

**Intract
Pharma**



Revolutionising The Way Biologics Are Delivered

Converting Injectable Antibodies into Safe and
Simple Oral Pills?

APS PharmSci, Sep 2019



Who We Are



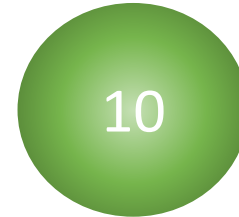
Founded



Spun-out



Founder



Team



Seed Funding

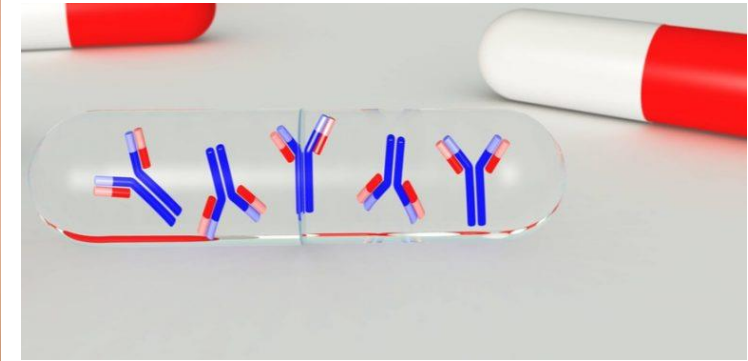


London BioScience
Innovation Centre

WHERE ENTERPRISE COMES TO SUCCEED



Our Mission



Transforming injectable antibody therapies into safe simple pills to revolutionize patient care

Antibodies are an Incredible Class of Therapeutics



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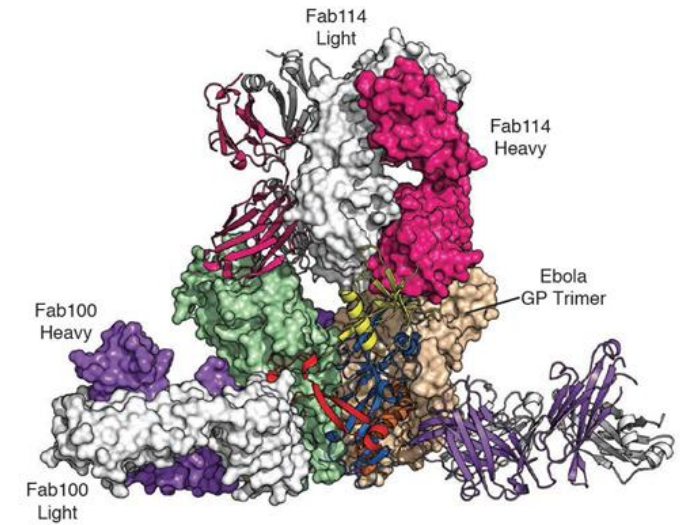
Ebola drugs show '90% survival rate' in breakthrough trial

13 August 2019



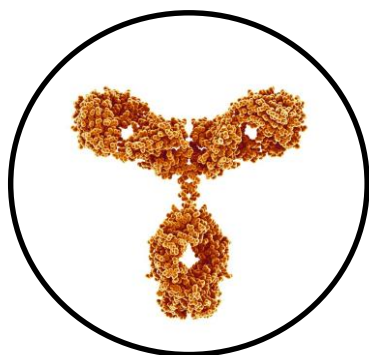
REUTERS

An outbreak of Ebola has killed more than 1,800 people in the Democratic Republic of Congo



Antibodies Dominate the Pharmaceutical Business

Top 10 Best Selling Drugs in the World (2018)



1	Humira (adalimumab)	\$19.9bn	Abbvie	Autoimmune Diseases
2	Eliquis (apixaban)	\$9.8bn	Bristol-Myers Squibb	Anti-coagulant
3	Revlimid (lenalidomide)	\$9.6bn	Celgene	Oncology
4	Opdivo (nivolumab)	\$7.5bn	Bristol-Myers Squibb	Oncology
5	Keytruda (pembrolizumab)	\$7.1bn	Merck	Oncology
6	Enbrel (etanercept)	\$7.1bn	Amgen	Autoimmune Diseases
7	Herceptin (trastuzumab)	\$7bn	Genentech	Oncology
8	Avastin (bevacizumab)	\$6.9bn	Genentech	Oncology
9	Rituxan (rituximab)	\$6.7bn	Genentech	Autoimmune/Oncology
10	Xarelto (rivaroxaban)	\$6.5bn	Bayer and J&J	Anti-coagulant

Budget vs Success Rate



Enormous Cost of Biologics Medicines



\$1

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US & Canada

The human cost of insulin in America

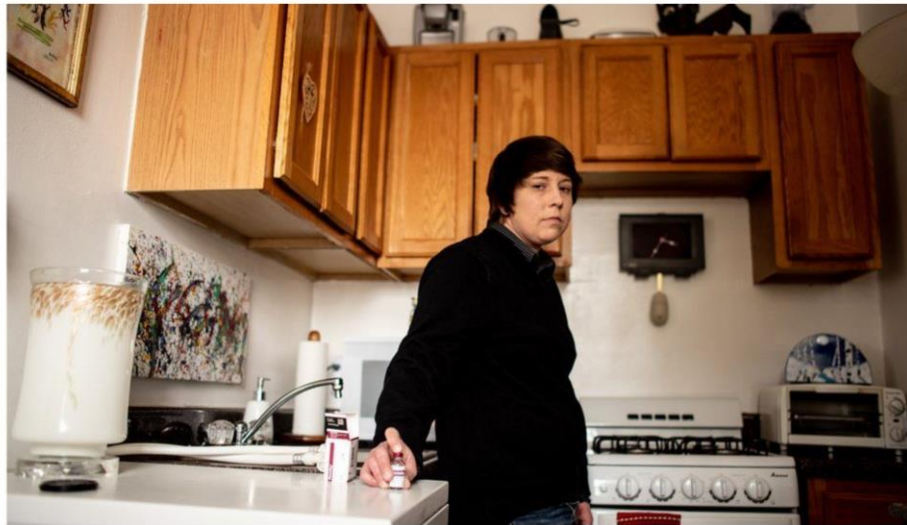
By Ritu Prasad
BBC News

© 14 March 2019

f t e Share



\$300



Our Major Therapeutic Focus

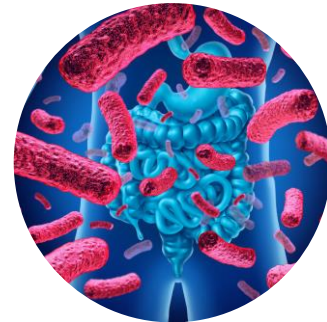
Gastrointestinal Diseases



Ulcerative colitis



Crohn's disease

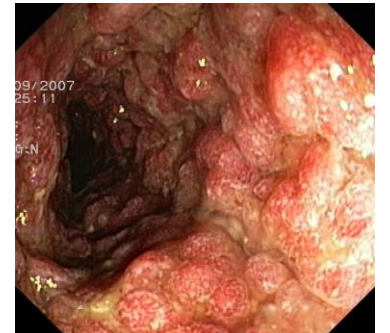


Infectious diseases of the gut e.g. C.difficile

Healthy Colon



Diseased Colon



Very Low Levels of mAb at the Site of Disease After IV Infusion

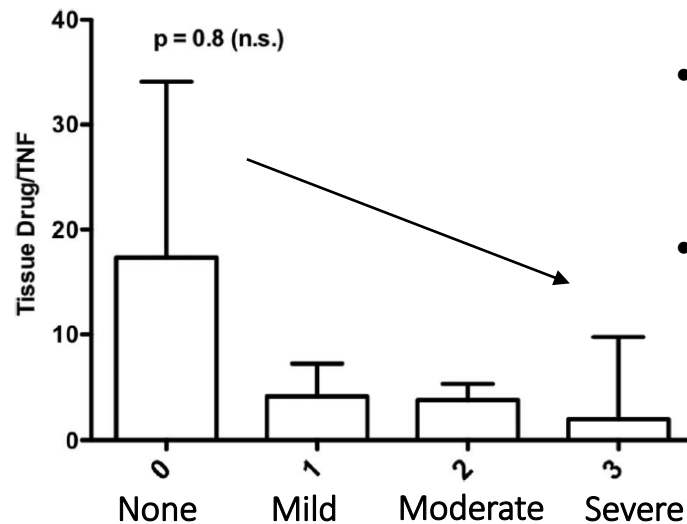
Inflammatory bowel disease

ORIGINAL ARTICLE

The association of tissue anti-TNF drug levels with serological and endoscopic disease activity in inflammatory bowel disease: the ATLAS study

Andres J Yarur,¹ Anjali Jain,² Daniel A Sussman,¹ Jamie S Barkin,¹ Maria A Quintero,¹ Fred Princen,² Richard Kirkland,² Amar R Deshpande,¹ Sharat Singh,² Maria T Abreu¹

- 30 IBD patients on anti-TNF mAb therapy (infliximab and adalimumab)
- Tissue biopsy and serum samples collected for drug analysis
- Response to therapy was correlated to serum and tissue PK of mAb



- Antibody levels in the inflamed tissue are low, even when serum levels are high
- >73% patients who did not respond to therapy had low tissue levels of antibody



