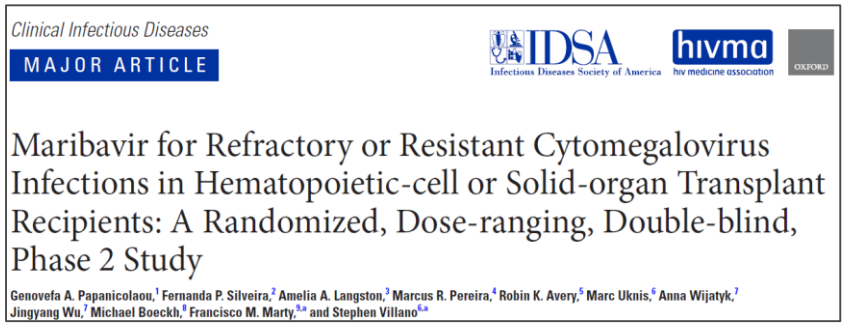
	TAK-620: Dose 400, 800 or 1200 mg BID All Doses (N=119)	VGV (N=40)
Neutropenia that occurred or worsened during treatment through week 12	5%	18%

1. Confirmed undetectable CMV DNA in plasma was defined as two consecutive CMV DNA polymerase-chain-reaction assay values measure during treatment that were below the level of quantitation (i.e., <200 copies per millimeter according to the central laboratory) separated by at least 5 days. For the primary analyses of confirmed undetectable CMV DNA within 3 weeks and 6 weeks, data were missing for 3 patients: 1 each in the 400-mg TAK-620 group, the 1200-mg TAK-620 group and the valganciclovir group
2. N Engl J Med 2019; 381:1136-47. Overall risk ratio (95% CI) relative to the Valganciclovir reference was 1.20 (0.95-1.51)

TAK-620: GRANTED BREAKTHROUGH DESIGNATION IN RESISTANT OR REFRACTORY CMV INFECTION

1 **Efficacy in seriously ill R/R CMV in SOT and HSCT recipients with multiple risk factors predictive of poor outcomes**

TAK-620 Dose: 400 mg, 800 mg, 1200 mg BID[1]	
Primary efficacy endpoint	**All doses (Total N = 120)**
Patients with confirmed undetectable plasma CMV DNA within 6 weeks in ITT[2] population	80 (66.7%)


Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America hivma hiv medicine association

Maribavir for Refractory or Resistant Cytomegalovirus Infections in Hematopoietic-cell or Solid-organ Transplant Recipients: A Randomized, Dose-ranging, Double-blind, Phase 2 Study

Genovefa A. Papanicolaou,[1] Fernanda P. Silveira,[2] Amelia A. Langston,[3] Marcus R. Pereira,[4] Robin K. Avery,[5] Marc Uknis,[6] Anna Wijatyk,[7] Jingyang Wu,[7] Michael Boeckh,[8] Francisco M. Marty,[9,a] and Stephen Villano[6,a]

Historical outcomes: High (~50%) failure rates / relapse rates[3,4,5]

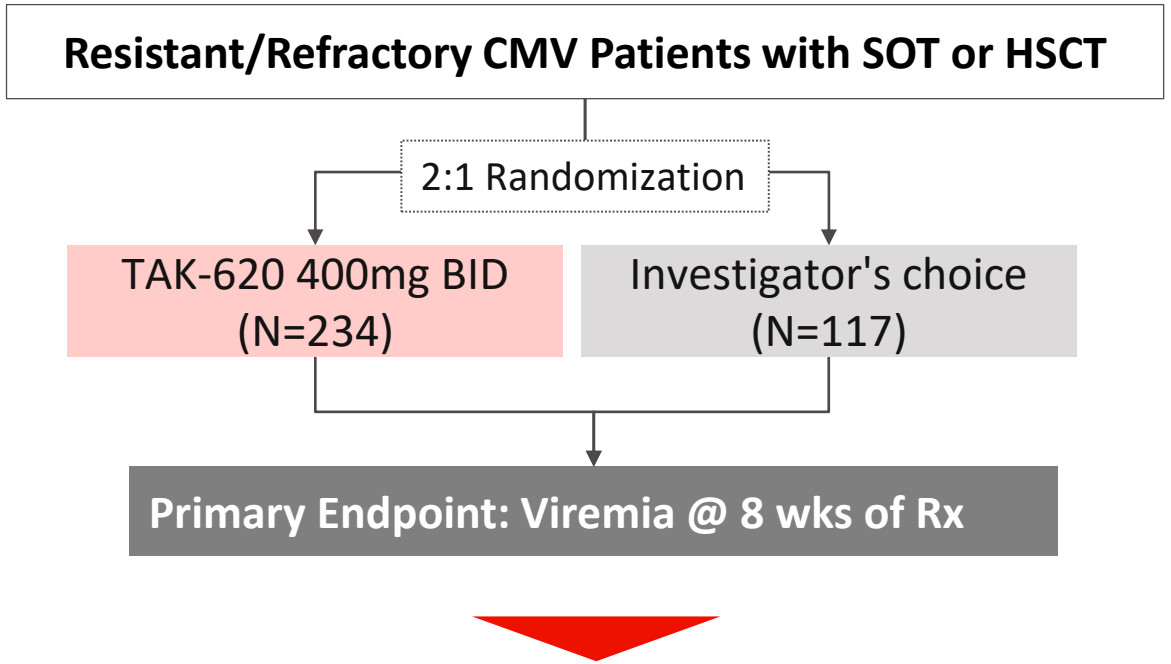
2 **Superior renal safety profile - did not result in treatment discontinuations**

Renal impairment is the primary reason for discontinuation with SOC (Foscarnet, Cidovir); nephrotoxicity is > 50%[6]

1. Clin Infect Dis. 2019 Apr 8;68(8):1255-1264; 2. ITT - Intent to treat; 3. Antimicrob Agents Chemother, 58, 128-35; 4. Mehta et al, 2016 American Transplant Congress, Meeting abstract C279; 5. J Heart Lung Transplant. 2019 Sep 10; 6. Transplantation. 2016 Oct; 100(10): e74–e80

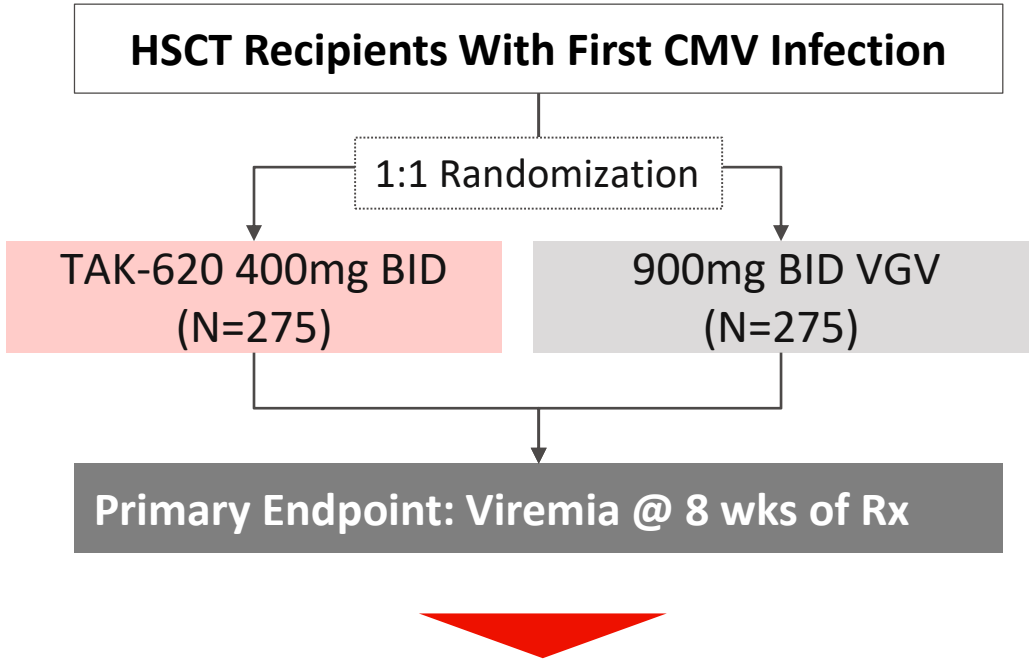
TAK-620: TWO ONGOING PIVOTAL STUDIES; EXPECT FIRST APPROVAL IN RESISTANT OR REFRACTORY CMV IN 2021

TAK-620 PHASE 3 STUDY 303



EXPECTED MILESTONES (FY)	2020	2021	2022
	2H 2020: Ph 3 Readout	2021: US Approval	2022: EU Approval

TAK-620 PHASE 3 STUDY 302



EXPECTED MILESTONES (FY)	2021	2022
	1H 2021: Ph 3 Readout	US Approval EU Approval

SELECTED TRANSFORMATIVE PROGRAMS

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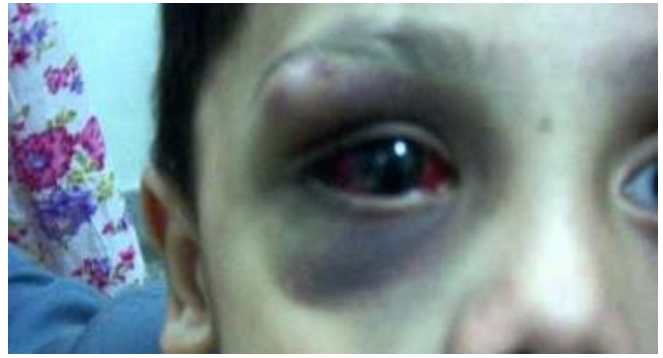
TAK-607	Potential first pharmacologic therapy in >20 years to prevent complications of prematurity. Recombinant IGF-1 growth factor.

CONGENITAL AND IMMUNE TTP HAVE SUBSTANTIAL MORTALITY AND MORBIDITY BURDEN DUE TO INADEQUATE SOC

CONGENITAL TTP (cTTP)

- Sub-therapeutic dose with plasma infusions
- Patients still experience ischemic injury of brain, kidneys and heart
- Poor long-term outcomes



IMMUNE TTP (iTTP)

- ~30% relapse rate with plasma exchange (PEX)
- New market entrant reduces relapse rate, but has significant limitations[3,4]
  - Enhanced risk of bleeding:
    Gingival bleeding 18% vs. 1% placebo
    Epistaxis 32% vs. 3% placebo

ADDRESSABLE POPULATION (WW)[1,2]	
cTTP	2,000 – 6,000
iTTP	5,000 – 18,000

1. Global major markets: US, Europe, Canada, JPN, and Global Emerging Markets; 2. Haematologica September 2010 95: 1444-1447; 3. N Engl J Med 2019;380:335-46.; 4. N Engl J Med 2016; 374:511-522

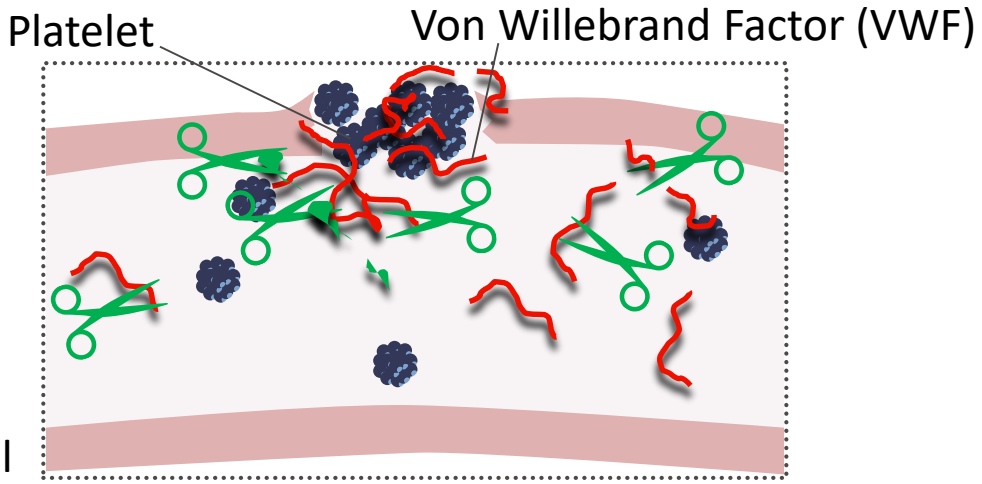
TAK-755 DIRECTLY ADDRESSES UNDERLYING CAUSE OF TTP

TAK-755 REPLACES ADAMTS13, DEFICIENCY OF WHICH LEADS TO TTP

Normal clotting cascade

ADAMTS13:

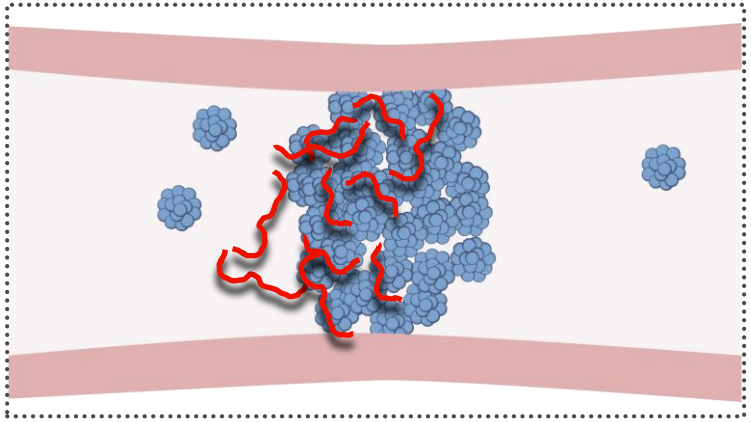
Cleaves VWF multimers that mediate platelet aggregation and clotting



TTP

ADAMTS13 deficiency:

