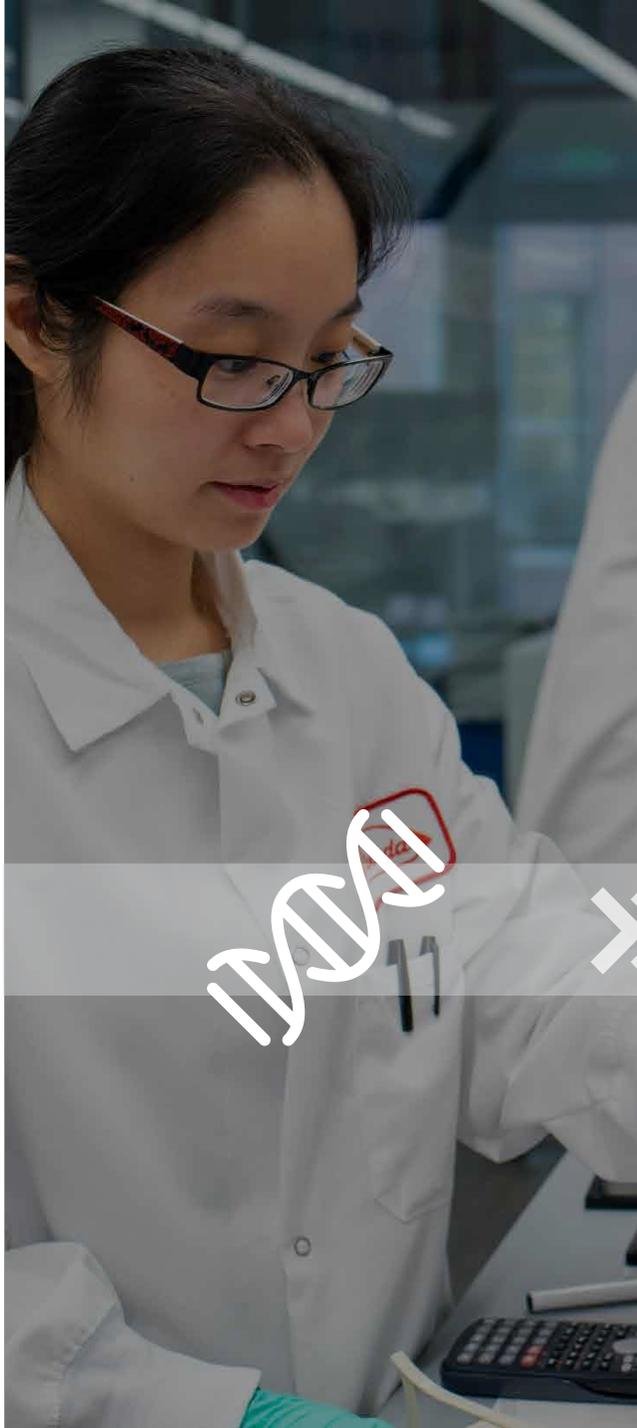


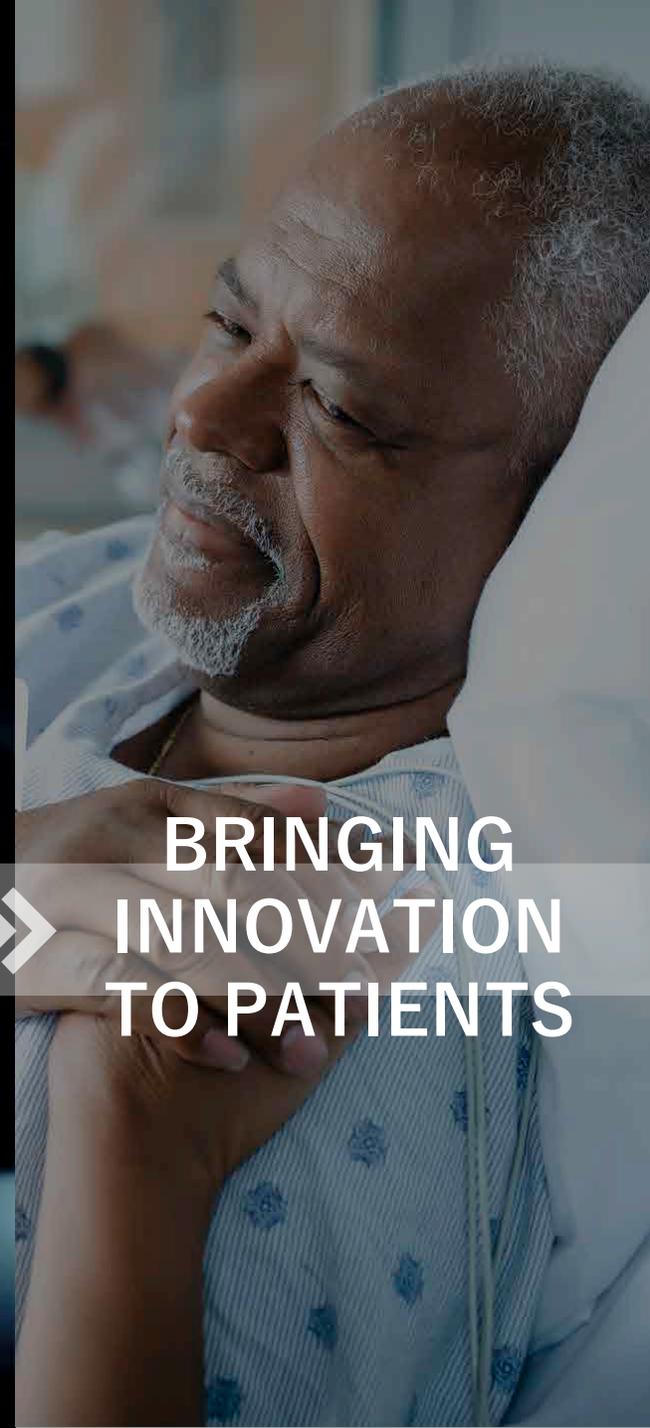
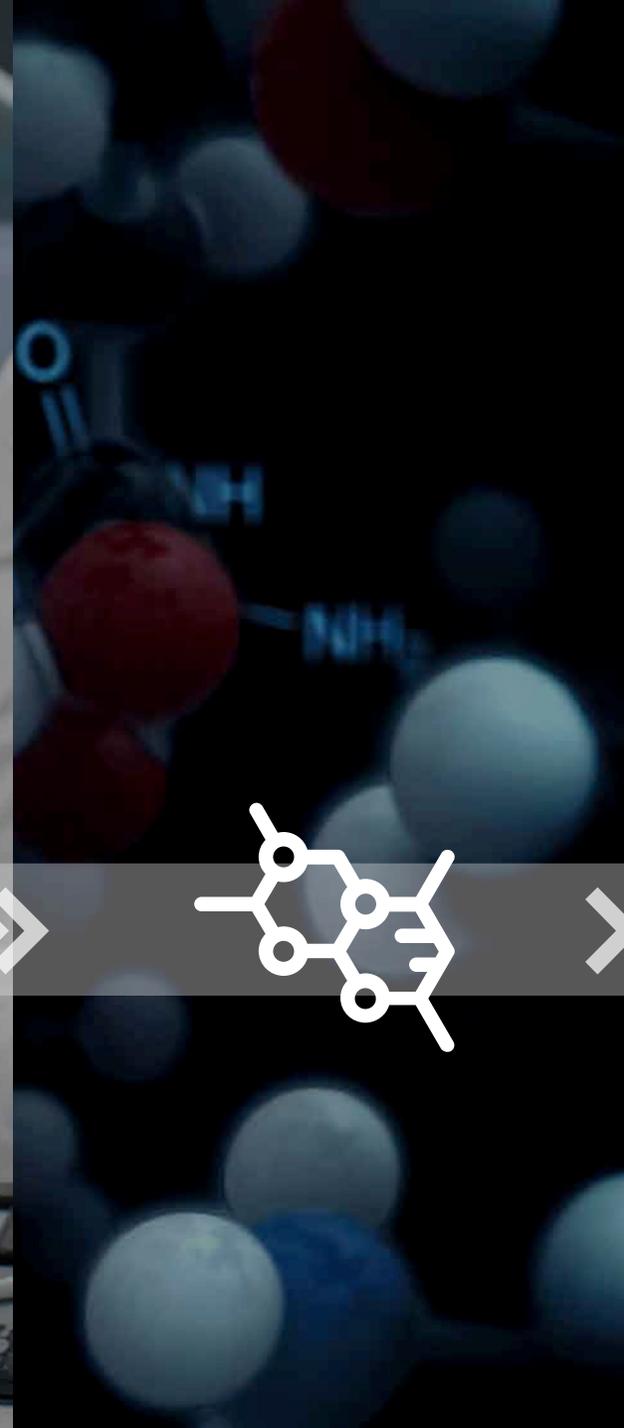
A woman with glasses and a ponytail, wearing a dark long-sleeved shirt, is holding a young child in a pink shirt and a grey hijab. She is pointing her right hand towards a city skyline with several tall buildings under a clear blue sky. The scene is brightly lit, suggesting daytime.

