



## THERAPEUTIC AREA FOCUS IN GI WITH SPOTLIGHT ON CELIAC DISEASE



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New York, NY

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Better Health, Brighter Future

## WE TARGET UNMET NEEDS THAT ALIGN WITH OUR STRENGTHS



### AREAS OF FOCUS



High unmet medical need



Potential to advance SoC through innovative science – by being first or best in class



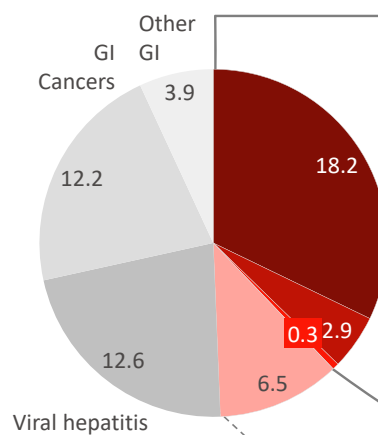
Fit with internal strengths



Ability to create a commercially - viable path

### GI WW RX SALES 2018 (USD Bn)

Total = \$57Bn



### TAKEDA GI DISEASE AREAS

GI inflammation

GI motility

Liver fibrosis

Acid related diseases

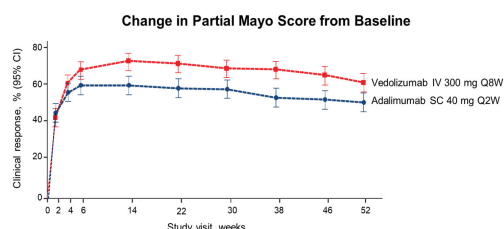
# WE STRENGTHEN ENTYVIO BY CONTINUOUSLY IMPROVING VALUE FOR PATIENTS



## COMPETITIVE POSITIONING

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

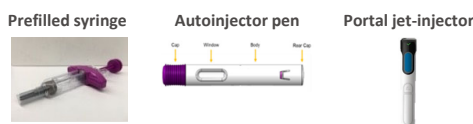
- Vedolizumab was superior to adalimumab on the primary endpoint of clinical remission at wk 52
- Onset of action as rapid as anti-TNF



## EXPANDED PATIENT POPULATIONS

### Entyvio Subcutaneous Development

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



### Gut GvHD prophylaxis

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



## GEOGRAPHIC EXPANSION

### Entyvio IV

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

### EXPECTED MILESTONES (FY)

2019  
Entyvio (SC UC) US approval

2020  
Entyvio (SC CD) US, EU approval  
Entyvio (SC UC) EU, JP approval  
Entyvio (IV) CN approval

2021  
Entyvio GvHD Ph3 readout






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

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

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# 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					FY25 AND BEYOND						
	FY20	FY21	FY22	FY23	FY24							
 ONCOLOGY		TAK-788 <sup>3</sup> 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 <sup>3</sup> HR-MDS		TAK-788 1L NSCLC		TAK-573 R/R MM	TAK-981 Multiple cancers					
 RARE DISEASES <small>Immunology Hematology Metabolic</small>		TAK-620 CMV infect. in transplant		TAK-611 MLD (IT)	TAK-607 Complications of prematurity	TAK-079 <sup>4</sup> MG, ITP	TAK-754 HemA	TAK-755 ITPP, SCD		GENE THERAPY		
		TAK-609 Hunter CNS (IT)		TAK-755 cTTP		TAK-531 Hunter CNS						
 NEUROSCIENCE				TAK-935 DEE	Orexin2R-ag (TAK-925/994) Narcolepsy T1	TAK-341 Parkinson's Disease	Orexin2R-ag Sleep Disorders	TAK-041 CIAS NS		GENE THERAPY	OTHER PLATFORMS RNA Modulation Antibody Transport Vehicle	
						TAK-418 Kabuki Syndrome	TAK-653 TRD	TAK-831 CIAS NS				
						WVE-120101 Huntington's Disease	WVE-120102 Huntington's Disease					
 GASTRO-ENTEROLOGY	TAK-721 EoE					Kuma062 Celiac Disease	TAK-101 Celiac Disease	TAK-018 Crohn's Disease (post-op and ileitis)	TAK-671 Acute Pancreatitis	GENE THERAPY	MICROBIOME	CELL THERAPY
						TAK-954 POGD	TAK-906 Gastroparesis	TAK-951 Nausea & vomiting				
 VACCINES		TAK-003 Dengue Vaccine				TAK-214 Noravirus Vaccine	TAK-426 Zika Vaccine	TAK-021 EV71 vaccine				