Formation of microthrombi due to accumulation of large VWF multimers

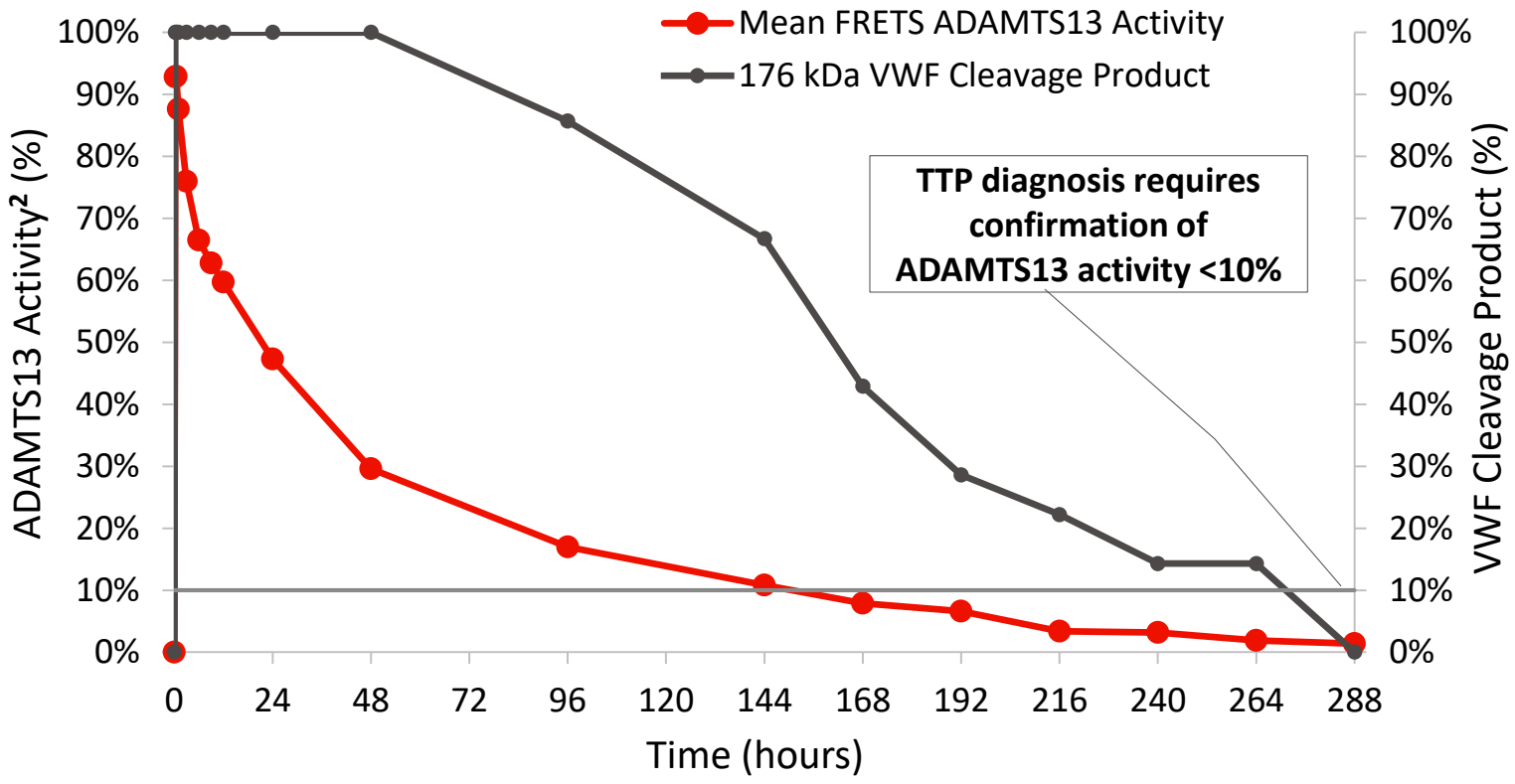


TAK-755: POTENTIAL TRANSFORMATIVE THERAPY FOR TTP

TAK-755 PHASE I, OPEN-LABEL, DOSE ESCALATION STUDY IN cTTP[1]

- Administered as a single dose in 15 cTTP patients
- TAK-755 was well tolerated
- No anti-ADAMTS13 antibodies detected

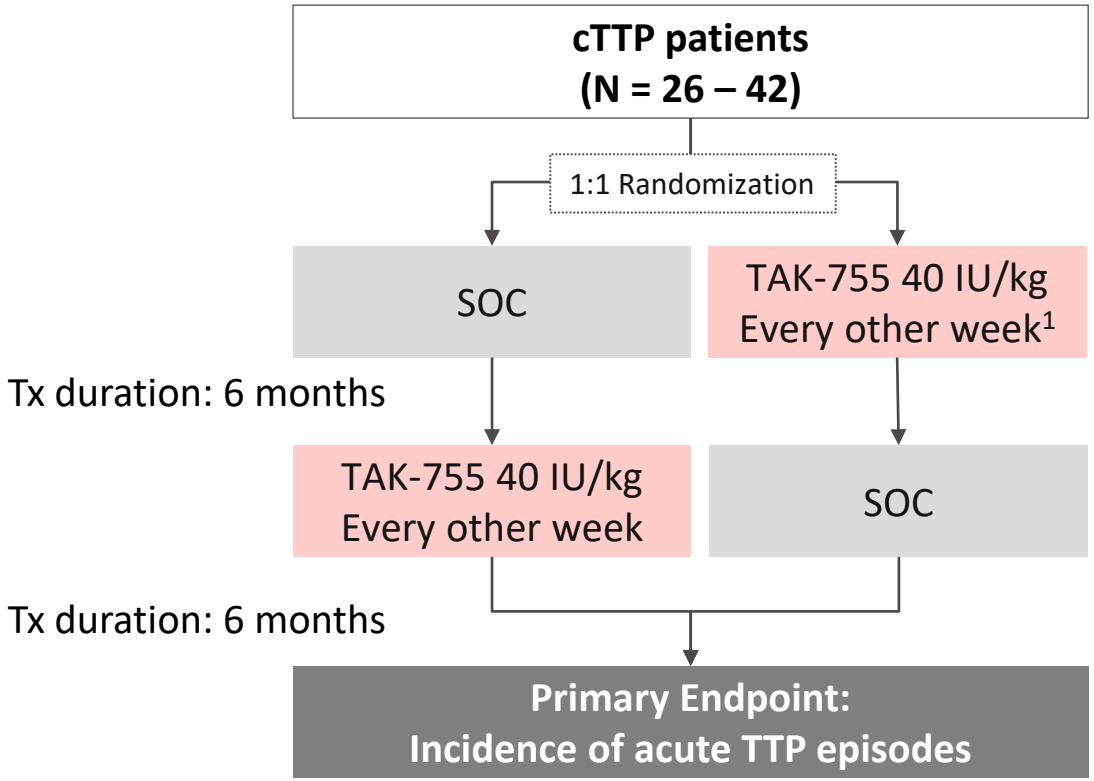
TAK-755 PK PROFILE AND PD EFFECT ON VWF CLEAVAGE AT 40 IU/KG



1. Blood 2017; vol. 130, number 19, 2055-63; 2. Measured using FRETS (fluorescence resonance energy transfer)

TAK-755: ONGOING PHASE 3 CONGENITAL TTP STUDY

TAK-755 PHASE 3 PROPHYLAXIS STUDY



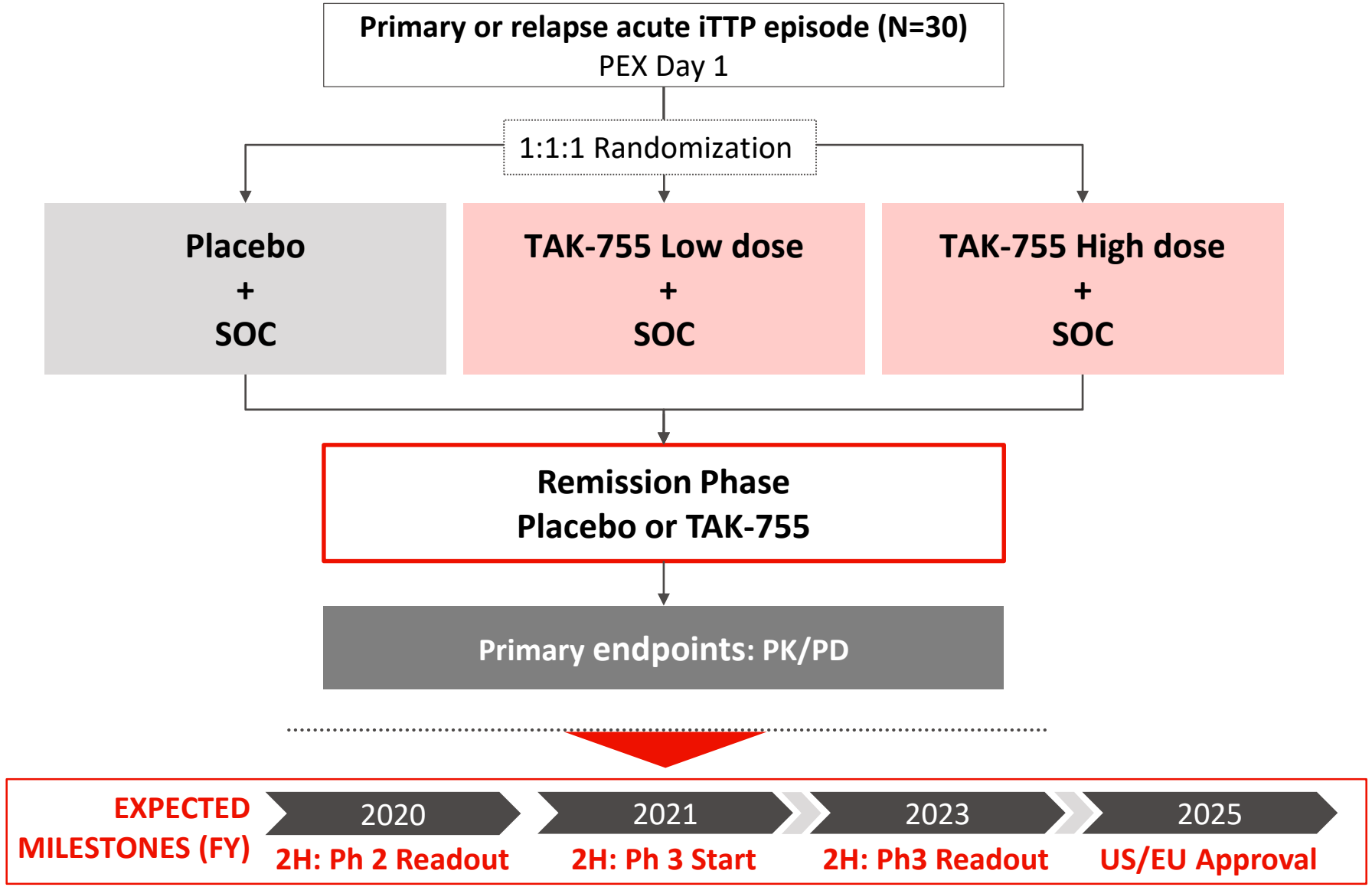
- All patients roll over to a 6 month TAK-755 extension
- Phase 3 study has a cohort of acute cTTP patients who receive TAK755. Patients are eligible to enter the prophylaxis study upon completion of acute treatment

EXPECTED MILESTONES (FY)

2019	2021	2023	2025
1H: Ph 3 initiated	2H: Ph 3 Readout	US Approval	EU Approval[2]

1. A single dose modification to 1x/week may be mandated based on clinical outcomes; 2. Plan to seek deferral of pediatric data requirement in EU for initial filing, which would enable possible approval in EU in 2023

TAK-755 IMMUNE TTP PHASE 2 STUDY DESIGN



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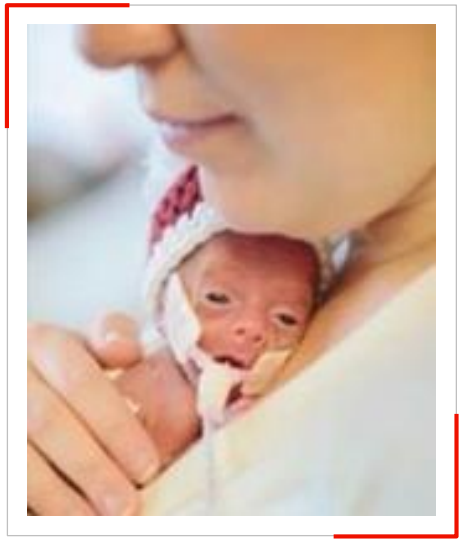
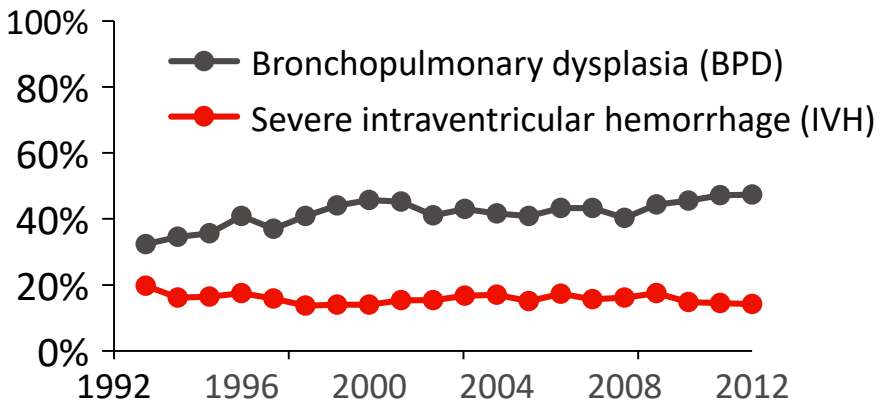
TAK-607	Potential first pharmacologic therapy in >20 years to prevent complications of prematurity. Recombinant IGF-1 growth factor.

EXTREMELY PREMATURE INFANTS EXPERIENCE CONSIDERABLE MORBIDITY



Morbidity (%) by birth year, US data[1]



~80,000-90,000 Extremely preterm babies (<28 wks gestational age) born WW[2,3]

0 Therapies for prevention of complications of prematurity

~40% have lung complications in addition to morbidities in brain, eye that adversely impact development and learning

~$200,000 hospitalization costs per infant [4]

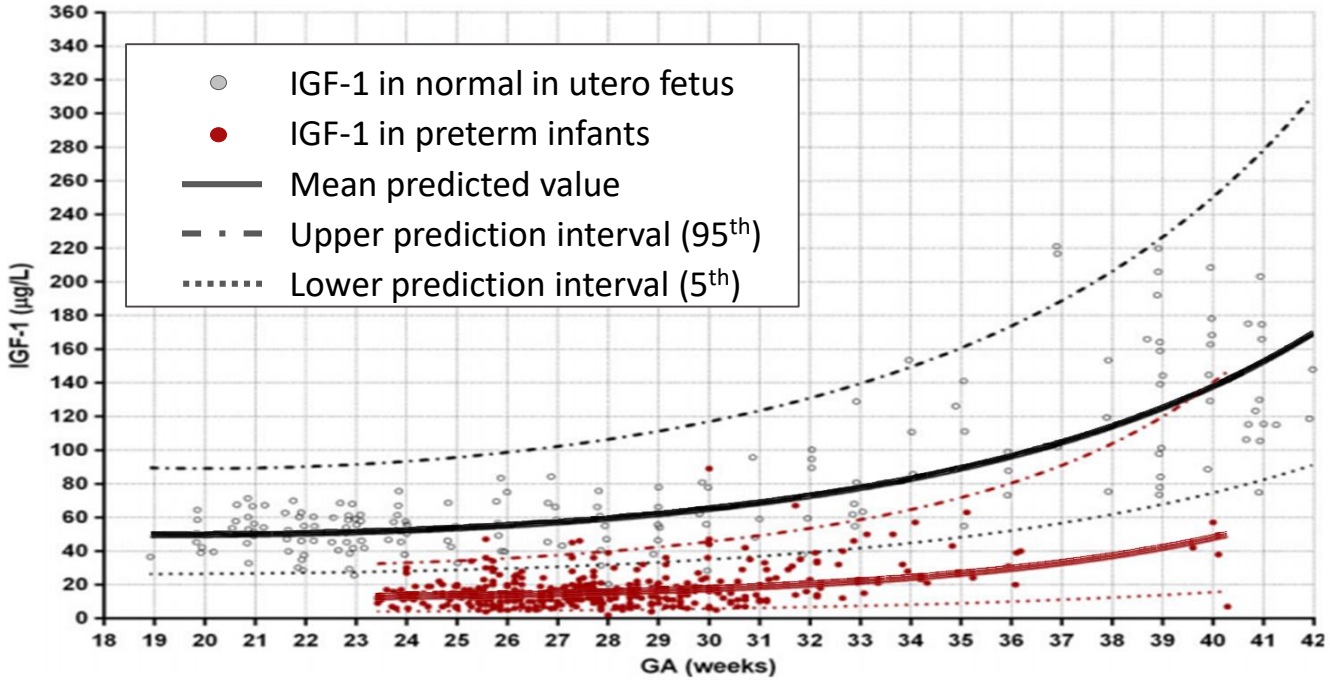
1. Stoll B, JAMA, 2015;314(10): 1039–1051; 2. CDC; 3. UN data and published sources; 4. Mowitz M et al. Co-occurrence and Burden of Complications of Prematurity Among Extremely Preterm Infants in the US AAP 2017 Poster 76

