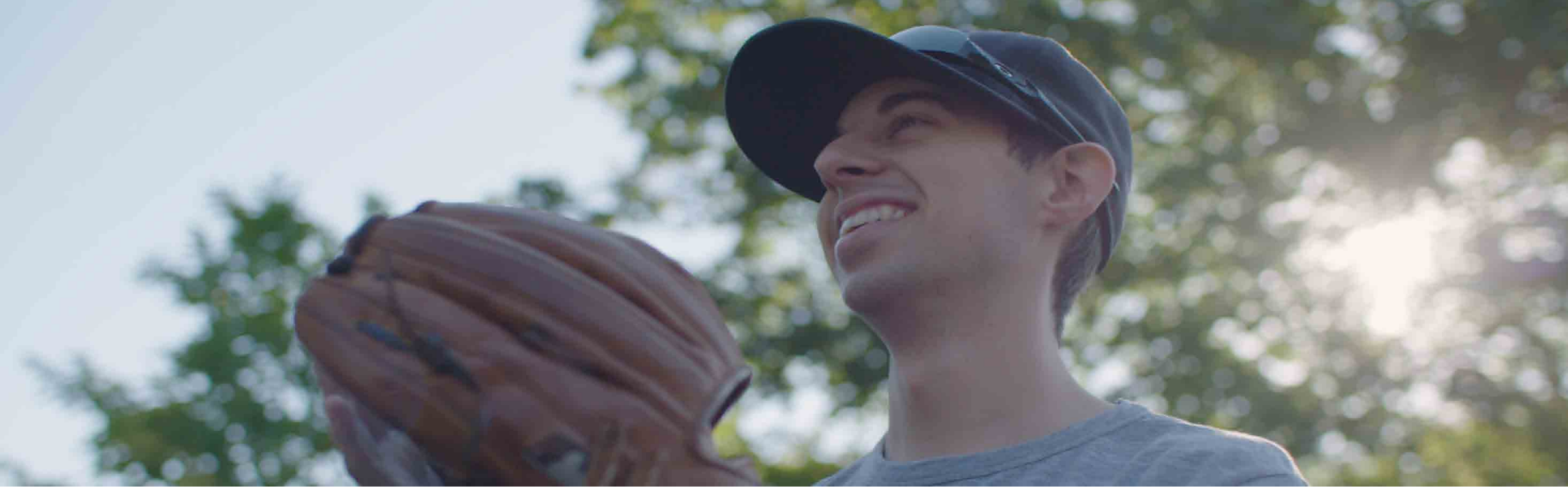


THERAPEUTIC AREA FOCUS IN GI WITH SPOTLIGHT ON CELIAC DISEASE

Asit Parikh, MD, PhD

Head Gastroenterology Therapeutic Area Unit

Takeda Pharmaceutical Company Limited

New York, NY

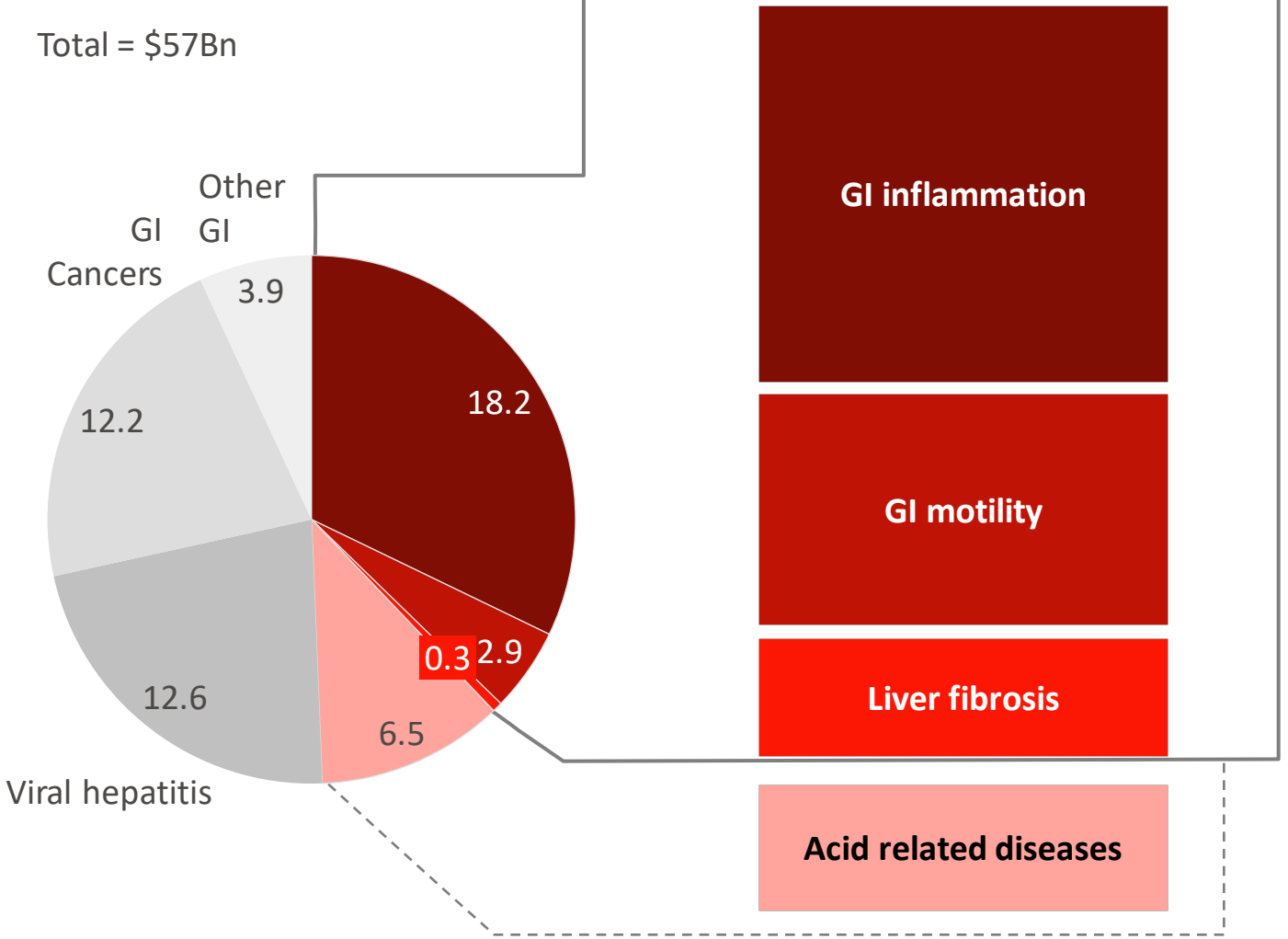
November 14, 2019

WE TARGET UNMET NEEDS THAT ALIGN WITH OUR STRENGTHS

AREAS OF FOCUS