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

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

3. Projected approval date assumes filing on Phase 2 data

4. TAK-079 to be developed in Rare Diseases indications myasthenia gravis (MG) and immune thrombocytopenic purpura (ITP) (FPI projected in each indication in 2H FY19)

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

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



## ADDRESSES SIGNIFICANT UNMET NEED

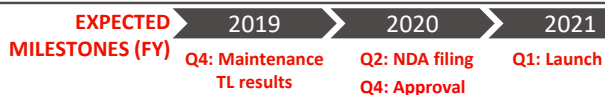
- Chronic, allergic, inflammatory condition of the esophagus that results in swallowing dysfunction
- Diagnosed prevalence is expected to increase significantly



No approved US medication  
SOC is food elimination, off-label use<sup>1</sup>



TAK-721 granted breakthrough therapy designation by FDA in 2016

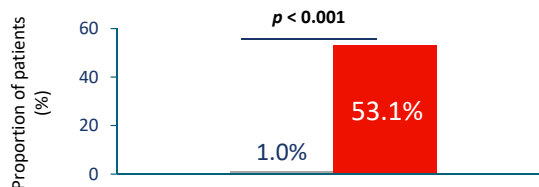


1. Swallowed use of glucocorticoids intended for asthma (e.g., home or compounded thickening of budesonide solution, or swallowing fluticasone aerosol).

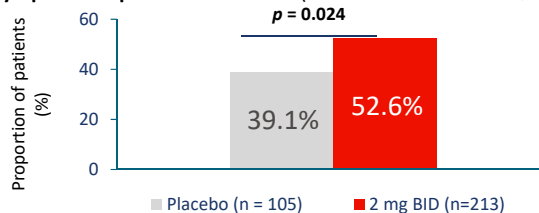
## INDUCTION DATA SHOWS SIGNIFICANT HISTOLOGIC AND SYMPTOM RESPONSE

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

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



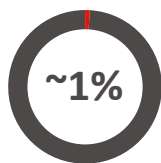
### Symptom Response at 12 Weeks (≥ 30% reduction in DSQ score)



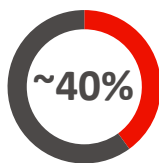
DSQ score: Dysphagia Symptom Questionnaire patient reported outcome score eos/hpf: peak eosinophils per high-powered field from endoscopic biopsies  
Eos/hpf: eosinophils per high-power field; BID: Twice daily; SOC: Standard of care; NDA: new drug application