# **LONG-TERM VALUE FOR PATIENTS, SOCIETY AND INVESTORS**

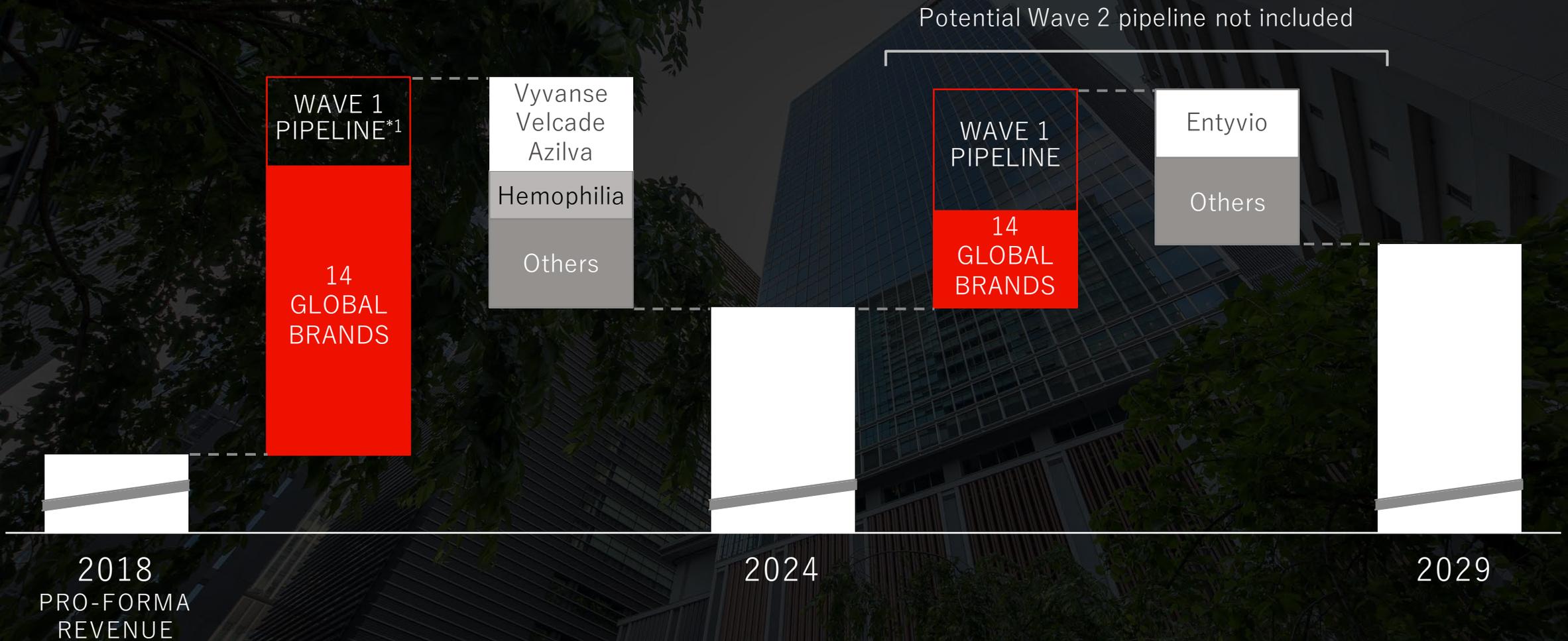
**SCIENCE  
DRIVEN  
COMPANY  
WITH A  
FOCUSED  
MIND**



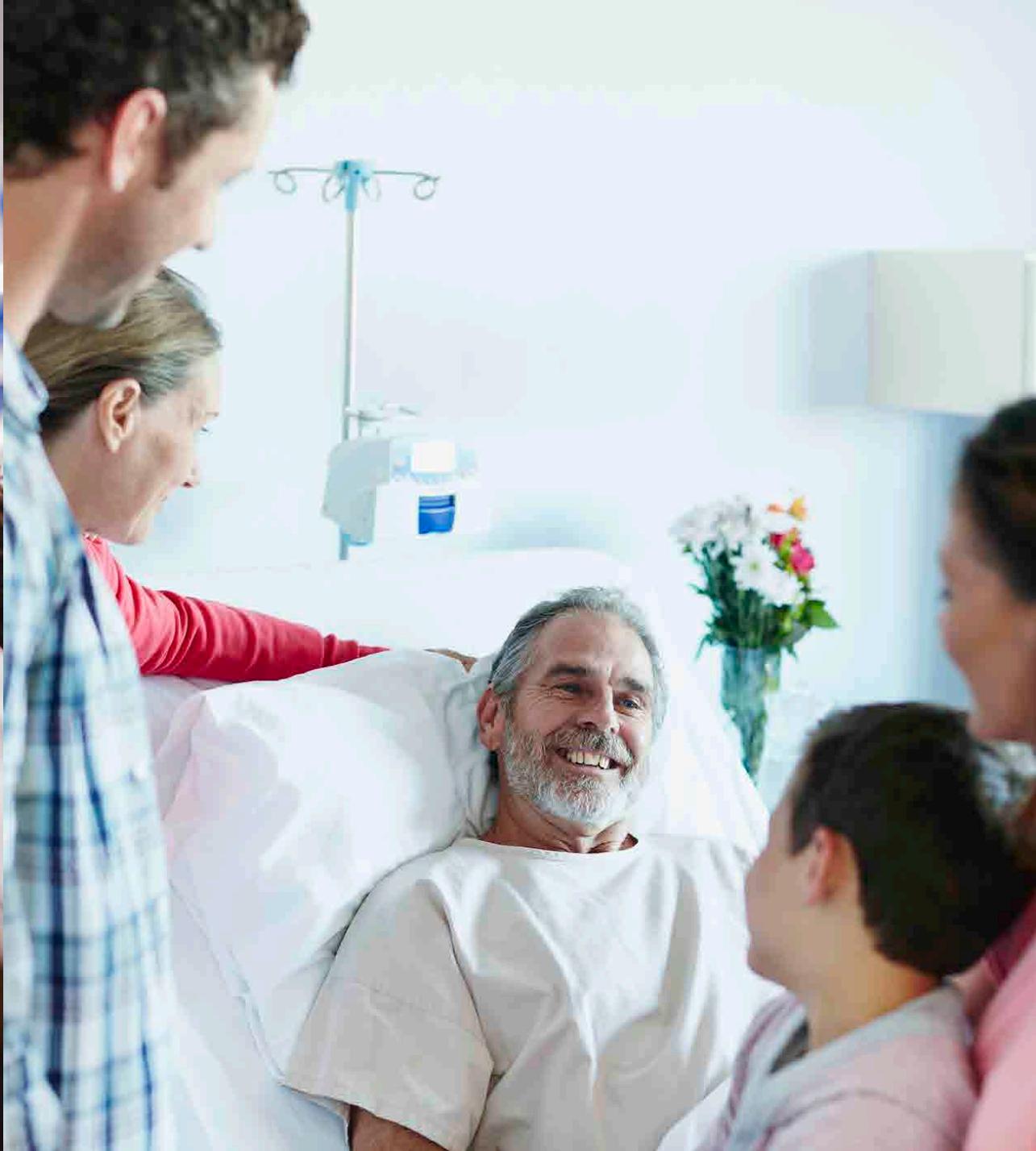
**BRINGING  
INNOVATION  
TO PATIENTS**



# 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.



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



TIME	AGENDA
12:30 – 12:35	<b>Welcome and Opening Remarks</b> <i>Sheelagh Cawley-Knopf, Head R&amp;D Global Portfolio Strategy</i>
12:35 – 12:45	<b>Takeda: A Global Values-Based, R&amp;D-Driven Biopharmaceutical Leader</b> <i>Christophe Weber, President &amp; CEO Takeda</i>
12:45 – 13:20	<b>Translating Science into Highly Innovative, Life-changing Medicines</b> <i>Andy Plump, President R&amp;D</i>
13:20 – 13:45	<b>Oncology and Cell Therapies with Spotlight on CAR-NK</b> <i>Chris Arendt, Head Oncology Drug Discovery Unit</i>
13:45 – 14:05	<b>Spotlight on Oncology Opportunities</b> <ul style="list-style-type: none"><li>• <b>TAK-788</b> : <i>Rachael Brake, Global Program Lead</i></li><li>• <b>Pevonedistat</b> : <i>Phil Rowlands, Head Oncology Therapeutic Area Unit</i></li></ul>
14:05 – 14:20	<b>Break</b>
14:20 – 14:45	<b>Rare Diseases &amp; Gene Therapy</b> <i>Dan Curran, Head Rare Disease Therapeutic Area Unit</i>
14:45 – 15:00	<b>Spotlight on Orexin2R agonists</b> <i>Deborah Hartman, Global Program Lead</i>
15:00 – 15:20	<b>Therapeutic Area Focus in GI with Spotlight on Celiac Disease</b> <i>Asit Parikh, Head GI Therapeutic Area Unit</i>
15:20 – 16:00	<b>Panel Q&amp;A Session</b>
16:00	<b>Drinks reception</b>



# 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

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

## INNOVATIVE BIOPHARMA



ONCOLOGY



RARE DISEASES



NEUROSCIENCE



GASTROENTEROLOGY

## PLASMA DERIVED THERAPIES



Complementing our  
rare disease focus

## VACCINES BUSINESS UNIT



Differentiated  
Dengue vaccine

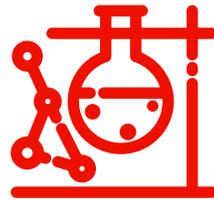
# WE ARE DOING MORE FOR OUR PATIENTS



8



POTENTIAL BIC/FIC NMEs IN PIVOTAL STUDIES<sup>1</sup>

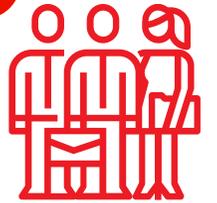


~40

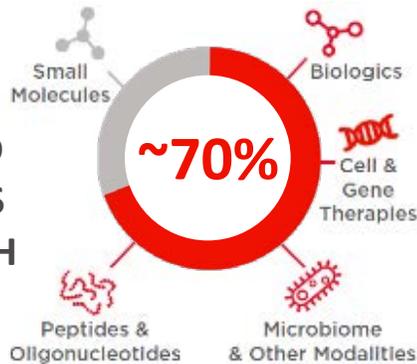
NEW MOLECULAR ENTITY CLINICAL STAGE ASSETS

~4,500

R&D EMPLOYEES GLOBALLY



DIVERSIFIED MODALITIES IN RESEARCH



PIPELINE WITH ORPHAN DRUG DESIGNATION<sup>2</sup>



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

*“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”*

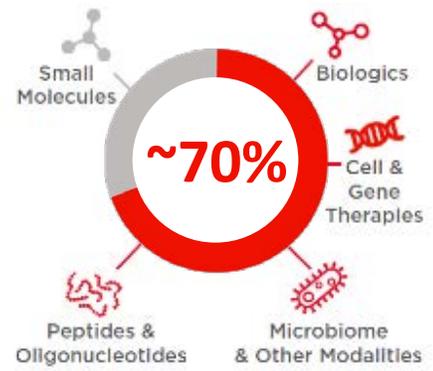


Dr. Makoto Honda, Sleep Disorders Project Leader, Tokyo Metropolitan Institute of Medical Science

Data presented at World Sleep conference

**NOVEL TARGET  
MECHANISMS WITH  
HUMAN VALIDATION**

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



**MODALITY  
DIVERSIFICATION**

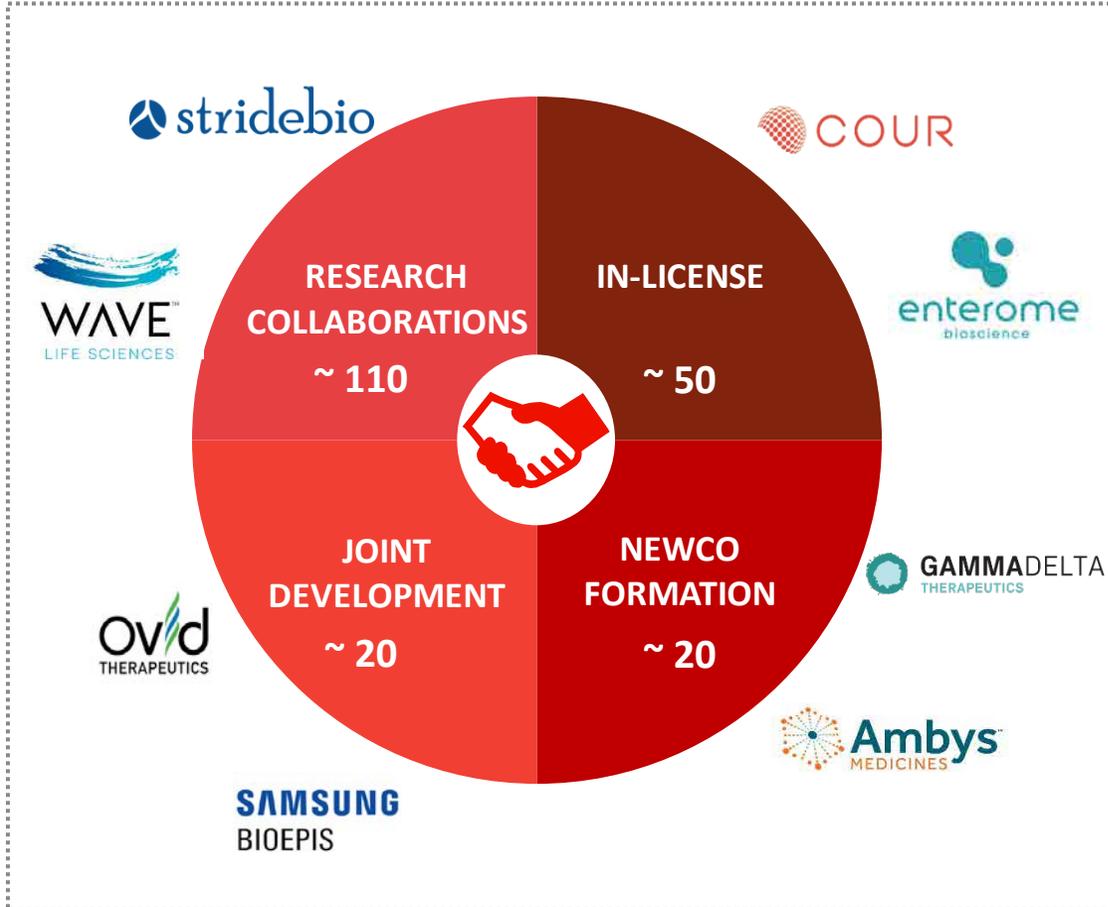
- 5** Accelerated programs
- 20** NME stage-ups since FY18
- 19** Indications terminated or externalized since FY18