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

GI WW RX SALES 2018 (USD BN)



TAKEDA GI DISEASE AREAS

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

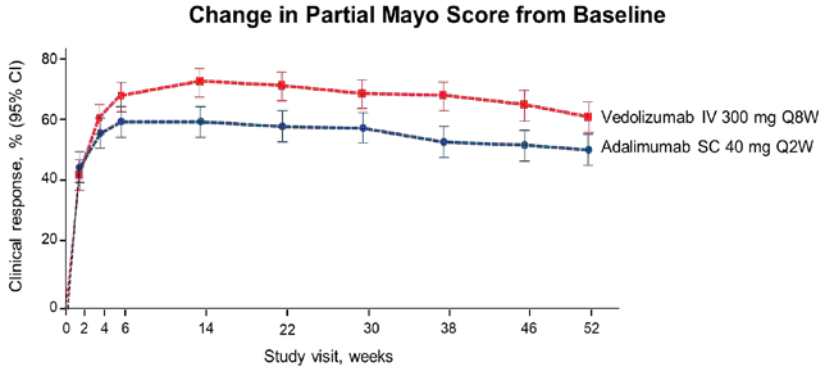
SOURCE: Evaluate Pharma indication specific sales, accessed May 29, 2019. Other GI includes: pancreatic insufficiency, hepatic encephalopathy, diarrhea, bowel clearance, gallstones, hemorrhoids