Increasing systemic dose not a practical option

All Marketed Antibodies for IBD Are Injections

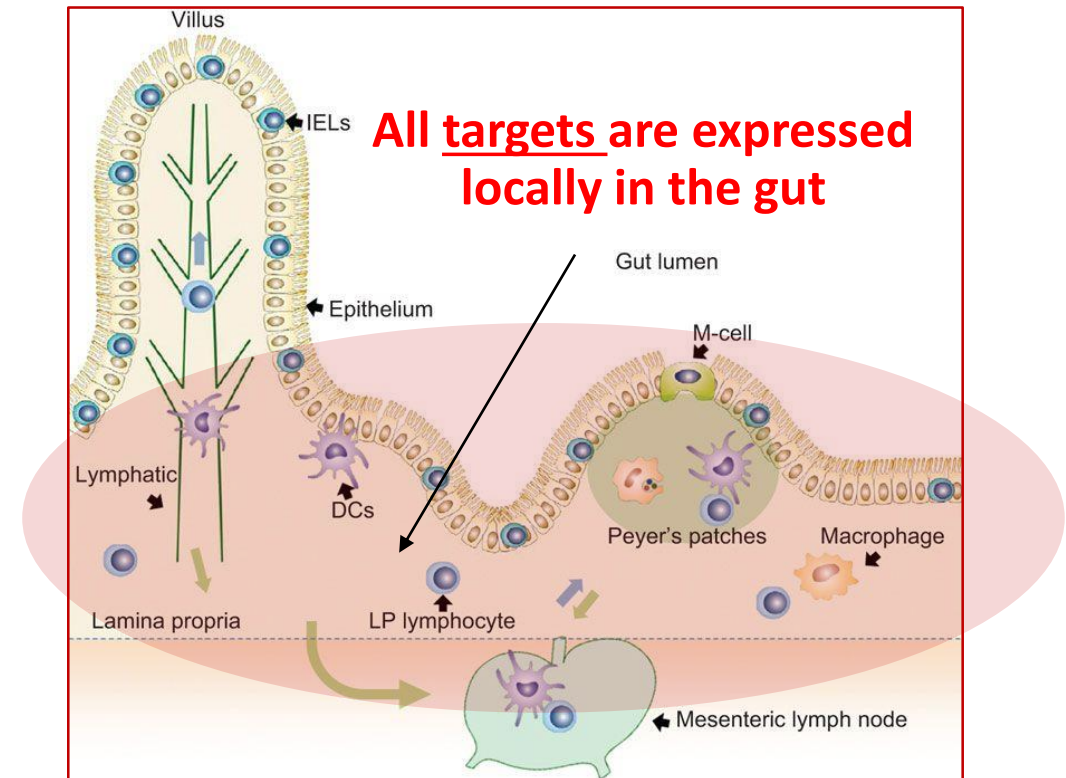
Anti-TNFs



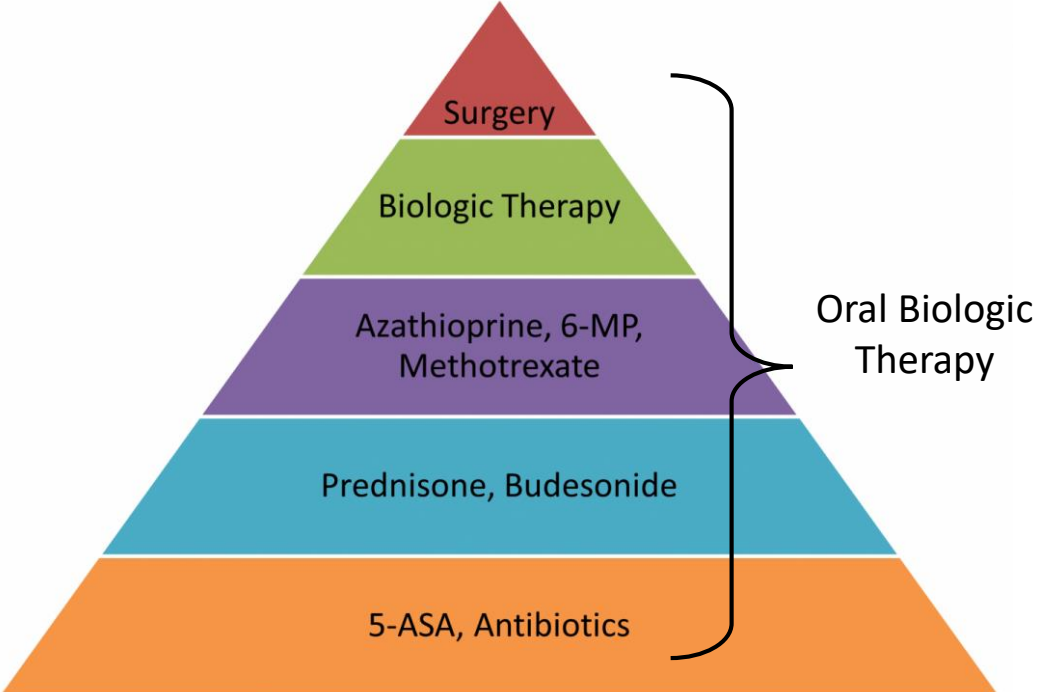
Anti-integrins



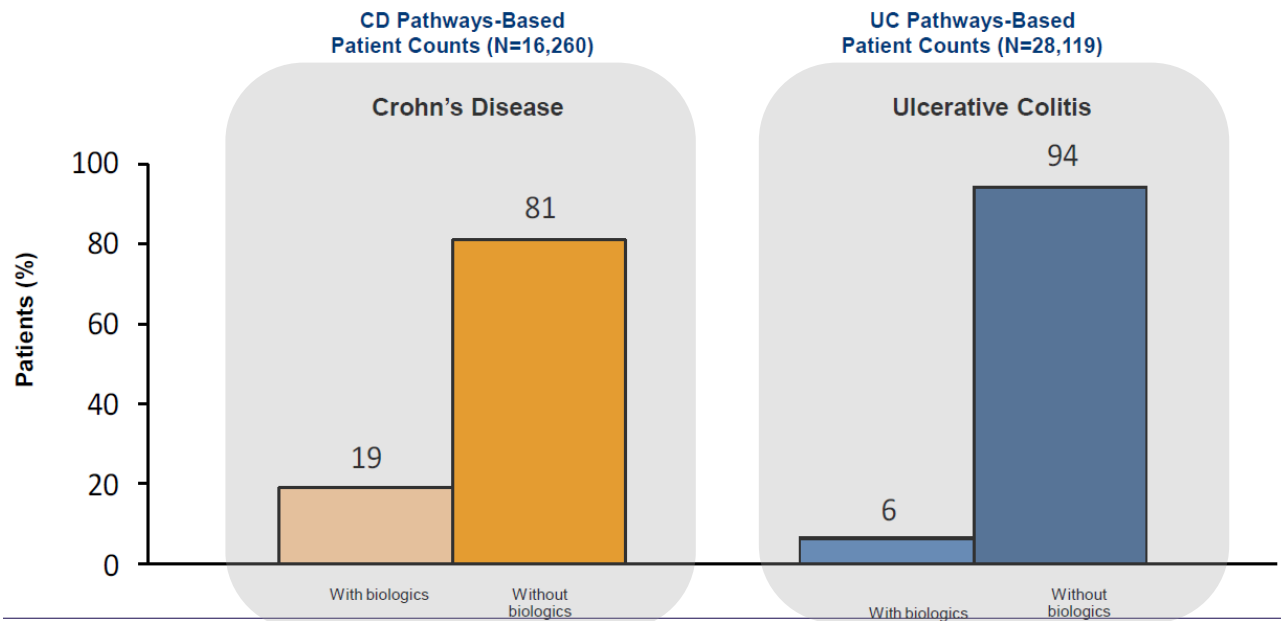
Anti-ILs



IBD Treatment Pyramid

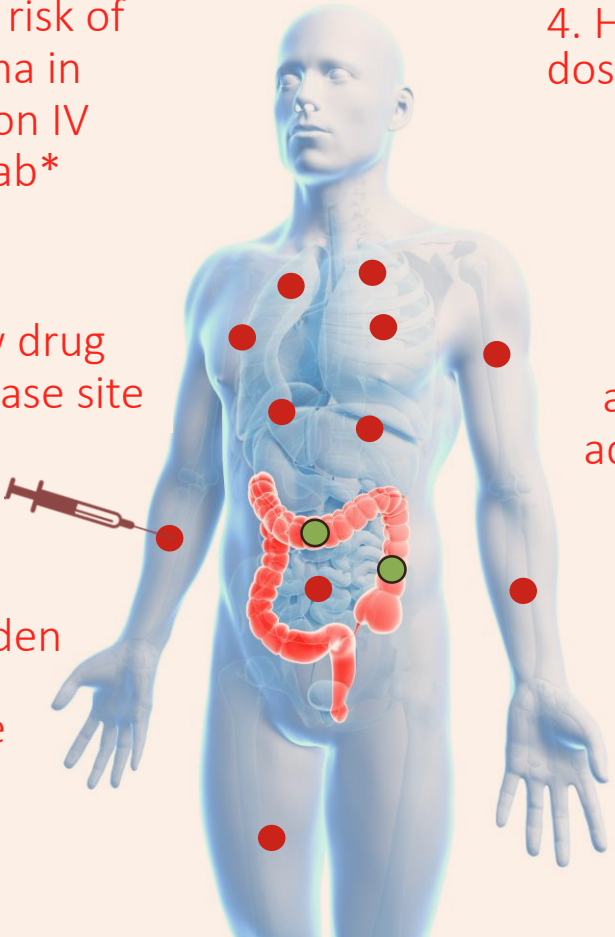


Overall use of biologics is low

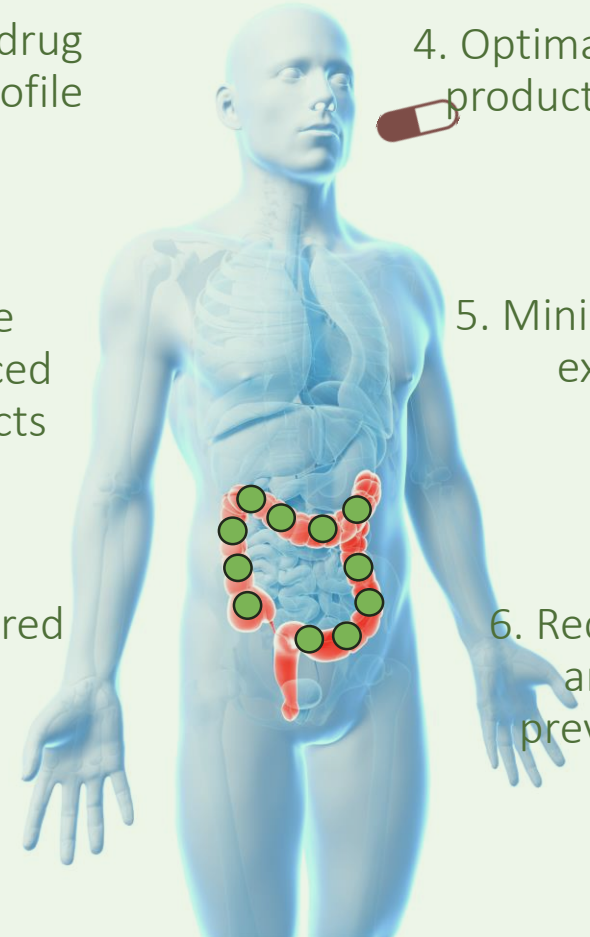


Why Oral Pills of Infliximab Instead of Injections?

