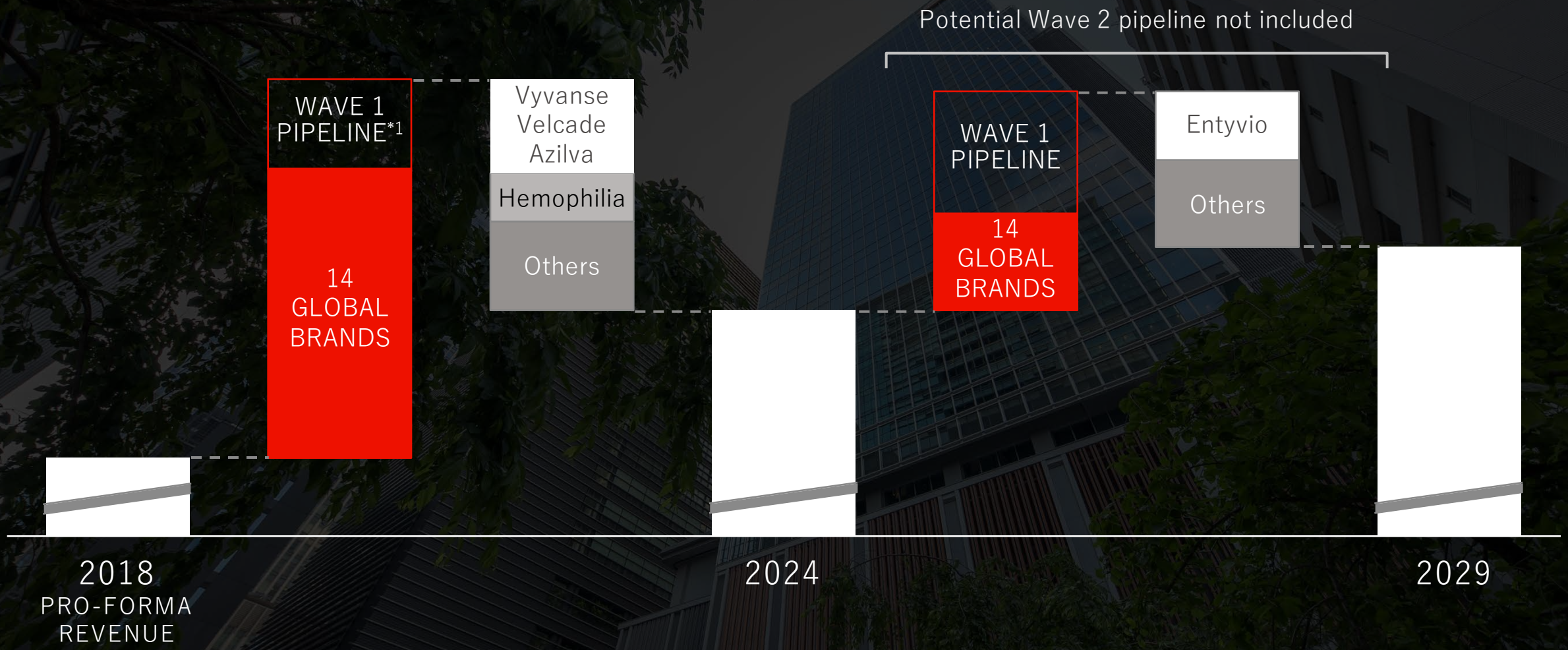
LONG-TERM VALUE FOR PATIENTS, SOCIETY AND INVESTORS

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

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**

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]					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*					
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						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*					

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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]

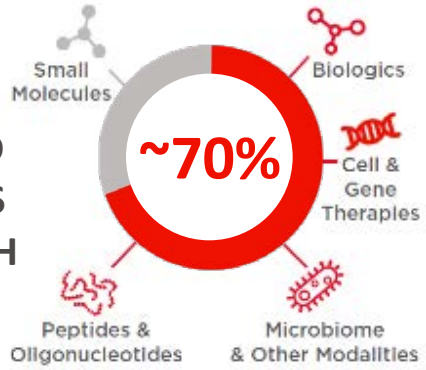
~40

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

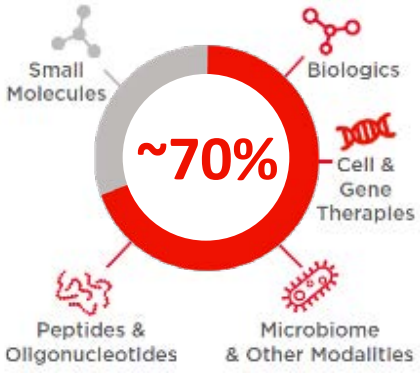
"There is a considerable need for improved treatments for individuals with NT1, which is caused by the loss of orexin-producing neurons in the brain"

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

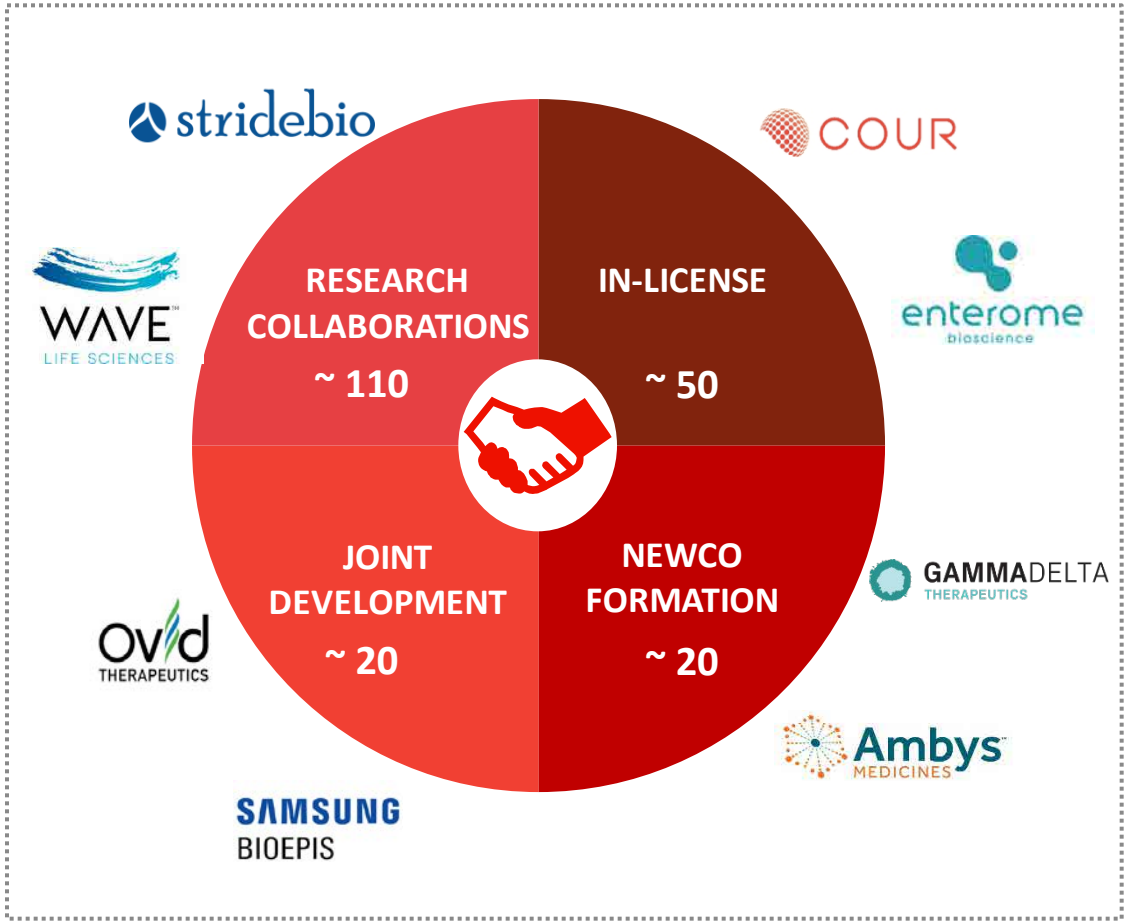
20 NME stage-ups since FY18

19 Indications terminated or externalized since FY18

FAST GO / NO-GO DECISION MAKING

WE ARE CULTIVATING THE BEST SCIENCE THROUGH DIFFERENTIATED PARTNERSHIPS…

*Select partnerships**



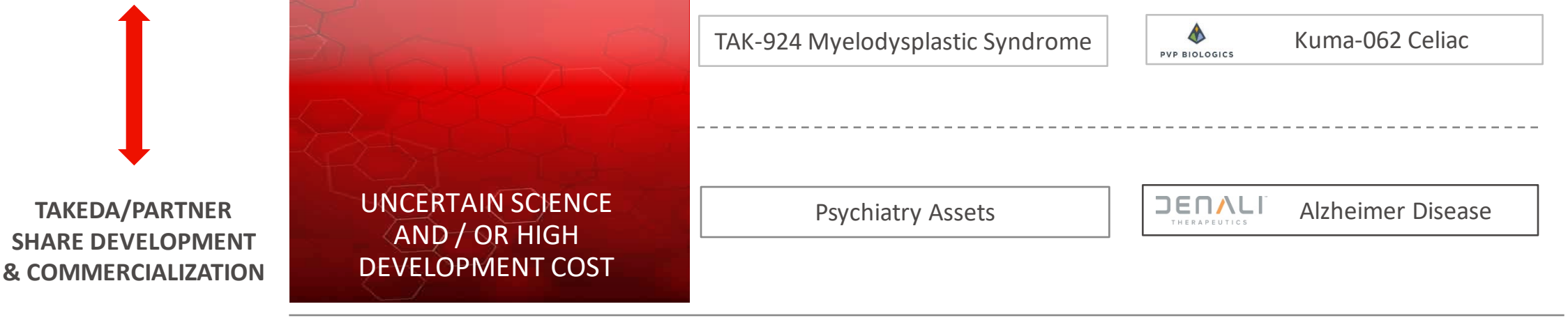
* Externalizations and venture investments are not included

- Access to Innovation
- Risk-Sharing
- Expanding Capacity

Total Value in Public & Private Equity

>$1B

WE ARE NURTURING INNOVATION WHEREVER IT OCCURS



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

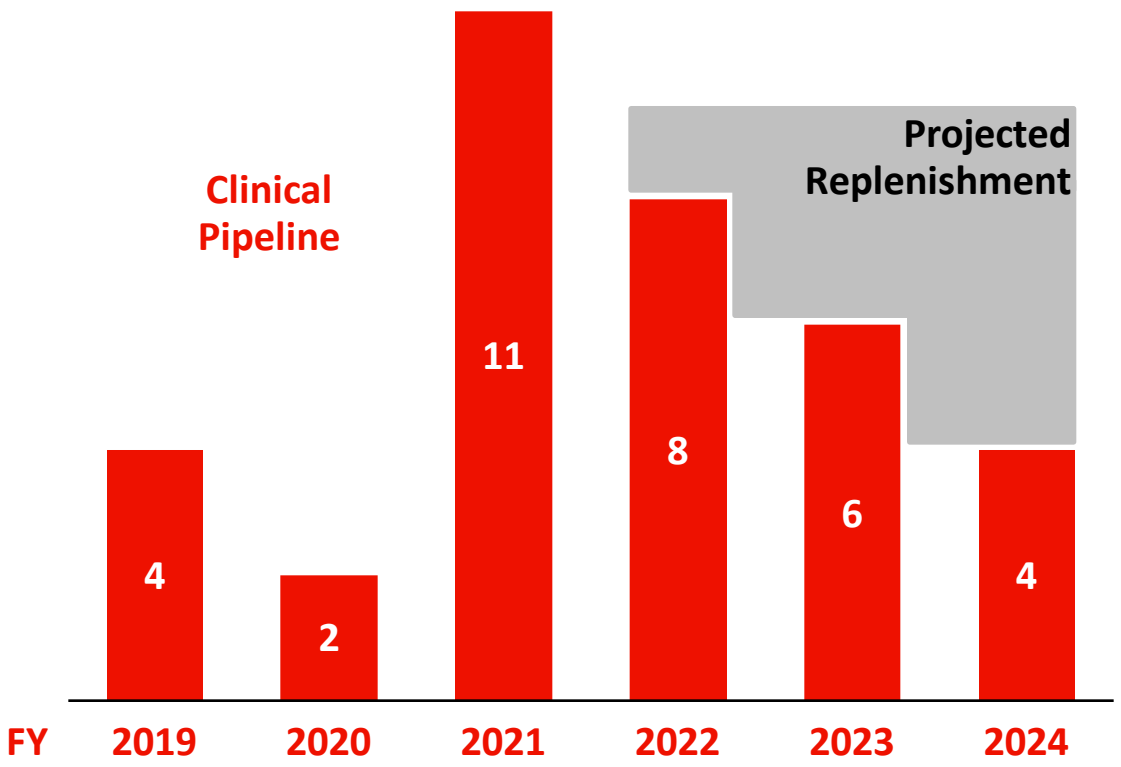
Smaller trials, lower costs, potential longer exclusivity