WE STRENGTHEN ENTYVIO BY CONTINUOUSLY IMPROVING VALUE FOR PATIENTS

COMPETITIVE POSITIONING

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

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



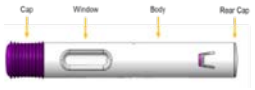
EXPANDED PATIENT POPULATIONS

Entyvio Subcutaneous Development

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

Prefilled syringe

Autoinjector pen



Portal jet-injector

Gut GvHD prophylaxis

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

GEOGRAPHIC EXPANSION

Entyvio IV

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

EXPECTED MILESTONES (FY)

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

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

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

WE ARE POSITIONED TO DELIVER NEAR-TERM & SUSTAINED GROWTH

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

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

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

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

ADDRESSES SIGNIFICANT UNMET NEED

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

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

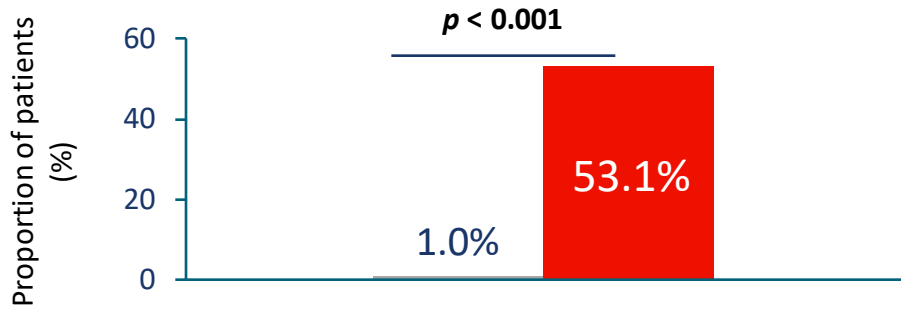
TAK-721 granted breakthrough therapy designation by FDA in 2016

EXPECTED MILESTONES (FY)	2019	2020	2021
	Q4: Maintenance TL results	Q2: NDA filing Q4: Approval	Q1: Launch

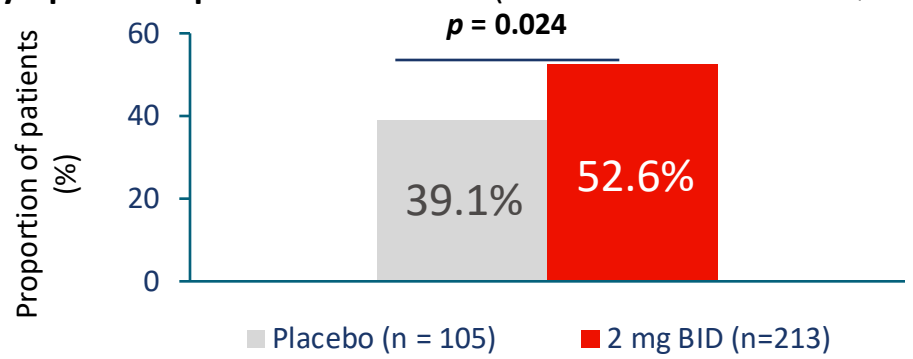
INDUCTION DATA SHOWS SIGNIFICANT HISTOLOGIC AND SYMPTOM RESPONSE

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

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



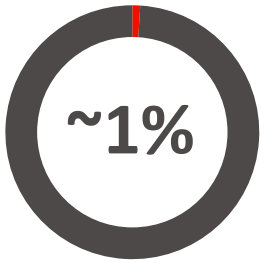
Symptom Response at 12 Weeks (≥ 30% reduction in DSQ score)



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

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

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



Global population affected by celiac[1]

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

Estimated global, eligible patient population[2]