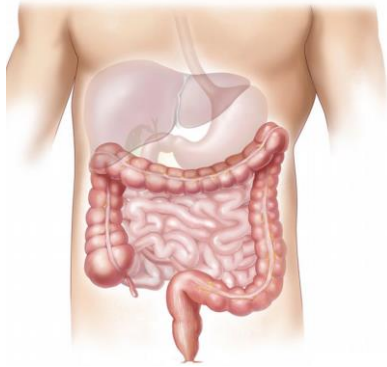
Injection

- 
1. Increase risk of lymphoma in patients on IV infliximab*
 2. Very low drug levels at disease site
 3. Patient burden & non-compliance
 4. Higher drug dose & cost of goods
 5. Systemic absorption & adverse effects
 6. >50% lose response over time

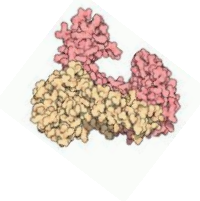
Targeted Oral Delivery

- 
1. Superior drug safety profile
 2. Higher tissue levels for enhanced therapeutic effects
 3. Patient preferred formulation
 4. Optimal, cost-effective product development
 5. Minimal systemic exposure
 6. Reduced anti-drug antibody and preventing loss of response

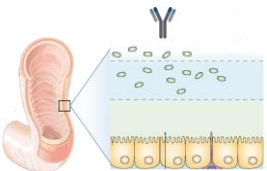
Challenges of Oral Delivery of Antibodies



Harsh pH conditions of stomach



High protease enzymes in the intestine



mAb size limits its absorption into tissue

MICROBIOME

Gut bacteria feast on the pills we pop

Mounting data raise the question: How will drug firms respond?

by *Megha Satyanarayana*

AUGUST 31, 2019 | APPEARED IN **VOLUME 97, ISSUE 34**



Credit: Mike Reddy

Human gut microbes chow down on the drugs we take every day, raising the question of whether the drug development process will soon incorporate microbial testing.

nature
International journal of science

Article | Published: 03 June 2019

Mapping human microbiome drug metabolism by gut bacteria and their genes

Michael Zimmermann, Maria Zimmermann-Kogadeeva, Rebekka Wegmann & Andrew L. Goodman [✉](#)

Nature **570**, 462–467 (2019) | [Download Citation](#) ↓

271
Drugs tested

66%
Metabolized



Portfolio of Oral Formulation Technologies



Phloral®

Dual-Trigger Enteric Coating for
Colon-Targeted Drug Delivery

- IP protection till 2027
- Mesalazine product on the market (in EU) by Swiss licensee Tillotts Pharma



Soteria®

Excipients to Stabilize Biologics
in the Intestine for oral delivery

- IP protection till 2036
- 7 programs in pre-clinical ongoing



DuoCoat®

Rapid release Enteric Coating
for Duodenal Targeting

- IP protection till 2026
- World's fastest enteric coating to release in drugs in duodenum
- Developed in partnership with Evonik

Our Approach To Oral Antibody Delivery



Ex-vivo Testing

Human Intestinal Stability and Permeability
Testing of Antibodies



Formulation into Proprietary Technologies



Phloral[®]

Dual-Trigger Enteric Coating for
Colon-Targeted Delivery of
Antibody



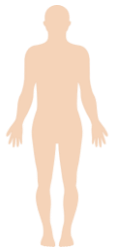
Soteria[®]

Excipients to Stabilize Antibody once
released in the Colon



In-vivo Testing

PK/Tox: Targeted Delivery of
Antibody to the Colon

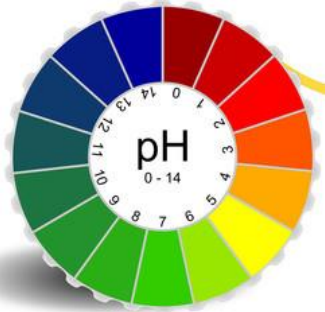
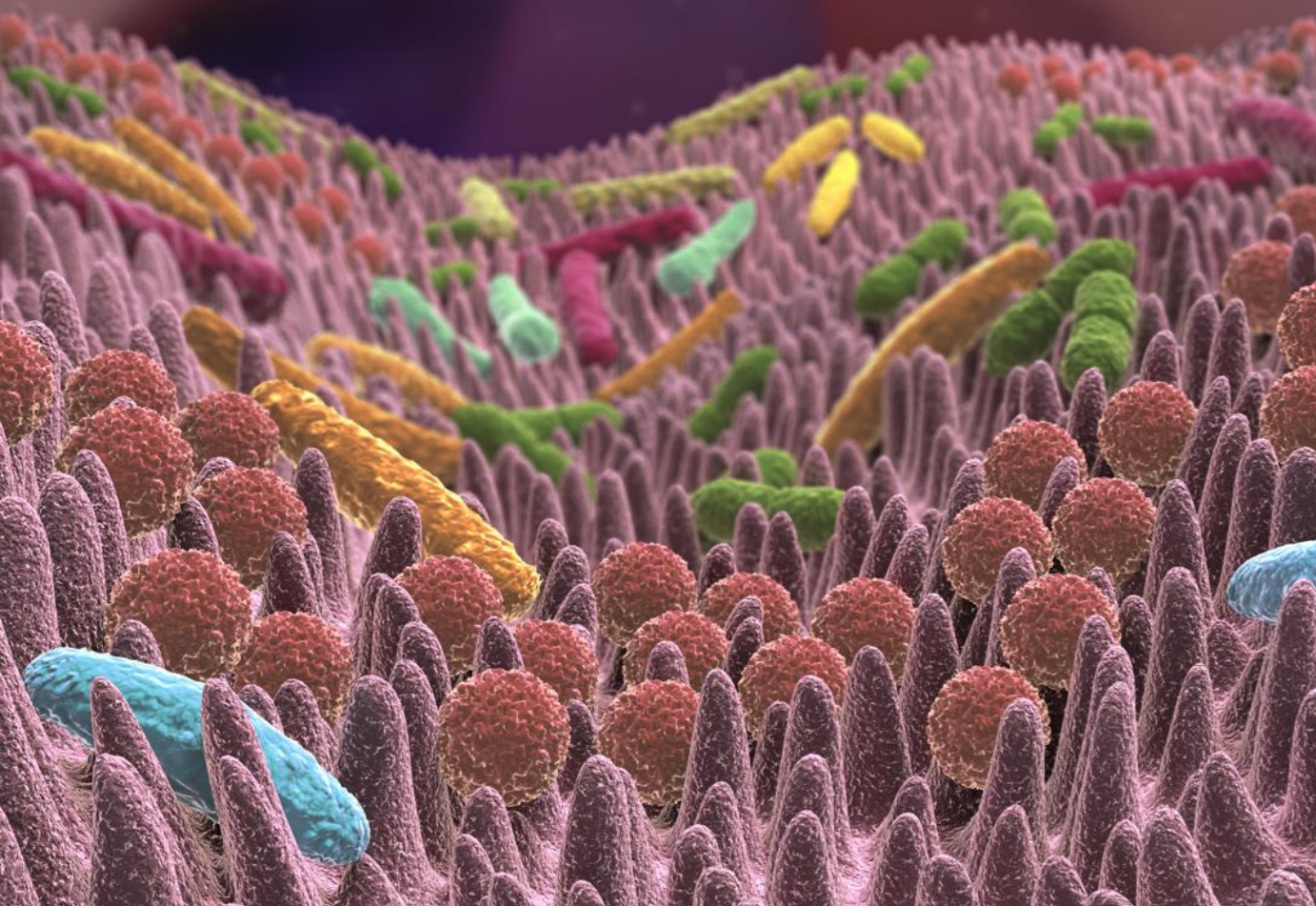


FIH Trials

Rapid Progression in to Trials in
IBD patients



Phloral® harnesses the power of the microbiota
Trillions of bacteria naturally residing in the colon



p
H



- flora -



oral

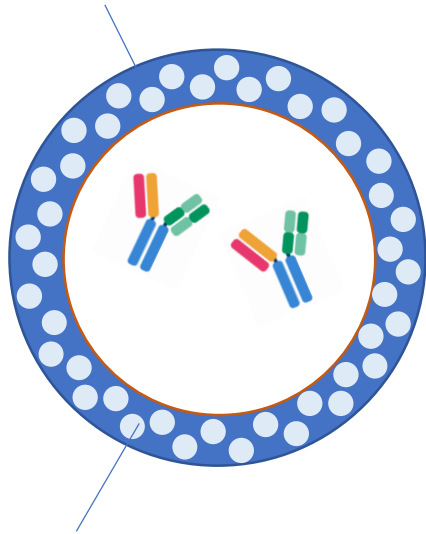
Phloral®

Innovative Mechanism of Action

Single Film Coating

Mixture of pH sensitive polymer and microbiome sensitive polysaccharide

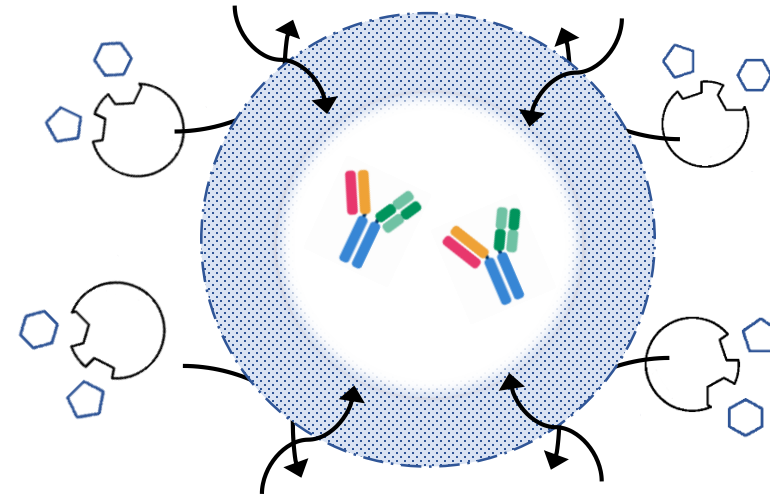
pH Sensitive Polymer:
Eudragit® S



Microbiome Sensitive
Polysaccharide: Resistant Starch

Dual Action and Fail-Safe Mechanism

If threshold pH is not reached in colon of subjects, trillions of bacteria in the colon digest the polysaccharide in the coating



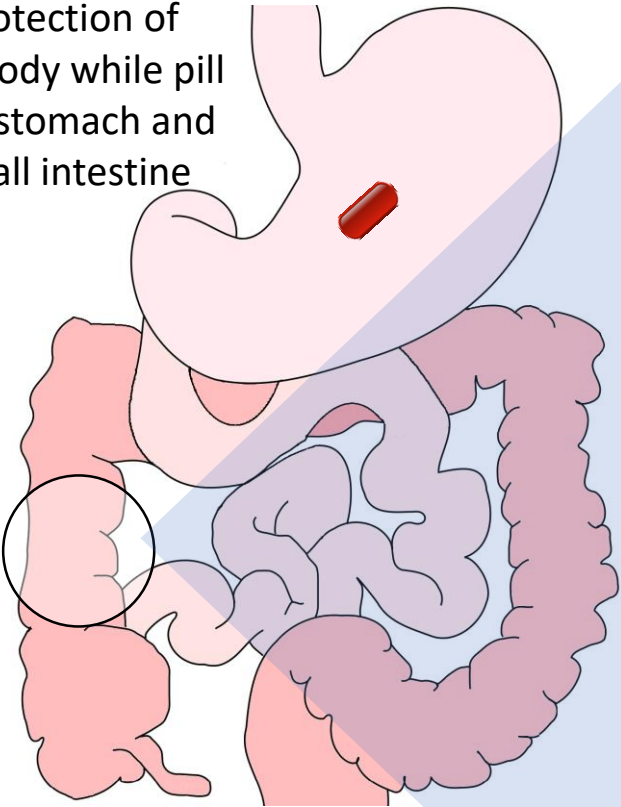
Phloral[®] Coating Now on the Market for IBD Treatment