PARTNERSHIP MODEL

Success driven milestone payments

A RESEARCH ENGINE FUELING A SUSTAINABLE PIPELINE

POTENTIAL NME PIVOTAL STUDY STARTS BY YEAR

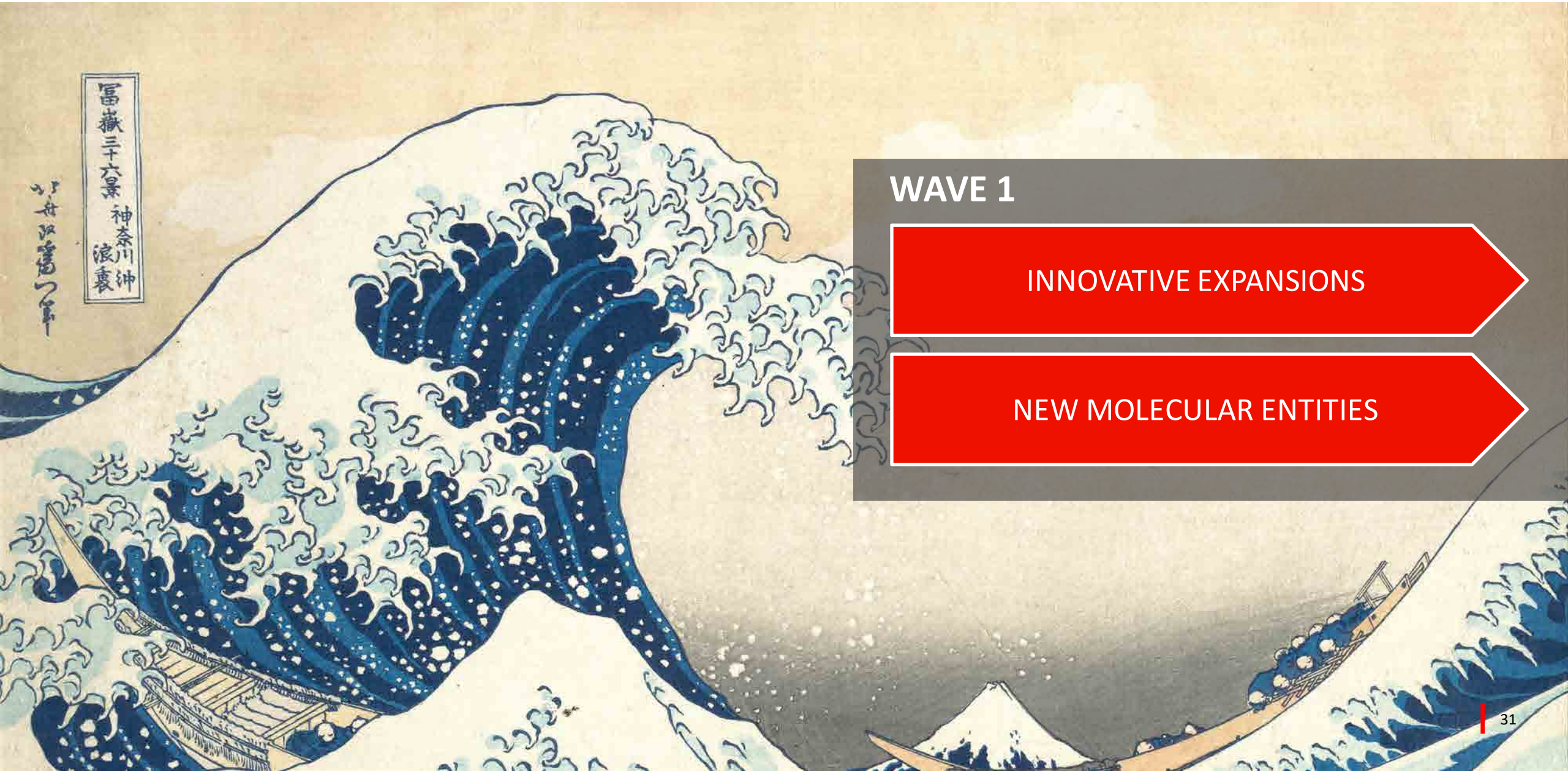


Note: Projections assume successful data readouts

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

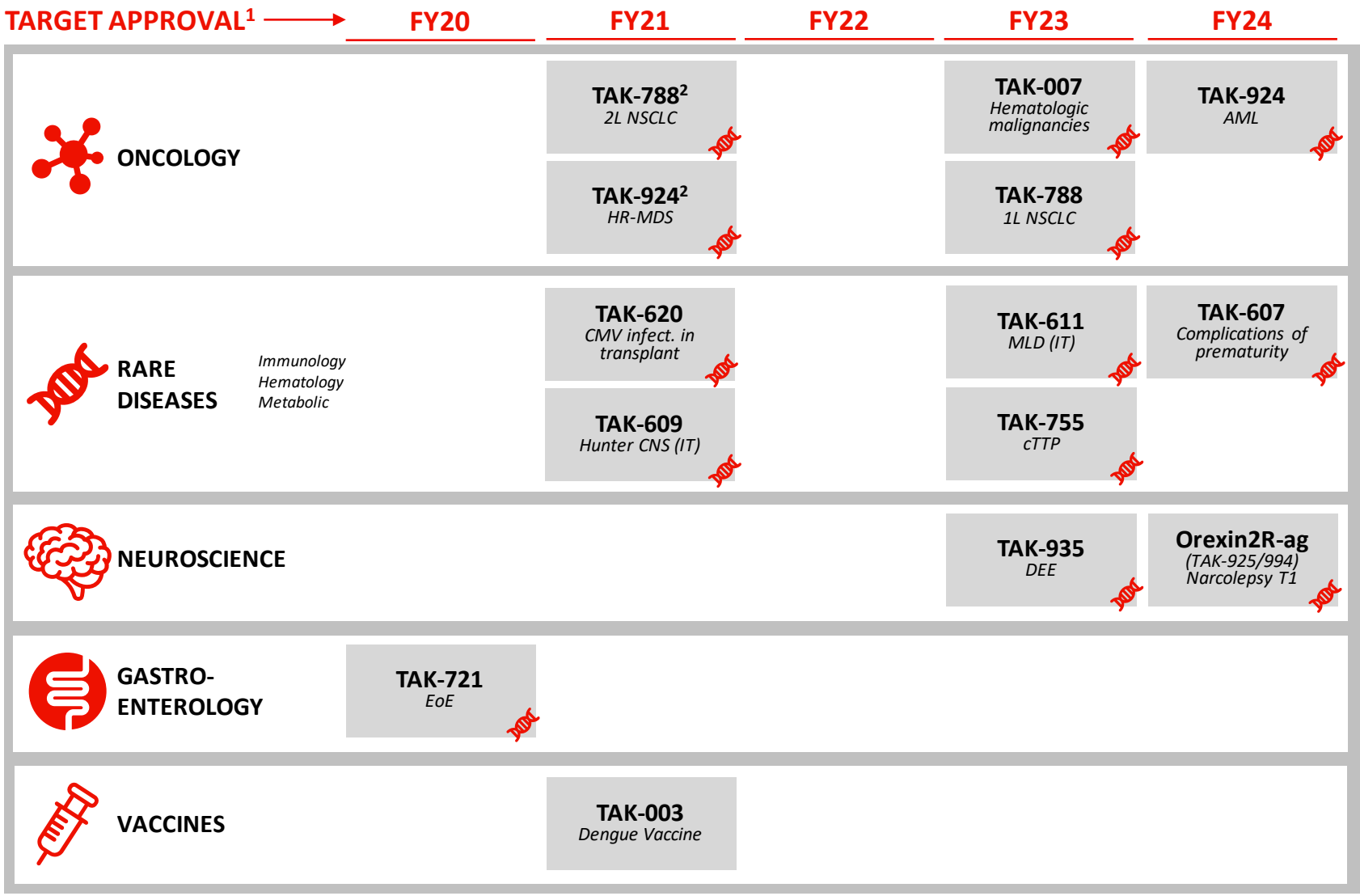
Region	Therapies
China	Entyvio® vedolizumab; ALUNBRIG® BRIGATINIB; TAKHZYRO® (lanadelumab-flyo) injection; VPRIV® velaglucerase alfa for injection; ADYNOVATE® [Antihemophilic Factor (Recombinant), PEGylated]