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



Global population affected by celiac<sup>1</sup>



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



Estimated global, eligible patient population<sup>2</sup>

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



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

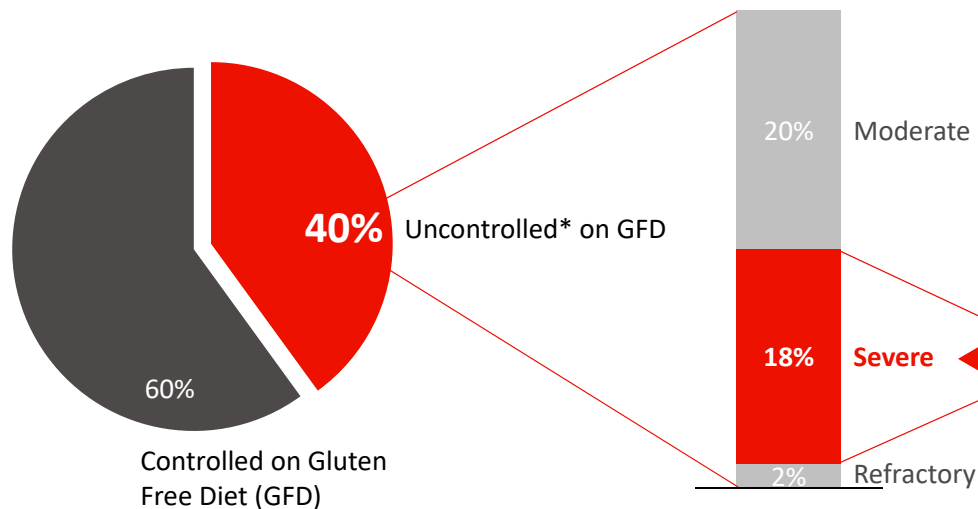
– Delisi, Celiac disease patient

1. Pooled global prevalence; Clin Gastroenterol Hepatol. 2018 Jun;16(6):823-836

2. Estimated number of patients projected eligible for treatment, in markets where the product is anticipated to be commercialized, subject to regulatory approval

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## WE ARE FOCUSING ON THE NARROWEST POPULATION WITH HIGH UNMET NEED



### Our focus:

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

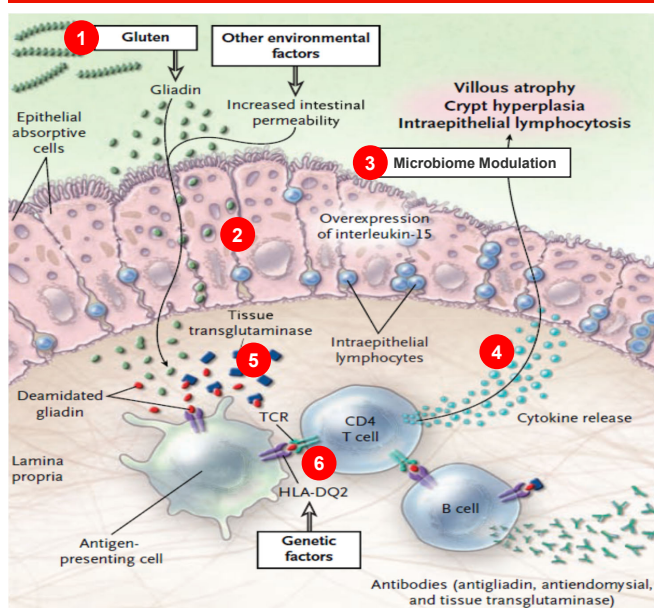
\*Uncontrolled defined as ongoing chronic moderate to severe symptoms with villous atrophy

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## OUR APPROACH TO TREATING CELIAC DISEASE



### TREATMENT OPPORTUNITIES FOR CELIAC DISEASE



Source: Green and Cellier, 2007

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



### PVP BIOLOGICS

Kuma062 promises greatly increased enzymatic efficiency and improved formulation over predecessors



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

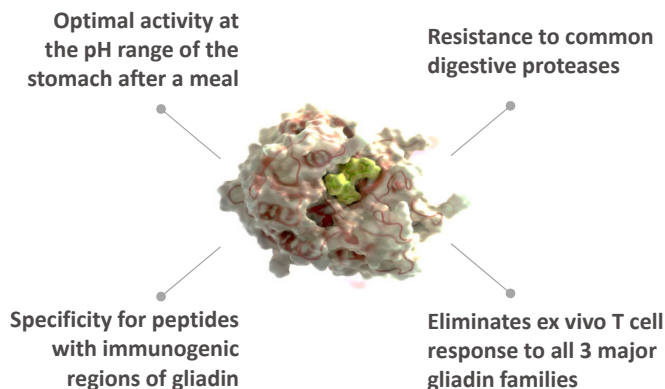
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# KUMA062: A HIGHLY POTENT ORAL GLUTENASE THAT COULD CHANGE THE STANDARD OF CARE IN CELIAC DISEASE