- ✓ Novel small molecule product (mesalamine) launched for Ulcerative Colitis in Europe in Jan 2019
- ✓ Phloral coating now the world's first and only dual-trigger coating to reach the market for colon targeting

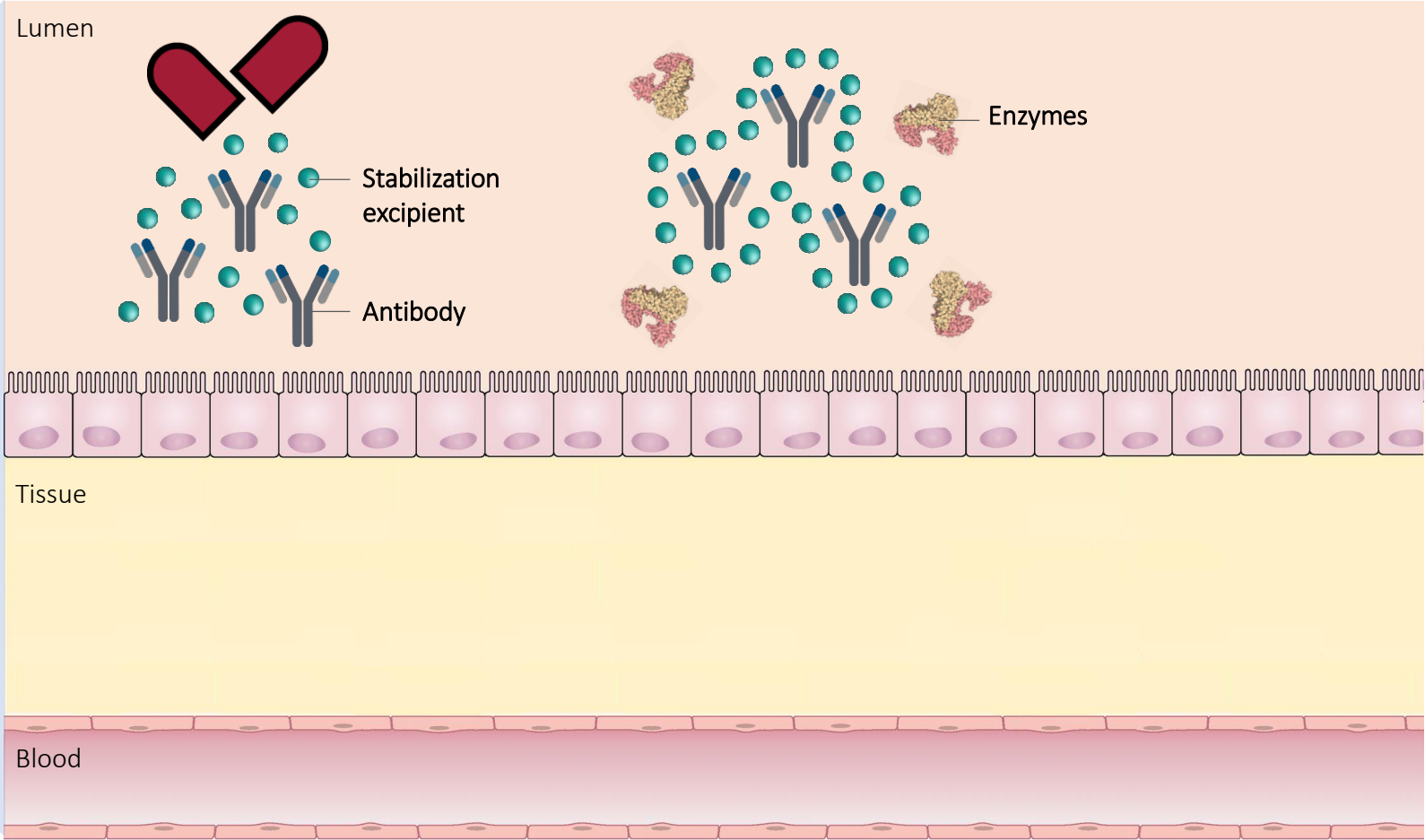
MOA of Intract's Oral Infliximab Approach for IBD Treatment

Protection of antibody while pill is in stomach and small intestine

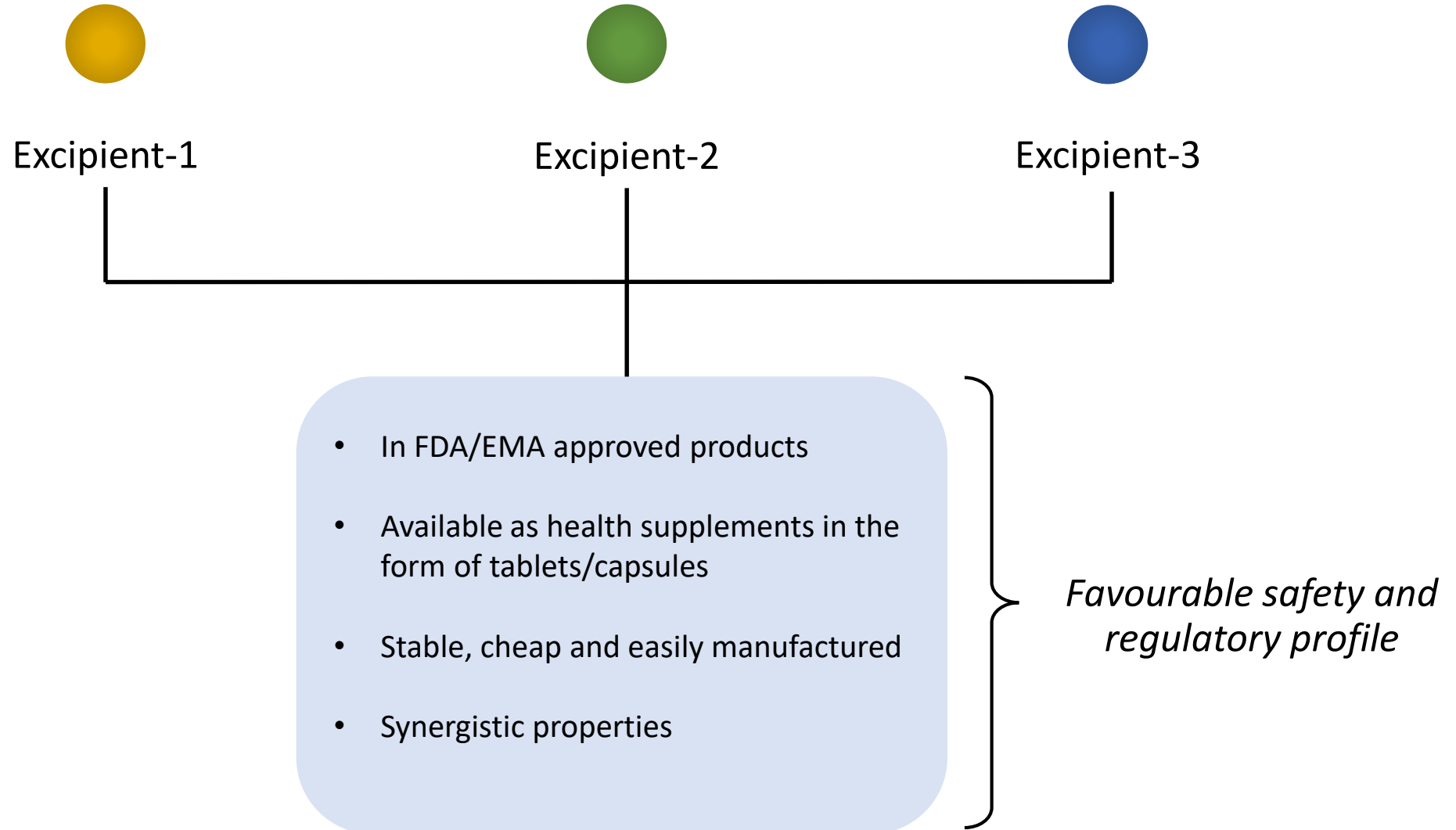


1. Release of Antibody from the Pill in the Colon

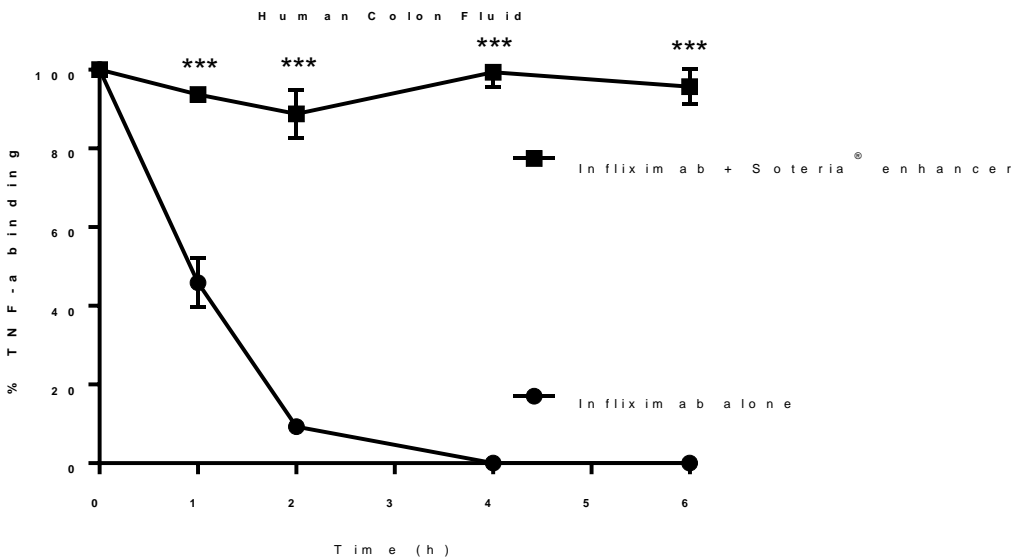
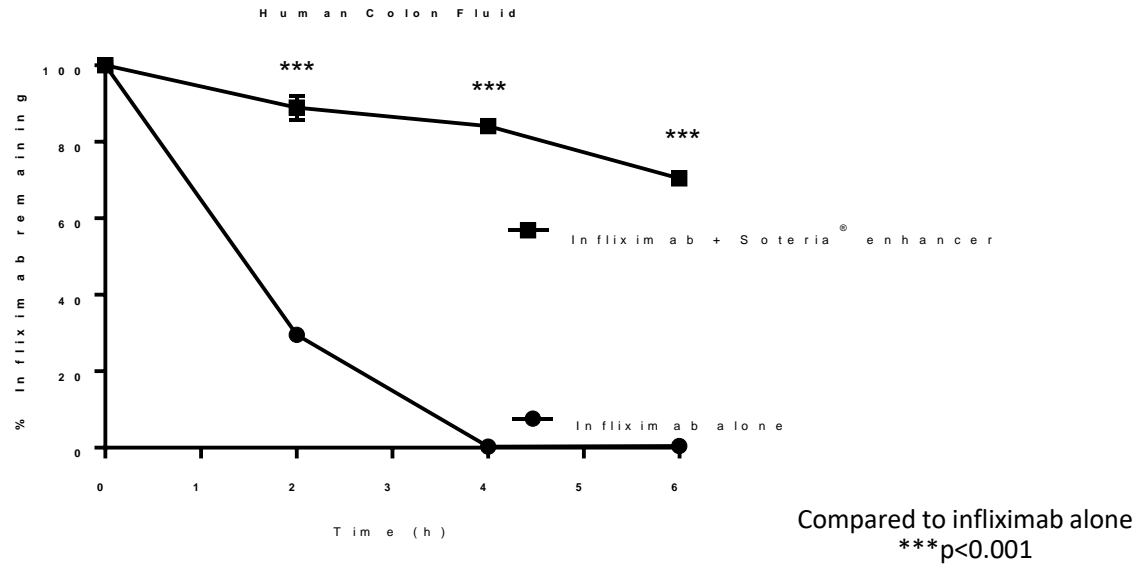
2. Stabilization of Antibody Against Proteases