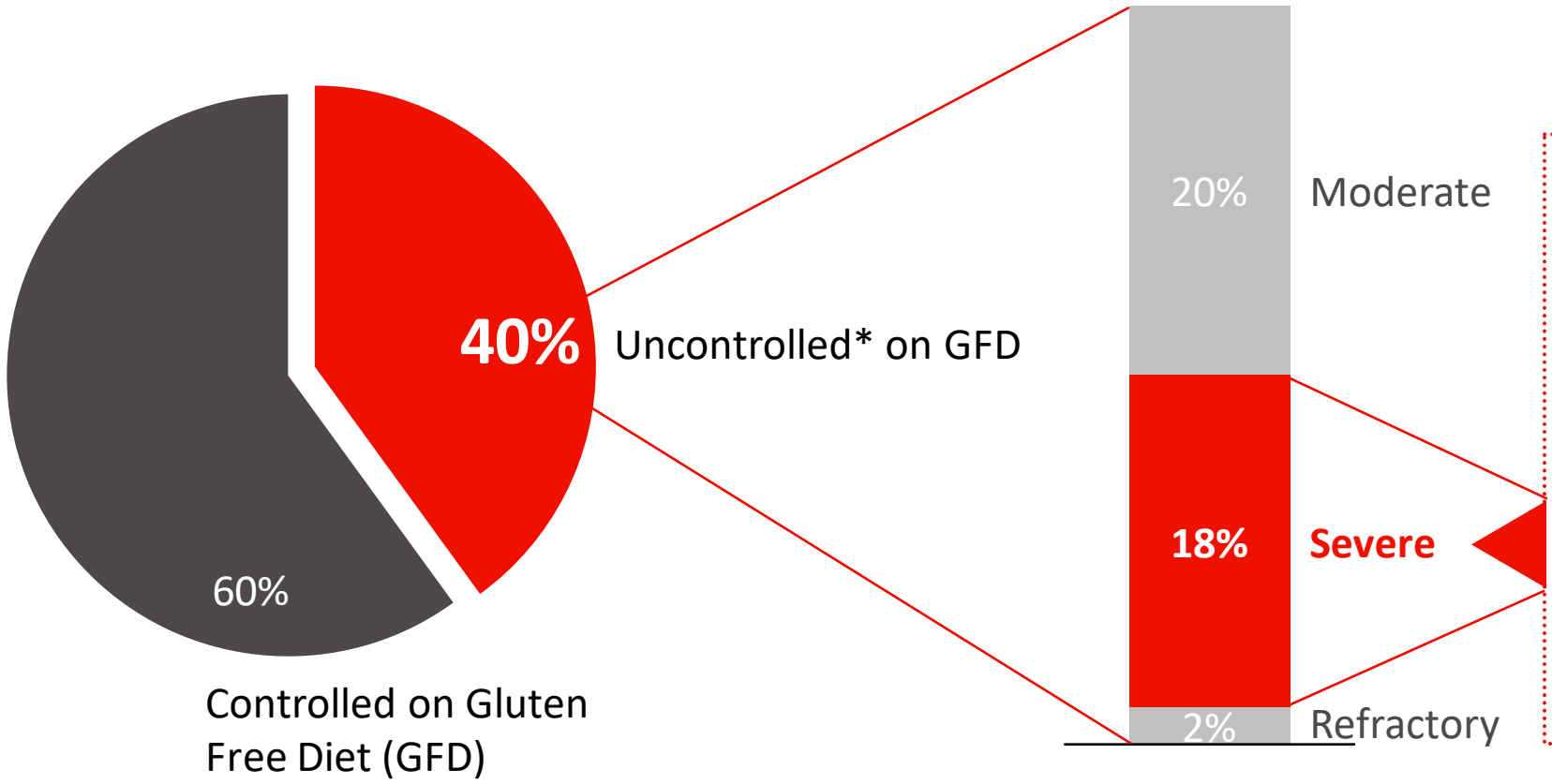
- Overlooked disease, growing prevalence
- Chronic symptoms
- Higher risk of certain cancers
- High treatment burden affecting the whole family
- No current pharmacologic therapies