TAK-607 REPLENISHES IGF-1, A FETAL GROWTH FACTOR THAT IS DECREASED IN PRETERM INFANTS

TAK-607: IGF-1 / IGFBP-3[1] COMPLEX

- IGF-1 is an important fetal growth factor supplied by the mother that is involved in the development of multiple organs
- IGF-1 is low or absent in premature infants born before 28 weeks[2]
- TAK-607 demonstrated beneficial effects in lung development and brain vasculature in preclinical models[3,4]

IGF-1 LEVELS ARE LOW IN PRETERM INFANTS[2]



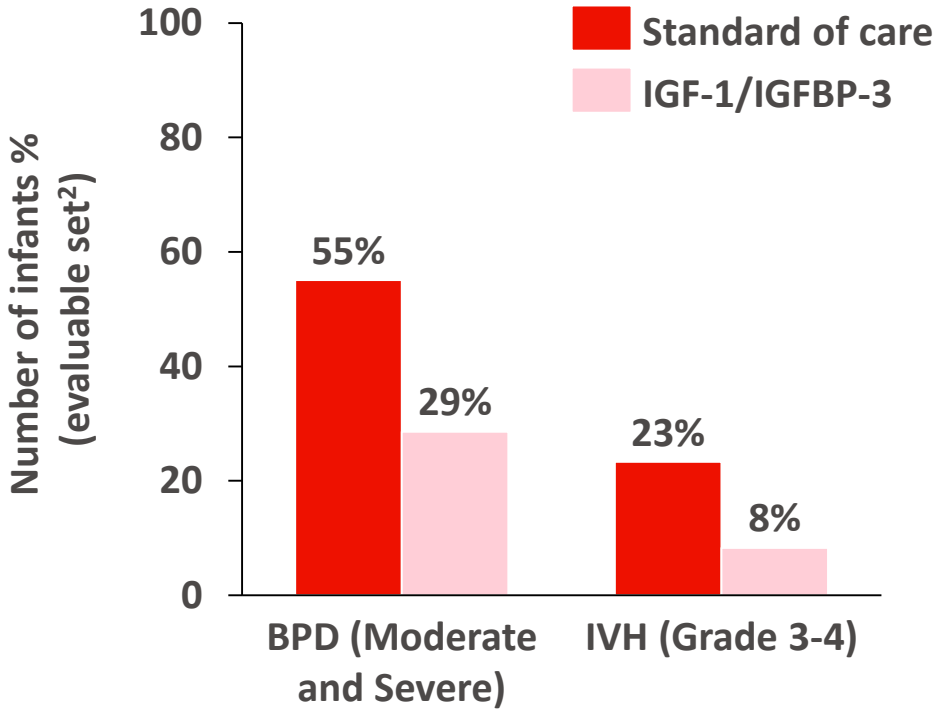
1. Recombinant insulin-like growth factor 1 (rIGF-1), IGFBP-3- IGF binding protein-3; 2. Hellstrom et al., Acta Pædiatrica 2016 105, pp. 576–586; 3. Seedorf G et al. EAPS. Geneva 2016 (manuscript in preparation)
4. Ley D et al. jENS 2019

TAK-607: PHASE 2 STUDY INFORMED DOSE AND ENDPOINT SELECTION

ROP-2008-01: RANDOMIZED, CONTROLLED PHASE 2 STUDY OF TAK-607

- Pre-term infants with a gestational age (GA) <28 weeks (N = 120)
- Assessed outcomes in ITT and "evaluable" sets (40% patients who achieved target exposure of IGF-1 levels)[1]
  - Primary endpoint: ROP not met
  - Pre-specified secondary endpoints: Bronchopulmonary Dysplasia (BPD) was reduced and Intra-Ventricular Hemorrhage (IVH) showed a positive trend
- Granted FDA fast-track designation

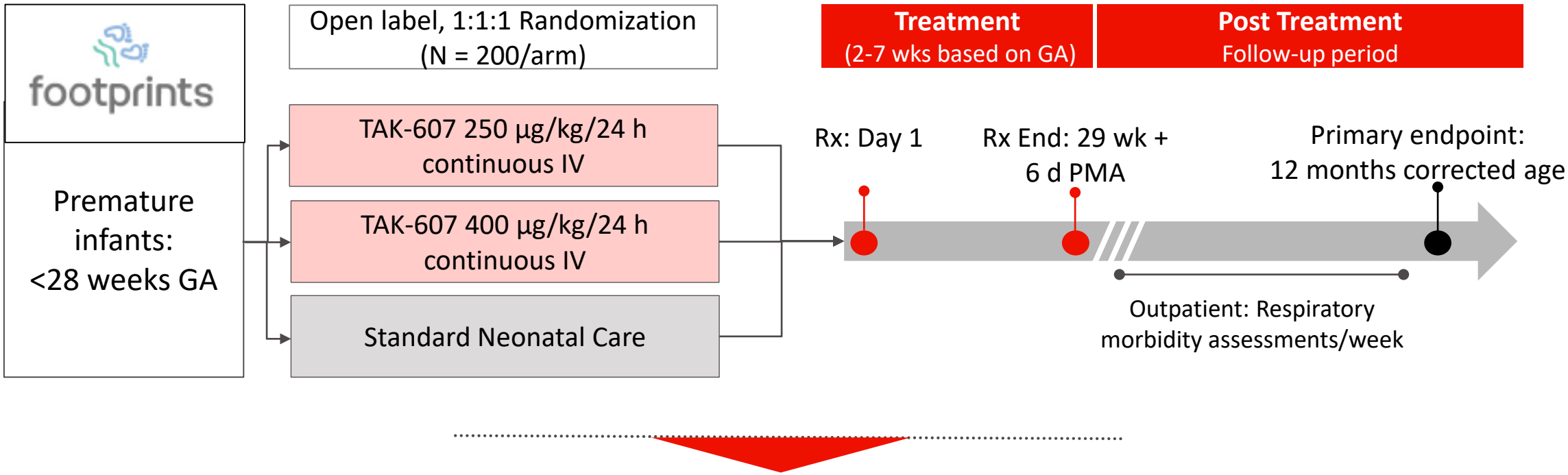
TAK-607 IMPACTED BPD AND IVH[2]



1. Evaluable set: ≥70% IGF-1 measurements within targeted intrauterine range (28–109 µg/L) AND ≥70% intended duration of treatment
2. Ley D, J Pediatrics, 2018

ROP – retinopathy of prematurity

TAK-607: FOOTPRINTS STUDY DESIGNED TO DEMONSTRATE REDUCTION IN THE COMPLICATIONS OF PREMATURITY



Primary endpoint: Duration of supplemental oxygen use through 1 year corrected age[1]

EXPECTED MILESTONES (FY)

2019 — **1H: Ph 2b initiated**

2023 — **1H: Ph 2b Readout**

1. Supplemental oxygen use defined by one of the following: a) Any fraction of inspired oxygen (FiO2) >21%, b) Non-invasive respiratory support delivered via a nasal interface (e.g., continuous positive airway pressure [CPAP], nasal cannula, etc.), c) Invasive respiratory support (mechanical ventilation) via an endotracheal tube or tracheostomy

NME MILESTONES ACHIEVED IN FY19 AND LOOKING AHEAD TO OTHER POTENTIAL MILESTONES[1] THROUGH FY20

PIVOTAL STUDY STARTS, APPROVALS

1H FY 2019

- ☑ TAK-611 — MLD — Ph 2 start[2]
- ☑ TAK-755 — cTTP — Ph 3 start
- ☑ TAK-925 — Narcolepsy — POC
- ☑ TAK-721 — EoE — Ph 3 data (induction)
- ☑ TAK-101 — Celiac Disease — POC

2H FY 2019

- ☑ PEVONEDISTAT TAK-924 — AML — Ph 3 start
- TAK-788 — 1L NSCLC — Ph 3 start
- ☑ PEVONEDISTAT TAK-924 — HR-MDS — Ph 2 Overall Survival
- ☑ TAK-007 — Hem. Malignancies — POC
- TAK-609 — Hunter (IT) — Ph 3 data 2yr extension
- mHTT ASO — Huntington's Disease — POC
- TAK-721 — EoE — Ph 3 data (maintenance)

1H FY 2020

- TAK-788 — 2L NSCLC — Ph 2 Pivotal
- TAK-573 — R/R MM, Solid Tumor — POC

2H FY 2020

- TAK-721 — EoE — Approval
- mHTT ASO — Huntington's Disease — Pivotal start
- TAK-620 — R/R CMV SOT & HSCT — Ph 3 data
- TAK-755 — iTTP — POC
- TAK-935 — DEE — POC
- TAK-906 — Gastroparesis — POC
- TAK-951 — Nausea & Vomiting — POC

Oncology

Rare Disease

Neuroscience

Gastroenterology

☑ Denotes milestones that have been achieved.

KEY DATA READOUTS

1. Potential key milestone dates as of November 14, 2019. The dates included herein are estimates based on current data and are subject to change
2. Potentially registration enabling

WE AIM TO PROVIDE CURATIVE THERAPY

As the global leader in Rare Diseases, we aspire to provide transformative and curative treatments to our patients

Transformative

Programs with transformative potential in devastating disorders with limited or no treatment options today

Curative

Emerging early pipeline of AAV gene therapies to redefine treatment paradigm in monogenic rare diseases

BUILDING A WORLD CLASS GENE THERAPY 'ENGINE'

TOP TIER GMP MANUFACTURING

GENE THERAPY AAV[1] PLATFORM

- Strong capabilities in **liver expression**
- Emerging capabilities in **CNS expression**

GENE THERAPY PIPELINE

TAKEDA THERAPEUTIC AREAS

Preclinical Development → Clinical Development

Liver expression

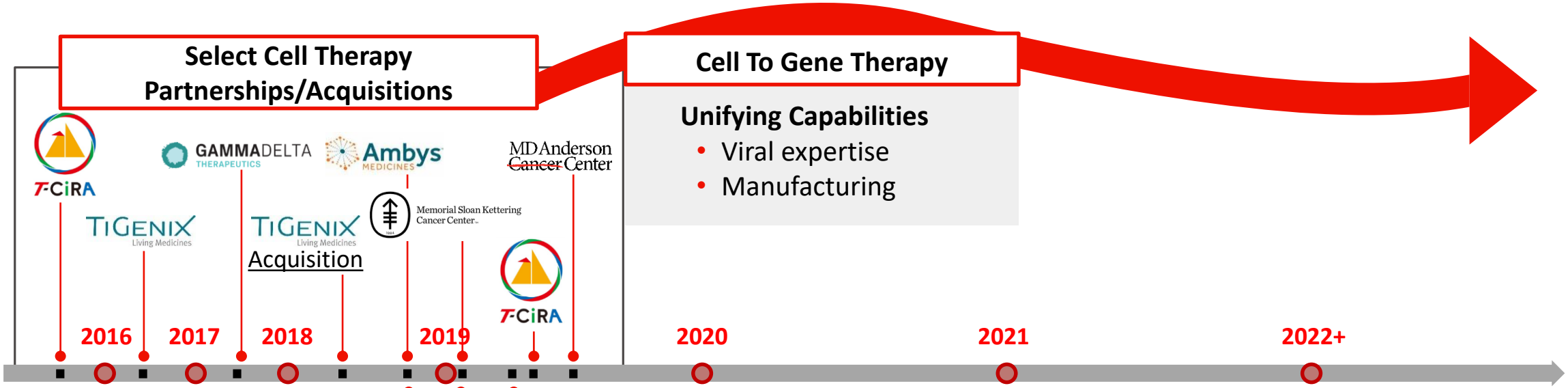
3+ Research Candidates	**NextGen** Hem A	**TAK-748** Hem B	**TAK-754** Hem A

CNS expression

StrideBio Research Candidate	**StrideBio** Friedreich Ataxia	**TAK-686** Huntington's Disease

1. Adeno-Associated Virus

WE WILL APPLY OUR CELL THERAPY PLAYBOOK AND UNIFYING CAPABILITIES TO BUILD A GENE THERAPY PIPELINE



Gene Therapy Platform

Ambys MEDICINES
Deliver protective or regenerative factors to hepatocytes

stridebio
Capsids to enhance biodistribution in CNS

Shire
Acquisition
AAV tool box and manufacturing platform

Focus of Future Gene Therapy Partnerships

1. Enable re-dosing
2. Lower dose and enhance biodistribution
3. Develop alternative gene delivery vehicles

SUMMARY

1

Takeda has the capabilities, scale, and innovative platforms to extend our leadership in Rare Diseases

2

We have a leading late stage portfolio of transformative programs that will establish or re-define the standard of care for highly underserved patients

3

We are building cutting - edge capabilities in gene therapy that aim to deliver ‘cures’ in monogenic rare diseases

R&D DAY AGENDA – NEW YORK, NOVEMBER 14, 2019

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

OX2R AGONISTS FOR THE TREATMENT OF NARCOLEPSY TYPE 1

Deborah Hartman, PhD

Global Program Leader, Neuroscience

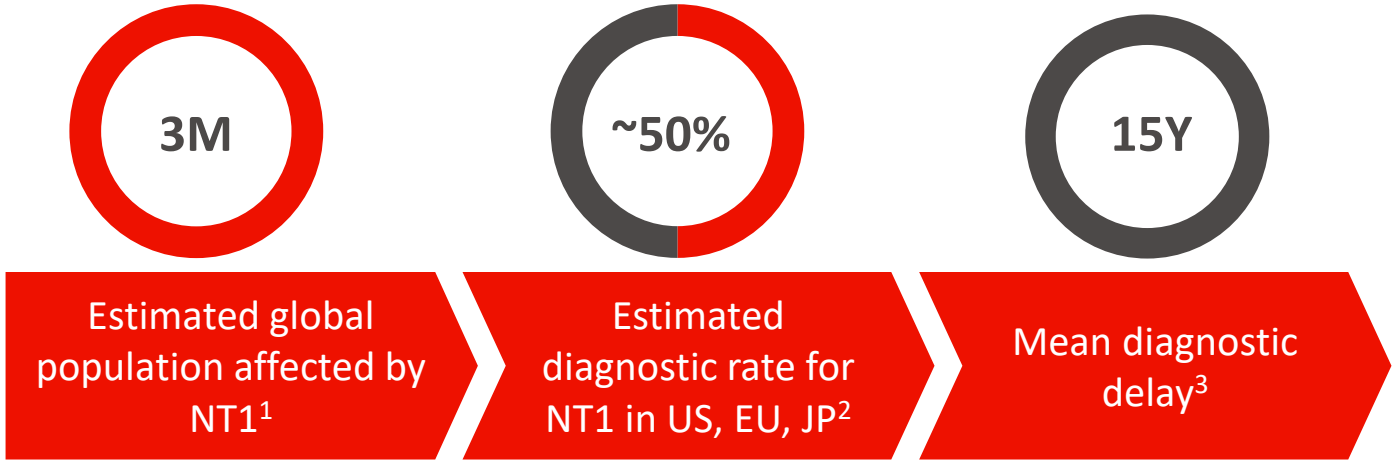
Takeda Pharmaceutical Company Limited

New York, NY

November 14, 2019

Better Health, Brighter Future

NARCOLEPSY TYPE 1 IS A RARE, ACQUIRED CHRONIC NEUROLOGICAL DISORDER



- Psychosocially devastating effects
- Current treatments are only partially effective
- Polypharmacy is common

When I'm awake, sleep is constantly intruding on that part of my life. And when I'm asleep, wakefulness is constantly intruding on that part of my life. It's frustrating because no matter how well you regulate your narcolepsy, you're always tired. You're exhausted.