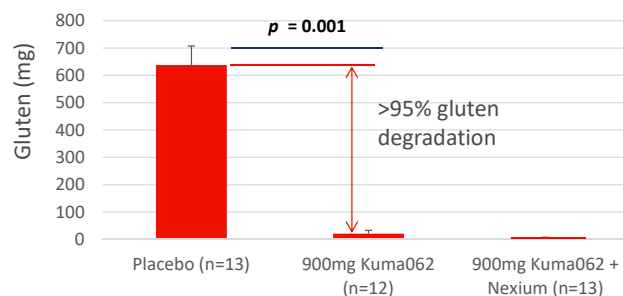
## ABOUT KUMA062

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



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

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



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

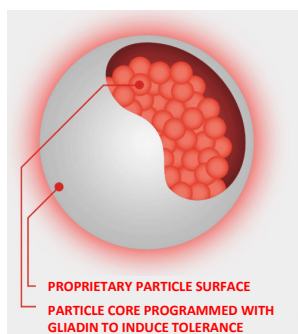
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# TAK-101: POTENTIAL BEST-IN-CLASS, INTRAVENOUS THERAPY FOR CELIAC DISEASE DESIGNED TO MODIFY T CELL RESPONSE



## ABOUT TAK-101\*

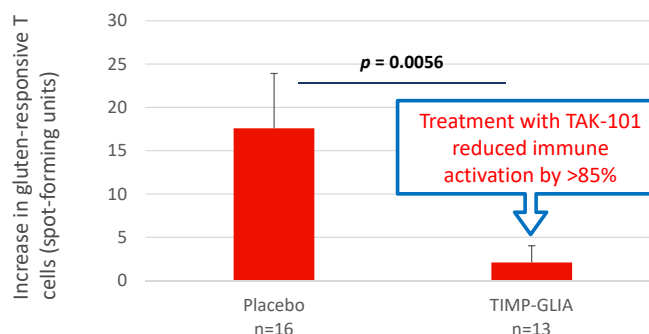
- Biodegradable polymer encapsulating antigen
- Designed to induce tolerance to gluten, reduce T cell responses to gliadin



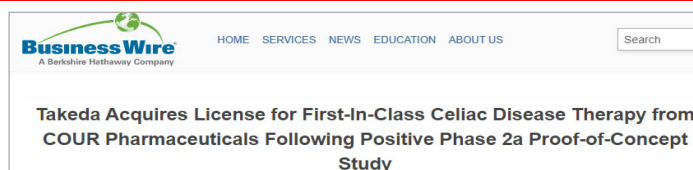
- Expected to provide durable (3 months or longer) down regulation of T cell responses to immunogenic gliadin peptides

## TAK-101 REDUCES IMMUNE ACTIVATION AFTER GLUTEN EXPOSURE

Interferon-gamma ELISPOT measurement of gluten-responsive T cells



## TAKEDA ACQUIRED EXCLUSIVE GLOBAL LICENSE TO TAK-101



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

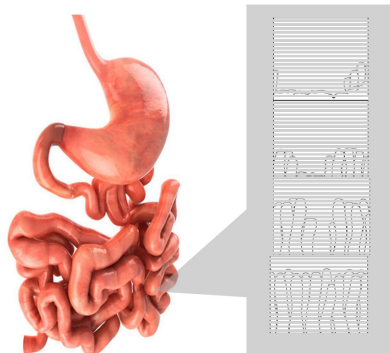
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## WE ARE LEADING THE SCIENCE IN CELIAC DISEASE WITH A NEW AI - BASED TOOL AND INGESTIBLE DEVICE