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

– **Delisi**, Celiac disease patient

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

WE ARE FOCUSING ON THE NARROWEST POPULATION WITH HIGH UNMET NEED



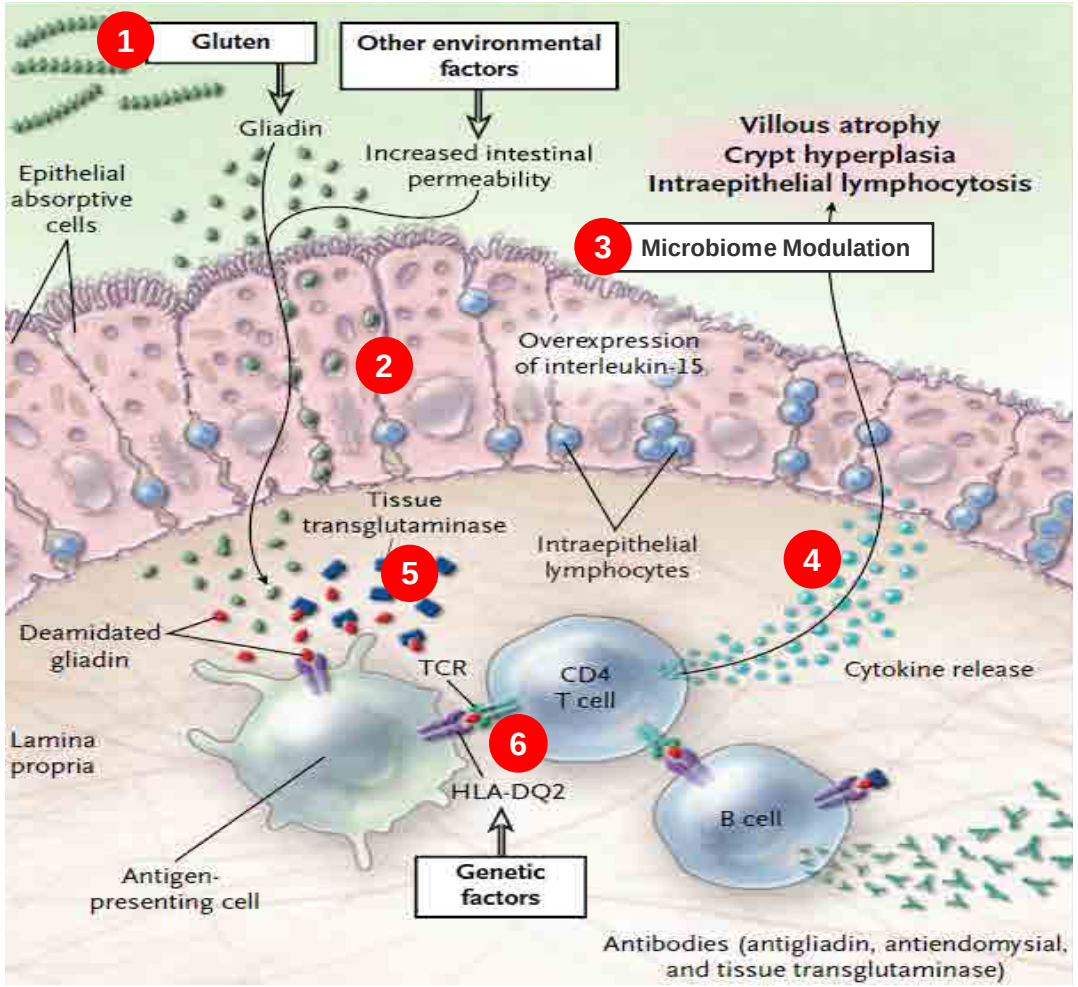
Our focus:

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

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

OUR APPROACH TO TREATING CELIAC DISEASE

TREATMENT OPPORTUNITIES FOR CELIAC DISEASE



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

PVP BIOLOGICS

Kuma062 promises greatly increased enzymatic efficiency and improved formulation over predecessors