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…



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

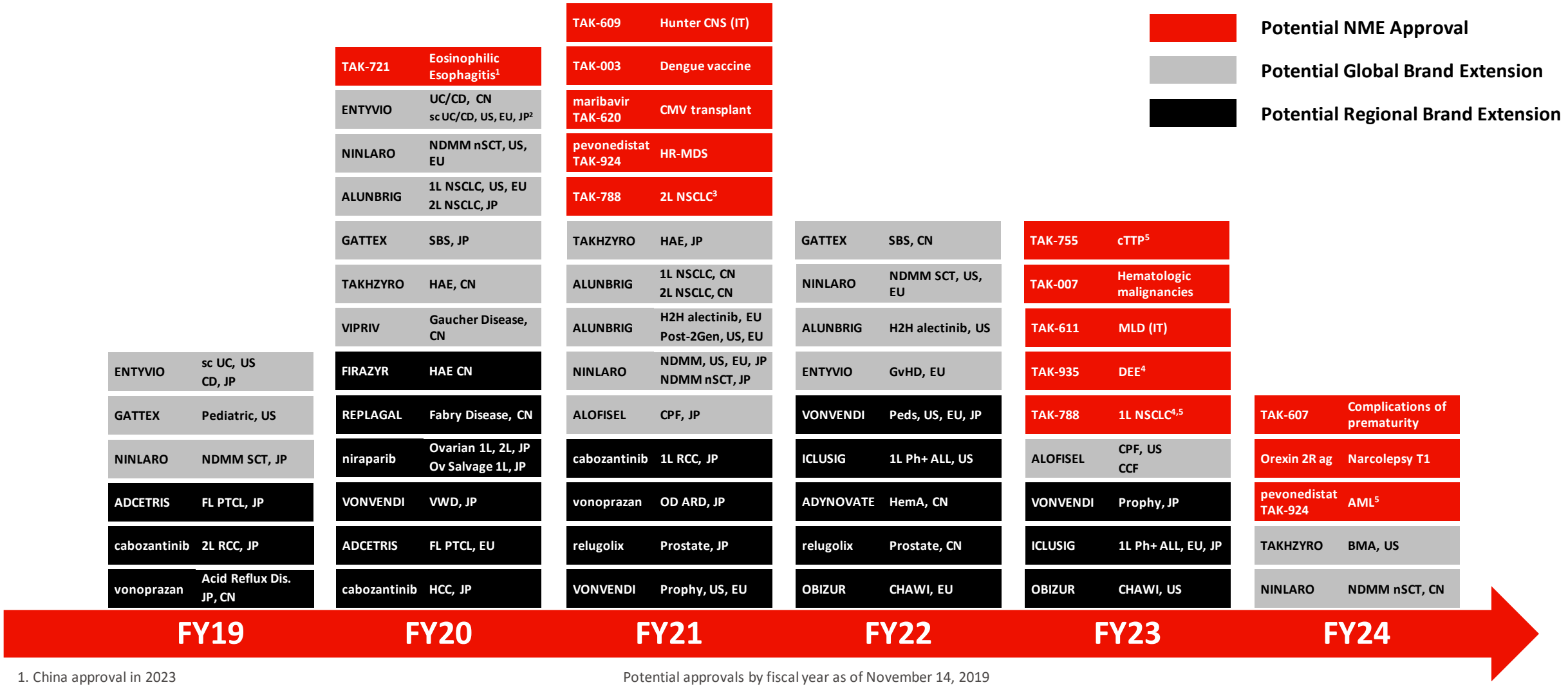
POTENTIAL FIRST-IN-CLASS OR BEST-IN-CLASS NMEs

	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

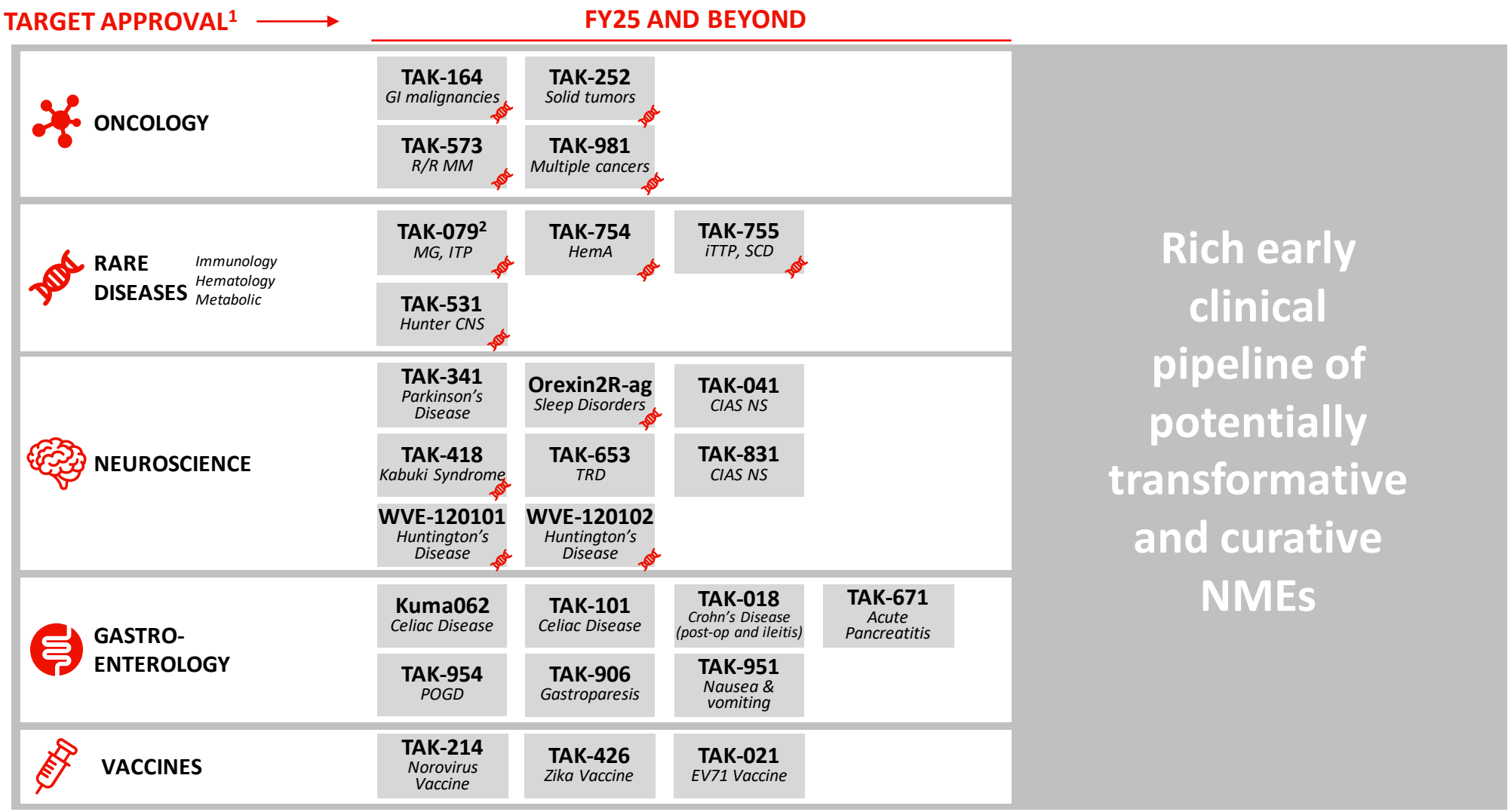
Potential approvals by fiscal year as of November 14, 2019
The target dates are estimates based on current data and subject to change

SUSTAINED GROWTH BEYOND FY25

WAVE 2

- NOVEL MECHANISMS
- NEXT-GENERATION PLATFORMS

DRIVEN BY A CLINICAL PIPELINE OF NOVEL MECHANISMS…



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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

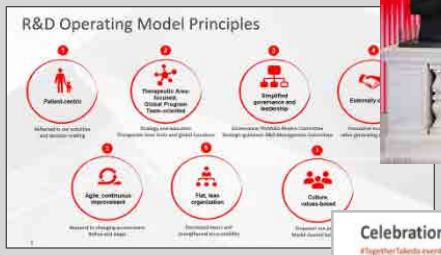
正直 Honesty

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

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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

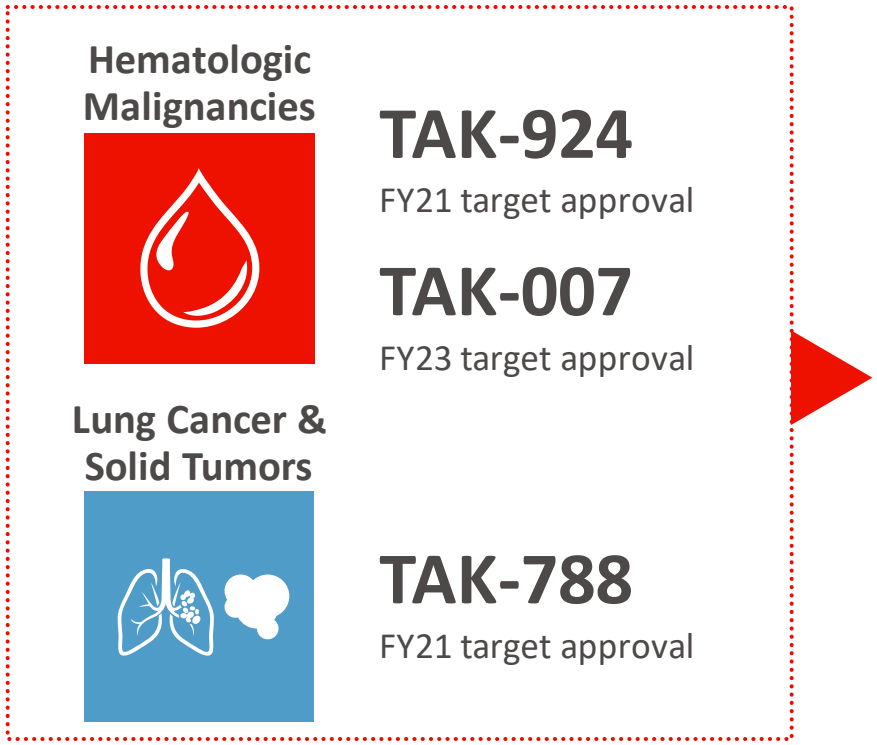
November 14, 2019

Better Health, Brighter Future

A CURATIVE-INTENT IMMUNO-ONCOLOGY PIPELINE IS TAKING SHAPE

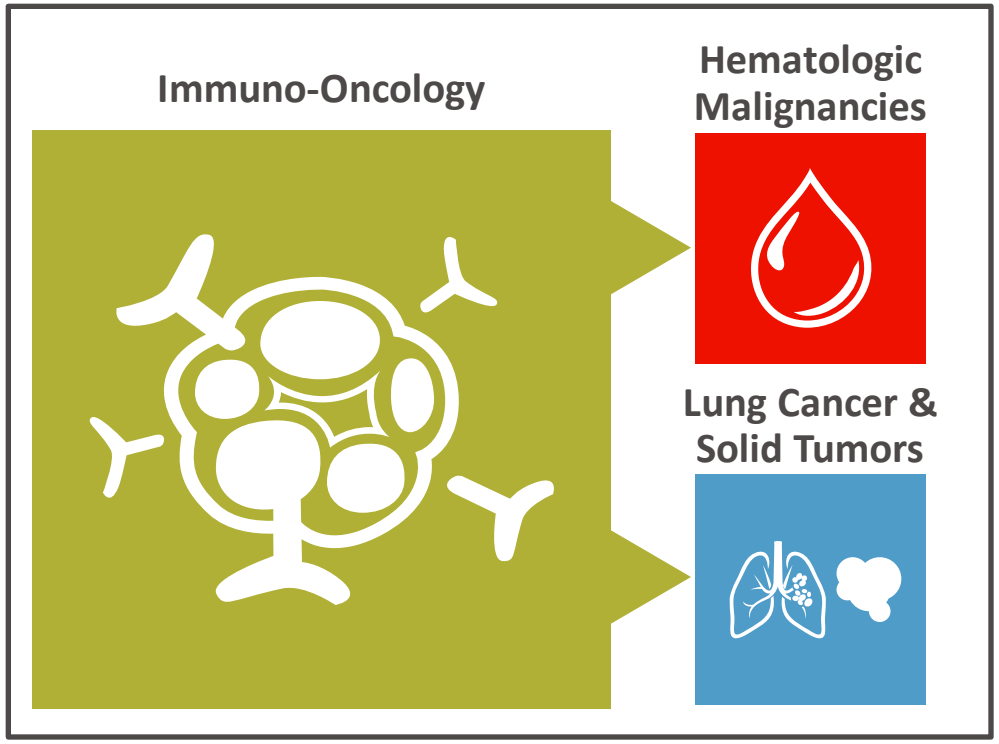
WAVE 1

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

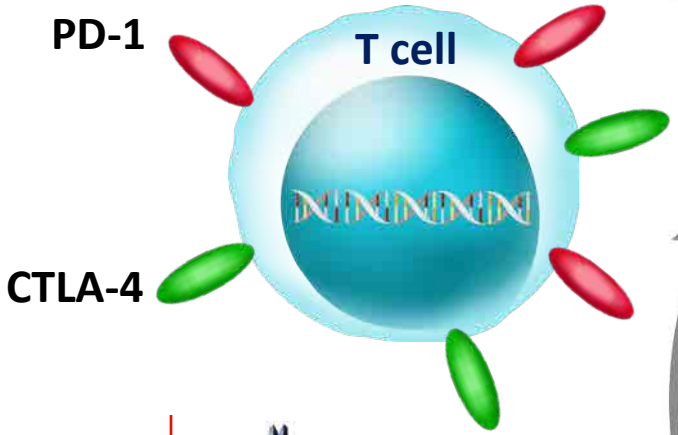
- Innovative, disruptive platforms
- Agility in ‘open lab’ model