**FAST GO / NO-GO  
DECISION MAKING**

# WE ARE CULTIVATING THE BEST SCIENCE THROUGH DIFFERENTIATED PARTNERSHIPS...



Select partnerships\*



\* Externalizations and venture investments are not included

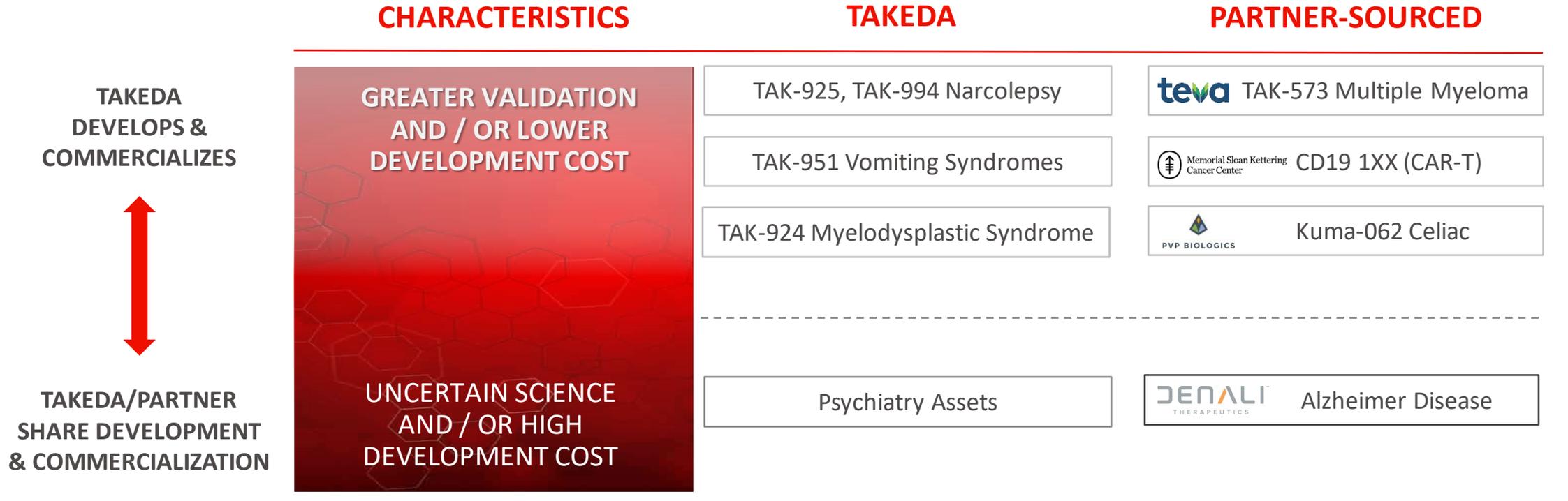
○ Access to Innovation

○ Risk-Sharing

○ Expanding Capacity

Total Value in Public & Private Equity  
**>\$1B**

# WE ARE NURTURING INNOVATION WHEREVER IT OCCURS



# 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



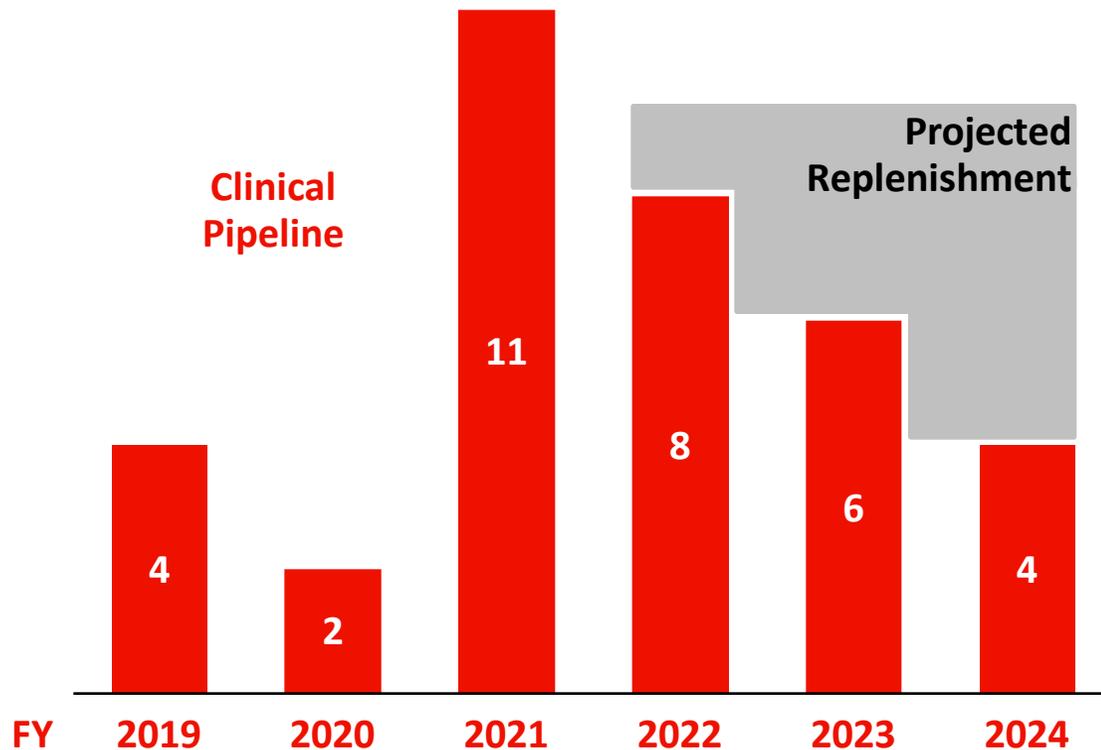
### PARTNERSHIP MODEL

Success driven milestone payments

# A RESEARCH ENGINE FUELING A SUSTAINABLE PIPELINE



## POTENTIAL NME PIVOTAL STUDY STARTS BY YEAR

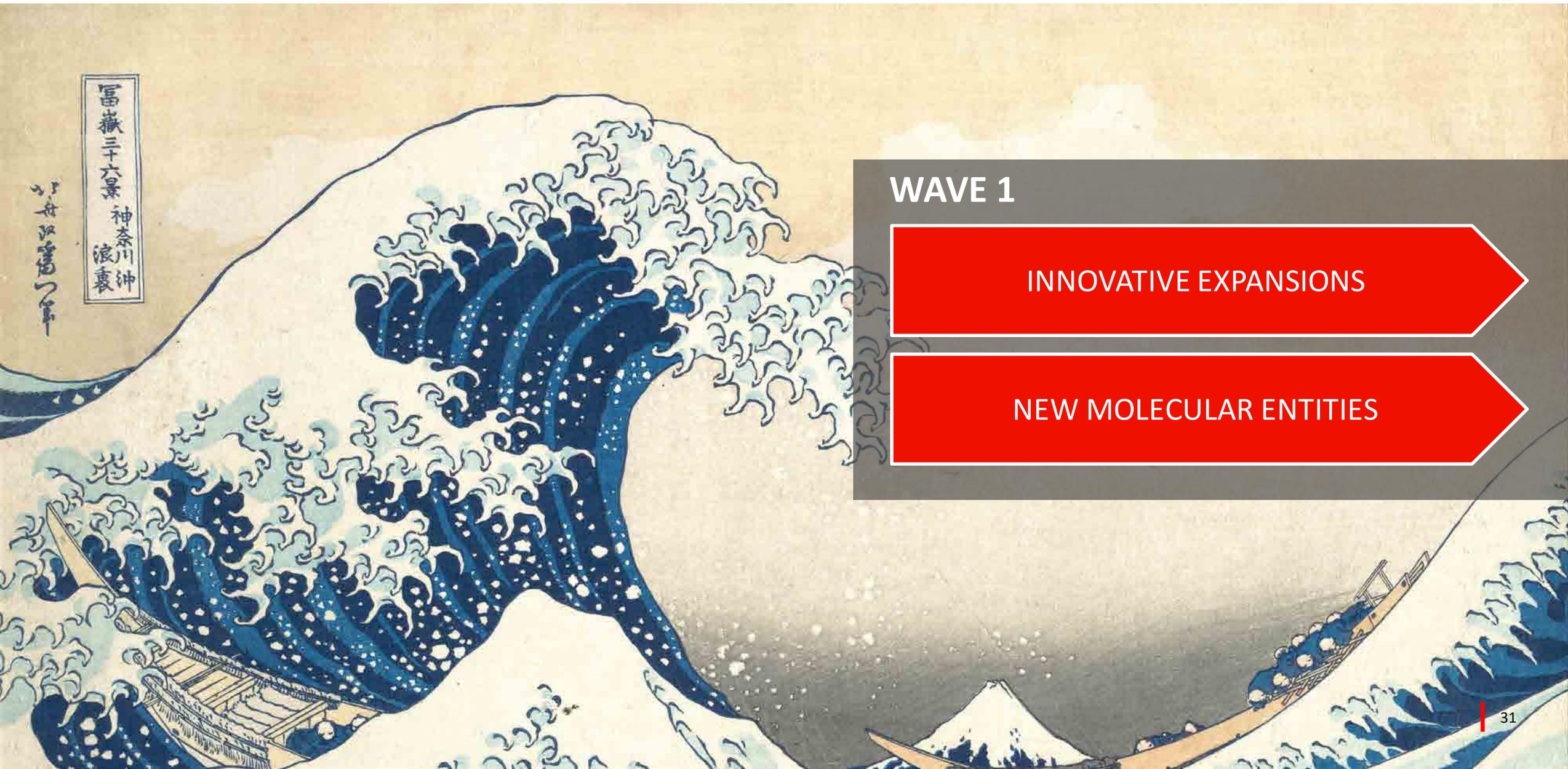


Note: Projections assume successful data readouts

## 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)
 <b>ONC</b>	 ALUNBRIG <sup>®</sup> BRIGATINIB 80mg TABLETS	1L Non Small Cell Lung Cancer	2020
	 NINLARO <sup>®</sup> (ixazomib) capsules	ND MM Maintenance (non-SCT and post-SCT)	2020 / 2022
 <b>Rare</b>	 TAKHZYRO <sup>®</sup> (lanadelumab-lyo) injection	Bradykinin Mediated Angioedema	2024
	 vonvendi*	Prophylactic Treatment of von Willebrand Disease	2021
 <b>GI</b>	 Entyvio <sup>®</sup> 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	Region	Therapies
China	 Entyvio <sup>®</sup> vedolizumab	Japan	 Takecab <sup>®</sup> relugolix, cabozantinib, niraparib
	 ALUNBRIG <sup>®</sup> BRIGATINIB 80mg TABLETS		
	 TAKHZYRO <sup>®</sup> (lanadelumab-lyo) injection		
	 VPRIV <sup>®</sup> velaglucerase alfa for injection		
	 ADYNOVATE <sup>®</sup> [Antihemophilic Factor (Recombinant), PEGylated]		

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...



TARGET APPROVAL <sup>1</sup> →	FY20	FY21	FY22	FY23	FY24
<b>ONCOLOGY</b>		<b>TAK-788<sup>2</sup></b> 2L NSCLC		<b>TAK-007</b> Hematologic malignancies	<b>TAK-924</b> AML
		<b>TAK-924<sup>2</sup></b> HR-MDS		<b>TAK-788</b> 1L NSCLC	
<b>RARE DISEASES</b> Immunology Hematology Metabolic		<b>TAK-620</b> CMV infect. in transplant		<b>TAK-611</b> MLD (IT)	<b>TAK-607</b> Complications of prematurity
		<b>TAK-609</b> Hunter CNS (IT)		<b>TAK-755</b> cTTP	
<b>NEUROSCIENCE</b>				<b>TAK-935</b> DEE	<b>Orexin2R-ag</b> (TAK-925/994) Narcolepsy T1
<b>GASTRO-ENTEROLOGY</b>	<b>TAK-721</b> EoE				
<b>VACCINES</b>		<b>TAK-003</b> 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) <sup>1</sup>	ADDRESSABLE POPULATION (IN US) <sup>2</sup>	ADDRESSABLE POPULATION (WW) <sup>2,3</sup>
 <b>ONCOLOGY</b>	● <b>TAK-788</b>	EGFR inhibitor (exon 20)	NSCLC – 2L / 1L	2021 <sup>4</sup> / 2023	~2k	~20 - 30k
	● <b>pevonedistat (TAK-924)</b>	NAE inhibitor	HR-MDS / AML	2021 <sup>4</sup> / 2024	~7k / ~12k	15 - 20k / 20 - 25k
	<b>TAK-007</b>	CD19 CAR-NK	Hematologic malignancies	2023	~9k	~15 - 25k
 <b>RARE DISEASES</b> <i>Immunology Hematology Metabolic</i>	● <b>TAK-609</b>	ERT / I2S replacement	Hunter CNS (IT)	2021	~250	~1 - 1.5k
	● <b>maribavir (TAK-620)</b>	UL97 kinase inh	CMV infect. in transpl.	2021	~7 - 15k	~25 - 45k
	<b>TAK-607</b>	IGF-1/ IGFBP3	Complications of prematurity	2024 <sup>5</sup>	~25k	~80 - 90k
	<b>TAK-611</b>	ERT / arylsulfatase A	MLD (IT)	2023	~350	~1 - 2k
	● <b>TAK-755</b>	ERT/ ADAMTS-13	cTTP / iTTP	2023 / 2025	~500 / ~2k	2 - 6k / 5 - 18k
 <b>NEUROSCIENCE</b>	<b>Orexin programs</b>	Orexin 2R agonist	Narcolepsy Type 1	2024	70 - 140k	300k - 1.2M
	<b>TAK-935</b>	CH24H inhibitor	Developmental and Epileptic Encephalopathies (DEE)	2023	~50k	~70 - 90k
 <b>GASTRO-ENTEROLOGY</b>	● <b>TAK-721</b>	Oral anti-inflammatory	Eosinophilic Esophagitis	2020	~150k	<i>Under evaluation</i>
 <b>VACCINES</b>	● <b>TAK-003</b>	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

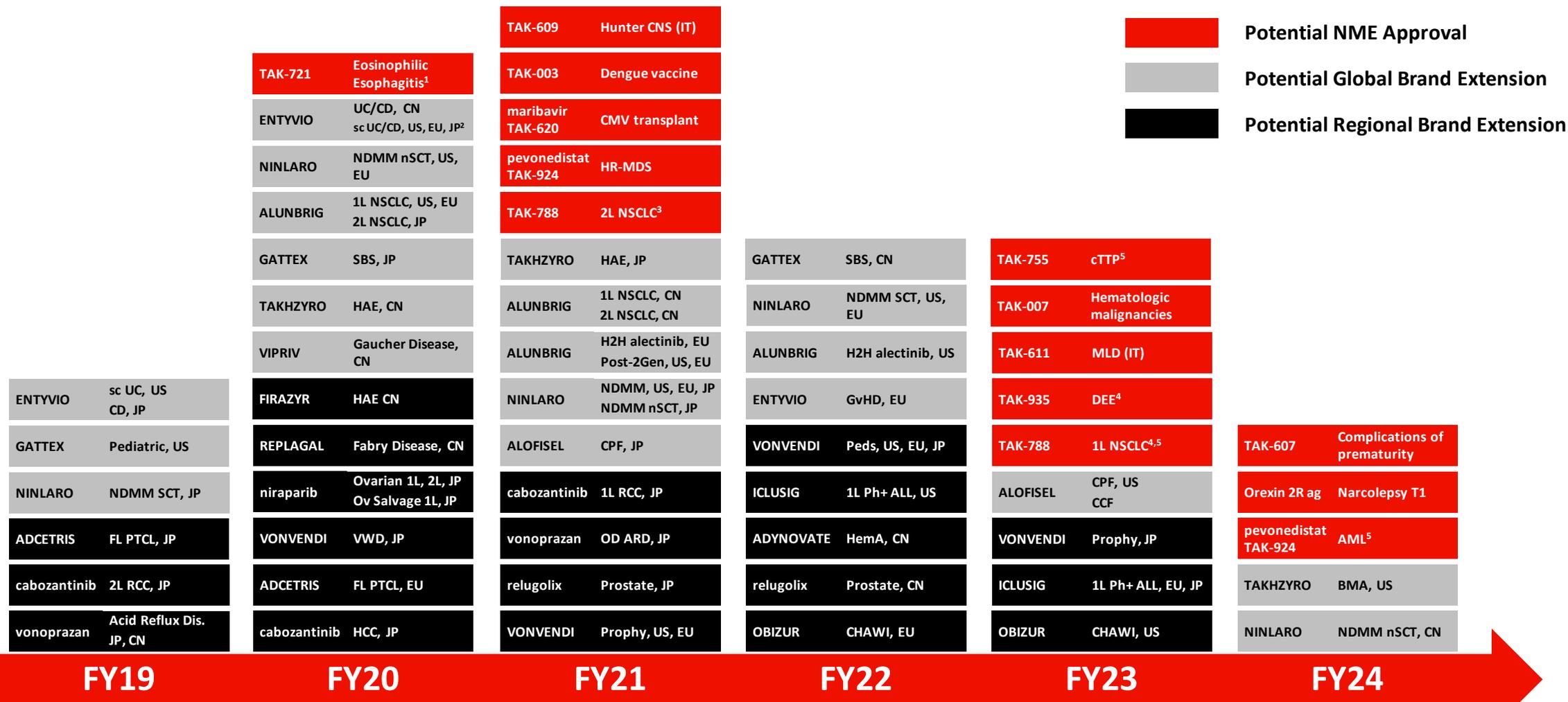
3. For TAK-788, TAK-924, TAK-007, TAK-607 and TAK-620 the addressable population represent annual incidence

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

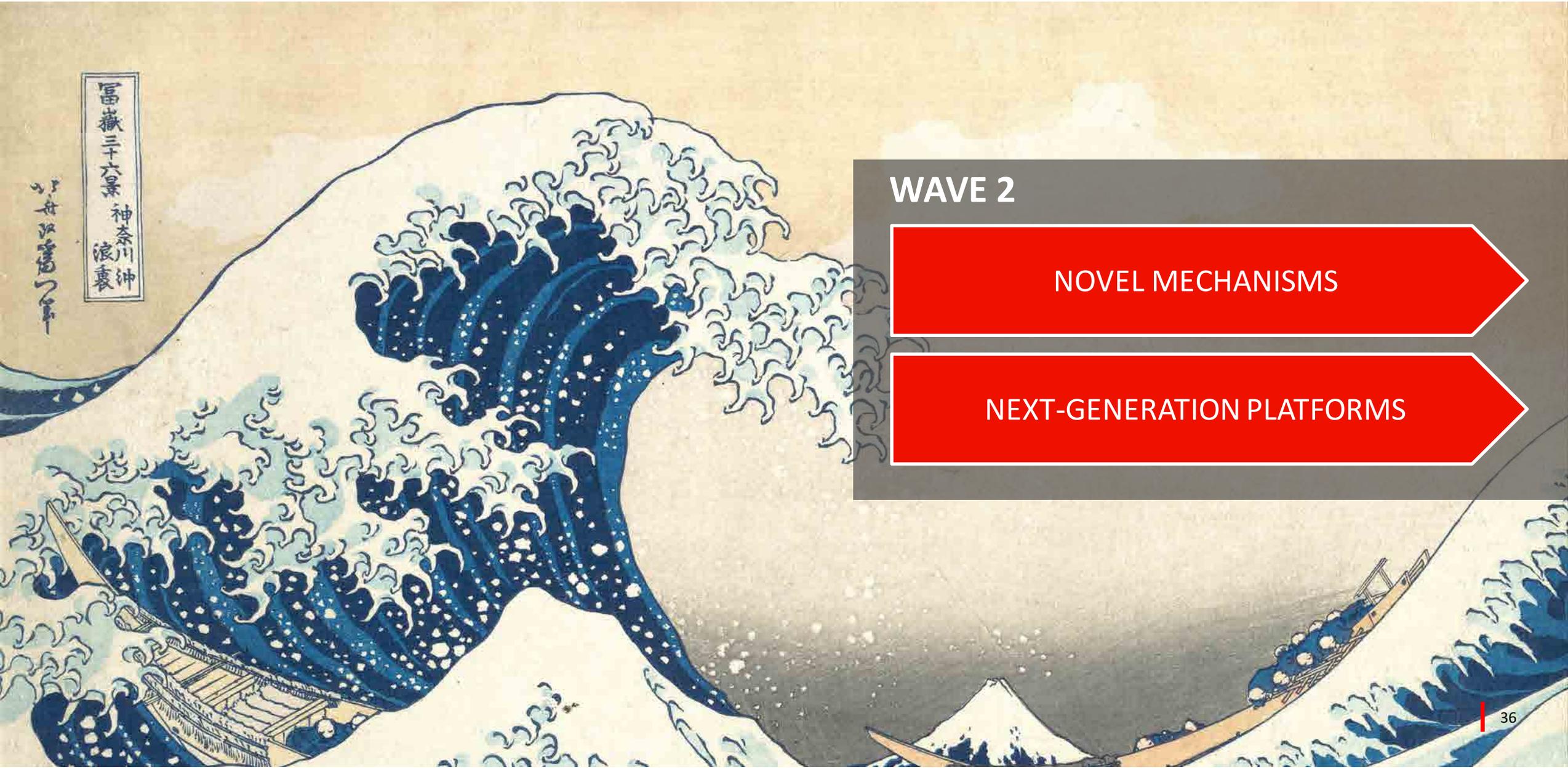
● Currently in pivotal study or potential for registration enabling Ph-2 study (note: table excludes relugolix)