COUR

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

Source: Green and Cellier, 2007

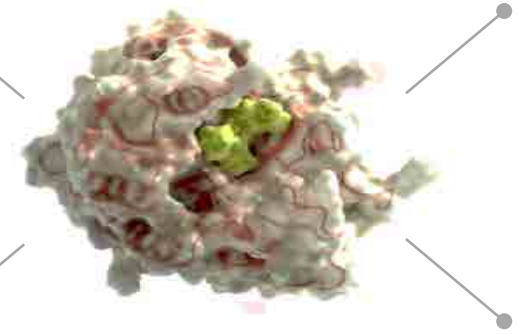
KUMA062: A HIGHLY POTENT ORAL GLUTENASE THAT COULD CHANGE THE STANDARD OF CARE IN CELIAC DISEASE

ABOUT KUMA062

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

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

Resistance to common digestive proteases

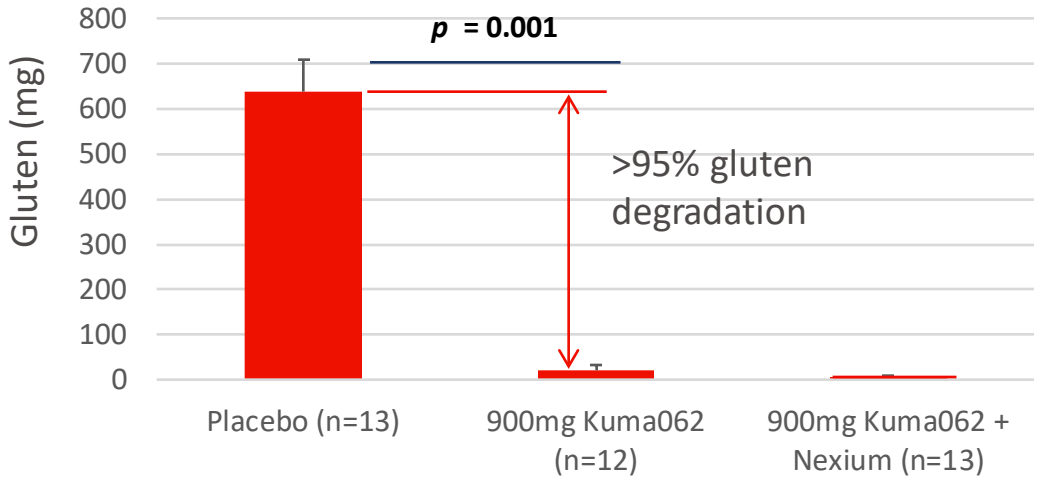


Specificity for peptides with immunogenic regions of gliadin

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

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

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

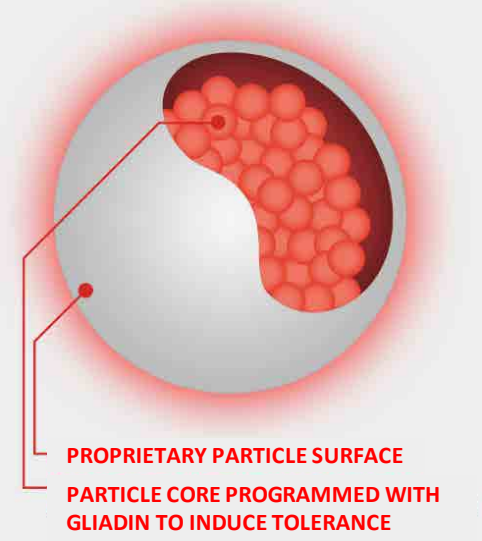


- Kuma well-tolerated, no identified safety concern
- Decision to acquire PVP Biologics expected Q3 FY2019