Differentiated Portfolio

- Harness innate immunity
- Eye towards solid tumors

THE FIRST BREAKTHROUGHS IN CANCER IMMUNOTHERAPY TARGET T CELLS

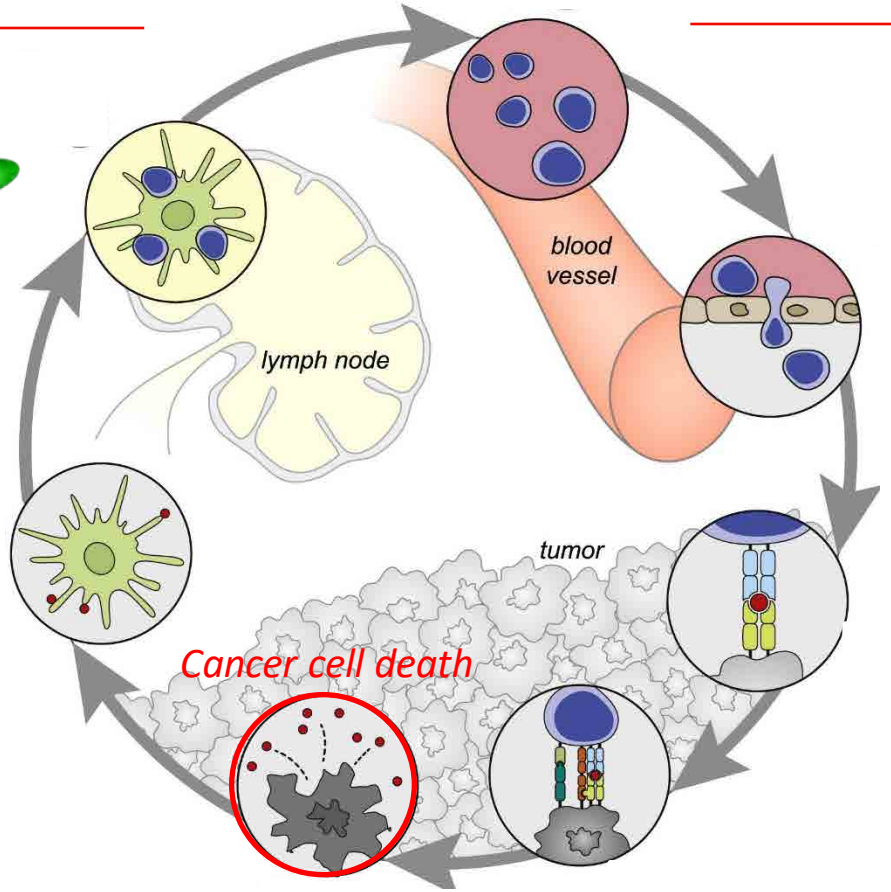
T CELL CHECKPOINT INHIBITORS



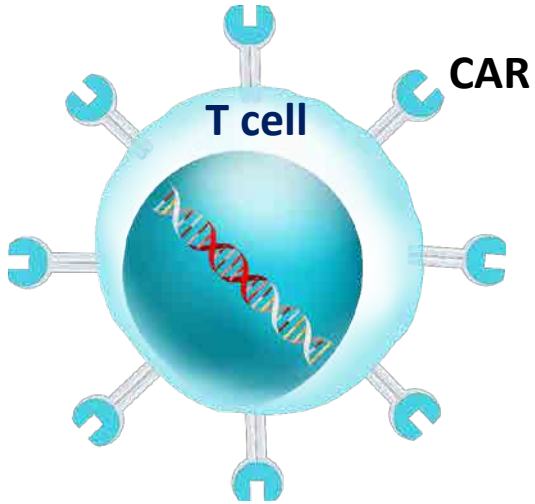
KEYTRUDA

OPDIVO (nivolumab)

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



FIRST-GEN CAR-Ts



YESCARTA (axicabtagene ciloleucel)

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

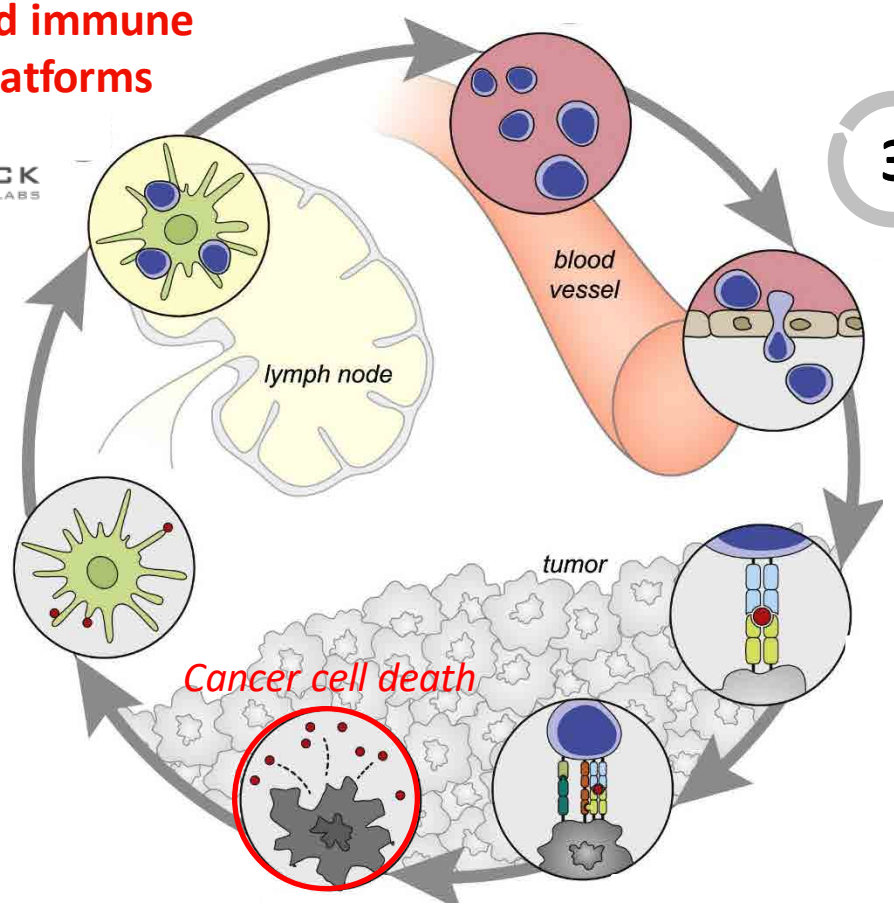
Crescendo biologics

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

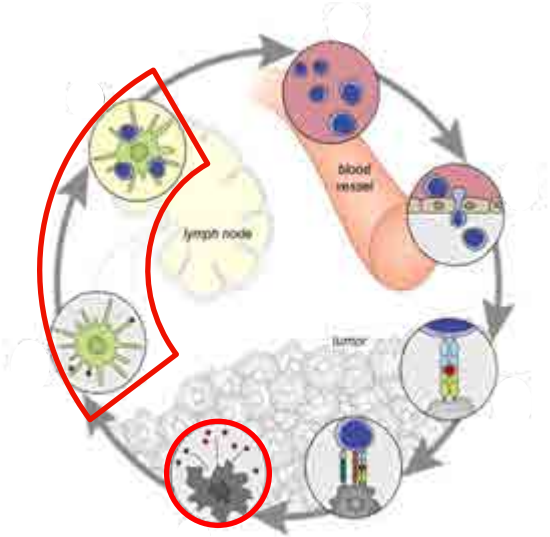
GAMMADELTA THERAPEUTICS

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	• 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™		

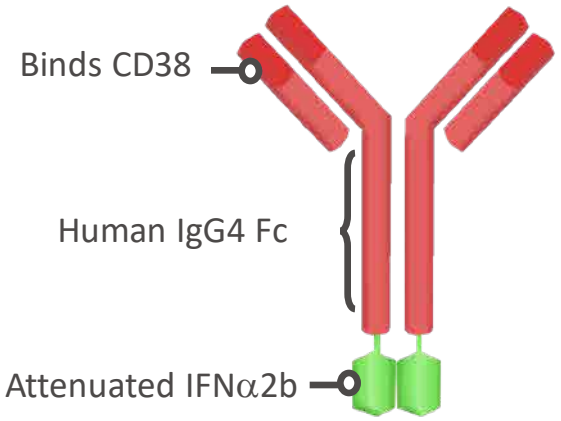
ADCC = Antibody-dependent cellular cytotoxicity

= first-in-class

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

TARGETED ATTENUATED TYPE I IFN PAYLOAD

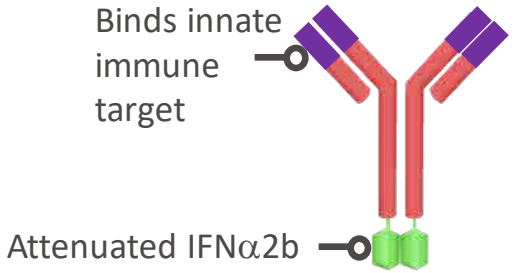
TAK-573



Immunomodulation in preclinical models

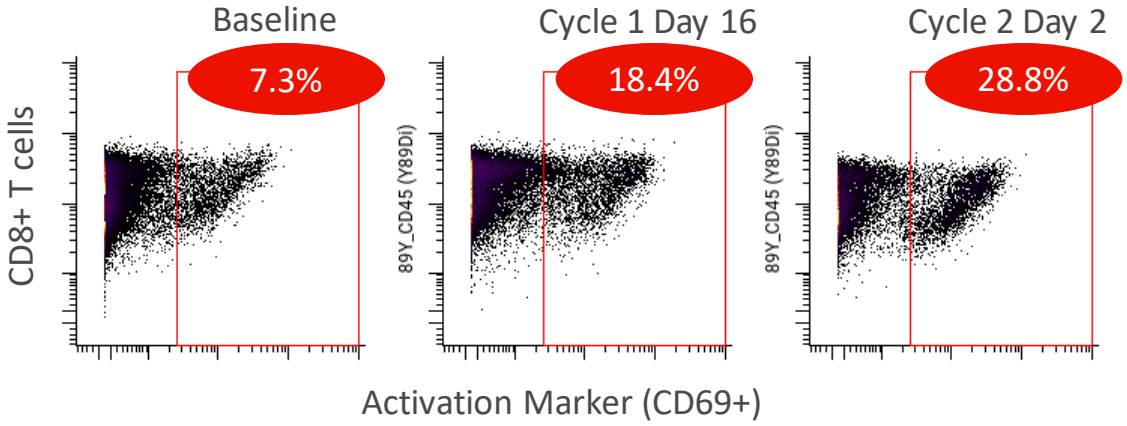
Includes CD8+ T cell migration / activation