# 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



## WAVE 2

NOVEL MECHANISMS

NEXT-GENERATION PLATFORMS

# DRIVEN BY A CLINICAL PIPELINE OF NOVEL MECHANISMS...



TARGET APPROVAL<sup>1</sup> →

FY25 AND BEYOND

<b>ONCOLOGY</b>	<b>TAK-164</b> <i>GI malignancies</i>	<b>TAK-252</b> <i>Solid tumors</i>	
	<b>TAK-573</b> <i>R/R MM</i>	<b>TAK-981</b> <i>Multiple cancers</i>	
<b>RARE DISEASES</b> <i>Immunology Hematology Metabolic</i>	<b>TAK-079<sup>2</sup></b> <i>MG, ITP</i>	<b>TAK-754</b> <i>HemA</i>	<b>TAK-755</b> <i>iTTP, SCD</i>
	<b>TAK-531</b> <i>Hunter CNS</i>		
<b>NEUROSCIENCE</b>	<b>TAK-341</b> <i>Parkinson's Disease</i>	<b>Orexin2R-ag</b> <i>Sleep Disorders</i>	<b>TAK-041</b> <i>CIAS NS</i>
	<b>TAK-418</b> <i>Kabuki Syndrome</i>	<b>TAK-653</b> <i>TRD</i>	<b>TAK-831</b> <i>CIAS NS</i>
	<b>WVE-120101</b> <i>Huntington's Disease</i>	<b>WVE-120102</b> <i>Huntington's Disease</i>	
<b>GASTRO-ENTEROLOGY</b>	<b>Kuma062</b> <i>Celiac Disease</i>	<b>TAK-101</b> <i>Celiac Disease</i>	<b>TAK-018</b> <i>Crohn's Disease (post-op and ileitis)</i>
	<b>TAK-954</b> <i>POGD</i>	<b>TAK-906</b> <i>Gastroparesis</i>	<b>TAK-951</b> <i>Nausea &amp; vomiting</i>
<b>VACCINES</b>	<b>TAK-214</b> <i>Norovirus Vaccine</i>	<b>TAK-426</b> <i>Zika Vaccine</i>	<b>TAK-021</b> <i>EV71 Vaccine</i>

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 →

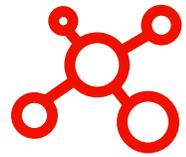
FY25 AND BEYOND

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

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

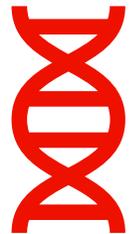
Some Wave 2 assets could be accelerated into Wave 1 if they have breakthrough data

Estimated dates as of November 14, 2019



## Cell Therapy

- 5 clinical programs by end of FY20
- Disruptive platforms, including off-the-shelf cell-therapies



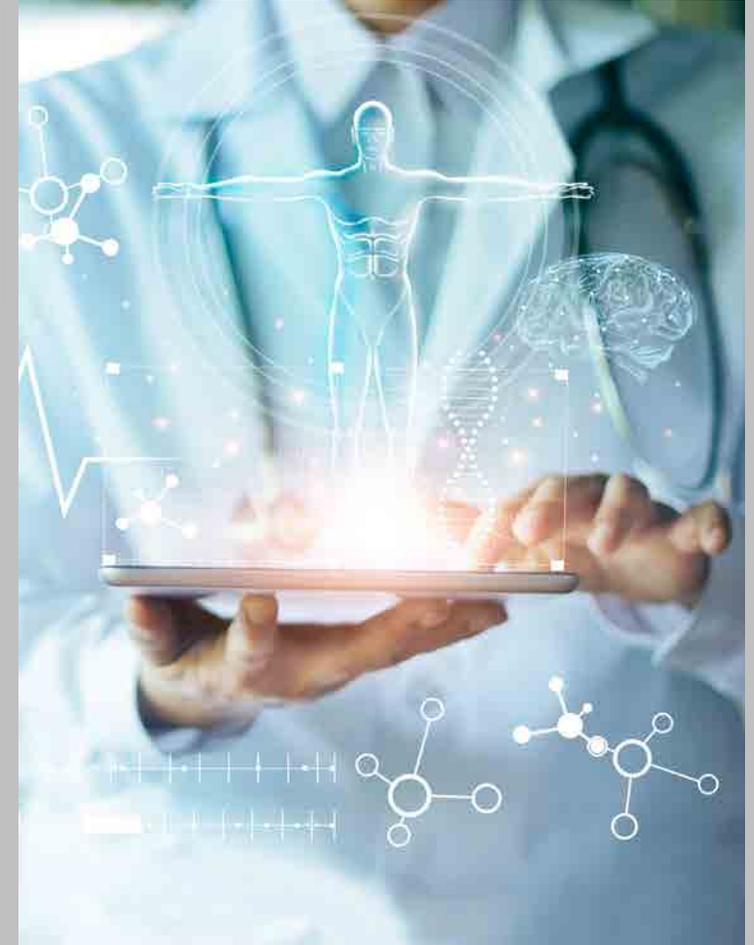
## Gene Therapy

- 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



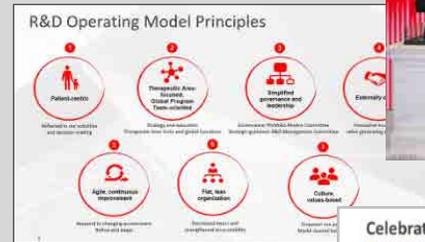
# COMMITTED TO OUR PEOPLE



# LIVING OUR VALUES THROUGHOUT THE INTEGRATION PROCESS



- 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 Sheikh 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



# WE ARE POSITIONED TO DELIVER NEAR-TERM & SUSTAINED GROWTH



TARGET APPROVAL →	WAVE 1 <sup>1</sup>					WAVE 2 <sup>2</sup>				PLATFORMS		
	CLINICAL-STAGE NMEs											
	FY20	FY21	FY22	FY23	FY24	FY25 AND BEYOND						
<b>ONCOLOGY</b>		<b>TAK-788<sup>3</sup></b> 2L NSCLC		<b>TAK-007</b> Hematologic malignancies	<b>TAK-924</b> AML	<b>TAK-164</b> GI malignancies	<b>TAK-252</b> Solid tumors			CELL THERAPY AND IMMUNE ENGAGERS	TARGETED INNATE IMMUNE MODULATION	NEXT-GEN CHECKPOINT MODULATORS
		<b>TAK-924<sup>3</sup></b> HR-MDS		<b>TAK-788</b> 1L NSCLC		<b>TAK-573</b> R/R MM	<b>TAK-981</b> Multiple cancers					
<b>RARE DISEASES</b> <i>Immunology Hematology Metabolic</i>		<b>TAK-620</b> CMV infect. in transplant		<b>TAK-611</b> MLD (IT)	<b>TAK-607</b> Complications of prematurity	<b>TAK-079<sup>4</sup></b> MG, ITP	<b>TAK-754</b> HemA	<b>TAK-755</b> iTTP, SCD		GENE THERAPY		
		<b>TAK-609</b> Hunter CNS (IT)		<b>TAK-755</b> cTTP		<b>TAK-531</b> Hunter CNS						
<b>NEUROSCIENCE</b>				<b>TAK-935</b> DEE	<b>Orexin2R-ag</b> (TAK-925/994) Narcolepsy T1	<b>TAK-341</b> Parkinson's Disease	<b>Orexin2R-ag</b> Sleep Disorders	<b>TAK-041</b> CIAS NS		GENE THERAPY	<b>OTHER PLATFORMS</b> RNA Modulation Antibody Transport Vehicle	
						<b>TAK-418</b> Kabuki Syndrome	<b>TAK-653</b> TRD	<b>TAK-831</b> CIAS NS				
<b>GASTRO-ENTEROLOGY</b>		<b>TAK-721</b> EoE				<b>Kuma062</b> Celiac Disease	<b>TAK-101</b> Celiac Disease	<b>TAK-018</b> Crohn's Disease (post-op and ileitis)	<b>TAK-671</b> Acute Pancreatitis	GENE THERAPY	MICROBIOME	CELL THERAPY
						<b>TAK-954</b> POGD	<b>TAK-906</b> Gastroparesis	<b>TAK-951</b> Nausea & vomiting				
<b>VACCINES</b>		<b>TAK-003</b> Dengue Vaccine				<b>TAK-214</b> Norovirus Vaccine	<b>TAK-426</b> Zika Vaccine	<b>TAK-021</b> 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	<b>Welcome and Opening Remarks</b> <i>Sheelagh Cawley-Knopf, Head R&amp;D Global Portfolio Strategy</i>
12:35 – 12:45	<b>Takeda: A Global Values-Based, R&amp;D-Driven Biopharmaceutical Leader</b> <i>Christophe Weber, President &amp; CEO Takeda</i>
12:45 – 13:20	<b>Translating Science into Highly Innovative, Life-changing Medicines</b> <i>Andy Plump, President R&amp;D</i>
13:20 – 13:45	<b>Oncology and Cell Therapies with Spotlight on CAR-NK</b> <i>Chris Arendt, Head Oncology Drug Discovery Unit</i>
13:45 – 14:05	<b>Spotlight on Oncology Opportunities</b> <ul style="list-style-type: none"><li>• <b>TAK-788</b> : <i>Rachael Brake, Global Program Lead</i></li><li>• <b>Pevonedistat</b> : <i>Phil Rowlands, Head Oncology Therapeutic Area Unit</i></li></ul>
14:05 – 14:20	<b>Break</b>
14:20 – 14:45	<b>Rare Diseases &amp; Gene Therapy</b> <i>Dan Curran, Head Rare Disease Therapeutic Area Unit</i>
14:45 – 15:00	<b>Spotlight on Orexin2R agonists</b> <i>Deborah Hartman, Global Program Lead</i>
15:00 – 15:20	<b>Therapeutic Area Focus in GI with Spotlight on Celiac Disease</b> <i>Asit Parikh, Head GI Therapeutic Area Unit</i>
15:20 – 16:00	<b>Panel Q&amp;A Session</b>
16:00	<b>Drinks reception</b>



# 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

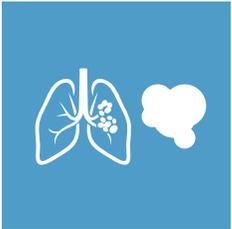
Better Health, Brighter Future

# A CURATIVE-INTENT IMMUNO-ONCOLOGY PIPELINE IS TAKING SHAPE



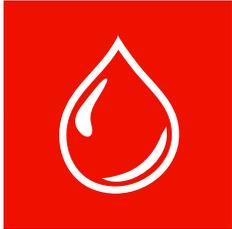
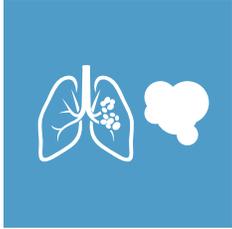
## WAVE 1

NMEs that complement our global brands

<b>Hematologic Malignancies</b> 	<b>TAK-924</b> FY21 target approval
<b>Lung Cancer &amp; Solid Tumors</b> 	<b>TAK-007</b> FY23 target approval
	<b>TAK-788</b> FY21 target approval

## WAVE 2

Leading platforms in immuno-oncology and cell therapies

<b>Immuno-Oncology</b> 	<b>Hematologic Malignancies</b> 
	<b>Lung Cancer &amp; Solid Tumors</b> 

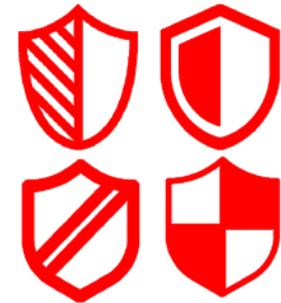
## Unique Partnership Model



- Innovative, disruptive platforms
- Agility in 'open lab' model



## Differentiated Portfolio

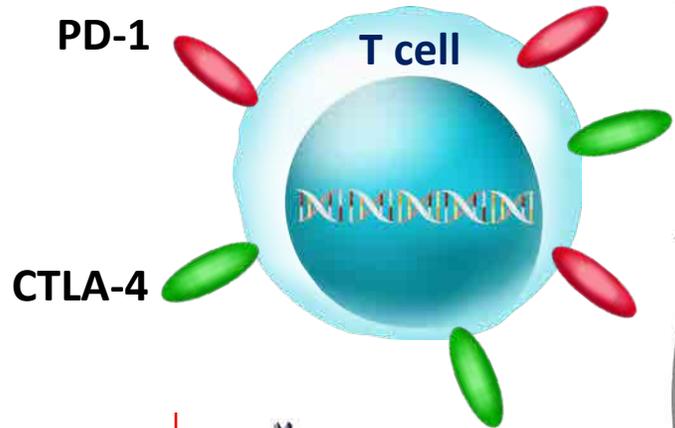


- Harness innate immunity
- Eye towards solid tumors

# THE FIRST BREAKTHROUGHS IN CANCER IMMUNOTHERAPY TARGET T CELLS



## T CELL CHECKPOINT INHIBITORS

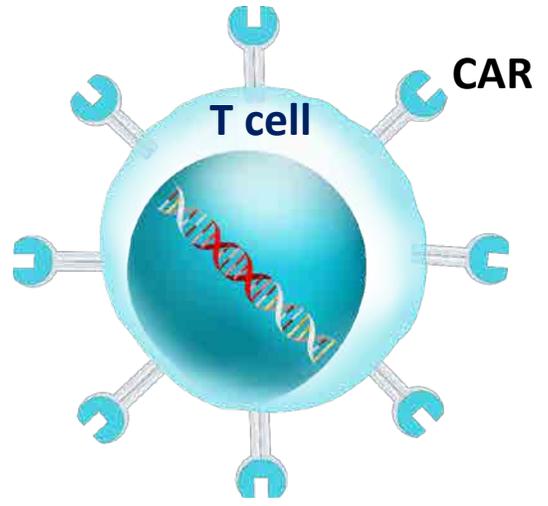


**KEYTRUDA**

**OPDIVO**  
(nivolumab)

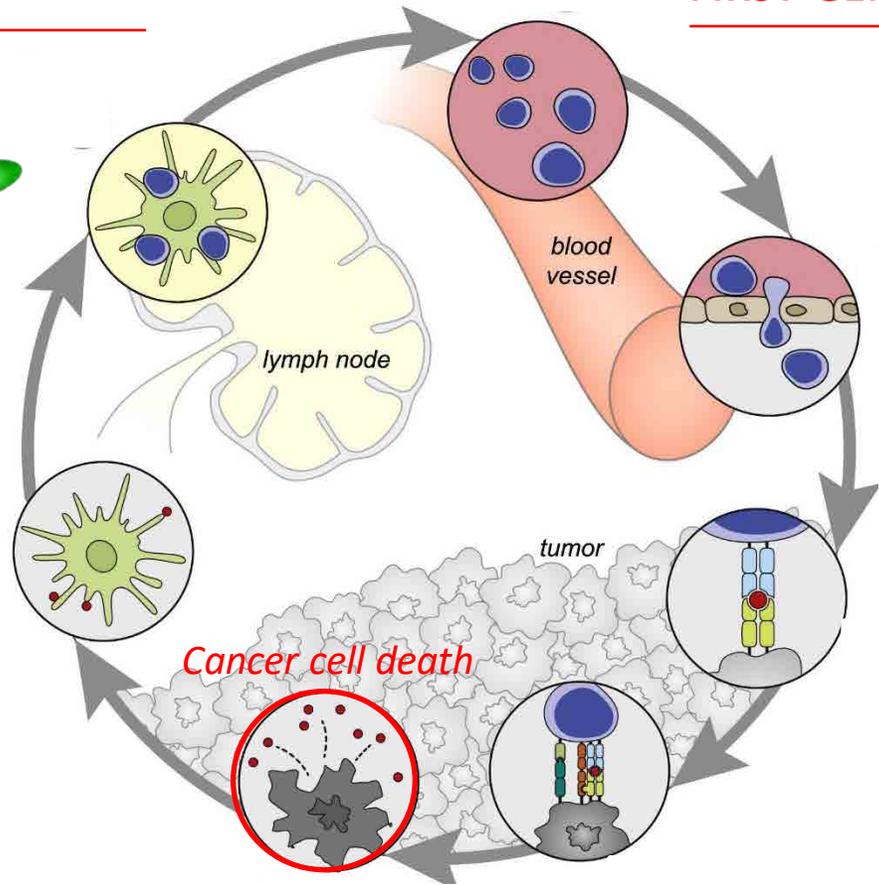
**YERVOY**  
(ipilimumab)  
Injection for intravenous use 5 mg/mL