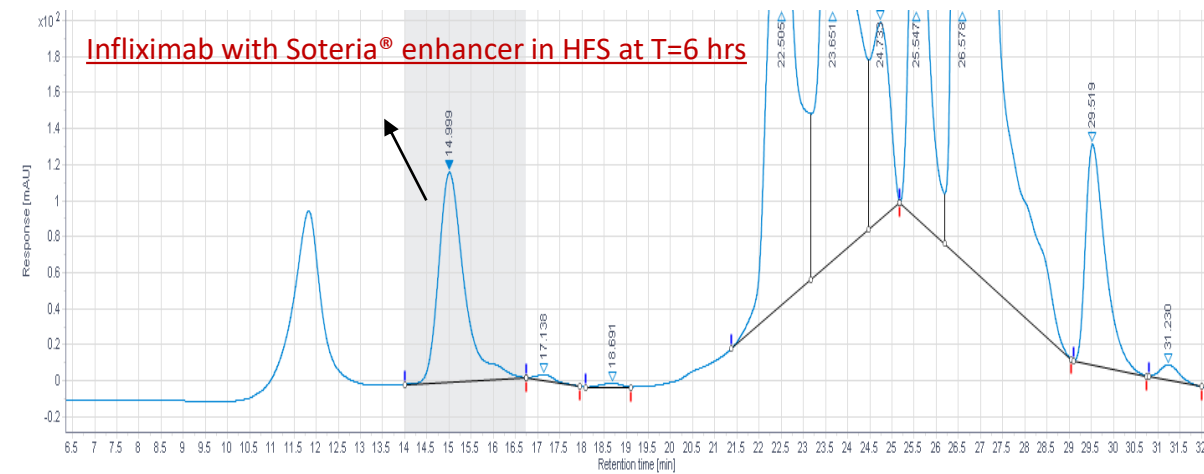
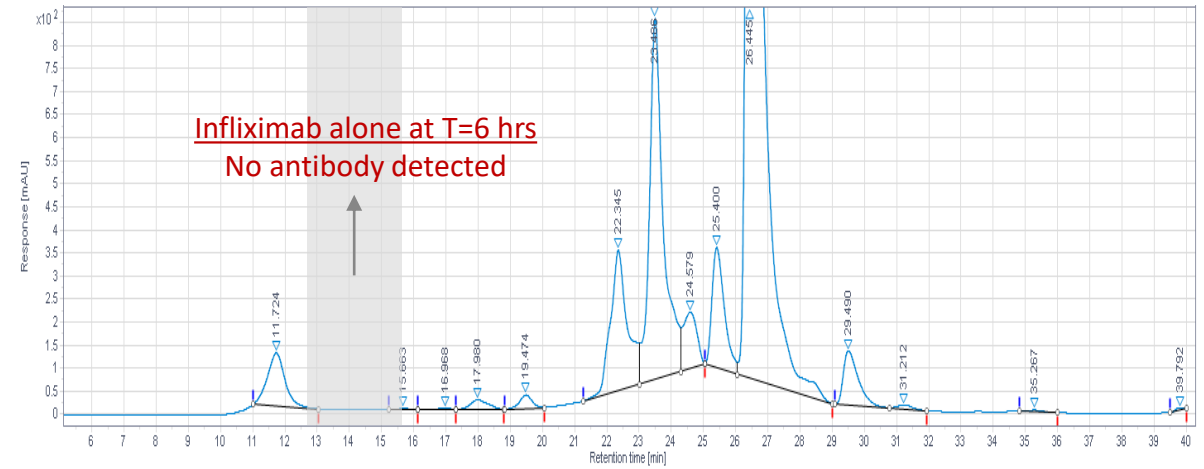
Soteria[®]: Stabilizing Enhancement Agents



Soteria[®]: Improved Stability of Infliximab in Human Colon



Size-exclusion chromatography

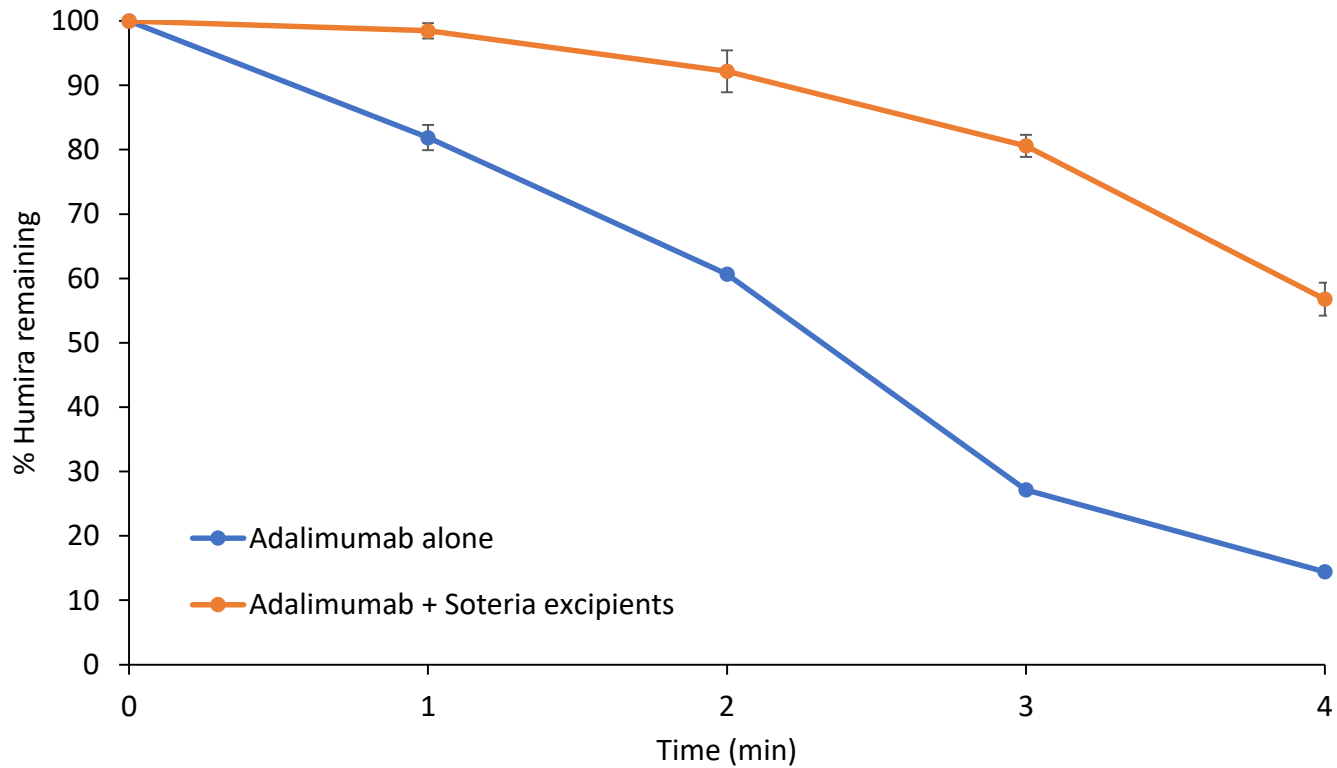


Soteria[®]: Improved Stability of Adalimumab

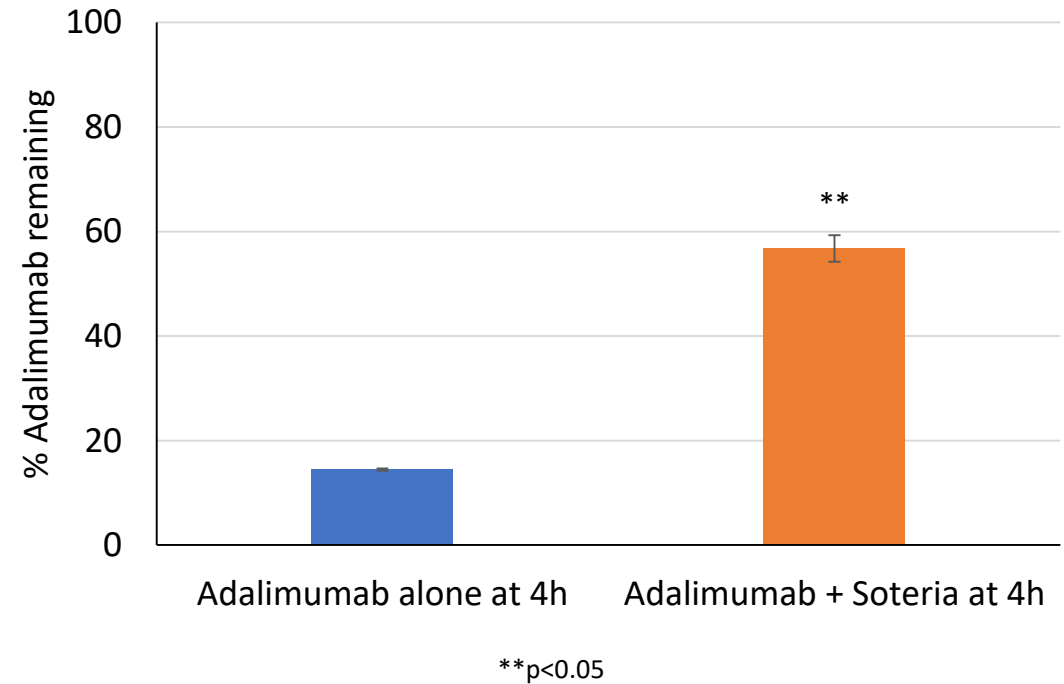
Potential to Expand Application of Technology to other Autoimmune Antibodies