NEXT-GEN ATTENUKINE™



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

Activation of CD8+ T cells in bone marrow

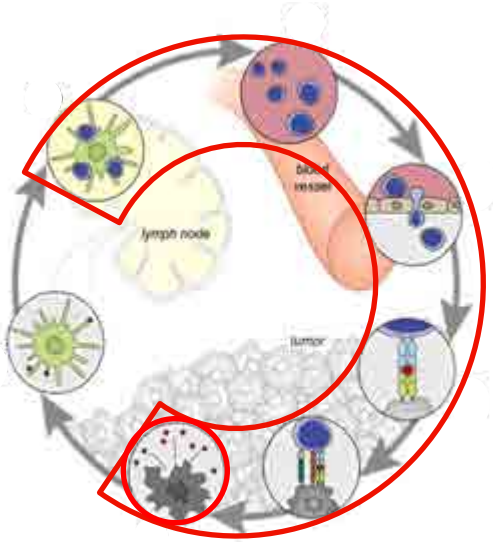


EXPECTED MILESTONES (FY)

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

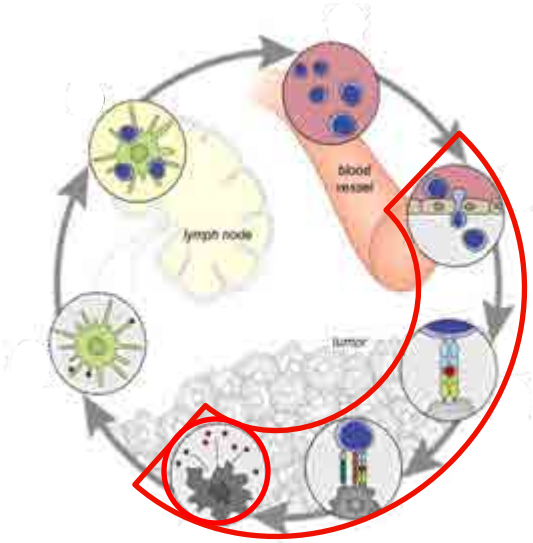
HIGH UNMET NEED	**Current checkpoint modulators fail to improve overall survival in majority of patients**
OUR DIFFERENTIATED APPROACH	**New classes of checkpoint inhibitors designed to increase breadth and depth of responses**

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)		

= first-in-class

Vh = Variable heavy domain

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

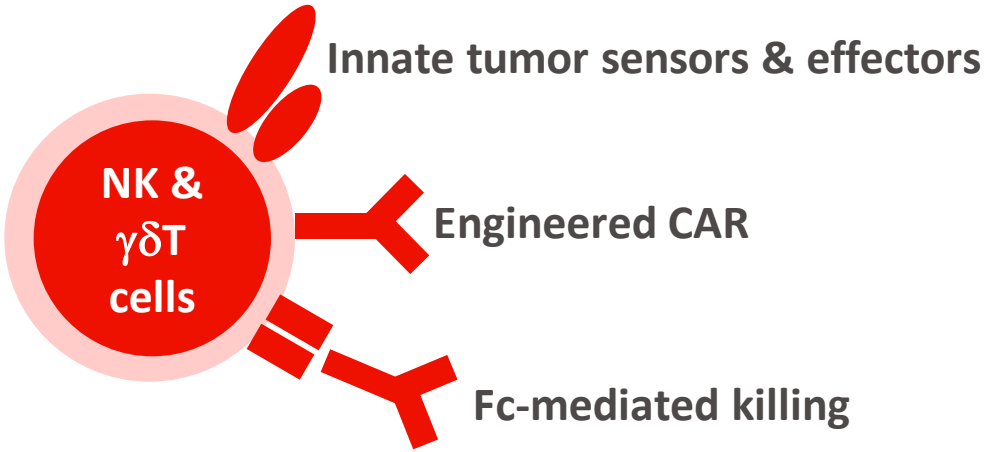


Cancer cell death

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

1 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
2016	2017	2018		2019	

★ Takeda Cell Therapy Translational Engine

★ First Development-Stage Partnership

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

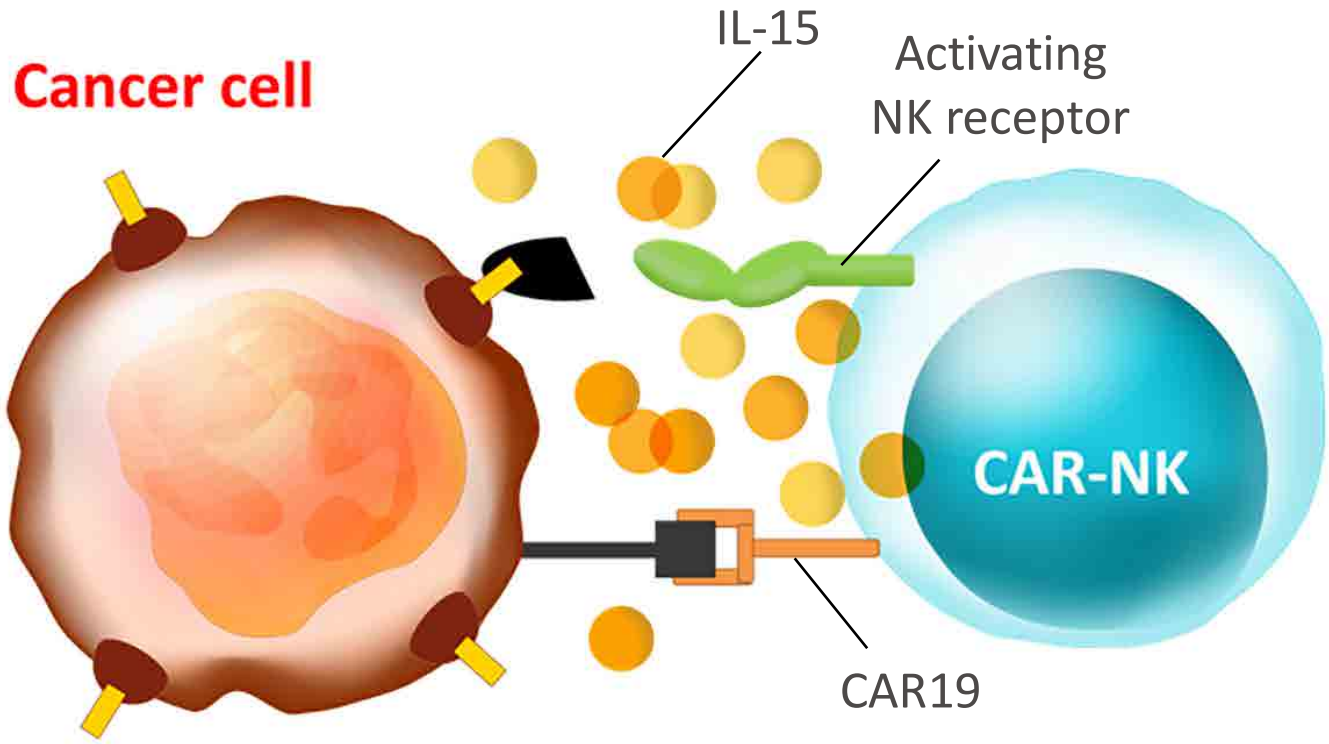
Takeda

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

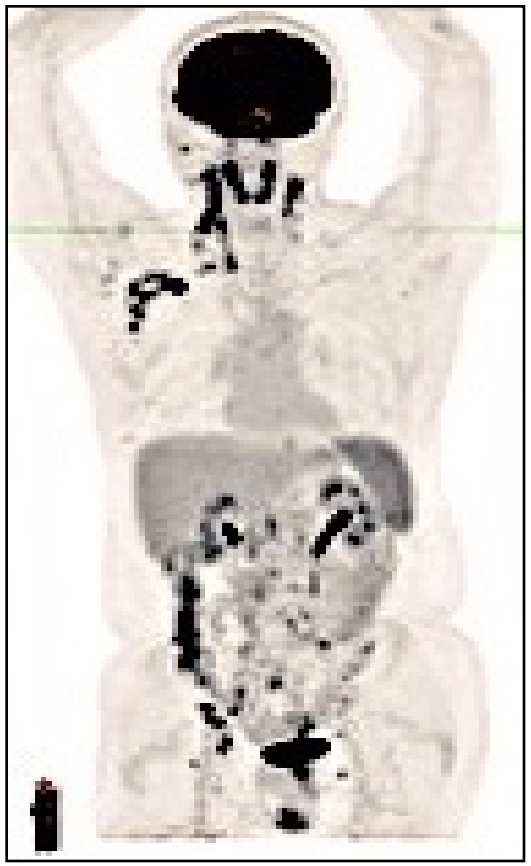
PLATFORM	PARTNER	MECHANISM-OF-ACTION	PROGRAMS	PRECLINICAL	PH 1
CAR-NK (allo cord blood)	MD Anderson Cancer Center – Dr. Katy Rezvani	• Non-autologous NK cell therapy	**TAK-007** (CD19 CAR-NK)		
			BCMA CAR-NK		
			Platform expansion		

= first-in-class

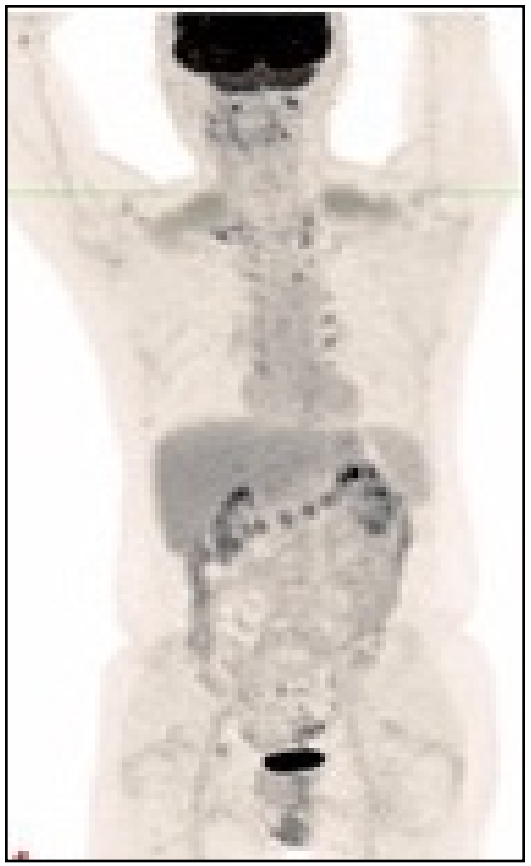
CLL = Chronic lymphocytic leukemia DLBCL = Diffuse large B-cell lymphoma iNHL = Indolent non-Hodgkin's lymphoma
*Estimated number of patients projected to be initially eligible for treatment in G7 markets, subject to regulatory approval