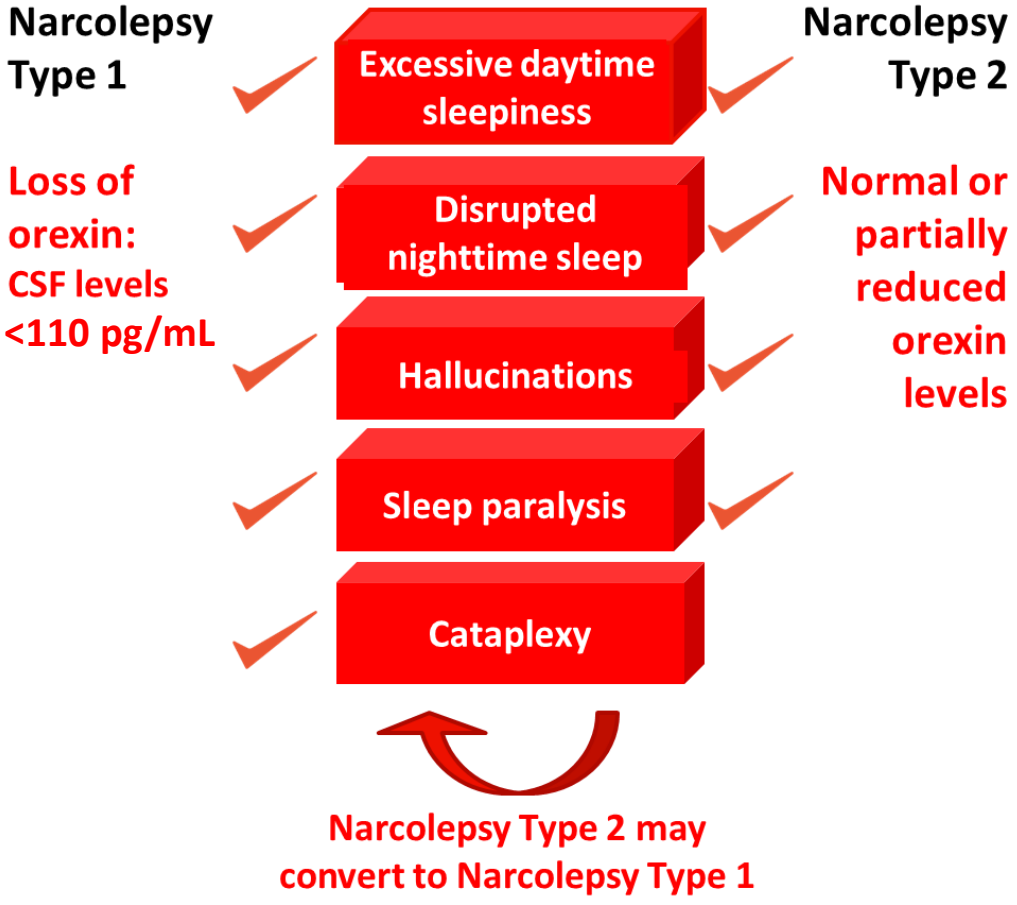
- Charlie, adviser with NT1

1. Narcolepsy Network. Narcolepsy Fast Facts. Available at: https://narcolepsynetwork.org/about-narcolepsy/narcolepsy-fast-facts/. Last Updated June 2015. Last Accessed Sept. 2019
2. Thorpy et al. Sleep Med. 2014 May;15(5):502-7
3. Frauscher B, J Clin Sleep Med 2013;9(8):805-12

NARCOLEPSY TYPE 1 IS DISTINGUISHED BY THE PRESENCE OF CATAPLEXY AND LOW OREXIN LEVELS

"It's not just about sleep, it's about quality of wakefulness … it's really about partnership with your extended family, your spouse, taking care of your children… it limits my ability to play with my kids."

-Sara, adviser with NT1



Other hypersomnia disorders

- Idiopathic Hypersomnia
- Residual Excessive Daytime Sleepiness in Obstructive Sleep Apnea[1]

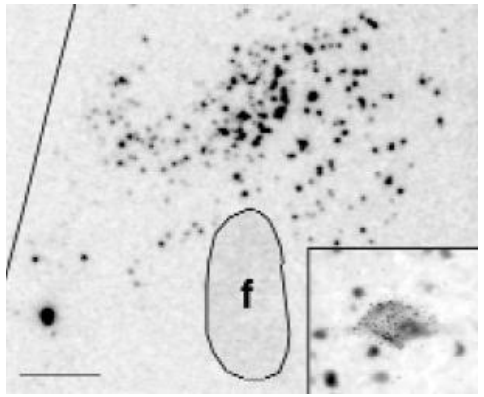
CSF: Cerebral spinal fluid; Orexin also referred to as hypocretin

1. Individuals with Obstructive Sleep Apnea who are compliant with use of continuous positive airway pressure at night

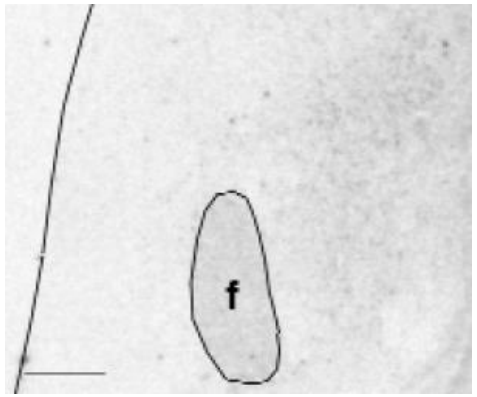
NARCOLEPSY TYPE I IS CAUSED BY PROFOUND LOSS OF OREXIN-PRODUCING NEURONS

OREXIN mRNA LABELLING OF POSTMORTEM HYPOTHALAMIC SECTIONS

Healthy control



Narcolepsy Type 1



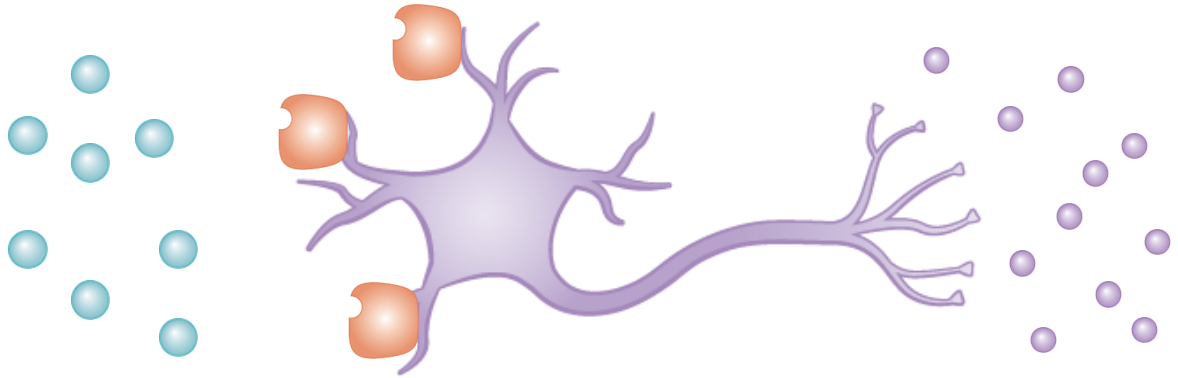
- Individuals with NT1 have >85% less orexin neurons than control, which are located in the hypothalamus[1, 2]

ACTIVATION OF OREXIN 2 RECEPTOR (OX2R) LEADS TO AROUSAL AND PROMOTES WAKEFULNESS[3]

Orexin neuropeptides A and B

Post-synaptic neurons with orexin 2 receptors

Downstream signalling promoting wakefulness



THE OREXIN HYPOTHESIS IN NARCOLEPSY TYPE I

An orexin 2 receptor agonist may replace the missing endogenous orexin peptide, addressing the underlying orexin deficiency of Narcolepsy Type 1 and reduce disease specific symptoms

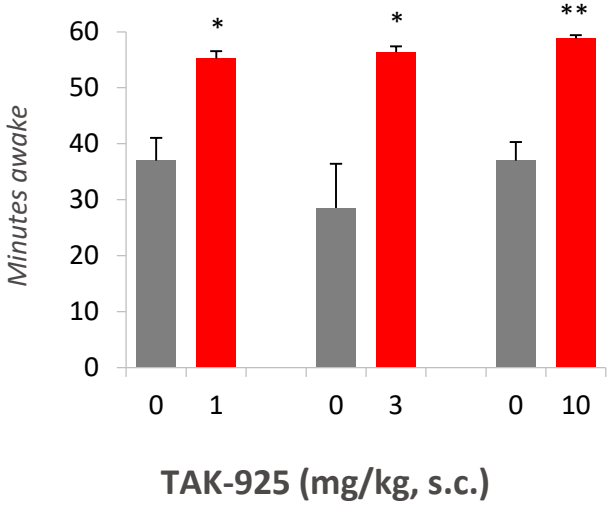
f: fornix

1. Reprinted by permission from Springer Nature. Peyron C, et al. Nat Med. 2000;6:991-997
2. Thannickal TC, et al. *Neuron.*2000;27:469–474
3. Tsujino N, et al. Pharmacol. Rev. 2009;61(2):162-176

TAK-925, A SELECTIVE OX2R AGONIST, REDUCES NARCOLEPSY-LIKE SYMPTOMS IN AN OREXIN-DEFICIENT MOUSE MODEL

TAK-925 FULLY RESTORED WAKEFULNESS

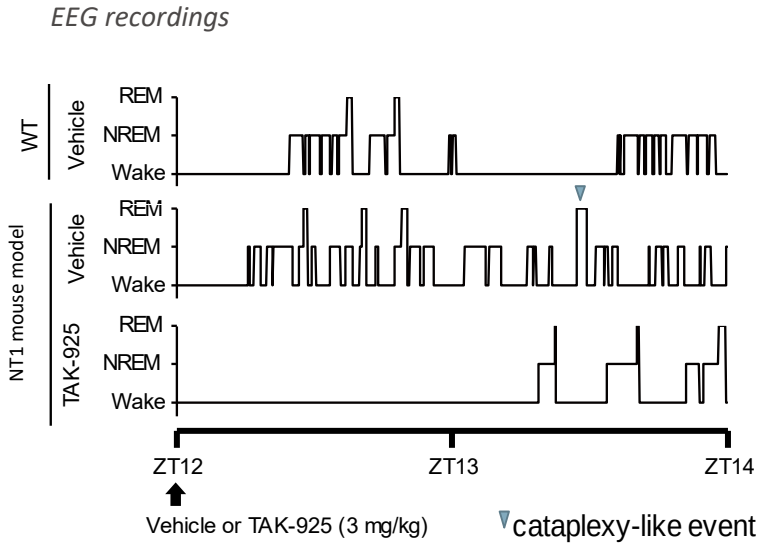
Wakefulness time of NT1 mouse model in active phase for one hour



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

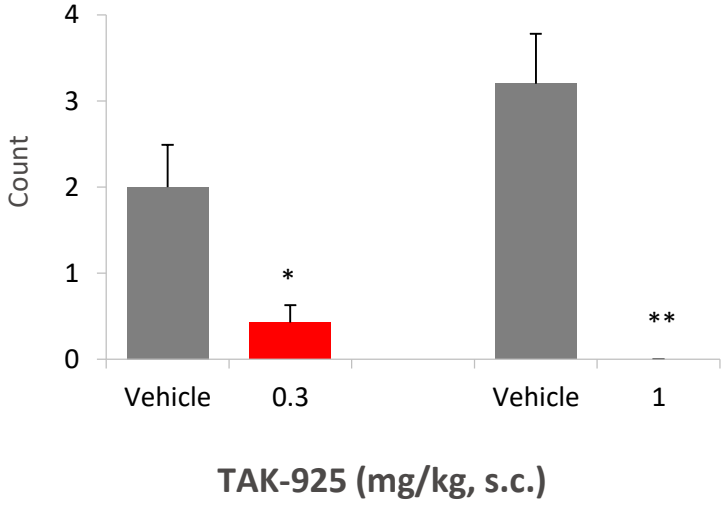
TAK-925 ELIMINATED SLEEP / WAKE TRANSITIONS

Hypnogram of sleep/wake transitions in NT1 mouse model



TAK-925 ABOLISHED CATAPLEXY-LIKE EPISODES

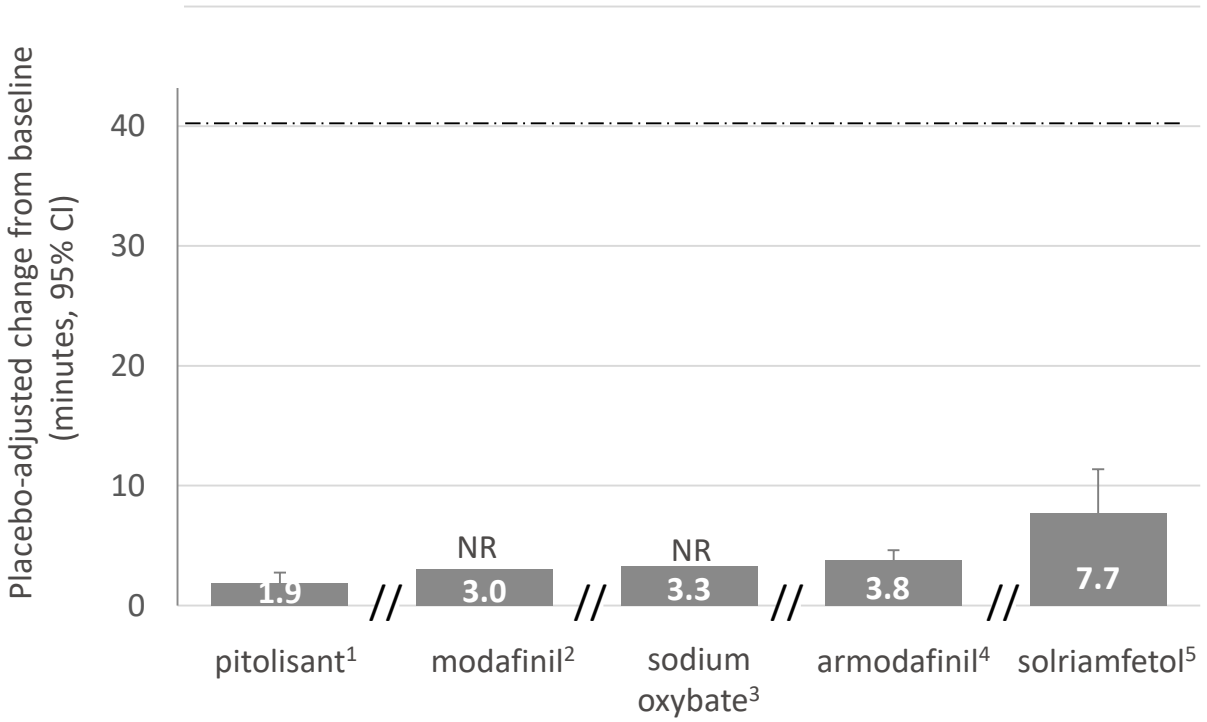
Cataplexy-like episodes in NT1 mouse model for three hours after chocolate