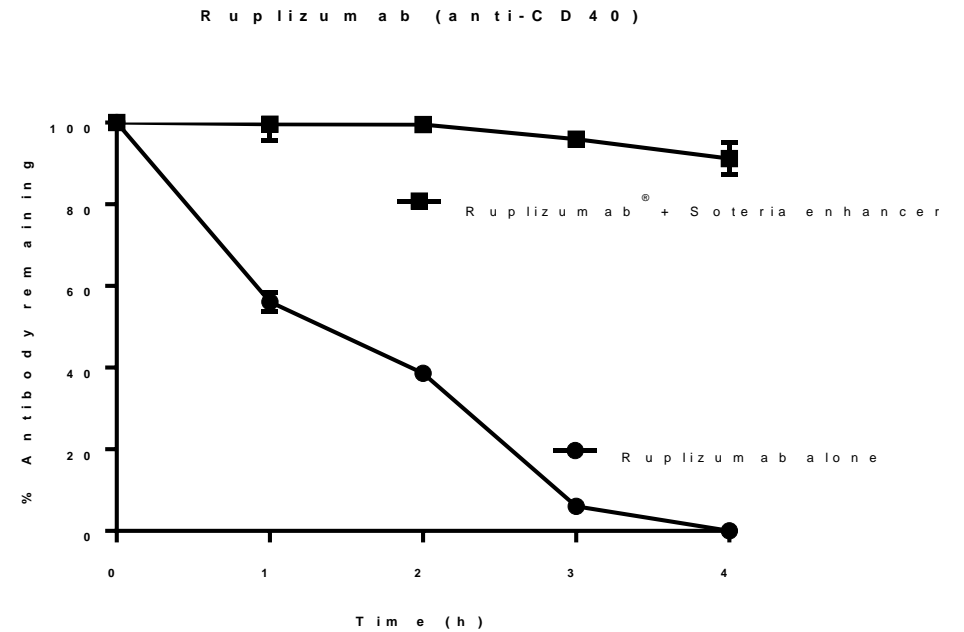
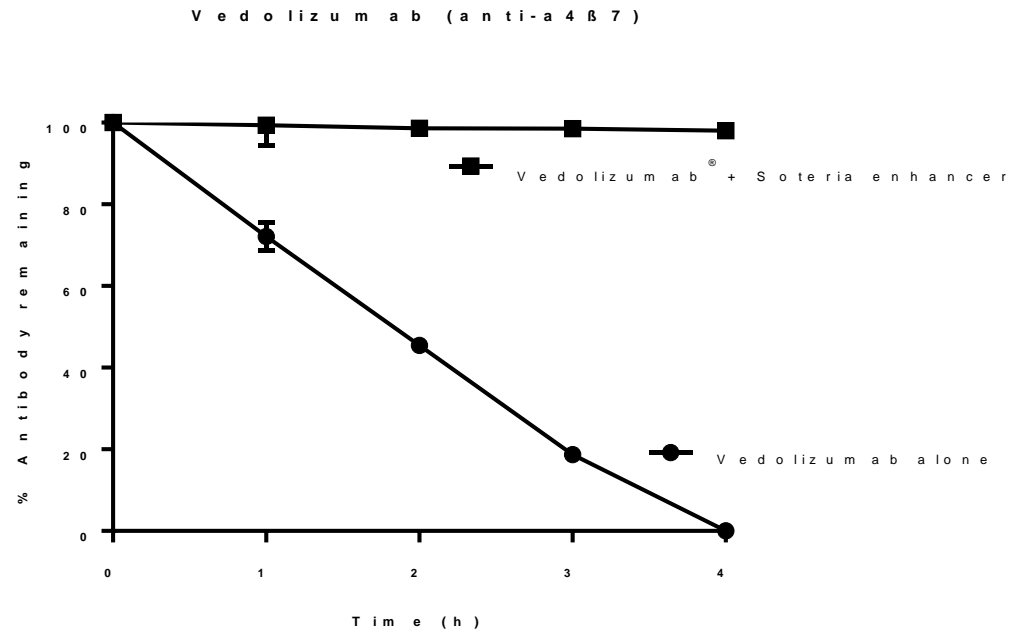
Stability of Adalimumab in Human Colon



% Recovery at 4h

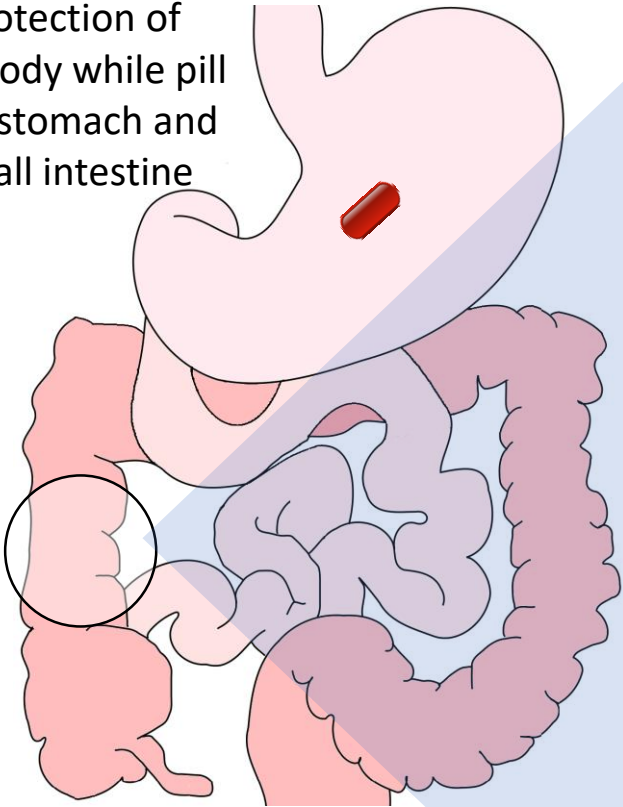


Ex-vivo Stability of Vedolizumab and Ruplizumab in Human Colon



MOA of Intract's Oral Infliximab Approach for IBD Treatment

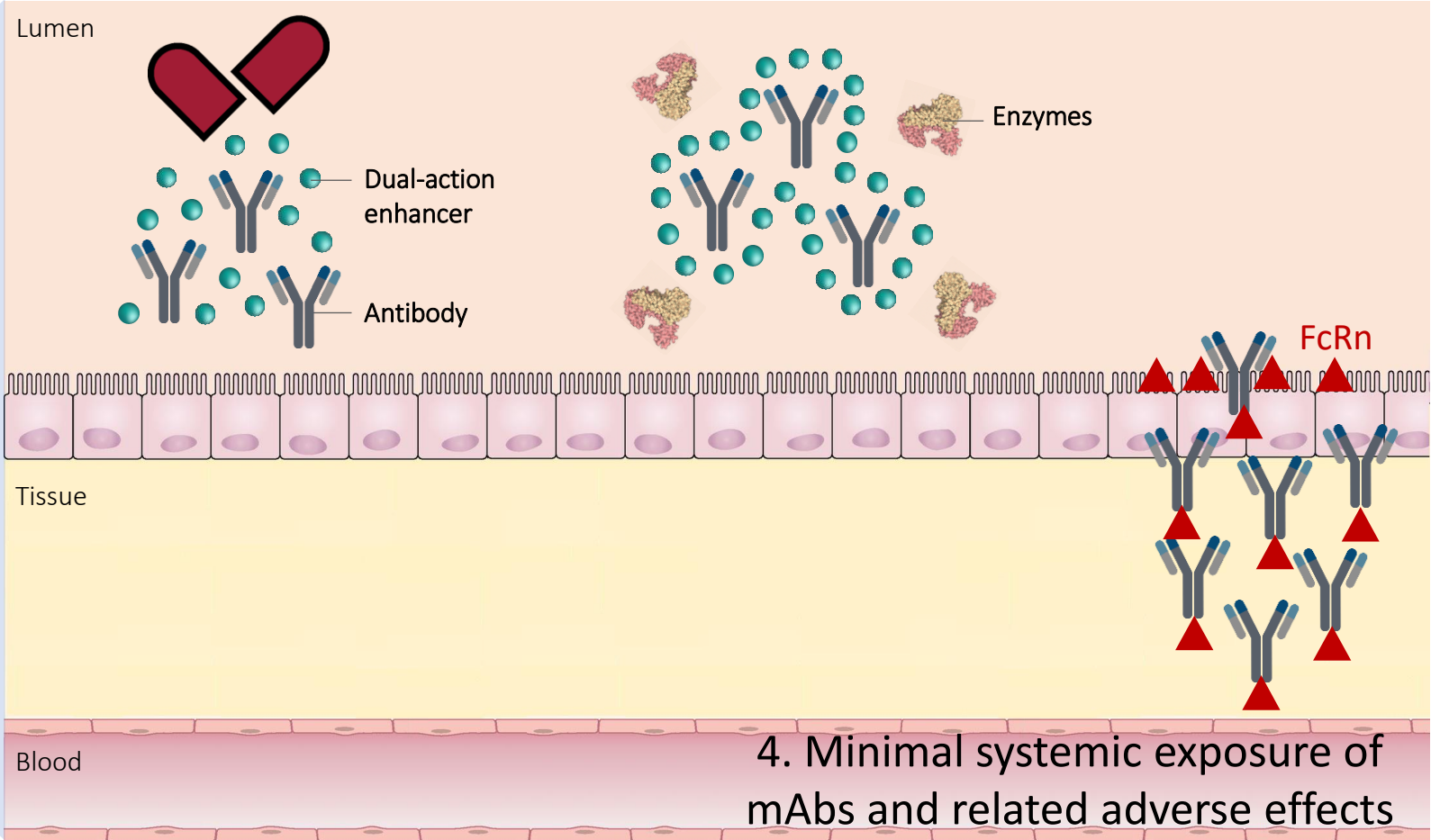
Protection of antibody while pill is in stomach and small intestine