1 DRAMATIC COMPLETE RESPONSE IN FIRST PATIENT TREATED

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

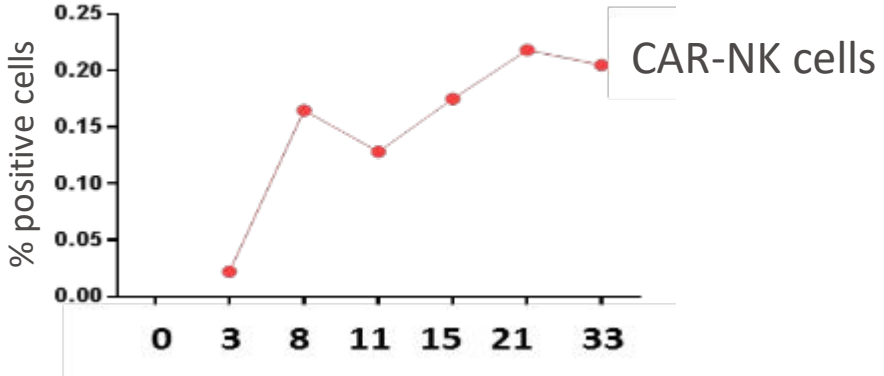


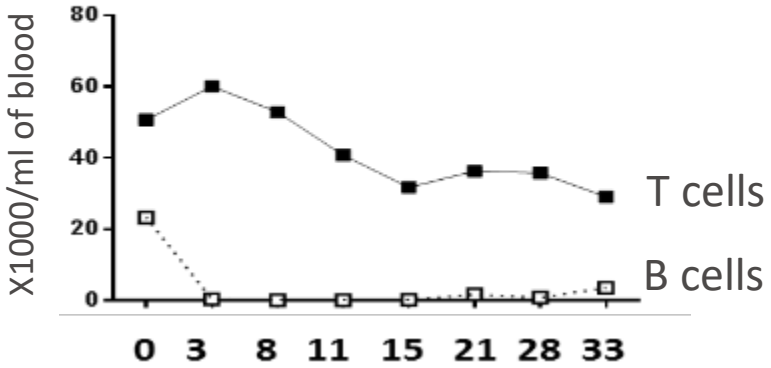
Baseline scan



Day 30 post CAR19-NK

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

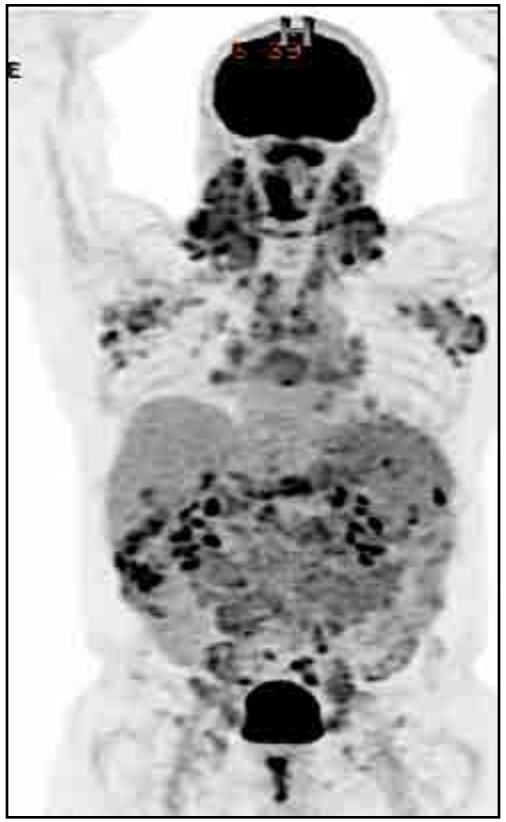




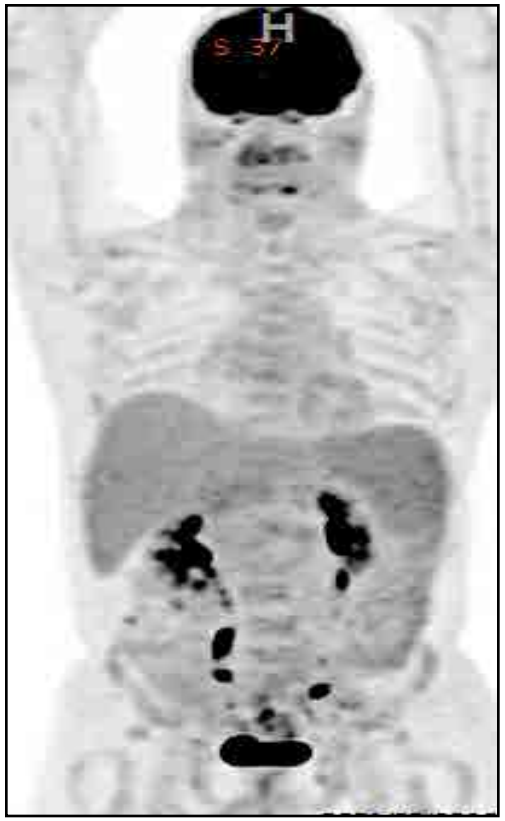
Data from Dr. Katy Rezvani, MD Anderson Cancer Center