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

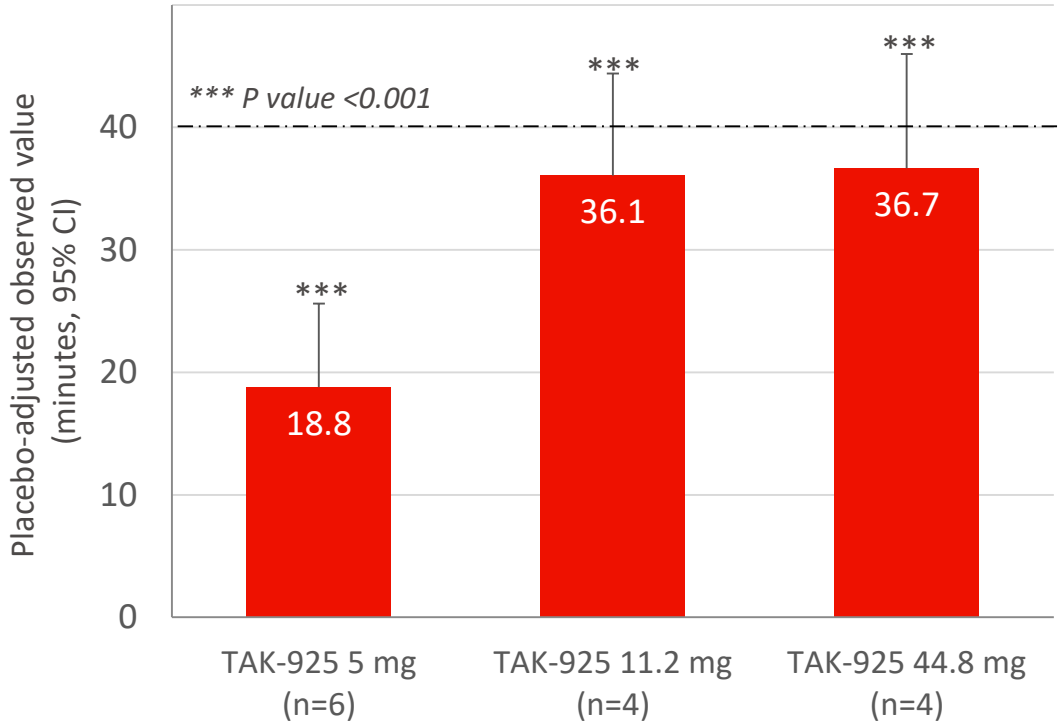
TAK-925 SHOWED PROMISING ABILITY TO MAINTAIN WAKEFULNESS IN AN EARLY PROOF OF CONCEPT STUDY IN NT1 PATIENTS

SLEEP LATENCY IN THE MAINTENANCE OF WAKEFULNESS TEST (MWT): CURRENT TREATMENTS



SLEEP LATENCY IN THE MAINTENANCE OF WAKEFULNESS TEST (MWT): TAK-925 (N=14)

(single dose nine hour continuous IV infusion during the day)[6]



- TAK-925 was well-tolerated; most AEs were mild and no SAEs were observed
- In this TAK-925-1001 study, four 40 minute MWTs were conducted per period
- Direct cross-study comparison can not be made between TAK-925 and treatments due to different studies with different designs

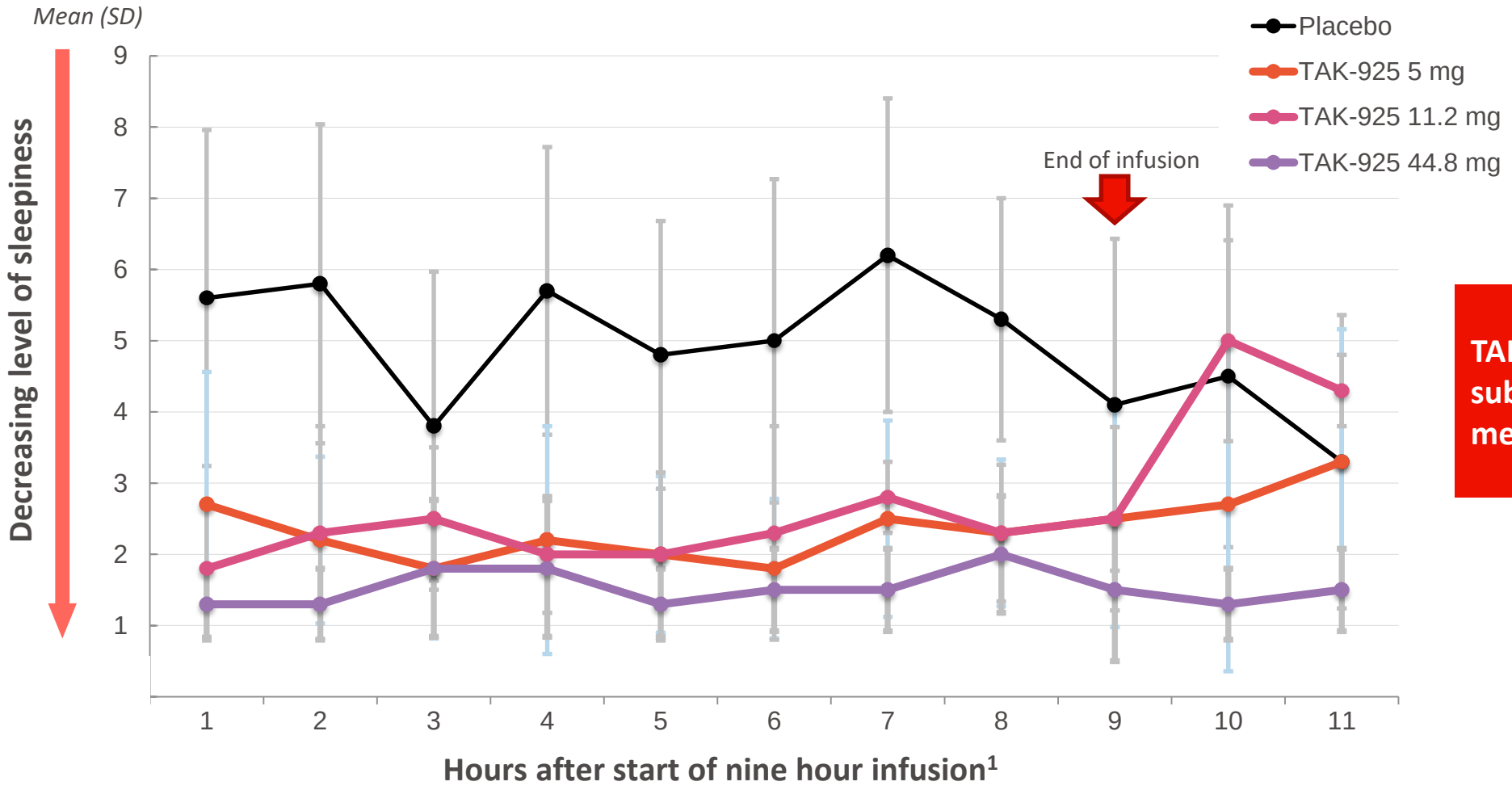
NR: 95% CI rot reported

1. Lancet Neurol. 2017 Mar;16(3):200-207; 2. FDA statistical Review: Page 5, 200 mg; 3. Label/Trial N4; 4. Clinicaltrials.gov (NCT00078377); 5. FDA Statistical Review, Study 14-002, 150 mg
6. Evans R, Tanaka S, Tanaka S, et al. 2019. A phase 1 single ascending dose study of a novel orexin 2 receptor agonist, TAK-925, in healthy volunteers (HV) and subjects with narcolepsy type 1 (NT1) to assess safety, tolerability, pharmacokinetics, and pharmacodynamic outcomes. Abstract presented at World Sleep 2019. Vancouver, Canada. http://www.professionalabstracts.com/ws2019/iPlanner/#/presentation/1832

TAK-925 ALSO REDUCED SUBJECTIVE SLEEPINESS IN THIS EARLY PROOF OF CONCEPT STUDY IN NT1

KAROLINSKA SLEEPINESS SCALE VALUES DURING AND AFTER ADMINISTRATION OF TAK-925

(single dose nine hour continuous IV infusion during the day)



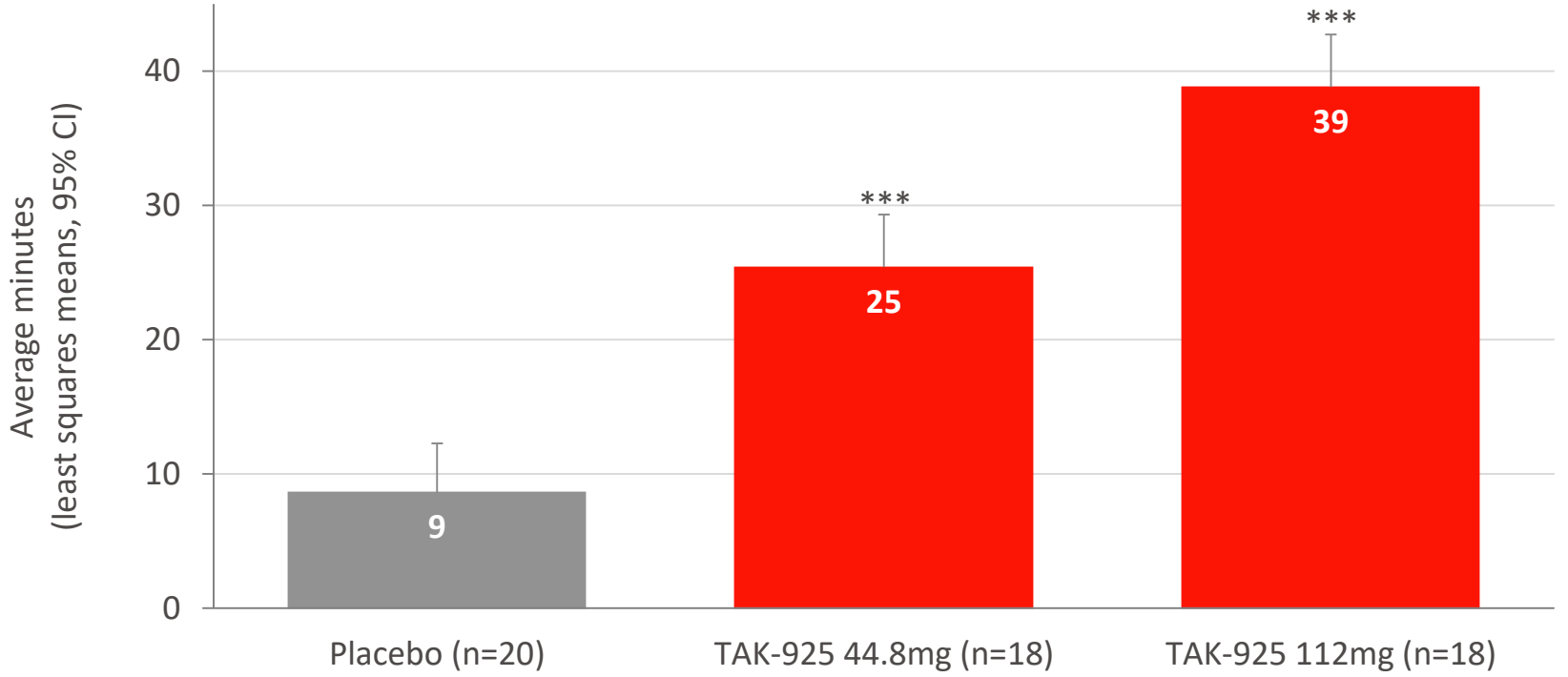
TAK-925 improved subjective and objective measures of wakefulness

1. TAK-925 effective plasma half-life <2 hours

Evans R, Tanaka S, Tanaka S, et al. 2019. A phase 1 single ascending dose study of a novel orexin 2 receptor agonist, TAK-925, in healthy volunteers (HV) and subjects with narcolepsy type 1 (NT1) to assess safety, tolerability, pharmacokinetics, and pharmacodynamic outcomes. Abstract presented at World Sleep 2019. Vancouver, Canada. http://www.professionalabstracts.com/ws2019/iPlanner/#/presentation/1832

TAK-925 MAINTAINED WAKEFULNESS IN SLEEP-DEPRIVED HEALTHY ADULTS IN A SECOND PHASE 1 STUDY

SLEEP LATENCY IN THE MAINTENANCE OF WAKEFULNESS TEST (MWT) IN SLEEP-DEPRIVED HEALTHY ADULTS[1]



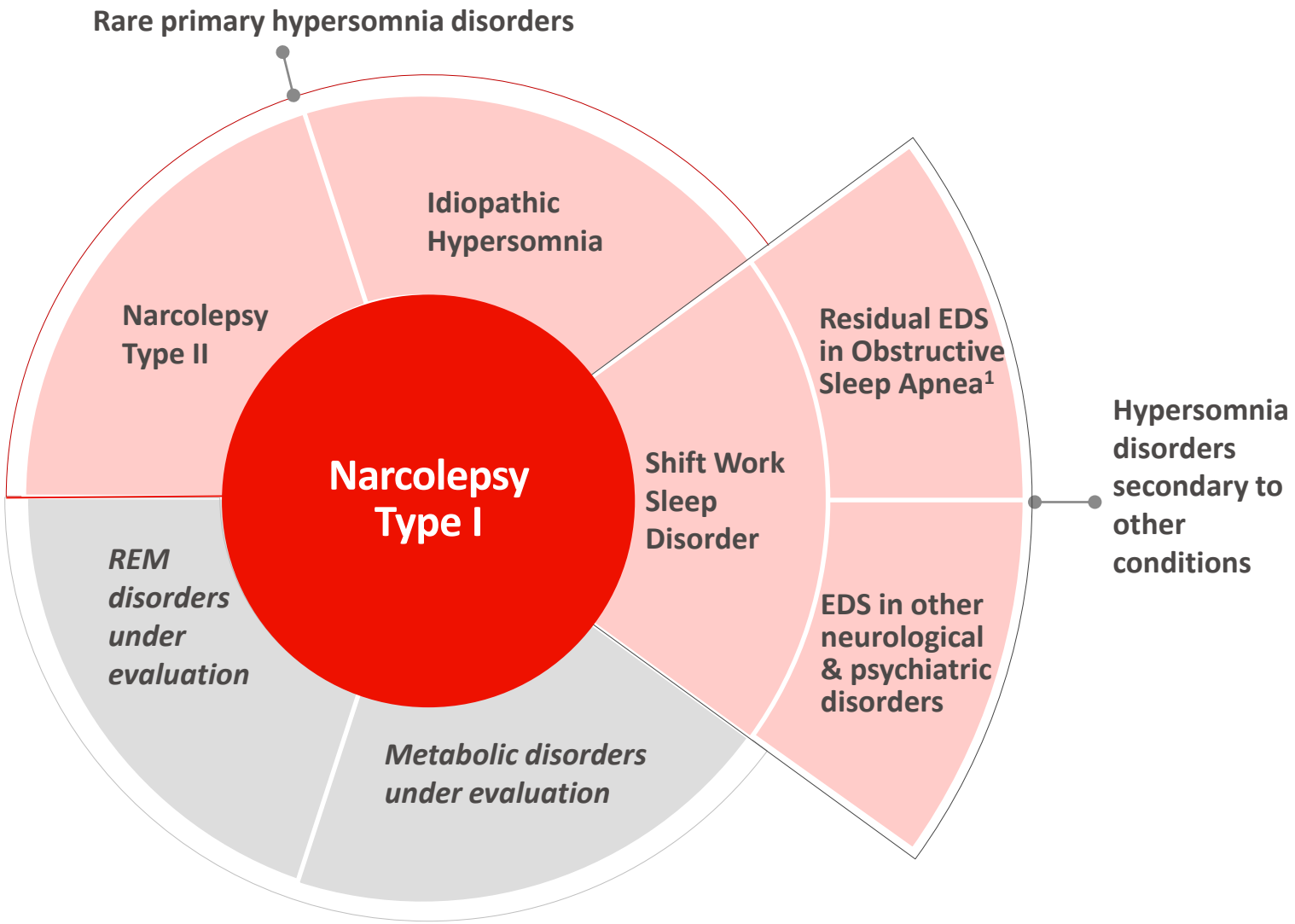
TAK-925 was well-tolerated; most AEs were mild and no SAEs were observed