1. Release of Antibody from the Pill in the Colon

2. Stabilization of Antibody Against Proteases

3. Improved Uptake into Tissue via FcRn



Formulation of Infliximab in a Capsule For Pre-Clinical Testing in Rats



Wistar rats

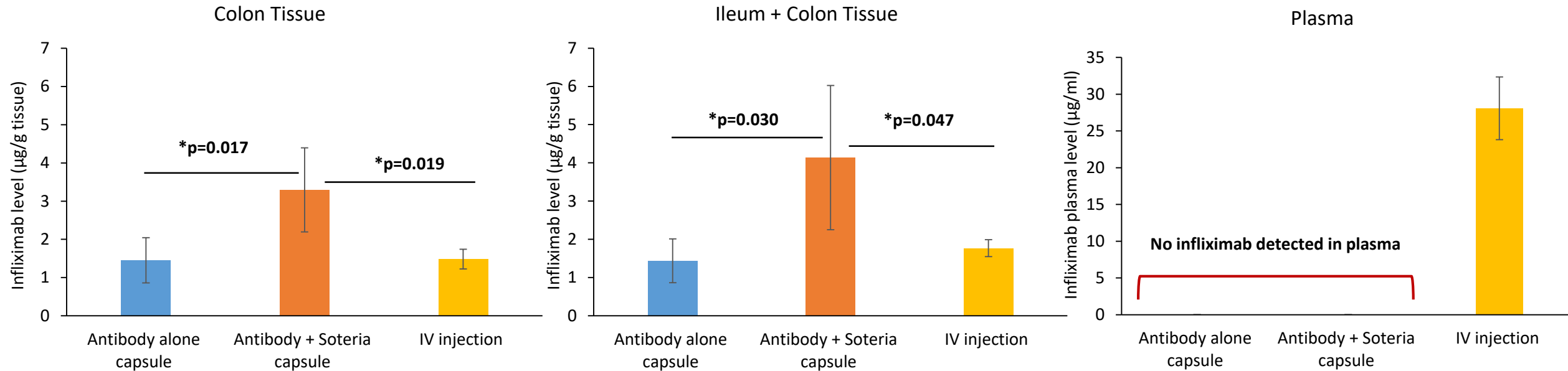
- Formulation into size 9h capsules compatible for oral dosing in rats
- Capsule core contains Infliximab + Soteria[®] excipients
- Outside of the capsule is coated with Phloral[®] to achieve colon targeting
- Sacrifice animal after 7hrs post dosing
- Plasma and Intestine tissue samples analysed for infliximab level by ELISA

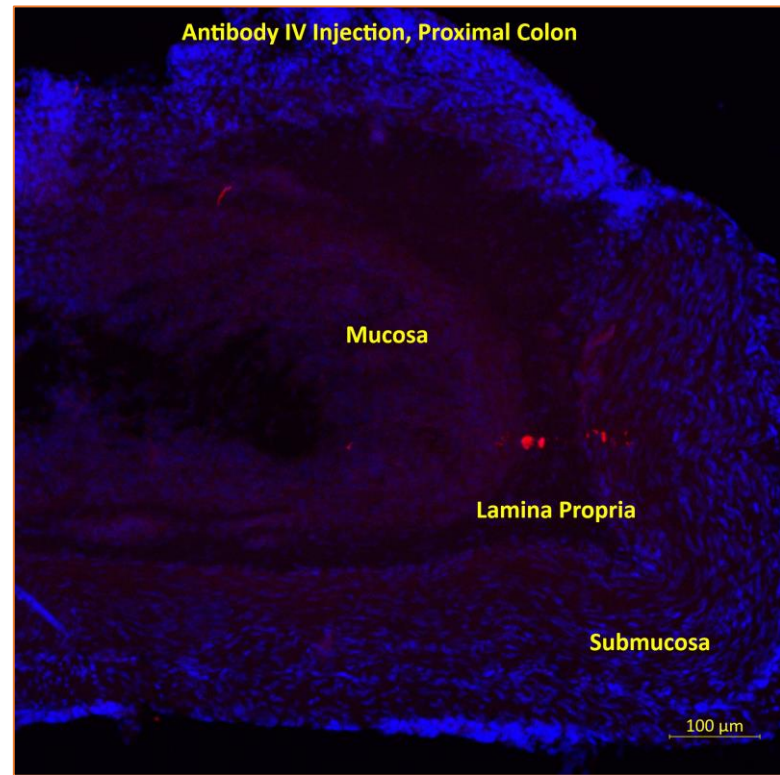
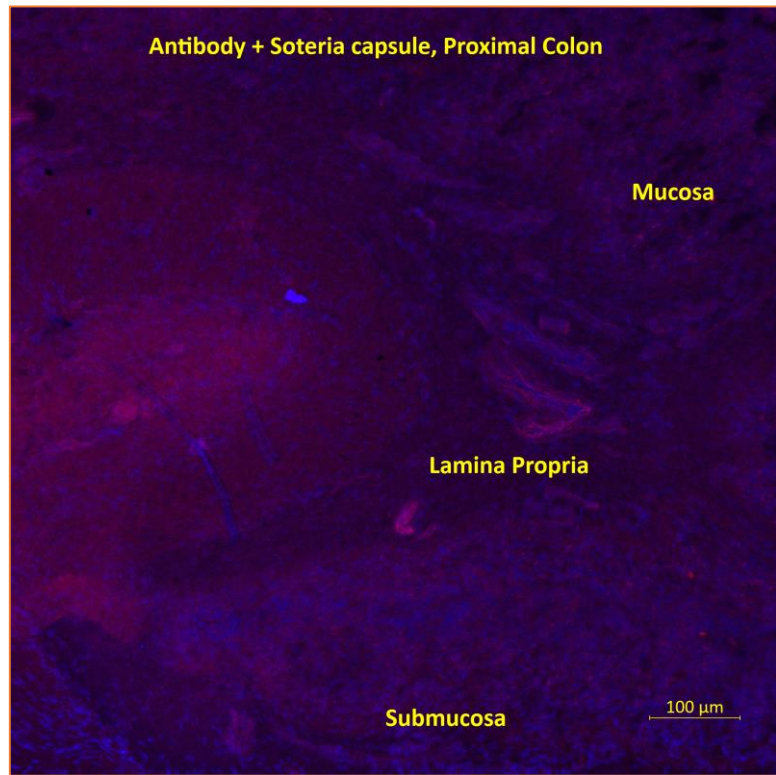
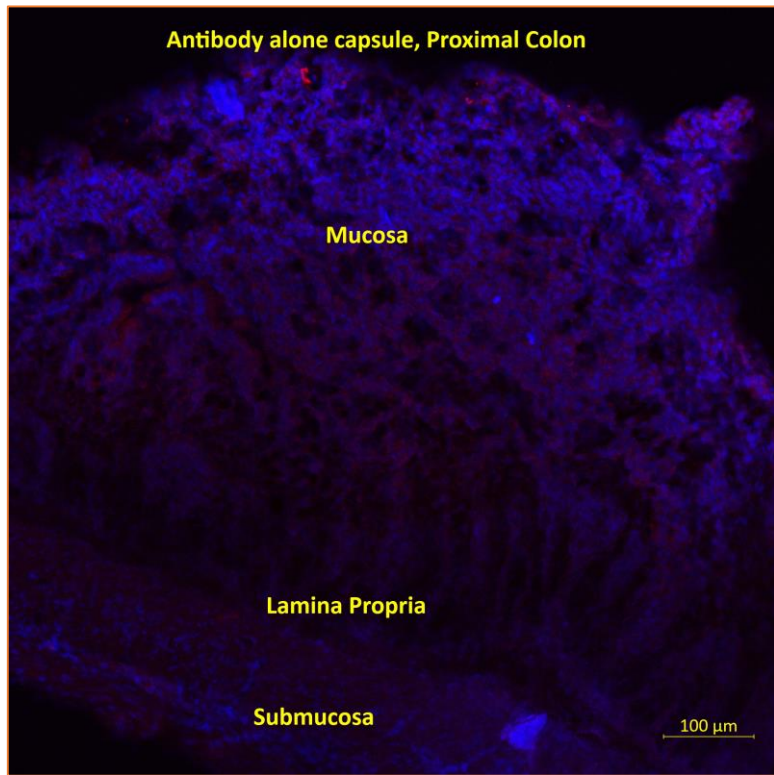
In-Vivo Dosing of Infliximab (0.7mg/kg) capsules ± Soteria vs IV



Single Dose PK, Animal Sacrificed 7h post Dosing

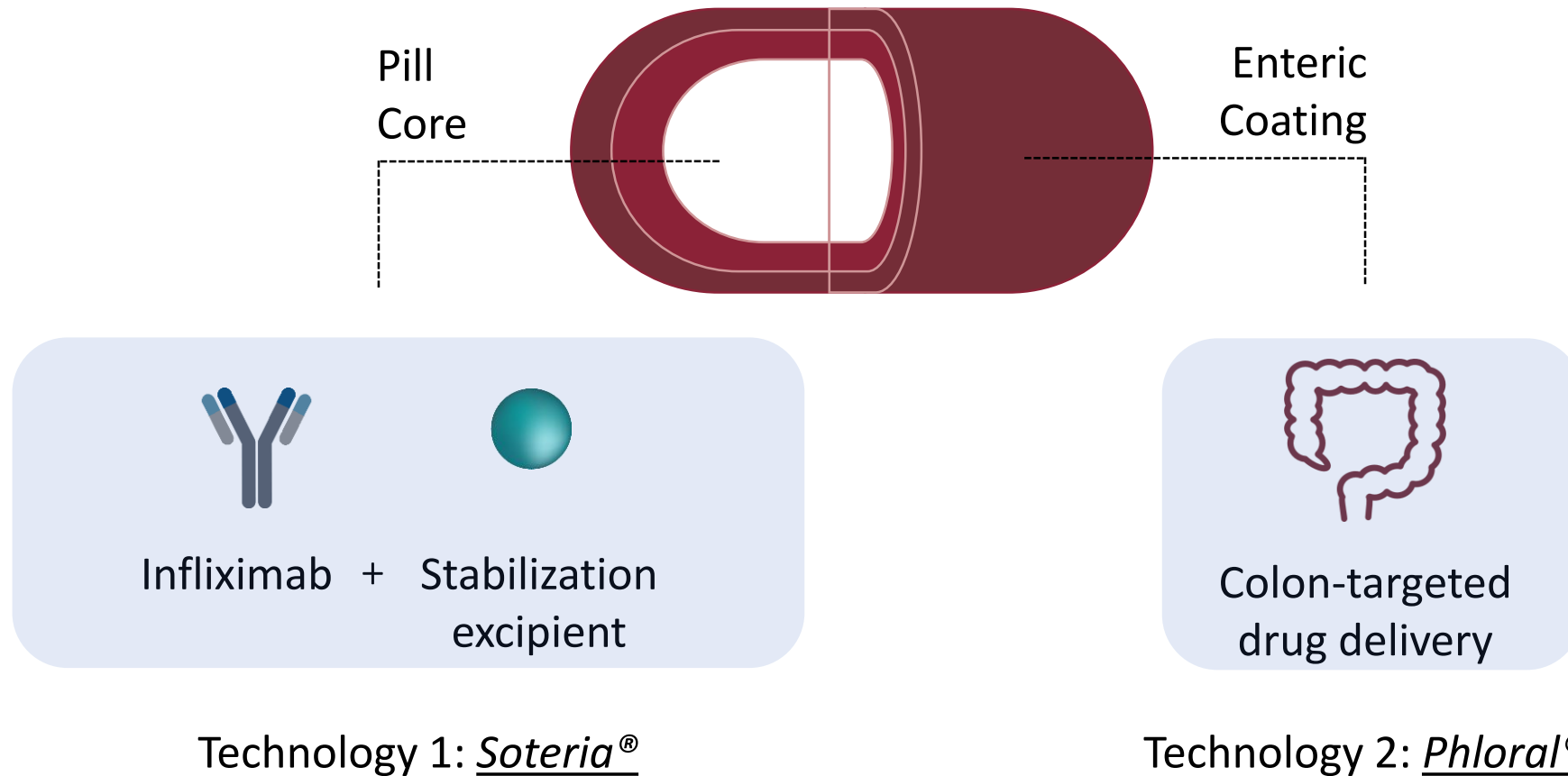
Quantification of infliximab in tissue and plasma by ELISA