1 IMPRESSIVE RESPONSES IN OTHER HEAVILY PRETREATED PATIENTS

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



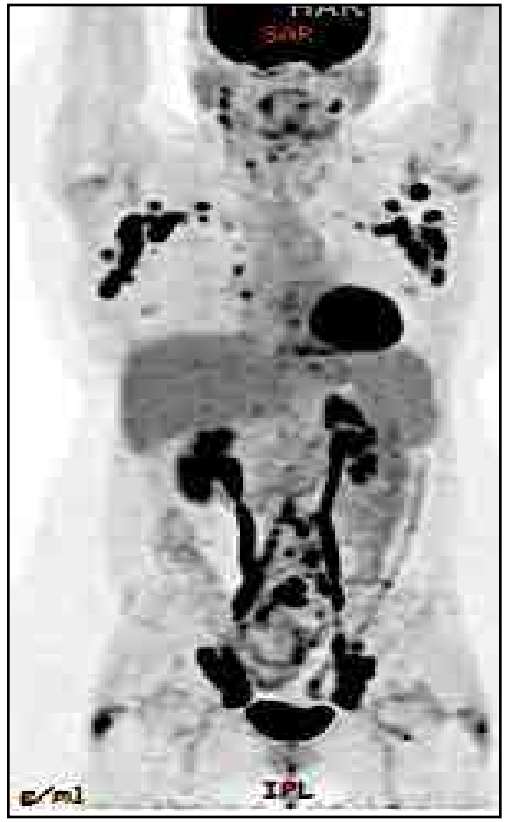
Baseline scan



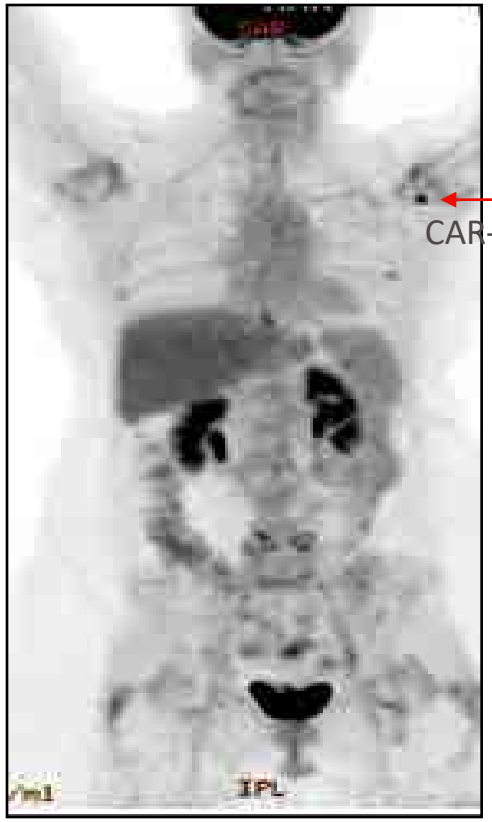
Day 30 post CAR19-NK

CR in Richter's; SD in CLL

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



Baseline scan

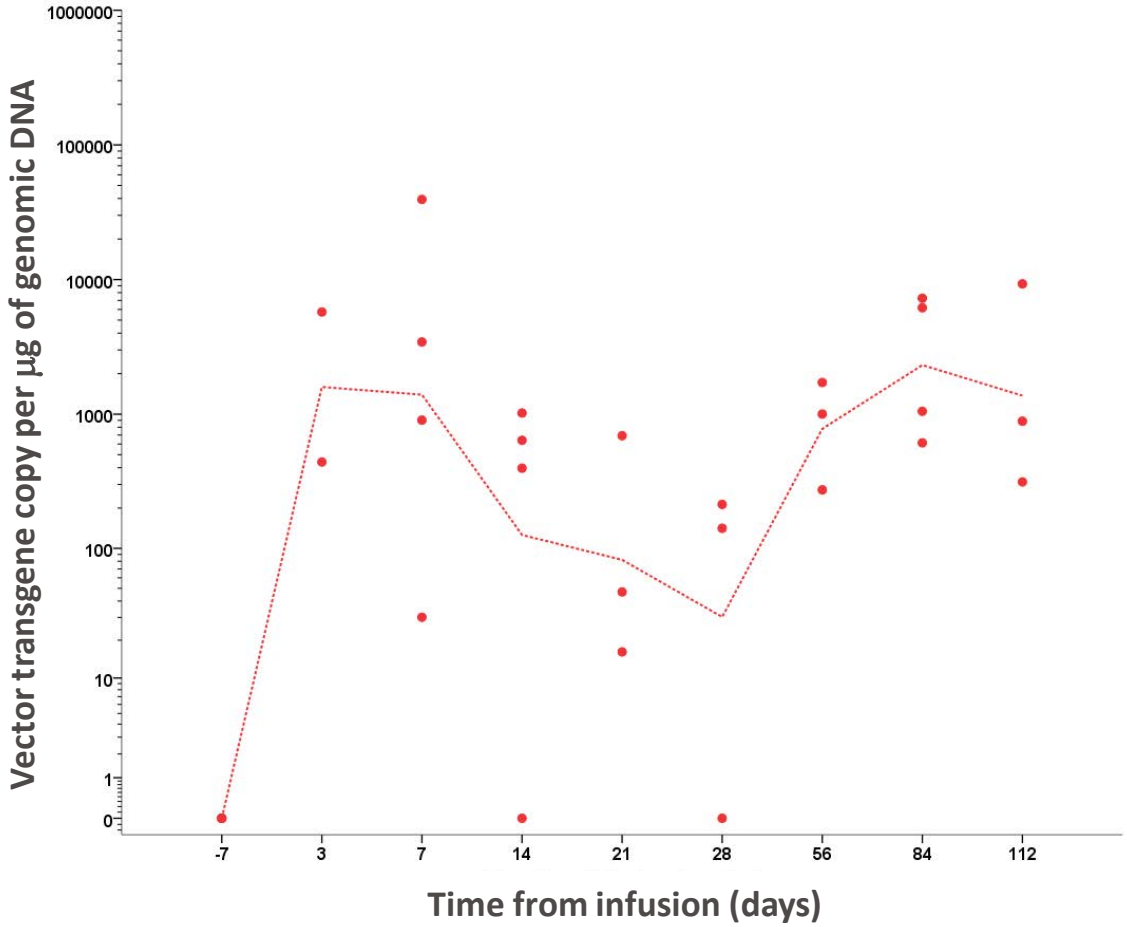


Day 30 post CAR19-NK

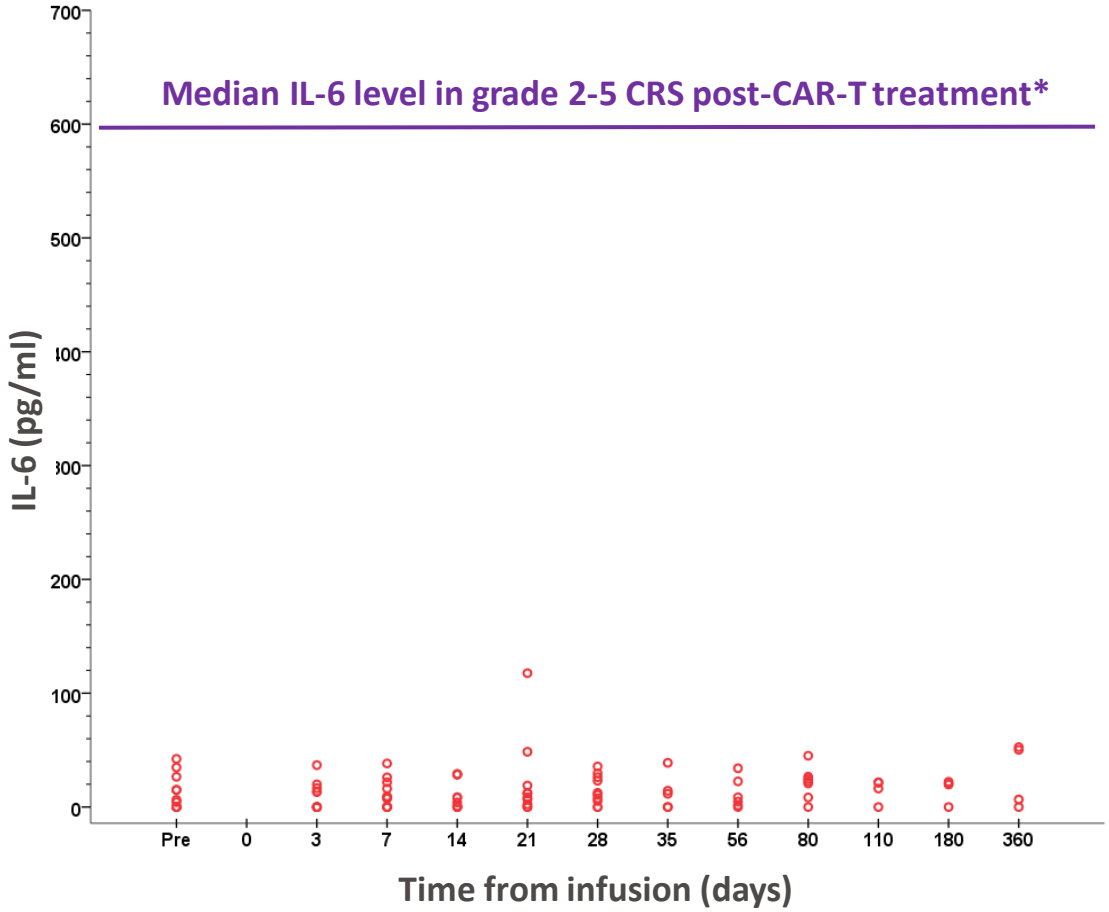
CLL = Chronic lymphocytic leukemia CR = Complete response SD = Stable disease
Data from Dr. Katy Rezvani, MD Anderson Cancer Center

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

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

FY20

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

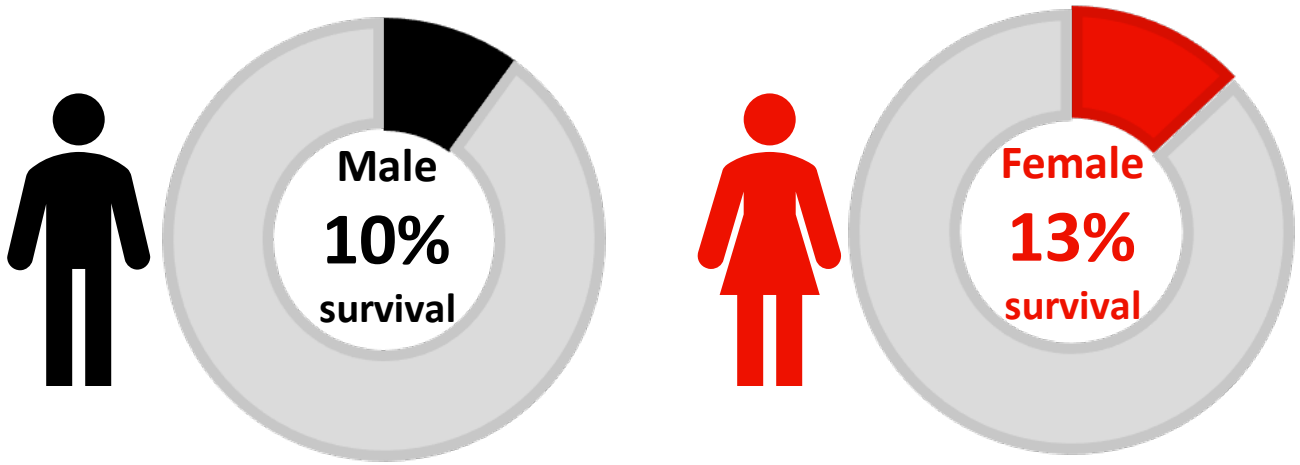
228,000[1]

New Lung cancer cases / year

143,000[1]

Lung cancer deaths/ yr
More than breast, colon, and prostate cancer <u>combined</u>

Survival of Lung cancer is amongst the lowest of all cancers

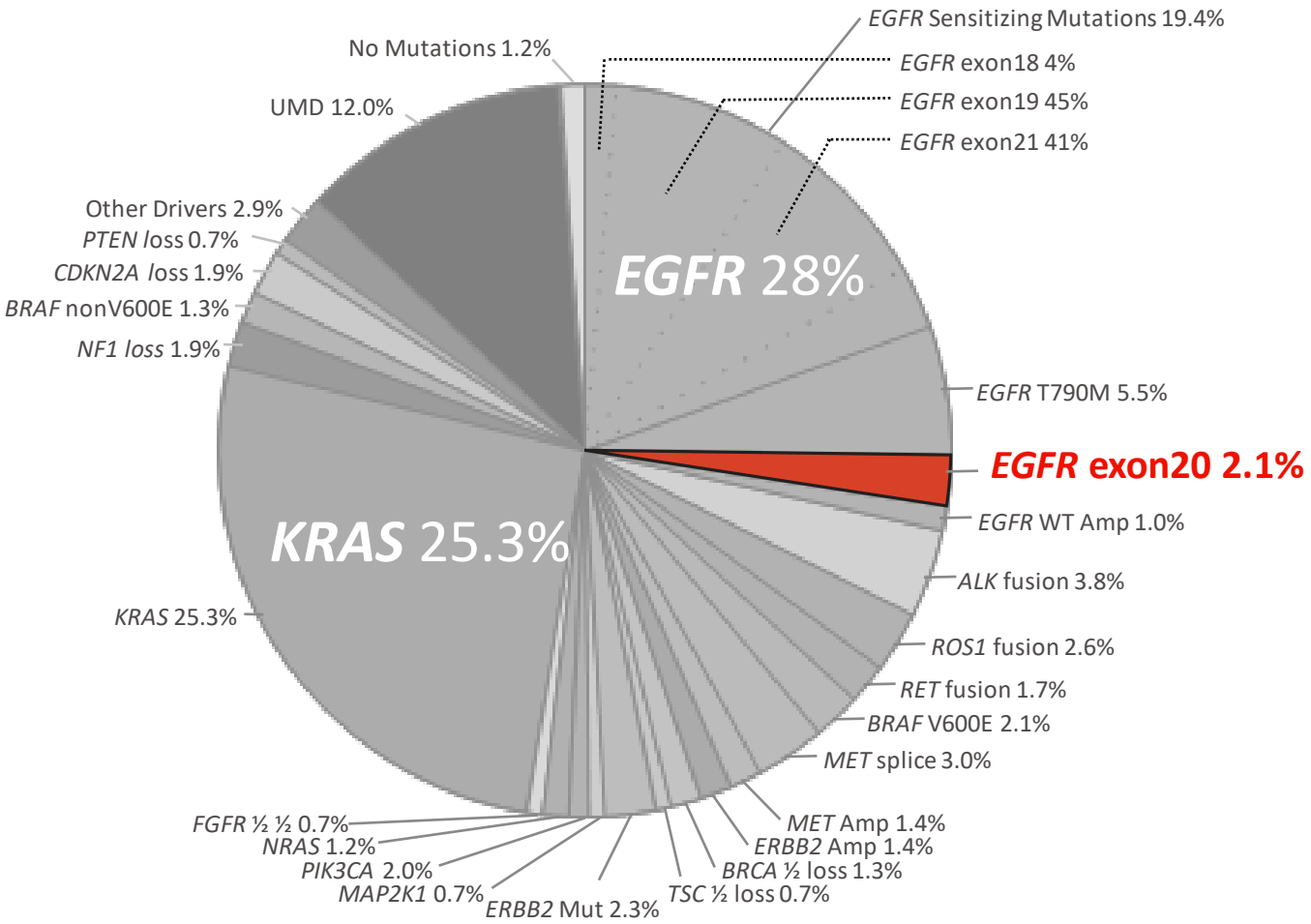


5 yr survival estimates among adults diagnosed with lung cancer between 2007-2011[2]

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%)

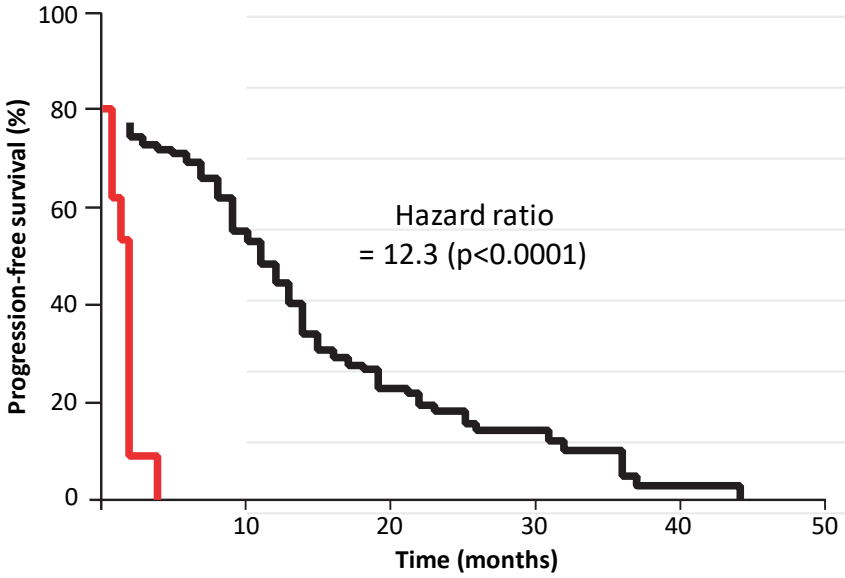
Sources: Leduc C et al., Ann Oncol 2017; Jorge S et al. Braz J Med Biol Res 2014; Kobayashi Y & Mitsudomi T. Cancer Sci 2016; Arcila M et al. Mol Cancer Ther 2013; Oxnard G et al. J Thorac Oncol 2013

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]

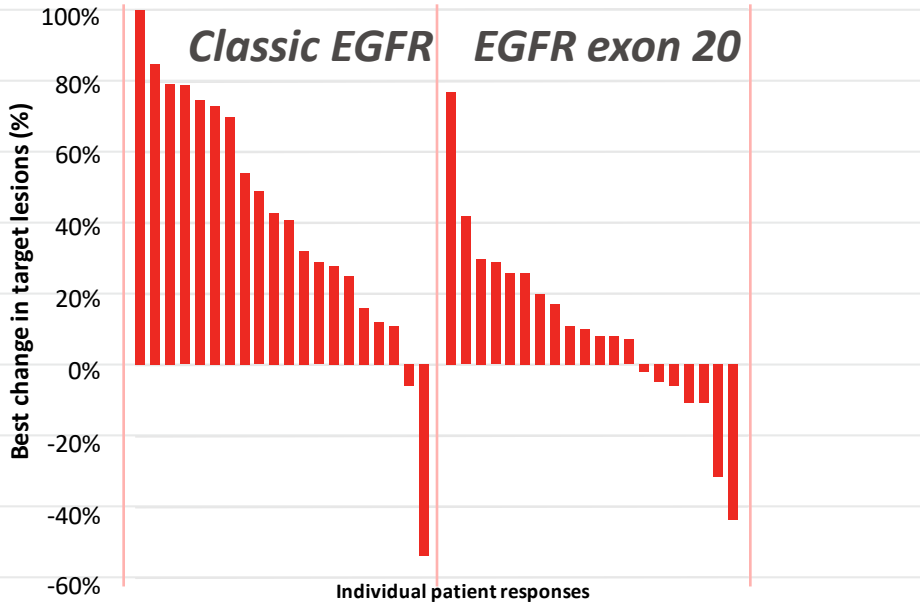
EGFR exon 20 insertions do not demonstrate significant PFS benefit with 1st and 2nd gen EGFR TKIs