### PIONEERING AT BOUNDARIES OF CLINICAL MEDICINE

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



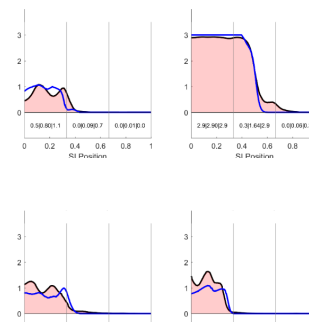
### INNOVATIVE USE OF TECHNOLOGY

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



### PRECISION MEASUREMENT USING AI

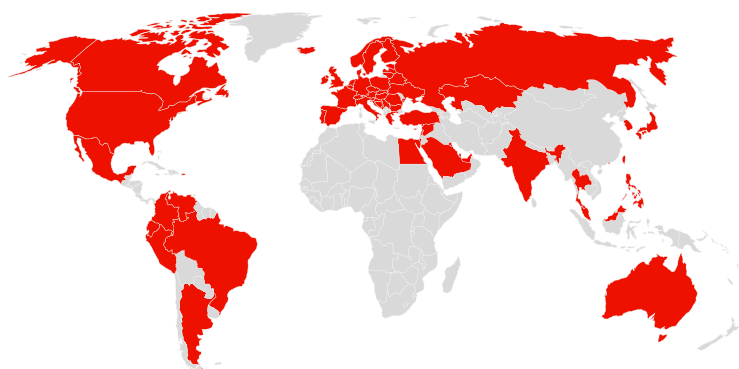
- Pioneering Automated Image assessment quantifies disease burden



## TAKEDA IS THE BEST COMPANY TO BRING CELIAC THERAPIES TO PATIENTS



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



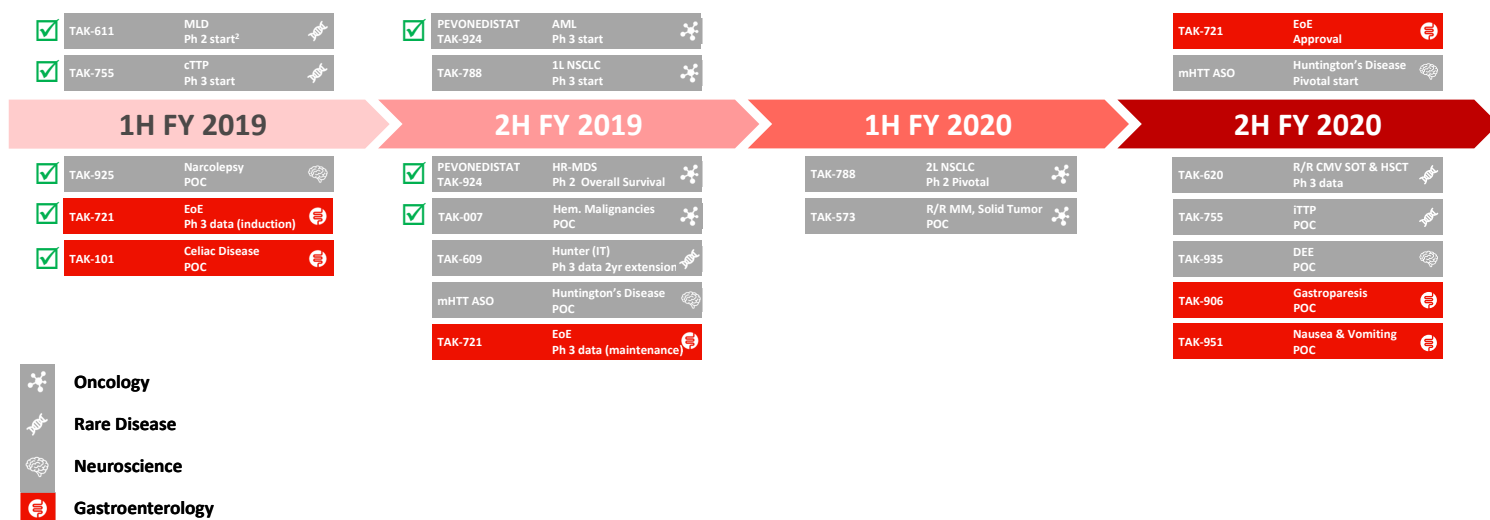
- Extensive GI clinical footprint
- Strong reputation for scientific excellence
- Lauded for calculated risk-taking by the GI community
- Experience with redefining guidelines and treatment paths



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



## PIVOTAL STUDY STARTS, APPROVALS



## 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

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## SUMMARY



# 1

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

# 2

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

# 3

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

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# 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>