## FIRST-GEN CAR-Ts



**YESCARTA**  
(axicabtagene ciloleucel)  
Suspension for IV infusion

**KYMRIAH**  
(tisaqenlecleucel)  
Suspension for IV infusion



Adapted from Chen & Mellman, *Immunity* 2013

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



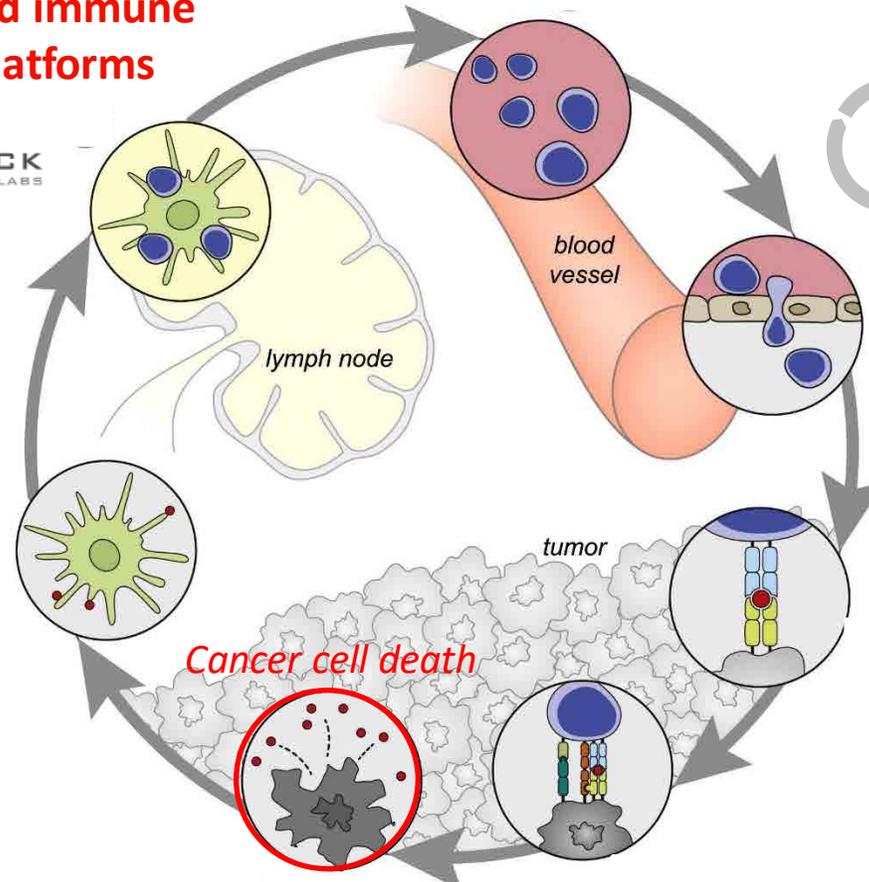
2

## Novel-scaffold immune checkpoint platforms



1

## Innate immuno-modulation



3

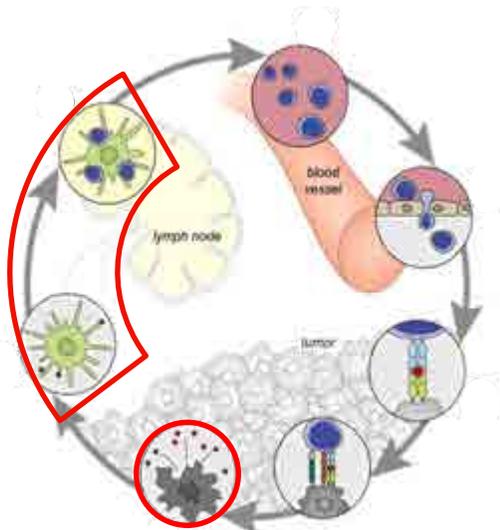
## Next-gen cell therapy & immune engager platforms



Memorial Sloan Kettering  
Cancer Center

# 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		<ul style="list-style-type: none"> <li>Innate-to-adaptive priming</li> </ul>	<b>TAK-676</b> (STING agonist) Targeted STING agonist		
SUMOylation		<ul style="list-style-type: none"> <li>Innate immune enhancer</li> </ul>	<b>TAK-981</b> TAK-981 (ADCC combo)		
Attenukine™		<ul style="list-style-type: none"> <li>Targeted attenuated IFN-α</li> </ul>	<b>TAK-573</b> (CD38-Attenukine™) Next-gen Attenukine™		

ADCC = Antibody-dependent cellular cytotoxicity

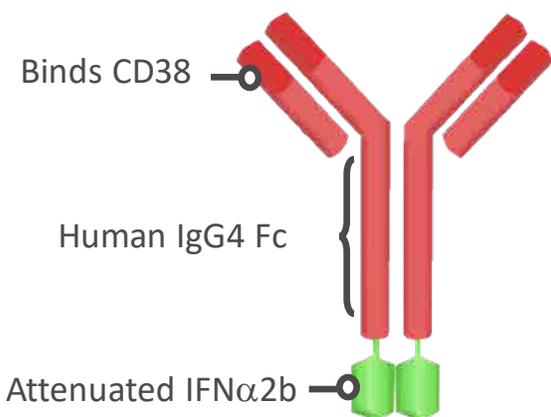
= first-in-class

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



## TARGETED ATTENUATED TYPE I IFN PAYLOAD

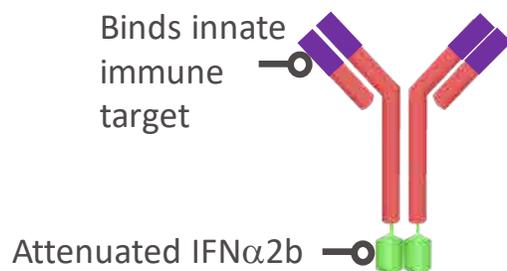
### TAK-573



Immunomodulation in preclinical models

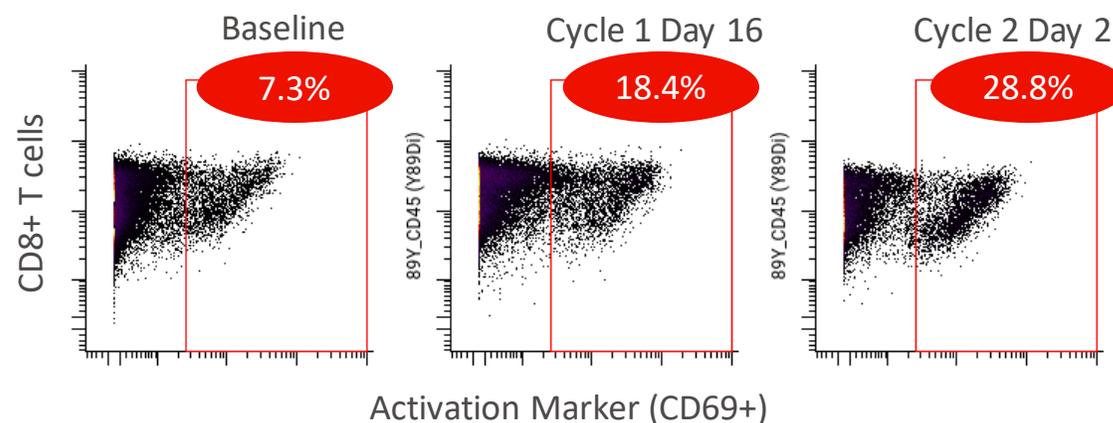
Includes CD8+ T cell migration / activation

### 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)**

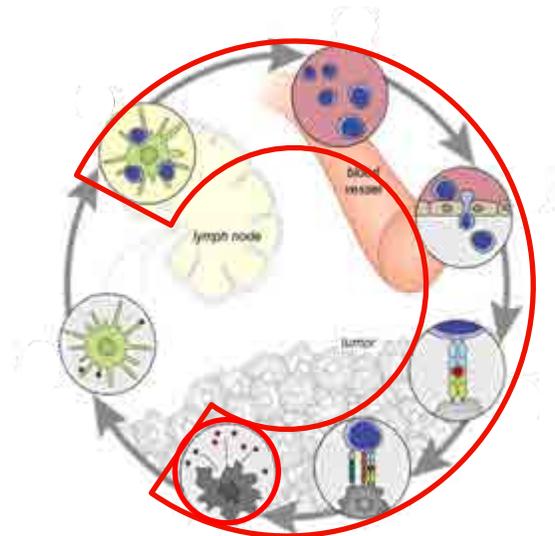
**2019**

Ph1 FPI in solid tumors

**2020**

Ph1b MM (incl. combinations)

# 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

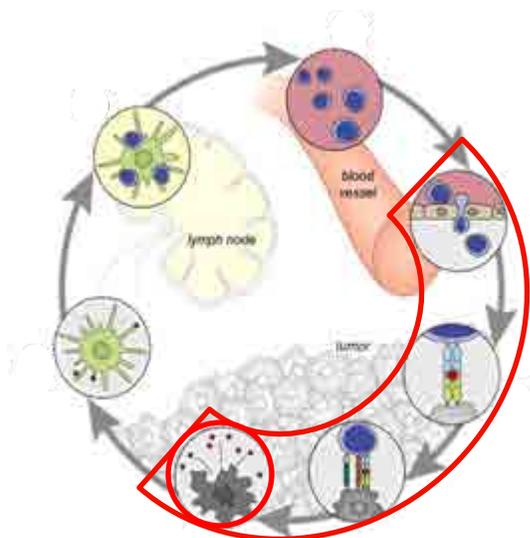
New classes of checkpoint inhibitors designed to increase breadth and depth of responses

PLATFORM	PARTNER	MECHANISM-OF-ACTION	PROGRAMS	PRE-CLINICAL	PH 1
Humabody Vh		<ul style="list-style-type: none"> <li>Unique pharmacology</li> </ul>	Concept 1 Concept 2	 	
Agonist-redirected checkpoints		<ul style="list-style-type: none"> <li>Co-inhibition &amp; co-stimulation</li> </ul>	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

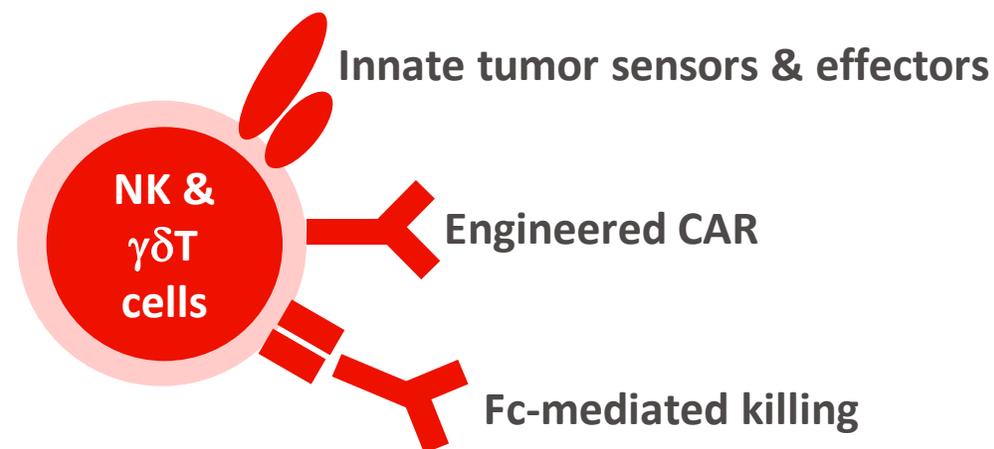
Current CAR-T therapies have significant challenges & fail to address solid tumors

## 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

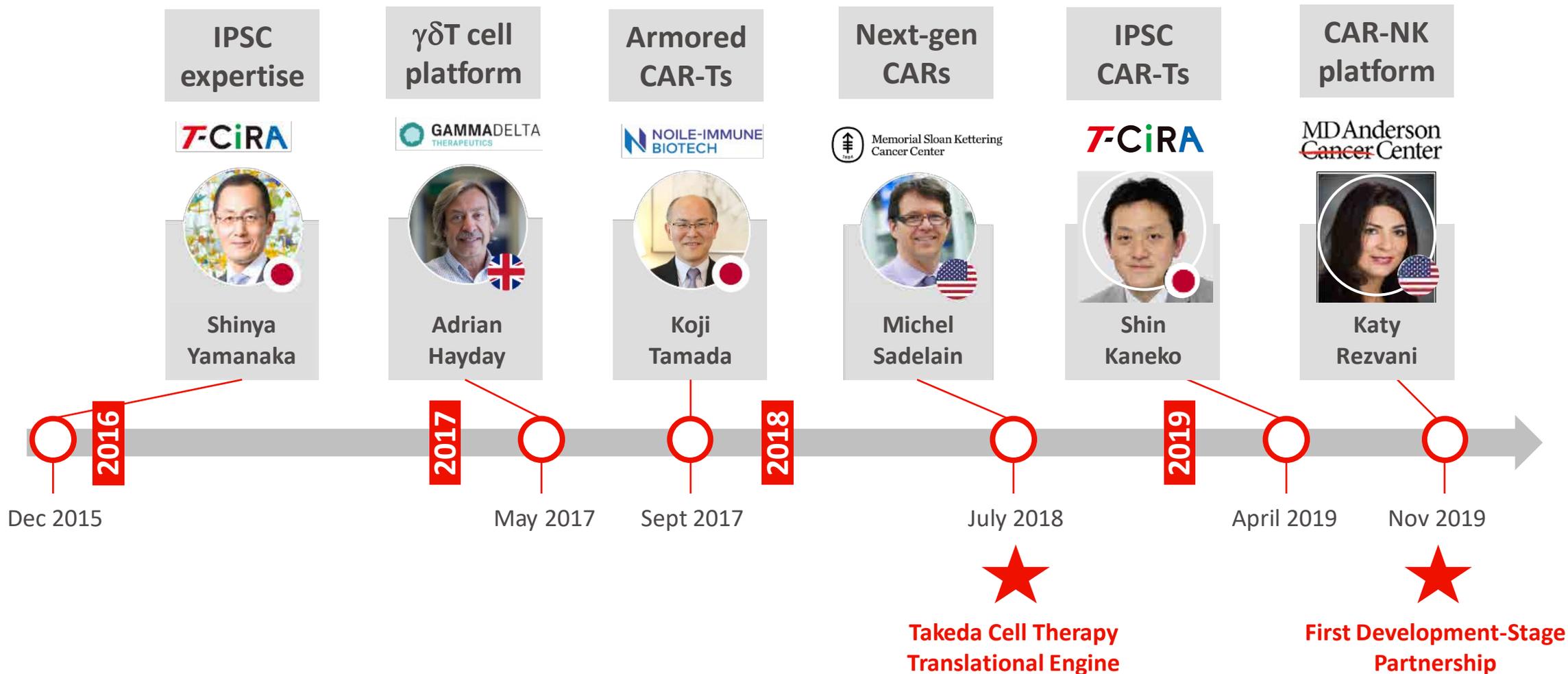


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# A NETWORK OF TOP INNOVATORS IS FUELING TAKEDA'S CELL THERAPY ENGINE