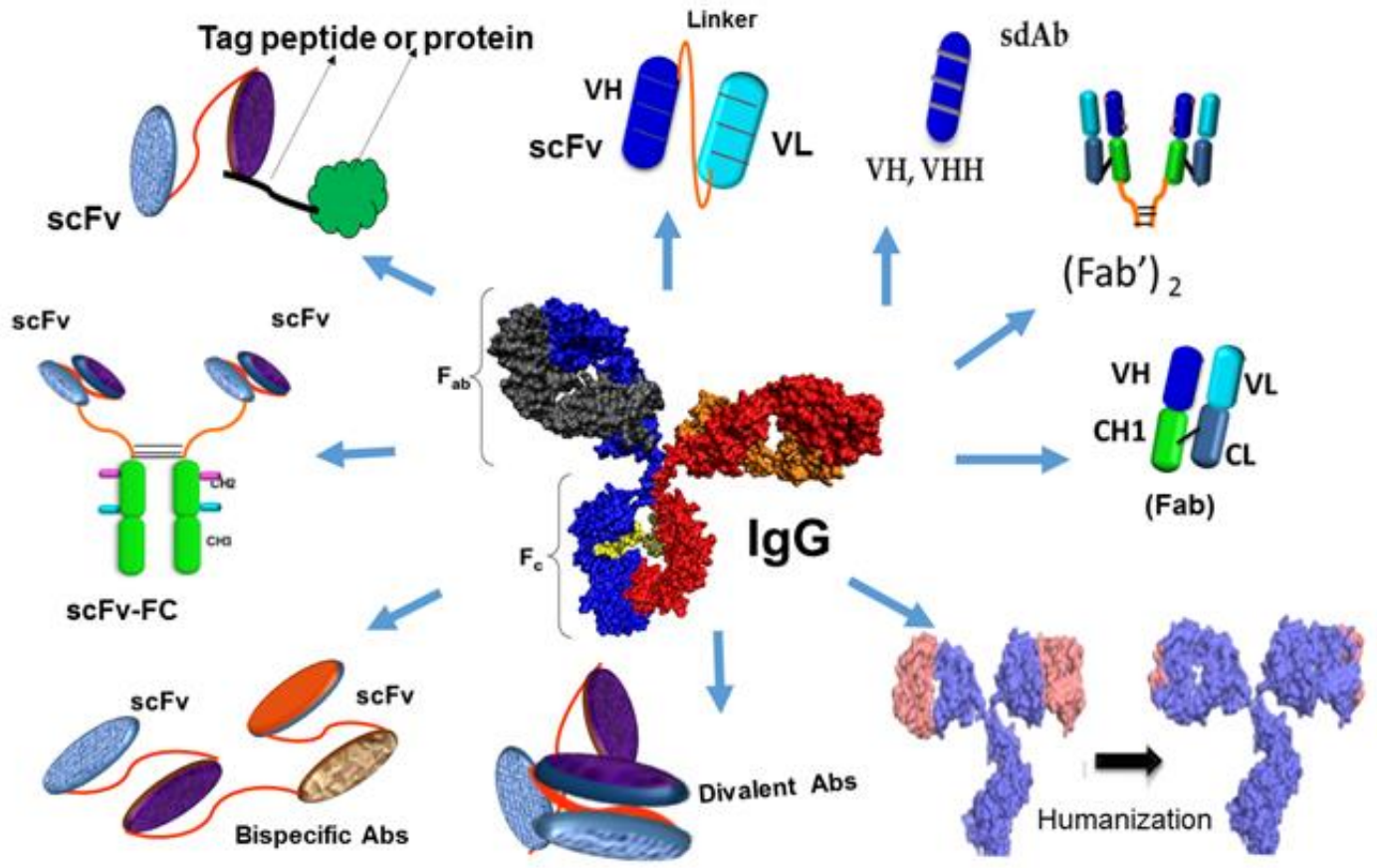




Target Product Profile: Infliximab + Soteria[®] + Phloral[®]




















A Breakthrough Technology for Oral Delivery of Antibodies





The image shows a screenshot of the Sanofi website header and a press release. The header includes the Sanofi logo and navigation links: **ABOUT US**, **YOUR HEALTH**, **SCIENCE & INNOVATION**, **OUR RESPONSIBILITY**, **CAREERS**, **INVESTORS**, and **MEDIA**. The press release text reads: **PRESS RELEASES • January 29 2018** and **Sanofi to acquire Ablynx for €3.9 Billion**.

Snapshot of Ongoing Programs

Drug (target)		Indication	Pre-clinical	Formulation Development	Phase 1	Phase 2	
INT-119 (Anti-TNF mAb)		Ulcerative colitis					
INT-120 (undisclosed target)		Crohn's disease Ulcerative Colitis					
Oral microbiome (cocktail of strains)	Undisclosed	Undisclosed					
Oral sIgA and IgG (Salmonella and Campylobacter Jejuni)		Intestinal infectious diseases					
Oral small molecule (undisclosed target)		IBD					
Oral small molecule (mitochondria modulating)		IBD					
Oral IgG and Fab	Undisclosed	Haemophilia A					
Oral mAb + Enhance® technology		Undisclosed					
Oral oligonucleotide (undisclosed)	Undisclosed	IBD					
Undisclosed		Undisclosed					Internal
						Partnered	

Core Team



Silvia Matiz
Formulation Scientist



Maria Scarpa
Research Scientist



Shehla Hridi
Senior Scientist



Shehla Hridi
Formulation Scientist



Dan Caplin
Lab Operations Manager



Eirini Poimenidou
Research Scientist

Advisory Team



Dr Peter Irving
MA MD MRCP
Consultant Gastroenterology



Dr Brian Bressler
MD MS FRCPC
Clinical Associate



Dr Heip Huatan
CMC Consultant



Dr Lesley Earl
Regulatory Consultant



Dr James Stones
IP Portfolio
Beck Greener LLP

Leadership



Bill Lindsay
CEO



Prof Abdul Basit
Founder & CSO



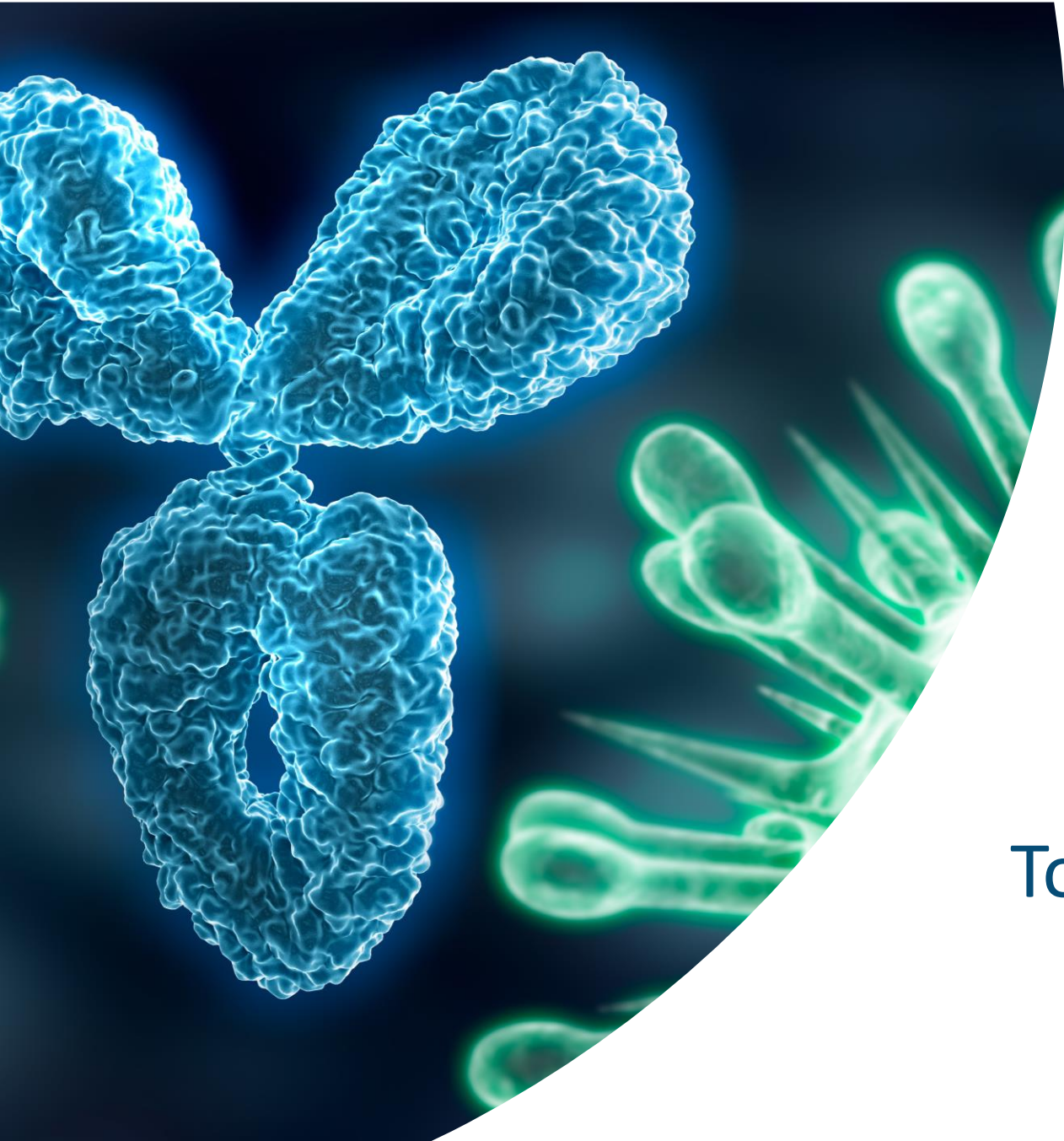
Vipul Yadav
Director, R&D



Keith Powel
Chairman



James Harrison
Executive Chairman, Cycle Pharma



**Intract
Pharma**



Innovating Technologies
To Revolutionise Patient Care