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]

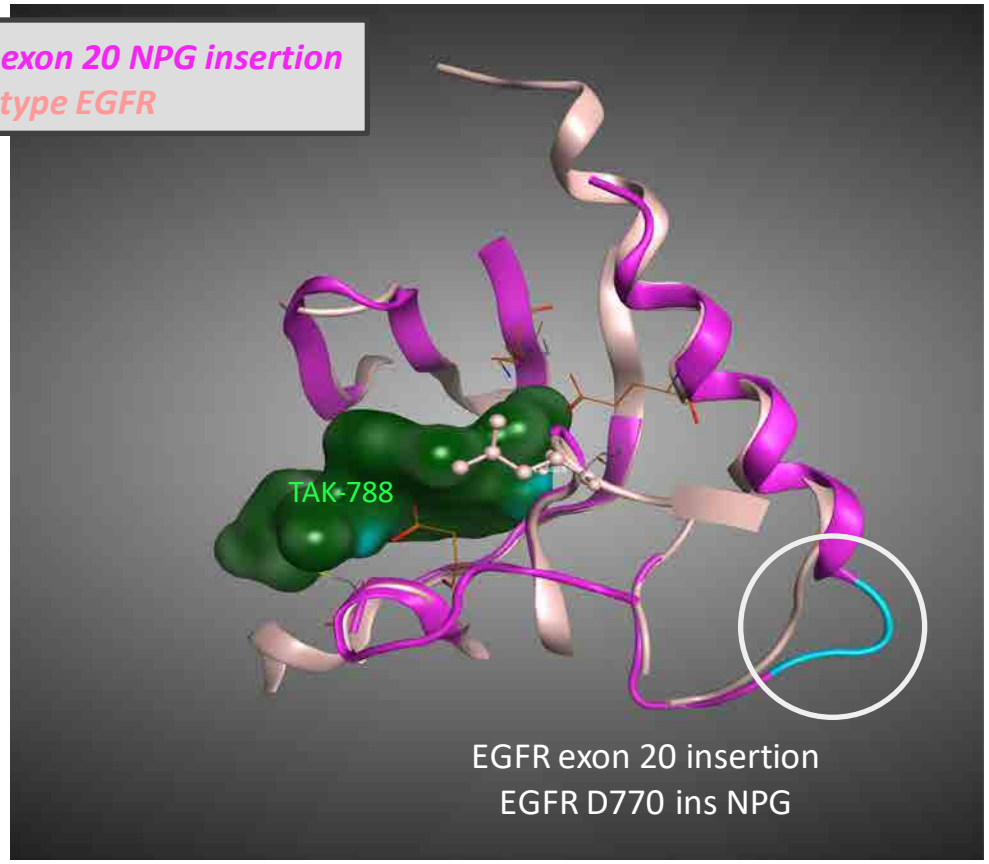
EGFR exon 20 ins patients demonstrate limited benefit to anti PD-1 directed therapy

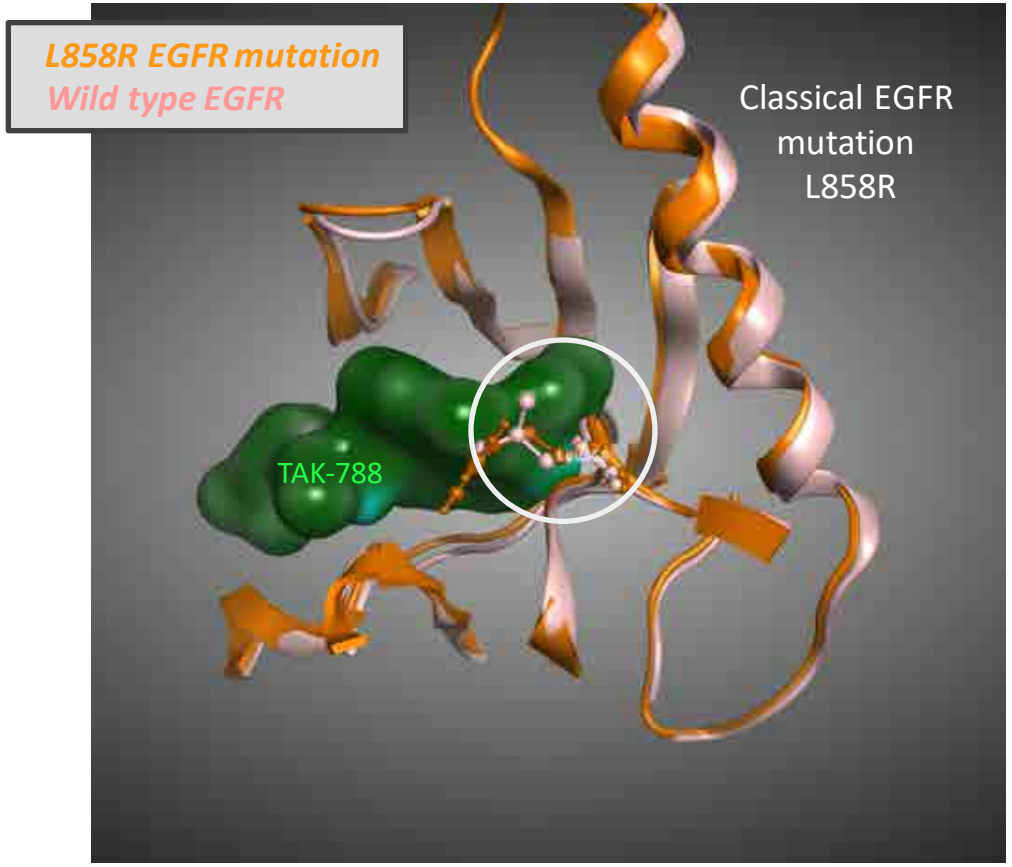


Group	Median PFS (months)	PDL-1 expression ≥1%
EGFR exon 20 ins (n=20)	2.7 (1.7-3.8)	40%
Classical EGFR mut (n=22)	1.8 (1.2-2.4)	25%

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

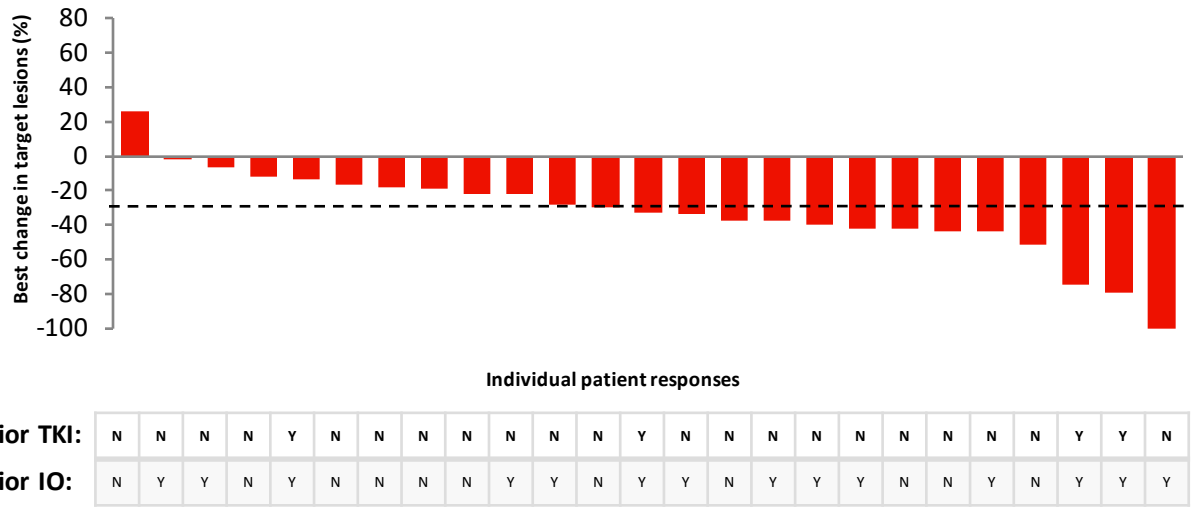
Source. TAK-788 bound to EGFR kinase domain containing D770 ins NPG, crystal structure (data on file)

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/

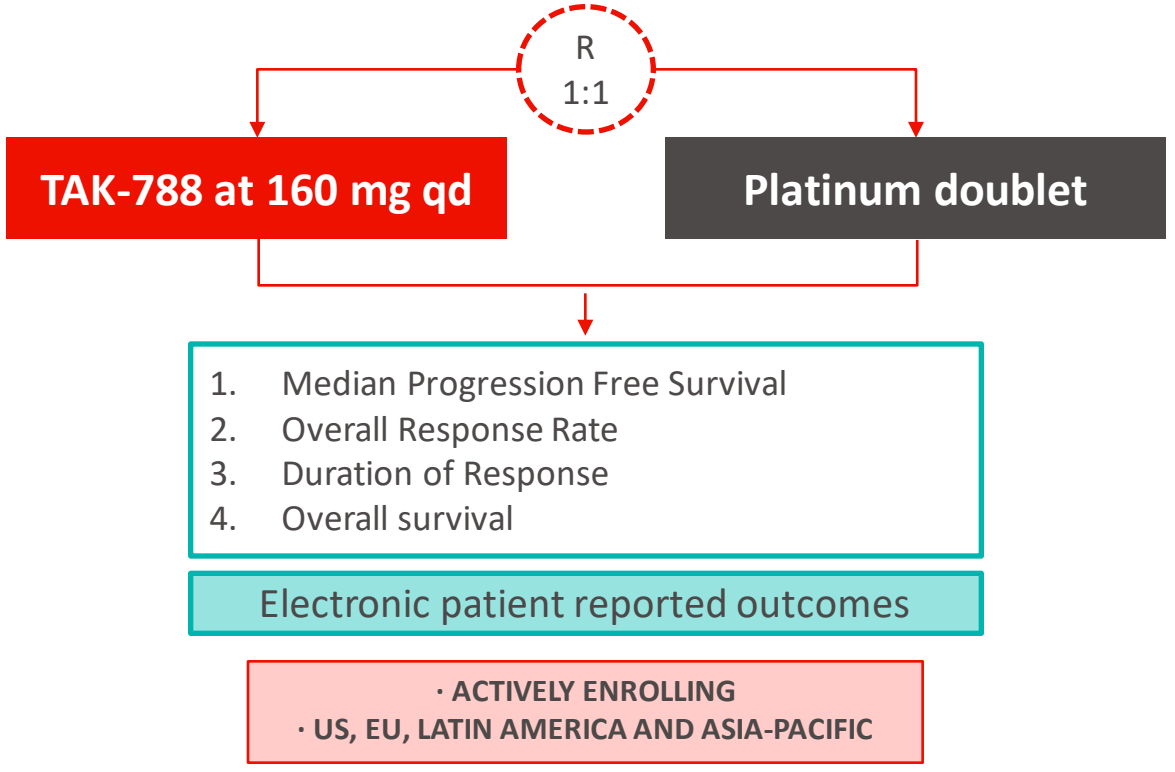
NEW ACTIVATION: A TRIAL FOR NEWLY DIAGNOSED PATIENTS

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



· ACTIVELY ENROLLING
· US, EU, LATIN AMERICA AND ASIA-PACIFIC

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