## CUTTING-EDGE ENGINEERING & CELL PLATFORMS



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

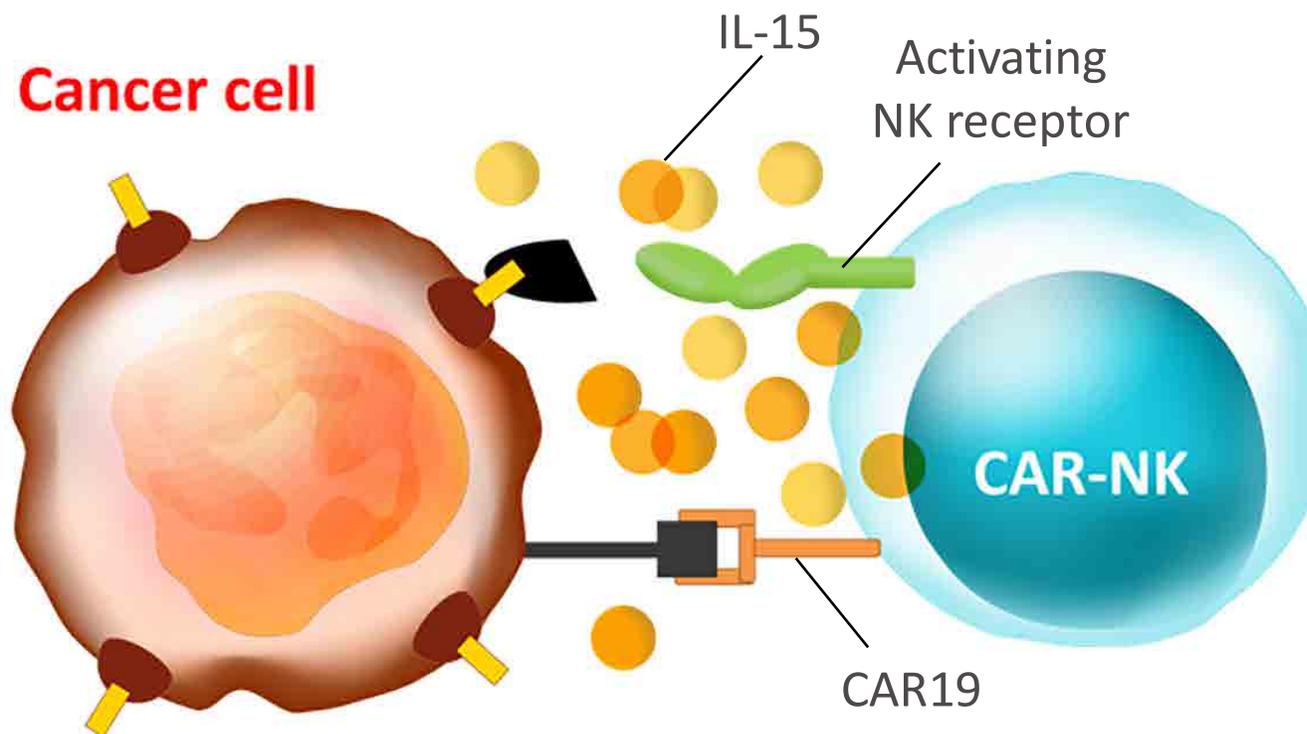
# TAKEDA IS EMBARKING ON A TRANSFORMATIVE CAR-NK PARTNERSHIP THAT COULD ENTER PIVOTAL TRIALS IN 2021



## NK CAR Platform

Multiple mechanisms of tumor killing

Potentiation of innate & adaptive immunity

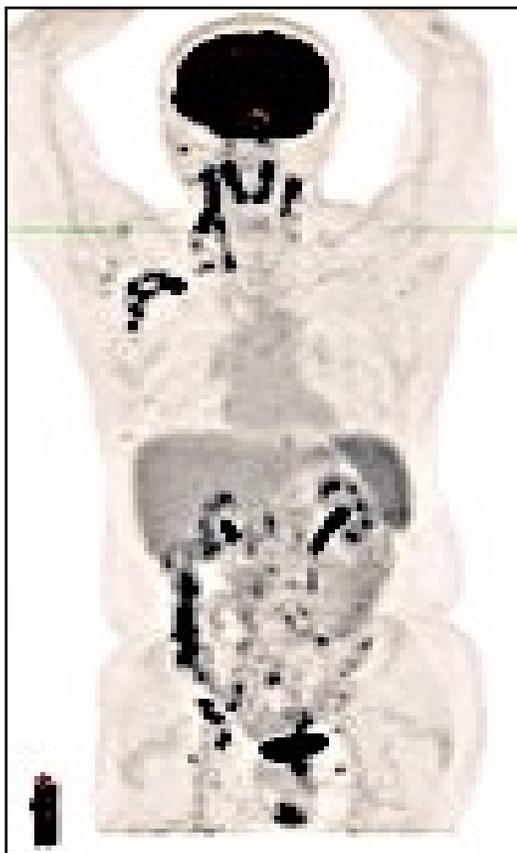




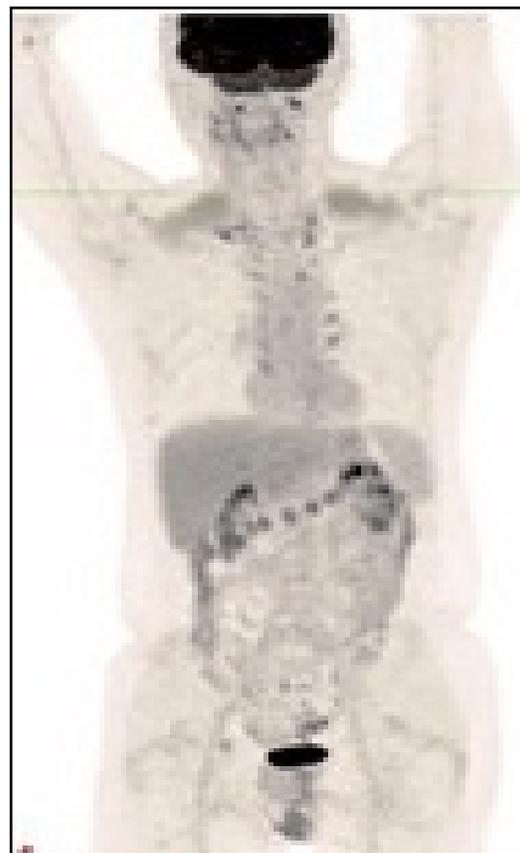
# 1 DRAMATIC COMPLETE RESPONSE IN FIRST PATIENT TREATED

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

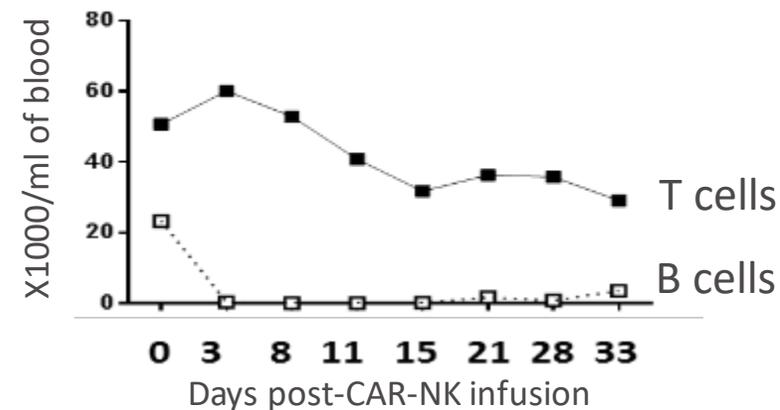
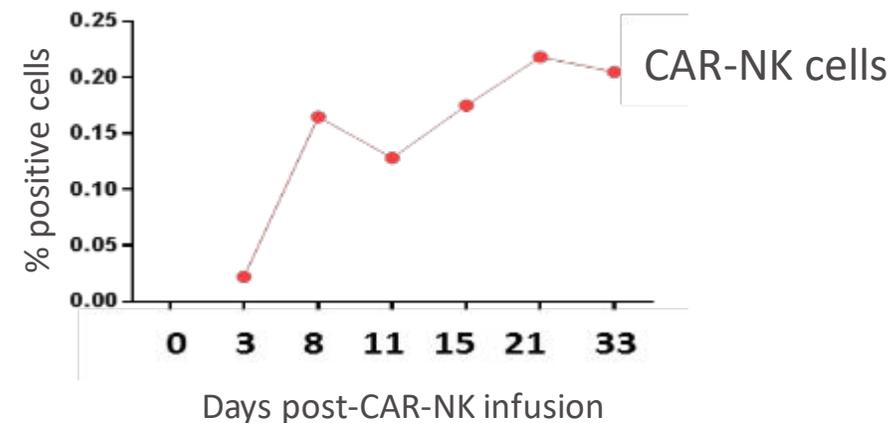
**KINETICS OF CAR-NK VERSUS ENDOGENOUS T AND B  
CELLS IN PERIPHERAL BLOOD**