Results suggest potential therapeutic use of TAK-925 in other hypersomnia disorders not associated with orexin deficiency

1. Evans R, Hazel J, Faessel H, et al. 2019. Results of a phase 1b, 4-period crossover, placebo-controlled, randomized, single dose study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of TAK-925, a novel orexin 2 agonist, in sleep-deprived healthy adults, utilizing modafinil as an active comparator. Abstract presented at World Sleep 2019. Vancouver, Canada. http://www.professionalabstracts.com/ws2019/iPlanner/#/presentation/2821
2. Int J Neurosci. 1990 May;52(1-2):29-37

***: p-value <0.001 relative to placebo

WE ARE COMMITTED TO LEADING INNOVATION IN OREXIN BIOLOGY AND EXPANDING THERAPEUTIC INDICATIONS FOR OX2R AGONISTS



- Top priority
- Other hypersomnia disorders
- Additional opportunities for expansion

- **TAK-925-1003** for Narcolepsy Type 2 (NCT03748979)
- **SPARKLE 2001** study for Residual EDS in Obstructive Sleep Apnea (NCT04091425)
- **SPARKLE 2002** study for Idiopathic Hypersomnia (NCT04091438)

REM: Rapid eye movement

1. Individuals with Obstructive Sleep Apnea who are compliant with use of continuous positive airway pressure at night

TAK-994 IS AN ORAL OX2R AGONIST PROGRESSING TO STUDIES IN NARCOLEPSY TYPE 1

TAK-994-1501 PROOF OF CONCEPT STUDY IN NARCOLEPSY TYPE 1

SPARKLE
OREXIN INNOVATION

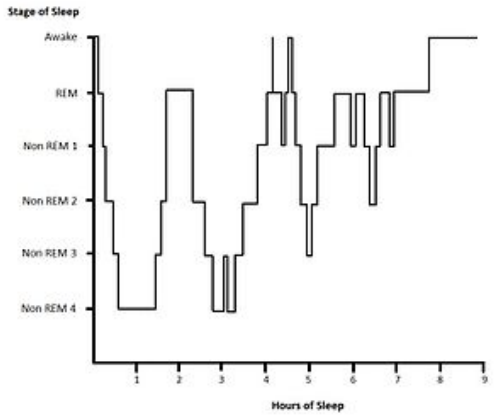
- Multi-center, placebo-controlled trial in North America and Japan
- Enrollment target: 72 adults
- Duration of treatment: 28 days dosing
- Exploratory outcome measures include Maintenance of Wakefulness Test (MWT), Epworth Sleepiness Scale (ESS), and Weekly Cataplexy Rate (WCR)

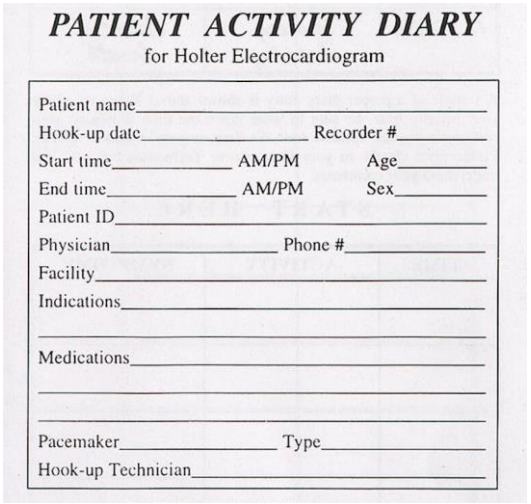
Proof of Concept trial: ClinicalTrials.gov Identifier: NCT04096560

DIGITAL TECHNOLOGIES ARE ENHANCING THE DEVELOPMENT OF OX2R AGONISTS FOR SLEEP DISORDERS

TRADITIONAL CLINICAL INSTRUMENTS DO NOT FULLY MEASURE SYMPTOMS OF SLEEP DISORDERS

Hand-scored polysomnography (PSG)[1]





PATIENT ACTIVITY DIARY

for Holter Electrocardiogram

Patient name_____

Hook-up date_____ Recorder #_____

Start time_____ AM/PM Age_____

End time_____ AM/PM Sex_____

Patient ID_____

Physician_____ Phone #_____

Facility_____

Indications_____

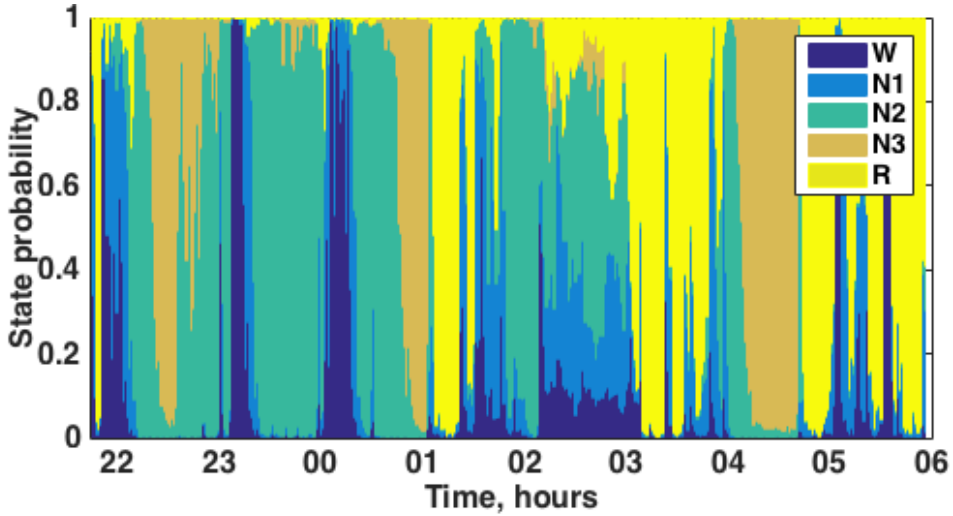
Medications_____

Pacemaker_____ Type_____

Hook-up Technician_____

DIGITAL MEASURES WILL FURTHER CHARACTERIZE SLEEP ARCHITECTURE AND SUPPORT CLINICAL TRIAL ASSESSMENTS

Automated analysis of NT1 nPSG[2]



- Real-time data capture to understand disease burden and effects of treatment
- Non-invasive measures to optimize therapy
- Patient stratification using digital fingerprints

nPSG – Night time polysomnography

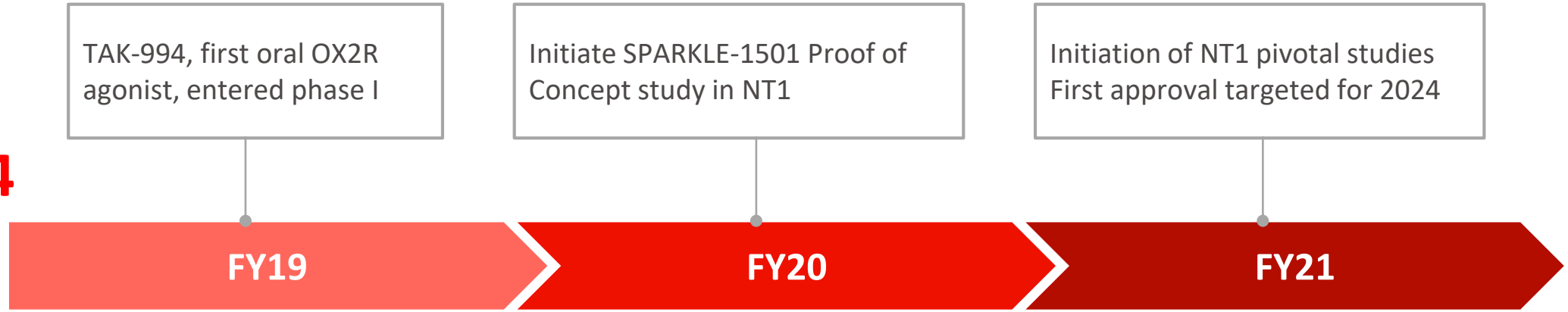
1. Approximately 80% interrater concordance based on Danker-Hopfe et al., J Sleep Res (2009) and Younes & Hanly, J Clin Sleep Med (2016); 2. Analysis shown is based on Stephansen et al., Nature Comm (2018)

WE ASPIRE TO BRING A POTENTIALLY TRANSFORMATIVE OX2R AGONIST SOLUTION TO INDIVIDUALS WITH NARCOLEPSY TYPE 1

TAK-925

- Achieved early Proof of Concept for NT1
- Awarded Breakthrough Therapy Designation
- Awarded Sakigake Designation
- Launched formulation development activities

TAK-994



Thank you to all the study participants who have enrolled in these early OX2R agonist clinical trials

SUMMARY

1

TAK-925 has achieved early Proof-of-Concept for OX2R agonists in Narcolepsy Type 1

2

TAK-925 has demonstrated potential of OX2R agonists for treatment of other sleep-related disorders

3

TAK-994 is an oral OX2R agonist progressing to studies in Narcolepsy Type 1

R&D DAY AGENDA – NEW YORK, NOVEMBER 14, 2019

TIME	AGENDA
12:30 – 12:35	**Welcome and Opening Remarks** *Sheelagh Cawley-Knopf, Head R&D Global Portfolio Strategy*
12:35 – 12:45	**Takeda: A Global Values-Based, R&D-Driven Biopharmaceutical Leader** *Christophe Weber, President & CEO Takeda*
12:45 – 13:20	**Translating Science into Highly Innovative, Life-changing Medicines** *Andy Plump, President R&D*
13:20 – 13:45	**Oncology and Cell Therapies with Spotlight on CAR-NK** *Chris Arendt, Head Oncology Drug Discovery Unit*
13:45 – 14:05	**Spotlight on Oncology Opportunities** • **TAK-788** : *Rachael Brake, Global Program Lead* • **Pevonedistat** : *Phil Rowlands, Head Oncology Therapeutic Area Unit*
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15:20 – 16:00	**Panel Q&A Session**
16:00	**Drinks reception**

THERAPEUTIC AREA FOCUS IN GI WITH SPOTLIGHT ON CELIAC DISEASE

Asit Parikh, MD, PhD

Head Gastroenterology Therapeutic Area Unit

Takeda Pharmaceutical Company Limited

New York, NY

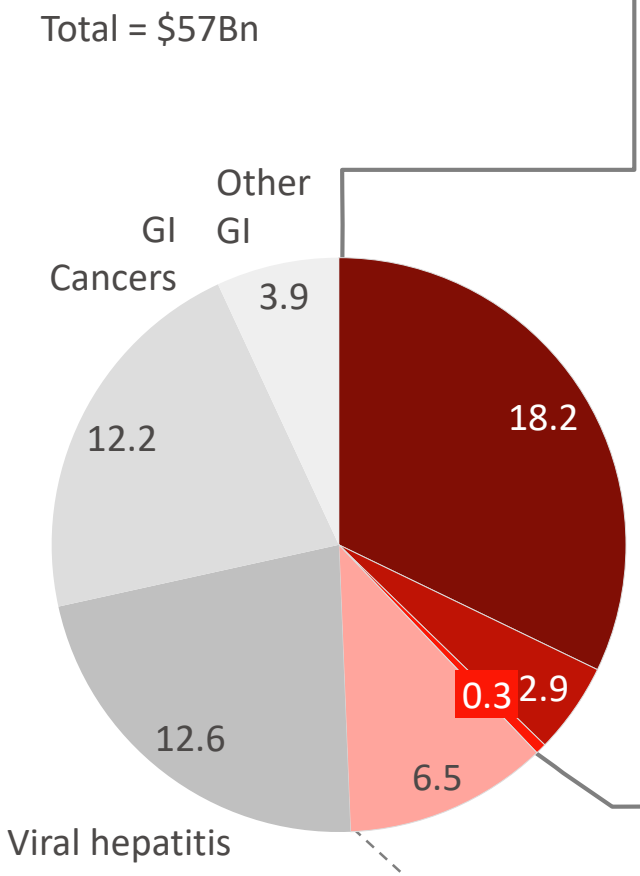
November 14, 2019

WE TARGET UNMET NEEDS THAT ALIGN WITH OUR STRENGTHS

AREAS OF FOCUS

- High unmet medical need
- Potential to advance SoC through innovative science – by being first or best in class
- Fit with internal strengths
- Ability to create a commercially - viable path

GI WW RX SALES 2018 (USD BN)



TAKEDA GI DISEASE AREAS

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

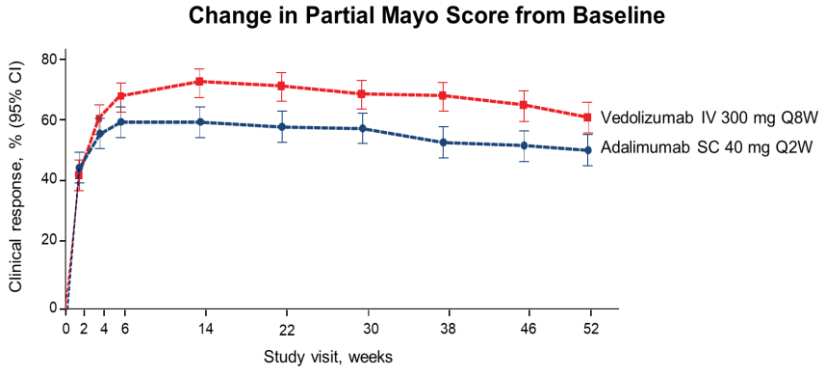
SOURCE: Evaluate Pharma indication specific sales, accessed May 29, 2019. Other GI includes: pancreatic insufficiency, hepatic encephalopathy, diarrhea, bowel clearance, gallstones, hemorrhoids

WE STRENGTHEN ENTYVIO BY CONTINUOUSLY IMPROVING VALUE FOR PATIENTS

COMPETITIVE POSITIONING

VARSITY: 1st Head-to-Head study in IBD (UC)