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

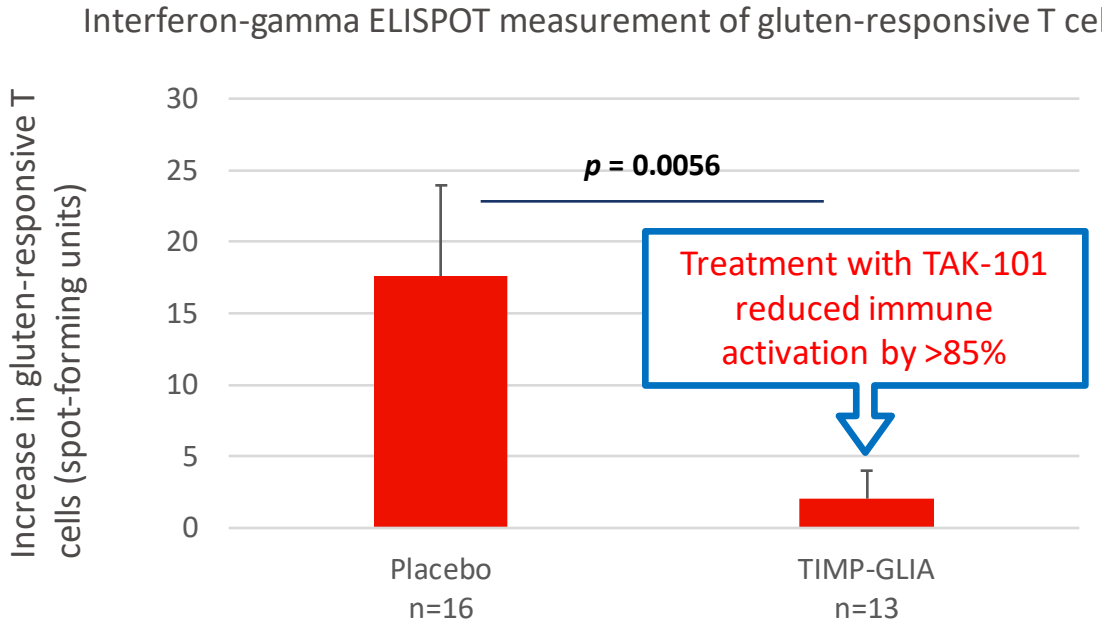
ABOUT TAK-101*

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



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

TAK-101 REDUCES IMMUNE ACTIVATION AFTER GLUTEN EXPOSURE



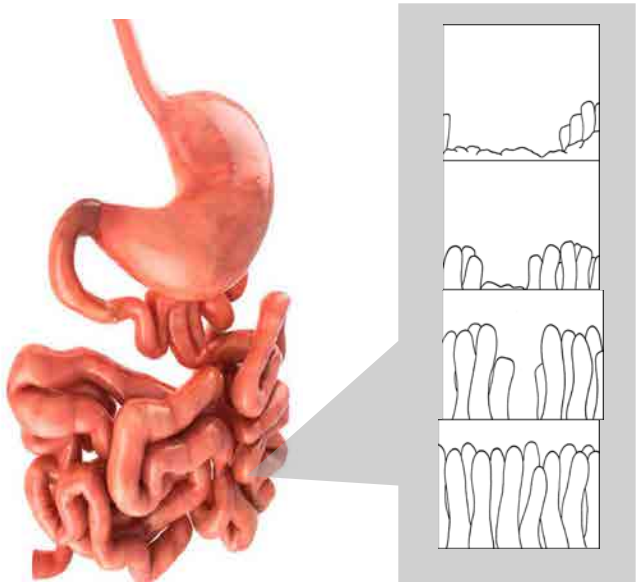
TAKEDA ACQUIRED EXCLUSIVE GLOBAL LICENSE TO TAK-101

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

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

PIONEERING AT BOUNDARIES OF CLINICAL MEDICINE

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

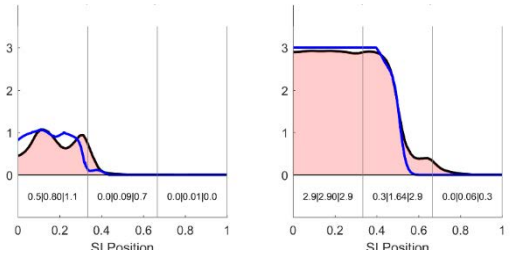


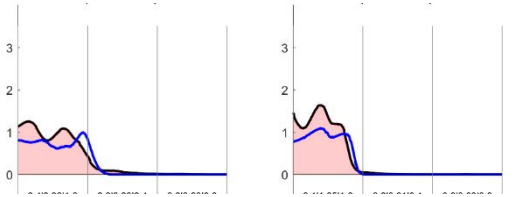
INNOVATIVE USE OF TECHNOLOGY

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

PRECISION MEASUREMENT USING AI

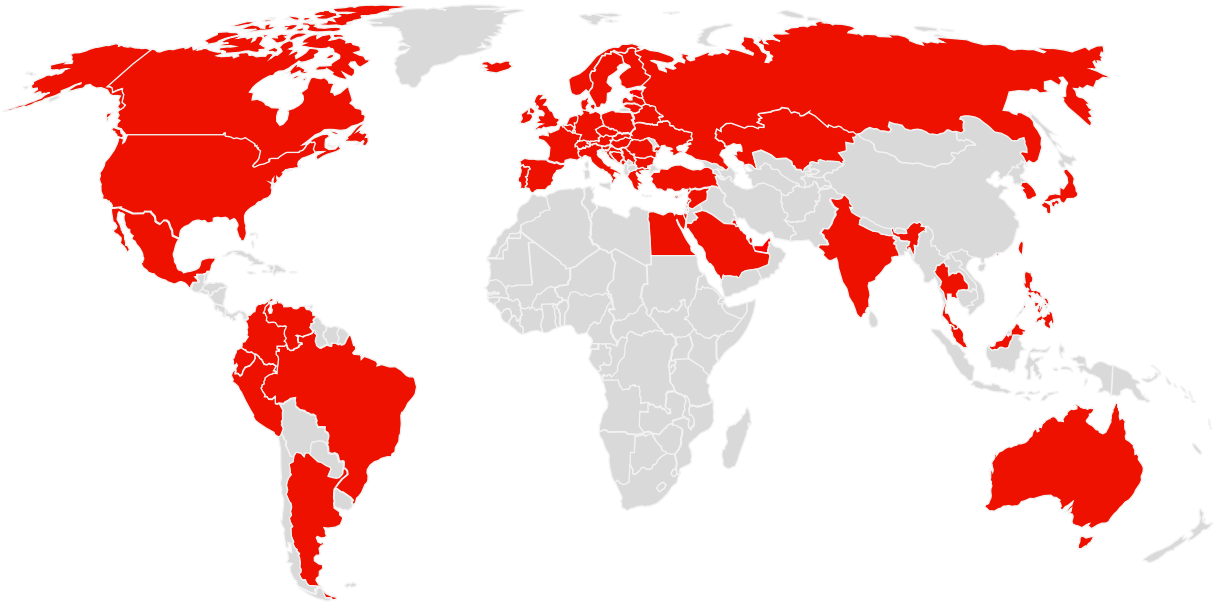
- Pioneering Automated Image assessment quantifies disease burden





TAKEDA IS THE BEST COMPANY TO BRING CELIAC THERAPIES TO PATIENTS

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



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

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

PIVOTAL STUDY STARTS, APPROVALS

1H FY 2019

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

2H FY 2019

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

1H FY 2020

- TAK-788 — 2L NSCLC — Ph 2 Pivotal
- TAK-573 — R/R MM, Solid Tumor — POC
- TAK-721 — EoE — Approval
- mHTT ASO — Huntington's Disease — Pivotal start

2H FY 2020

- TAK-620 — R/R CMV SOT & HSCT — Ph 3 data
- TAK-755 — iTTP — POC
- TAK-935 — DEE — POC
- TAK-906 — Gastroparesis — POC
- TAK-951 — Nausea & Vomiting — POC

Oncology

Rare Disease

Neuroscience

Gastroenterology

☑ Denotes milestones that have been achieved.

KEY DATA READOUTS

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

SUMMARY

1

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

2

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

3

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

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

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

Panel Q&A Session