Baseline scan



Day 30 post CAR19-NK



# 1 IMPRESSIVE RESPONSES IN OTHER HEAVILY PRETREATED PATIENTS

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

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

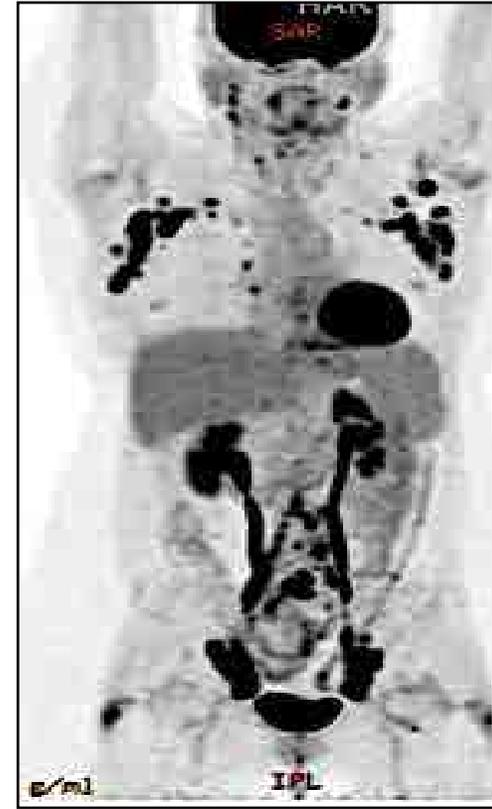


Baseline scan

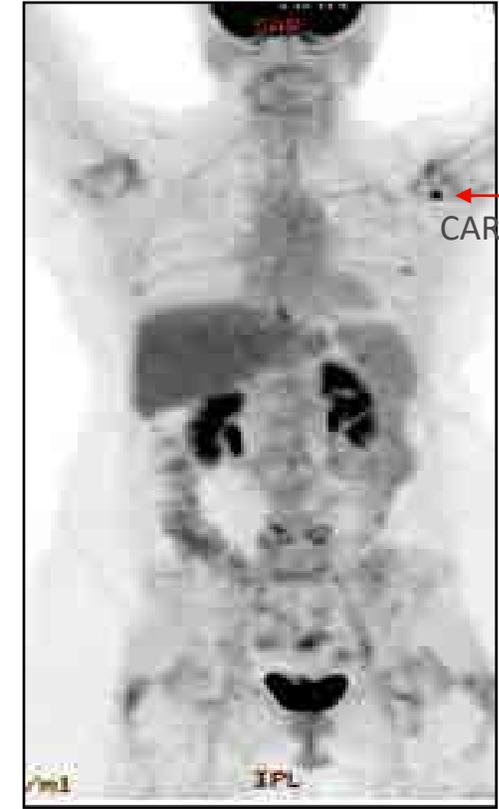


Day 30 post CAR19-NK

**CR in Richter's; SD in CLL**



Baseline scan



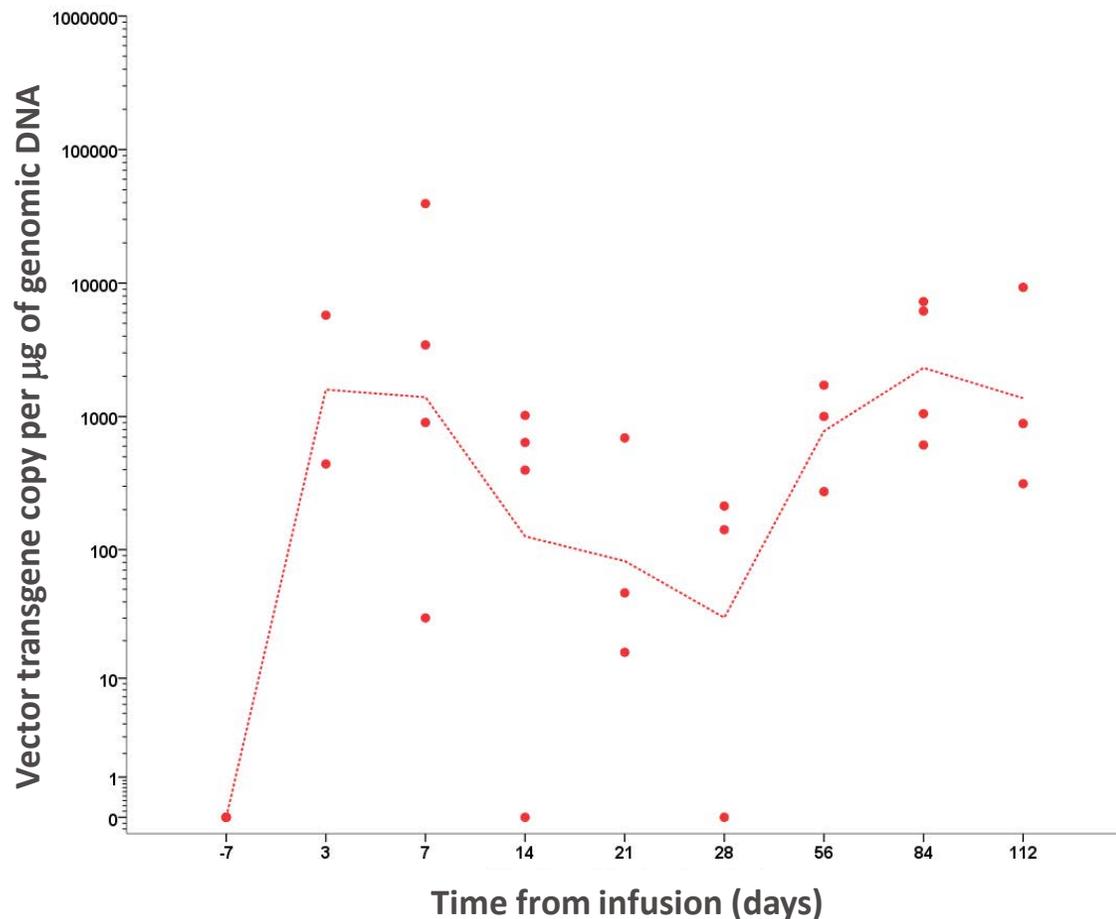
Day 30 post CAR19-NK

1

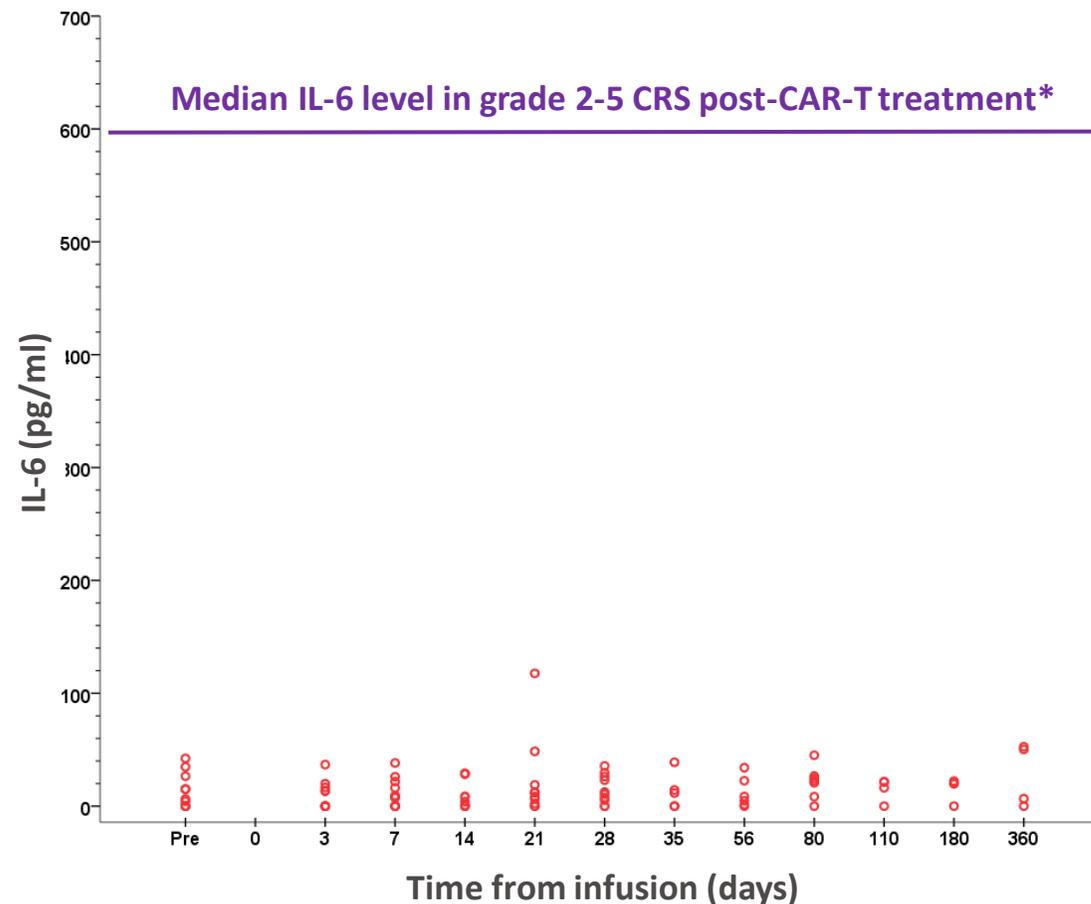
# CAR-NK CELLS PERSIST IN PATIENTS AND DO NOT TRIGGER CYTOKINE RELEASE SYNDROME (CRS)



## CAR-NK CELLS PERSIST UP TO 4 MONTHS POST INFUSION



## IL-6 LEVELS 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 MULTIPLE 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

1

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



## 5 CLINICAL-STAGE PROGRAMS EXPECTED BY END OF FY20



**TAK-007**

MD Anderson  
Cancer Center

*Off-the-shelf  
CAR-NK product*



**TAK-102**



*Cytokine +  
chemokine  
armed CAR-T*



**CD19 1XX-CAR-T**



Memorial Sloan Kettering  
Cancer Center

*Next-gen CART  
signaling domain*



**GDX012**



*Gamma-delta  
T cells*



**GCC CAR-T**



*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	PRECLINICAL	PH1
STING agonism				<ul style="list-style-type: none"> <li>Innate-to-adaptive priming</li> </ul>	TAK-676 (STING agonist)	
					Targeted STING agonist	
SUMOylation				<ul style="list-style-type: none"> <li>Innate immune enhancer</li> </ul>	TAK-981	
					TAK-981 (ADCC combo)	
Attenukine™				<ul style="list-style-type: none"> <li>Targeted attenuated IFN-α</li> </ul>	TAK-573 (CD38-Attenukine™)	
Agonist-redirected checkpoints				<ul style="list-style-type: none"> <li>Co-inhibition &amp; co-stimulation</li> </ul>	TAK-252 / SL-279353	
					TAK-254 / SL-115154	
Shiga-like toxin A				<ul style="list-style-type: none"> <li>Novel cytotoxic payload</li> </ul>	TAK-169 (CD38-SLTA)	
IGN toxin				<ul style="list-style-type: none"> <li>Solid tumor-targeted ADC</li> </ul>	TAK-164 (GCC-ADC)	
Conditional T cell engagers				<ul style="list-style-type: none"> <li>Novel solid tumor platform</li> </ul>	MVC-101 (EGFR COBRA™)	
Cell therapy platforms				<ul style="list-style-type: none"> <li>Off-the-shelf cell therapies</li> </ul>	TAK-007 (CD19 CAR-NK)	
					<b>5 cell therapies expected in clinic by end of FY20</b>	

## UNDISCLOSED TARGETS



= first-in-class

Hematology Solid tumors

# NME MILESTONES ACHIEVED IN FY19 AND LOOKING AHEAD TO OTHER POTENTIAL MILESTONES<sup>1</sup> THROUGH FY20



## PIVOTAL STUDY STARTS, APPROVALS

✓ TAK-611	MLD Ph 2 start <sup>2</sup>		✓ PEVONEDISTAT TAK-924	AML Ph 3 start		TAK-721	EoE Approval	
✓ TAK-755	cTTP Ph 3 start		TAK-788	1L NSCLC Ph 3 start		mHTT ASO	Huntington's Disease Pivotal start	



✓ TAK-925	Narcolepsy POC		✓ PEVONEDISTAT TAK-924	HR-MDS Ph 2 Overall Survival		TAK-788	2L NSCLC Ph 2 Pivotal		TAK-620	R/R CMV SOT & HSCT Ph 3 data	
✓ TAK-721	EoE Ph 3 data (induction)		✓ TAK-007	Hem. Malignancies POC		TAK-573	R/R MM, Solid Tumor POC		TAK-755	iTTP POC	
✓ TAK-101	Celiac Disease POC		TAK-609	Hunter (IT) Ph 3 data 2yr extension					TAK-935	DEE POC	
			mHTT ASO	Huntington's Disease POC					TAK-906	Gastroparesis POC	
			TAK-721	EoE Ph 3 data (maintenance)					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

# 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	<b>Welcome and Opening Remarks</b> <i>Sheelagh Cawley-Knopf, Head R&amp;D Global Portfolio Strategy</i>
12:35 – 12:45	<b>Takeda: A Global Values-Based, R&amp;D-Driven Biopharmaceutical Leader</b> <i>Christophe Weber, President &amp; CEO Takeda</i>
12:45 – 13:20	<b>Translating Science into Highly Innovative, Life-changing Medicines</b> <i>Andy Plump, President R&amp;D</i>
13:20 – 13:45	<b>Oncology and Cell Therapies with Spotlight on CAR-NK</b> <i>Chris Arendt, Head Oncology Drug Discovery Unit</i>
13:45 – 14:05	<b>Spotlight on Oncology Opportunities</b> <ul style="list-style-type: none"><li>• <b>TAK-788</b> : <i>Rachael Brake, Global Program Lead</i></li><li>• <b>Pevonedistat</b> : <i>Phil Rowlands, Head Oncology Therapeutic Area Unit</i></li></ul>
14:05 – 14:20	<b>Break</b>
14:20 – 14:45	<b>Rare Diseases &amp; Gene Therapy</b> <i>Dan Curran, Head Rare Disease Therapeutic Area Unit</i>
14:45 – 15:00	<b>Spotlight on Orexin2R agonists</b> <i>Deborah Hartman, Global Program Lead</i>
15:00 – 15:20	<b>Therapeutic Area Focus in GI with Spotlight on Celiac Disease</b> <i>Asit Parikh, Head GI Therapeutic Area Unit</i>
15:20 – 16:00	<b>Panel Q&amp;A Session</b>
16:00	<b>Drinks reception</b>



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



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New York, NY

November 14, 2019

# THE SIZE OF THE LUNG CANCER CHALLENGE IS VAST



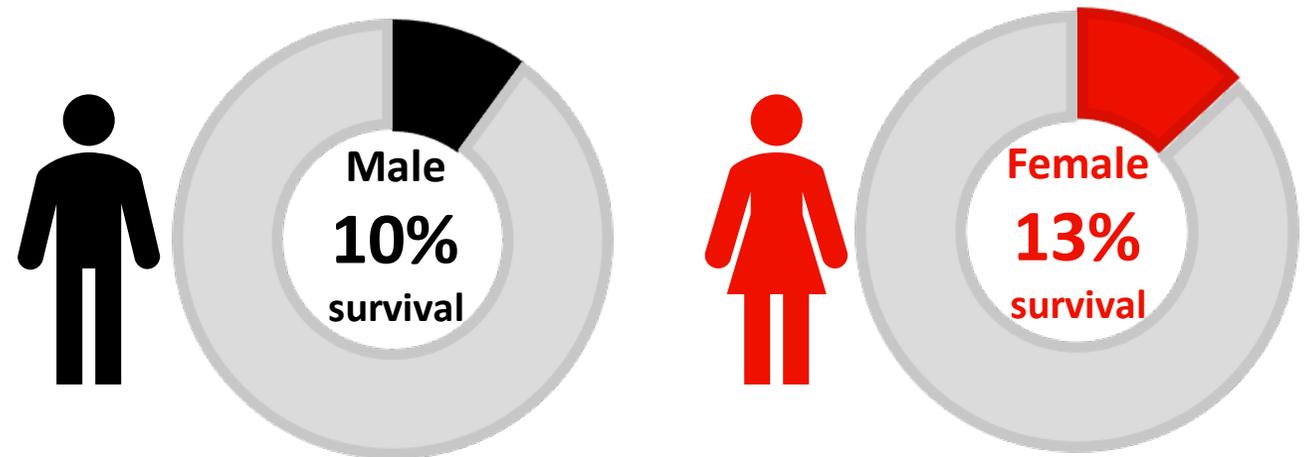
**228,000<sup>1</sup>**

**New Lung cancer cases / year**

**143,000<sup>1</sup>**

**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<sup>2</sup>

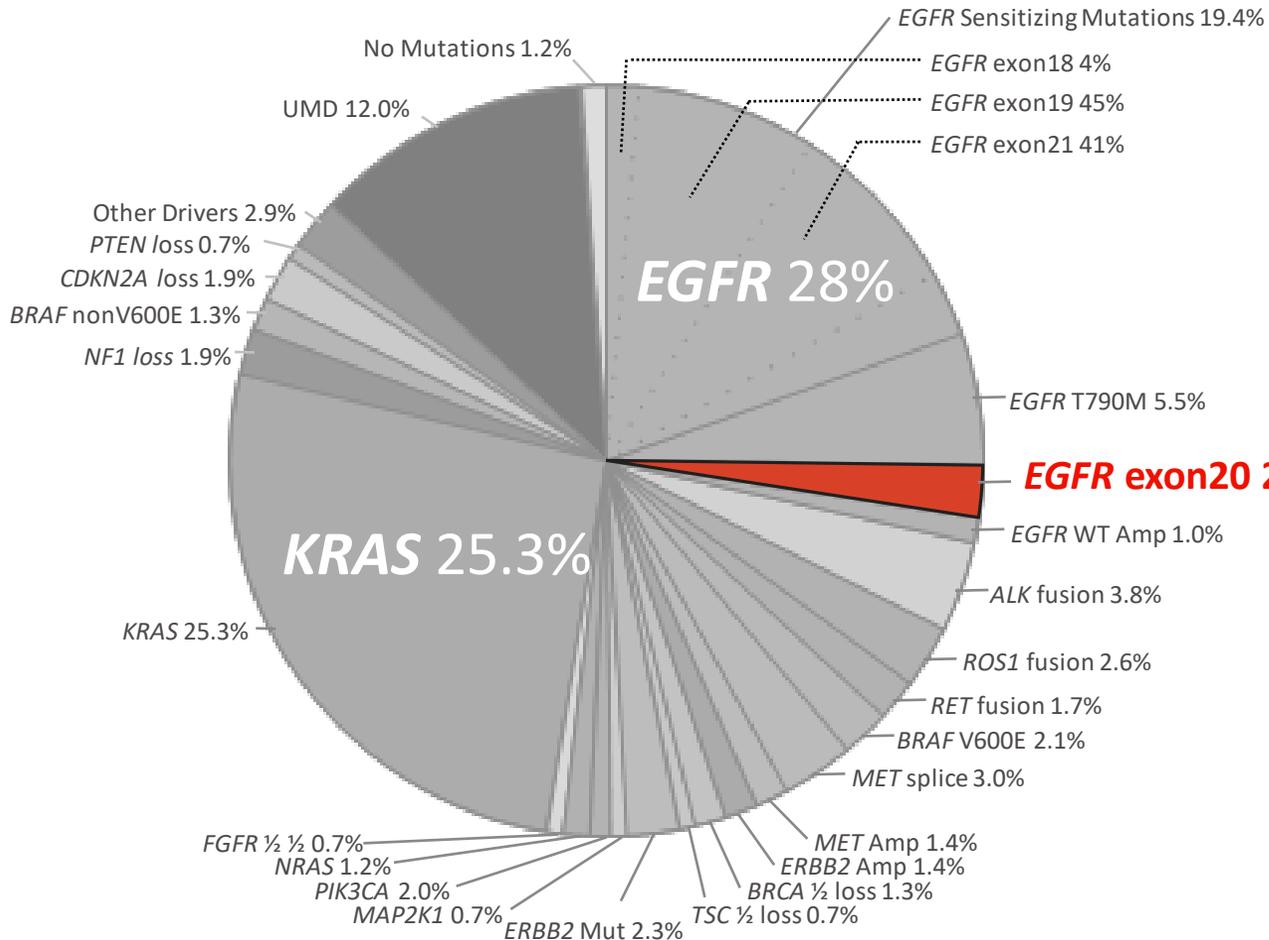
1. American Cancer Society; Cancer facts and figures 2019  
2. Office for National Statistics UK ([www.ons.gov.uk](http://www.ons.gov.uk))