- Vedolizumab was superior to adalimumab on the primary endpoint of clinical remission at wk 52
- Onset of action as rapid as anti-TNF



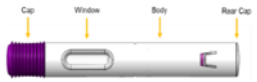
EXPANDED PATIENT POPULATIONS

Entyvio Subcutaneous Development

- Positive VISIBLE UC and CD trials
- Subject to regulatory approval, on track to launch exclusive, digital, needle-free jet-injector by 2022

Prefilled syringe

Autoinjector pen



Portal jet-injector

Gut GvHD prophylaxis

- Could **transform SoC** for cancer patients undergoing allo stem-cell transplants

GEOGRAPHIC EXPANSION

Entyvio IV

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

EXPECTED MILESTONES (FY)

2019	2020	2021
Entyvio (SC UC) US approval	Entyvio (SC CD) US, EU approval Entyvio (SC UC) EU, JP approval Entyvio (IV) CN approval	Entyvio GvHD Ph3 readout

Source: Sands *et al*. Vedolizumab versus Adalimumab for Moderate-to-Severe Ulcerative Colitis. N Engl J Med 2019; 381:1215-1226

IBD: Inflammatory Bowel Disease; UC: ulcerative colitis; CD: Crohn's Disease; IV=intravenous; SC=subcutaneous; TNF=tumour necrosis factor; SoC: standard of care; CN: China; JP: Japan; GvHD: graft versus host disease; Clinical remission: Complete Mayo score of ≤2 points and no individual subscore >1 point

WE ARE POSITIONED TO DELIVER NEAR-TERM & SUSTAINED GROWTH

TARGET APPROVAL →	WAVE 1[1]					WAVE 2[2]					PLATFORMS
	CLINICAL-STAGE NMEs										
	FY20	FY21	FY22	FY23	FY24	FY25 AND BEYOND					
ONCOLOGY		**TAK-788**[3] *2L NSCLC*		**TAK-007** *Hematologic malignancies*	**TAK-924** *AML*	**TAK-164** *GI malignancies*	**TAK-252** *Solid tumors*				CELL THERAPY AND IMMUNE ENGAGERS; TARGETED INNATE IMMUNE MODULATION; NEXT-GEN CHECKPOINT MODULATORS
		TAK-924[3] *HR-MDS*		**TAK-788** *1L NSCLC*		**TAK-573** *R/R MM*	**TAK-981** *Multiple cancers*				
RARE DISEASES *Immunology Hematology Metabolic*		**TAK-620** *CMV infect. in transplant*		**TAK-611** *MLD (IT)*	**TAK-607** *Complications of prematurity*	**TAK-079**[4] *MG, ITP*	**TAK-754** *HemA*	**TAK-755** *iTTP, SCD*			GENE THERAPY
		TAK-609 *Hunter CNS (IT)*		**TAK-755** *cTTP*		**TAK-531** *Hunter CNS*					
NEUROSCIENCE				**TAK-935** *DEE*	**Orexin2R-ag** *(TAK-925/994) Narcolepsy T1*	**TAK-341** *Parkinson's Disease*	**Orexin2R-ag** *Sleep Disorders*	**TAK-041** *CIAS NS*			GENE THERAPY; OTHER PLATFORMS *RNA Modulation Antibody Transport Vehicle*
						TAK-418 *Kabuki Syndrome*	**TAK-653** *TRD*	**TAK-831** *CIAS NS*			
						WVE-120101 *Huntington's Disease*	**WVE-120102** *Huntington's Disease*				
GASTRO-ENTEROLOGY	**TAK-721** *EoE*					**Kuma062** *Celiac Disease*	**TAK-101** *Celiac Disease*	**TAK-018** *Crohn's Disease (post-op and ileitis)*	**TAK-671** *Acute Pancreatitis*		GENE THERAPY; MICROBIOME; CELL THERAPY
						TAK-954 *POGD*	**TAK-906** *Gastroparesis*	**TAK-951** *Nausea & vomiting*			
VACCINES		**TAK-003** *Dengue Vaccine*				**TAK-214** *Norovirus Vaccine*	**TAK-426** *Zika Vaccine*	**TAK-021** *EV71 vaccine*			

1. Projected timing of approvals depending on data read-outs; some of these Wave 1 target approval dates assume accelerated approval
2. Some Wave 2 assets could be accelerated into Wave 1 if they have breakthrough data
3. Projected approval date assumes filing on Phase 2 data
4. TAK-079 to be developed in Rare Diseases indications myasthenia gravis (MG) and immune thrombocytopenic purpura (ITP) (FPI projected in each indication in 2H FY19)

Orphan potential in at least one indication
Estimated dates as of November 14, 2019

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

ADDRESSES SIGNIFICANT UNMET NEED

- Chronic, allergic, inflammatory condition of the esophagus that results in swallowing dysfunction
- Diagnosed prevalence is expected to increase significantly

No approved US medication
SOC is food elimination, off-label use[1]

TAK-721 granted breakthrough therapy designation by FDA in 2016

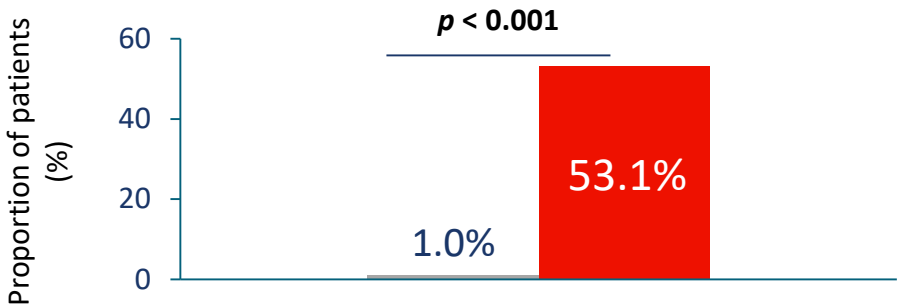
EXPECTED MILESTONES (FY)

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

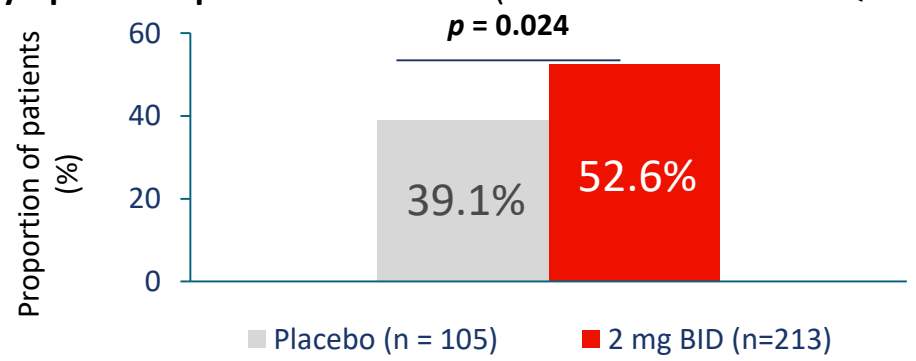
INDUCTION DATA SHOWS SIGNIFICANT HISTOLOGIC AND SYMPTOM RESPONSE

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

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



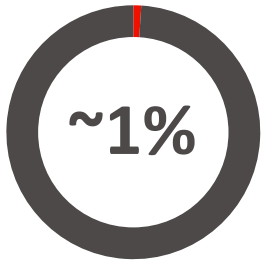
Symptom Response at 12 Weeks (≥ 30% reduction in DSQ score)



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

DSQ score: Dysphagia Symptom Questionnaire patient reported outcome score eos/hpf: peak eosinophils per high-powered field from endoscopic biopsies
Eos/hpf: eosinophils per high-power field; BID: Twice daily; SOC: Standard of care; NDA: new drug application

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



Global population affected by celiac[1]

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

Estimated global, eligible patient population[2]

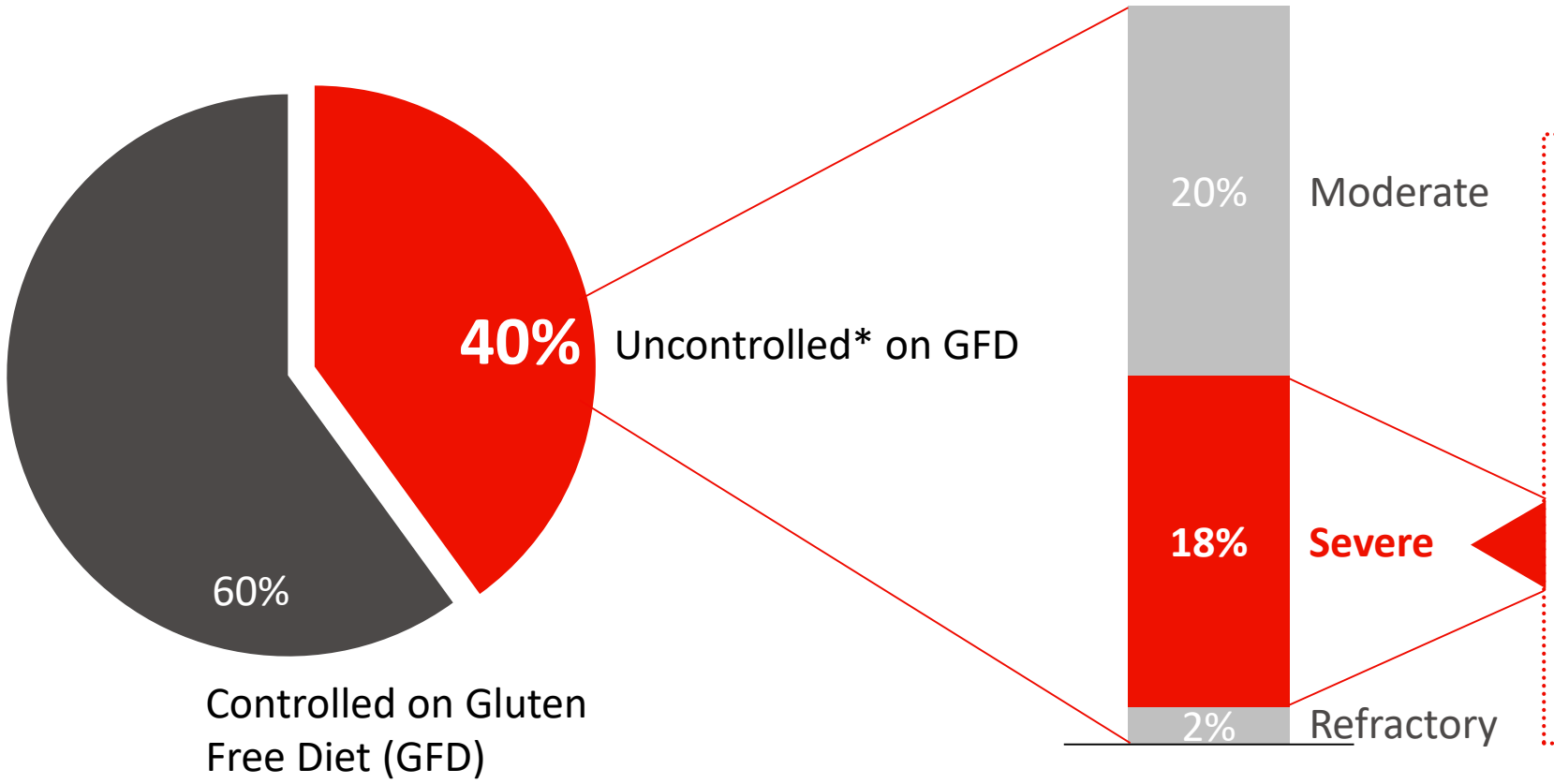
- Overlooked disease, growing prevalence
- Chronic symptoms
- Higher risk of certain cancers
- High treatment burden affecting the whole family
- No current pharmacologic therapies

“Some of us are so extremely sensitive that one little crumb will make us extremely sick. I'm one of those people, and there is really nothing I can do about it”

– **Delisi**, Celiac disease patient

1. Pooled global prevalence; Clin Gastroenterol Hepatol. 2018 Jun;16(6):823-836
2. Estimated number of patients projected eligible for treatment, in markets where the product is anticipated to be commercialized, subject to regulatory approval

WE ARE FOCUSING ON THE NARROWEST POPULATION WITH HIGH UNMET NEED



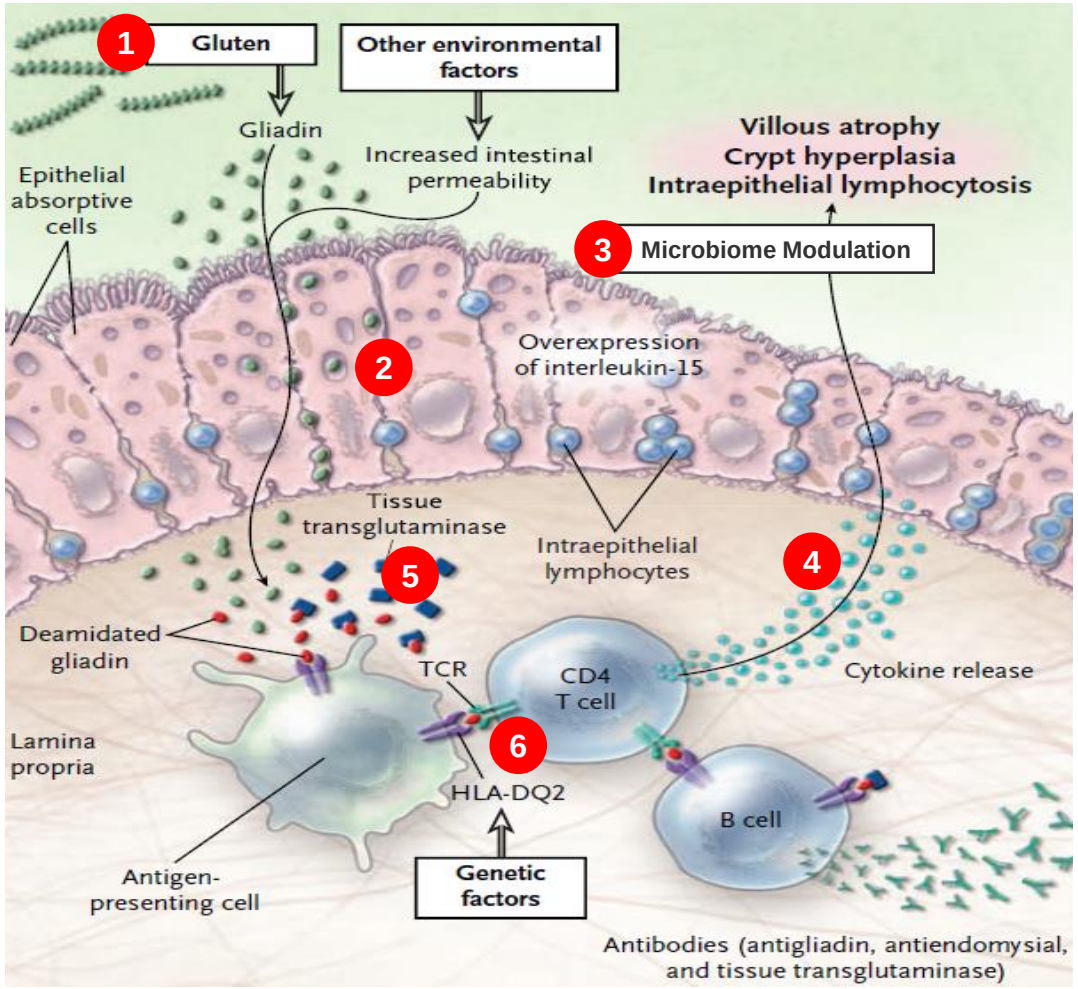
Our focus:

- Niche patient segment with the highest unmet need
- Severe symptoms with villous atrophy
- Continue to suffer despite the GFD and are highly likely to take a therapy

*Uncontrolled defined as ongoing chronic moderate to severe symptoms with villous atrophy

OUR APPROACH TO TREATING CELIAC DISEASE

TREATMENT OPPORTUNITIES FOR CELIAC DISEASE



1. Enzymatic digestion of gluten
2. Reduce intestinal permeability
3. Microbiome modulation
4. Cytokine inhibition
5. Transglutaminase inhibition
6. Promote Immune tolerance

PVP BIOLOGICS

Kuma062 promises greatly increased enzymatic efficiency and improved formulation over predecessors

COUR

TAK-101 (TIMP-GLIA) has the potential to be a first in class, tolerizing immune therapy for celiac disease

Source: Green and Cellier, 2007

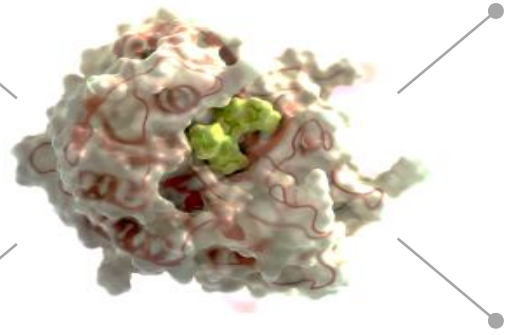
KUMA062: A HIGHLY POTENT ORAL GLUTENASE THAT COULD CHANGE THE STANDARD OF CARE IN CELIAC DISEASE

ABOUT KUMA062

- Kuma062 is an oral, computationally-engineered super glutenase
- Enhanced catalytic activity compared to other glutenases

Optimal activity at the pH range of the stomach after a meal

Resistance to common digestive proteases

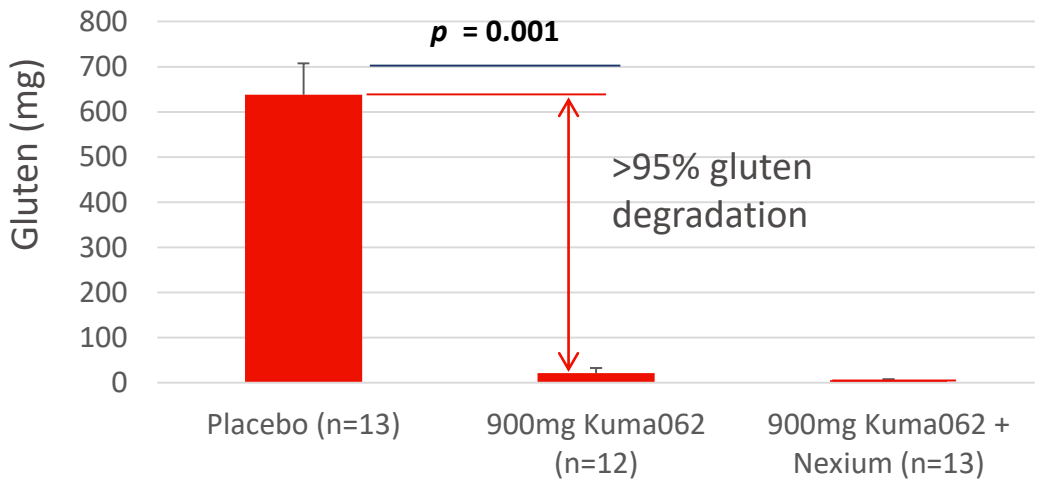


Specificity for peptides with immunogenic regions of gliadin

Eliminates ex vivo T cell response to all 3 major gliadin families

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

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

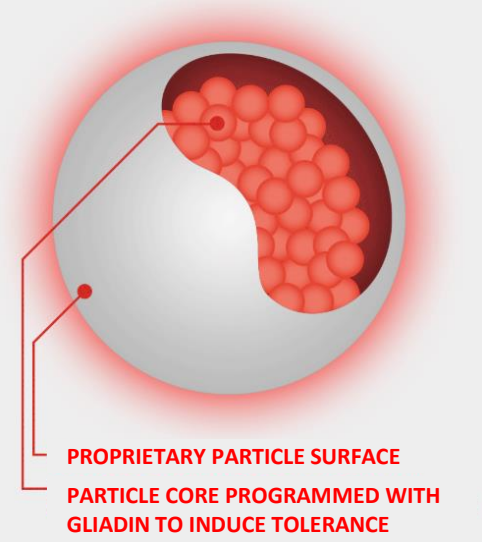


- Kuma well-tolerated, no identified safety concern
- Decision to acquire PVP Biologics expected Q3 FY2019

TAK-101: POTENTIAL BEST-IN-CLASS, INTRAVENOUS THERAPY FOR CELIAC DISEASE DESIGNED TO MODIFY T CELL RESPONSE

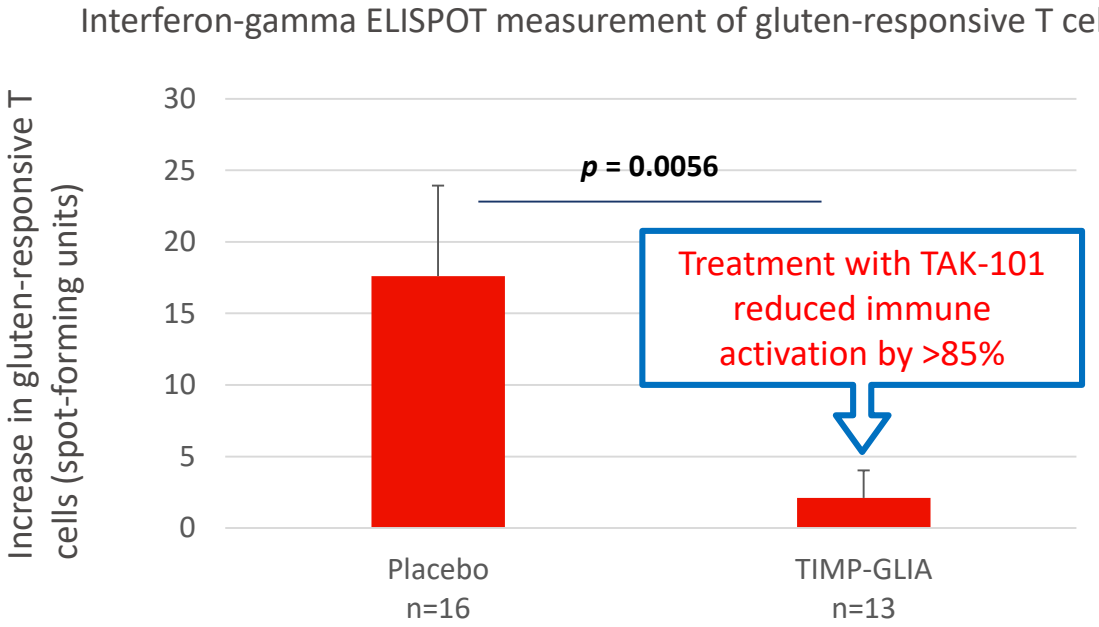
ABOUT TAK-101*

- Biodegradable polymer encapsulating antigen
- Designed to induce tolerance to gluten, reduce T cell responses to gliadin



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

TAK-101 REDUCES IMMUNE ACTIVATION AFTER GLUTEN EXPOSURE



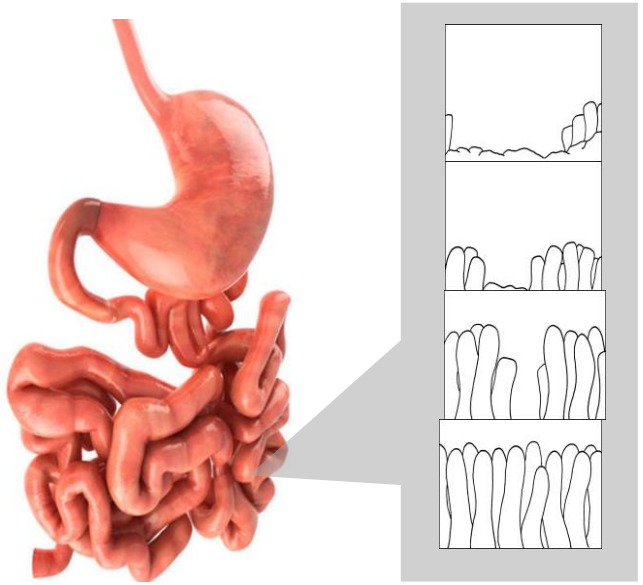
TAKEDA ACQUIRED EXCLUSIVE GLOBAL LICENSE TO TAK-101

*Formerly TIMP-GLIA
Source: https://www.courpharma.com/our-technology/

WE ARE LEADING THE SCIENCE IN CELIAC DISEASE WITH A NEW AI - BASED TOOL AND INGESTIBLE DEVICE

PIONEERING AT BOUNDARIES OF CLINICAL MEDICINE

- Innovative, non-invasive, patented method of measuring total burden of intestinal disease

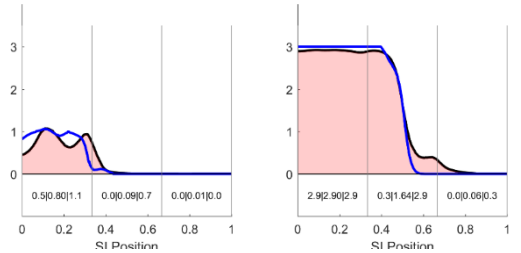


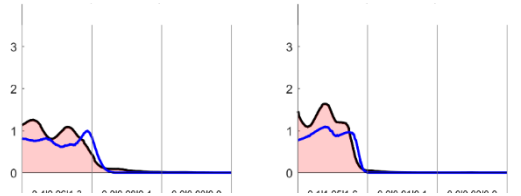
INNOVATIVE USE OF TECHNOLOGY

- Ingestible high resolution camera pill
- Modern machine-learning/ AI based image processing

PRECISION MEASUREMENT USING AI

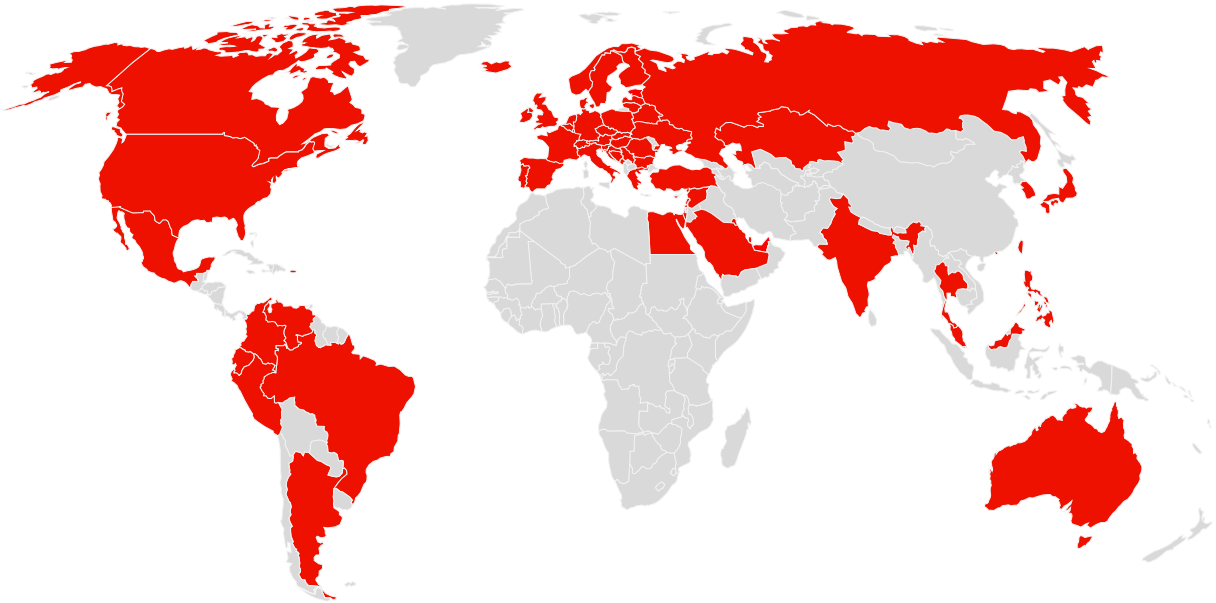
- Pioneering Automated Image assessment quantifies disease burden





TAKEDA IS THE BEST COMPANY TO BRING CELIAC THERAPIES TO PATIENTS

World-class, fully connected GI commercial infrastructure across 65+ countries that supports $6bn+ revenues



- Extensive GI clinical footprint
- Strong reputation for scientific excellence
- Lauded for calculated risk-taking by the GI community
- Experience with redefining guidelines and treatment paths

NME MILESTONES ACHIEVED IN FY19 AND LOOKING AHEAD TO OTHER POTENTIAL MILESTONES[1] THROUGH FY20

PIVOTAL STUDY STARTS, APPROVALS

1H FY 2019

- ☑ TAK-611 — MLD — Ph 2 start[2]
- ☑ TAK-755 — cTTP — Ph 3 start
- ☑ TAK-925 — Narcolepsy — POC
- ☑ TAK-721 — EoE — Ph 3 data (induction)
- ☑ TAK-101 — Celiac Disease — POC

2H FY 2019

- ☑ PEVONEDISTAT TAK-924 — AML — Ph 3 start
- TAK-788 — 1L NSCLC — Ph 3 start
- ☑ PEVONEDISTAT TAK-924 — HR-MDS — Ph 2 Overall Survival
- ☑ TAK-007 — Hem. Malignancies — POC
- TAK-609 — Hunter (IT) — Ph 3 data 2yr extension
- mHTT ASO — Huntington's Disease — POC
- TAK-721 — EoE — Ph 3 data (maintenance)

1H FY 2020

- TAK-788 — 2L NSCLC — Ph 2 Pivotal
- TAK-573 — R/R MM, Solid Tumor — POC

2H FY 2020

- TAK-721 — EoE — Approval
- mHTT ASO — Huntington's Disease — Pivotal start
- TAK-620 — R/R CMV SOT & HSCT — Ph 3 data
- TAK-755 — iTTP — POC
- TAK-935 — DEE — POC
- TAK-906 — Gastroparesis — POC
- TAK-951 — Nausea & Vomiting — POC

Oncology

Rare Disease

Neuroscience

Gastroenterology

☑ Denotes milestones that have been achieved.

KEY DATA READOUTS

1. Potential key milestone dates as of November 14, 2019. The dates included herein are estimates based on current data and are subject to change
2. Potentially registration enabling

SUMMARY

1

We have built an industry-leading portfolio rooted in unparalleled scientific excellence and outstanding global commercial strength

2

We are well positioned to bring the first therapies to celiac patients that could change the standard of care

3

We have multiple milestones, including expected key approvals in the next 2 years that will be transformative for patients

R&D DAY AGENDA – NEW YORK, NOVEMBER 14, 2019

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

Panel Q&A Session