# EXON 20 INSERTIONS ARE A RARE SUBSET OF EGFR MUTANT NSCLC



Non-Sq NSCLC  
200,000 pts/yr<sup>1</sup>

EGFR Exon 20 insertions  
2,000 pts/yr<sup>2</sup>



## Insertion variants

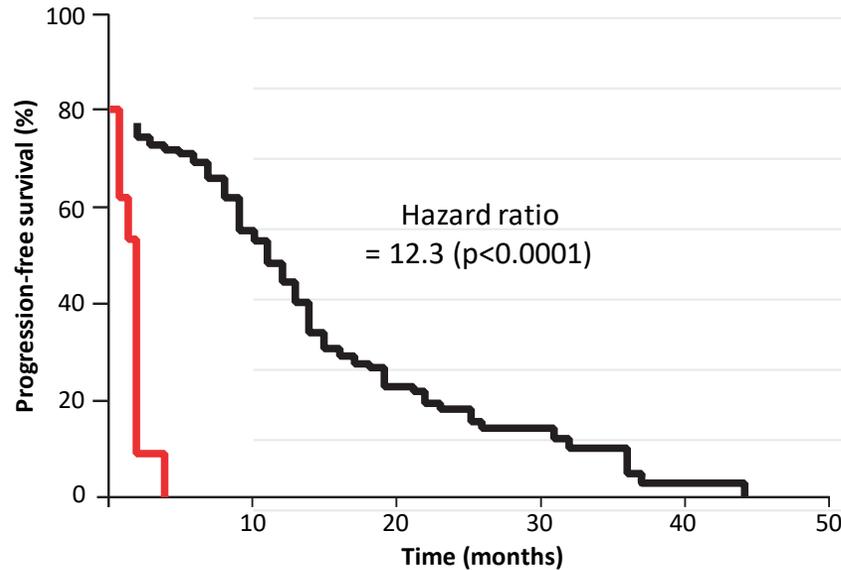
- V769\_D770insASV (≈20%)
- D770\_N771insSVD (≈19%)
- H773\_V774insH (≈8%)
- A763\_Y764insFQEA (≈7%)
- H773\_v774insPH (≈5%)
- H773\_V774insNPH (≈4%)
- N771\_P772insN (≈3%)
- H773\_V774insAH (≈3%)
- Other (≈31%)

# PATIENTS WITH EGFR EXON 20 INSERTIONS HAVE NO EFFECTIVE THERAPY



## POOR RESPONSE TO EXISTING TKIs <sup>1</sup>

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

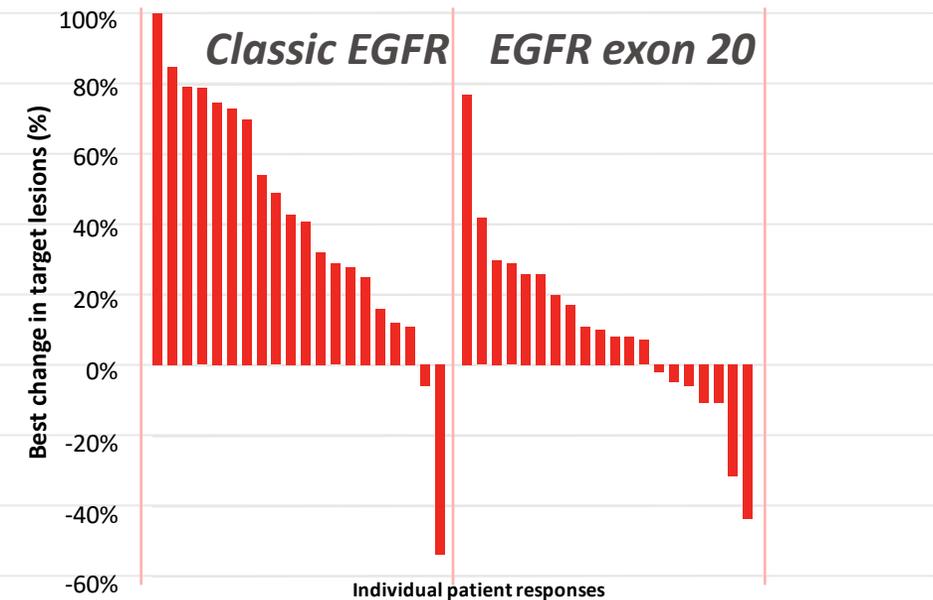


Group	Median PFS (months)
EGFR exon 20 ins (n=9)	2.0
Classical EGFR mut (n=129)	12.0



## POOR RESPONSE TO ANTI PD-1/PDL-1 THERAPY <sup>2</sup>

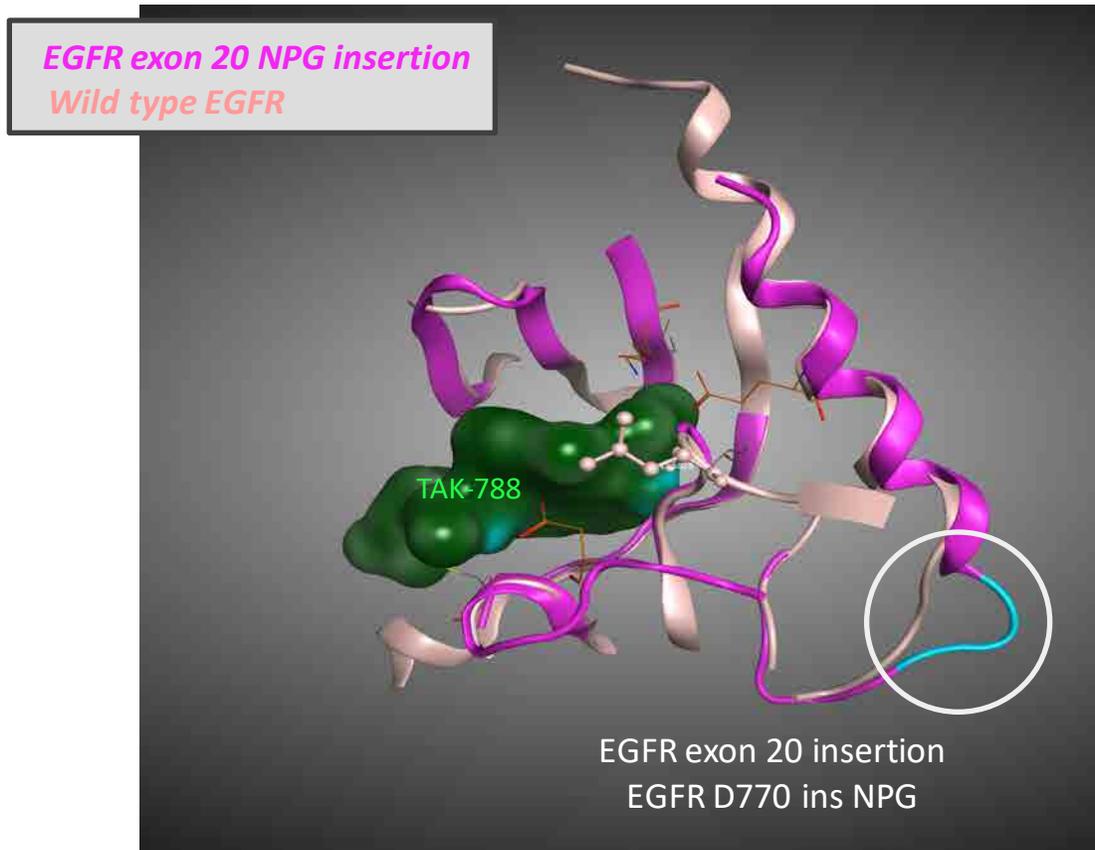
EGFR exon 20 ins patients demonstrate limited benefit to anti PD-1 directed therapy



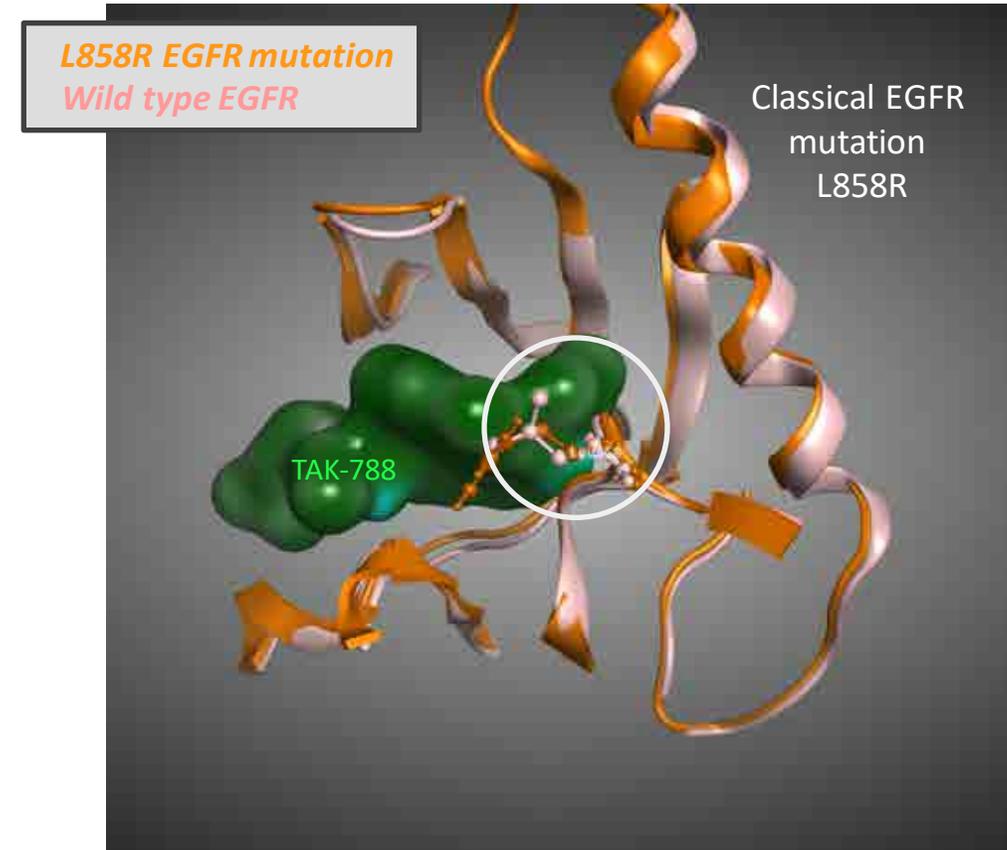
Group	Median PFS (months)	PDL-1 expression ≥1%
EGFR exon 20 ins (n=20)	2.7 (1.7-3.8)	40%
Classical EGFR mut (n=22)	1.8 (1.2-2.4)	25%

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**

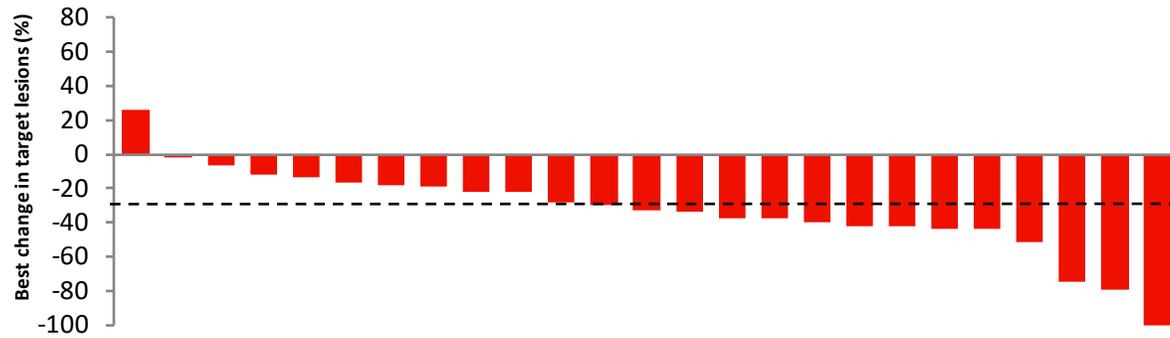
# TAK-788 PROOF OF CONCEPT DATA IN EGFR EXON 20 INSERTIONS



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



Individual patient responses

Prior TKI:	N	N	N	N	Y	N	N	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	N	N	Y	Y	N
Prior IO:	N	Y	Y	N	Y	N	N	N	N	Y	Y	N	Y	Y	N	Y	Y	Y	N	N	Y	N	Y	Y	Y	

## 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 <sup>1</sup> n=28	Poziotinib <sup>2</sup> n=50	Afatinib <sup>3</sup> n=23	Osimertinib <sup>4</sup> 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 <sup>1</sup> n=72	Poziotinib <sup>2</sup> n=63	Afatinib <sup>5</sup> n=229	Osimertinib <sup>6</sup> 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 al., 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  
  
Comprehensive  
diarrhea management  
guidelines  
implemented earlier

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

# 2021: EXPECTED FIRST APPROVAL IN EGFR EXON 20 INSERTIONS



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

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



**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

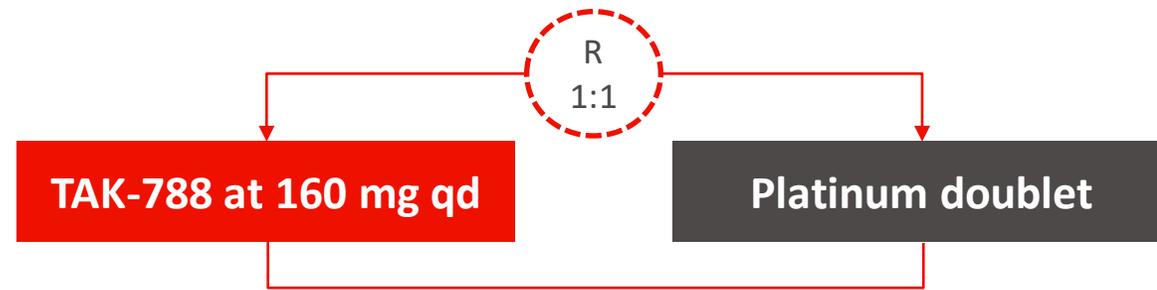
# NEW ACTIVATION: A TRIAL FOR NEWLY DIAGNOSED PATIENTS



**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



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

Electronic patient reported outcomes

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

# 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