# InDex Pharmaceuticals
## R&D day

## Introduction and welcome

Peter Zerhouni, CEO

*December 8, 2020*

# Forward Looking Statement

This presentation contains certain forward-looking statements reflecting the Company's current view of future events and financial and operational performance. Such forward-looking statements are associated with both known and unknown risks and circumstances outside the Company's control. All statements in this presentation other than statements of historical or current facts or circumstances are forward-looking statements. Forward-looking statements are made in several sections of the presentation and can be identified by the use of terms or expressions such as "may", "could", "should", "anticipated", "estimated", "expected", "likely", "forecasted", "plans to", "aims to", or conjugations of such terms or similar terms. The forward-looking statements only apply as of the date of this presentation. The Company has no intent or obligation to publish updated forward-looking statements or any other information contained in this presentation based on new information, future events etc. other than required by applicable law, regulation or regulatory framework.



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# Agenda and Speakers

**Introduction and welcome**
Peter Zerhouni, CEO, InDex Pharmaceuticals

**Ulcerative colitis – a debilitating disease with high unmet medical need**
Professor William J. Sandborn, University of California San Diego

**Living with ulcerative colitis – the patient perspective**
Jonas Ericsson, ulcerative colitis patient and board member of the Swedish patient association Mag- och tarmförbundet

**Cobitolimod – a late stage first-in-class immunotherapeutic**
Professor Raja Atreya, University of Erlangen-Nürnberg

**Planned phase III program with cobitolimod**
Thomas Knittel, CMO and Pernilla Sandwall, COO, InDex Pharmaceuticals

**Feedback from IBD specialists and payers on cobitolimod through primary market research**
David Cotterell, Managing Director, Apex Healthcare Consulting

**The commercial potential of cobitolimod**
Peter Zerhouni, CEO, InDex Pharmaceuticals

**Moderator**
Charlotte Admyre, InDex Pharmaceuticals

**Questions and Answers**
All speakers (send questions to info@indexpharma.com or via the chat)

**Should not Emma and other patients with ulcerative colitis get the chance to live a normal life?**



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# InDex Pharmaceuticals in Brief

- Cobitolimod for ulcerative colitis in late stage clinical development
- Broad portfolio of pre-clinical stage assets from DIMS platform
  - DNA based ImmunoModulatory Sequences
- Based in Stockholm, Sweden with origins from Karolinska Institutet
- Listed on the Nasdaq First North Growth Market Stockholm (ticker INDEX)
- Main shareholders: SEB Venture Capital, Industrifonden, Linc, 4th AP Fund

Cobitolimod



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# Cobitolimod – A Late Stage, First-in-Class Immunotherapeutic

- Cobitolimod is a potential new medication for moderate to severe ulcerative colitis
- Primary endpoint met in phase IIb study CONDUCT with an excellent safety profile
- 4 previous completed clinical studies support efficacy and safety demonstrated in CONDUCT
- Phase III to start Q2, 2021 – subject to covid-19

- Competitive efficacy
- Superior safety profile
- Local treatment, provides rapid onset
- Novel mechanism of action
- Potential for combination therapy

Cobitolimod has blockbuster potential with an outstanding combination of efficacy and safety



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# Ulcerative colitis - A Debilitating Disease with High Unmet Medical Need

Professor William J. Sandborn
University of California San Diego

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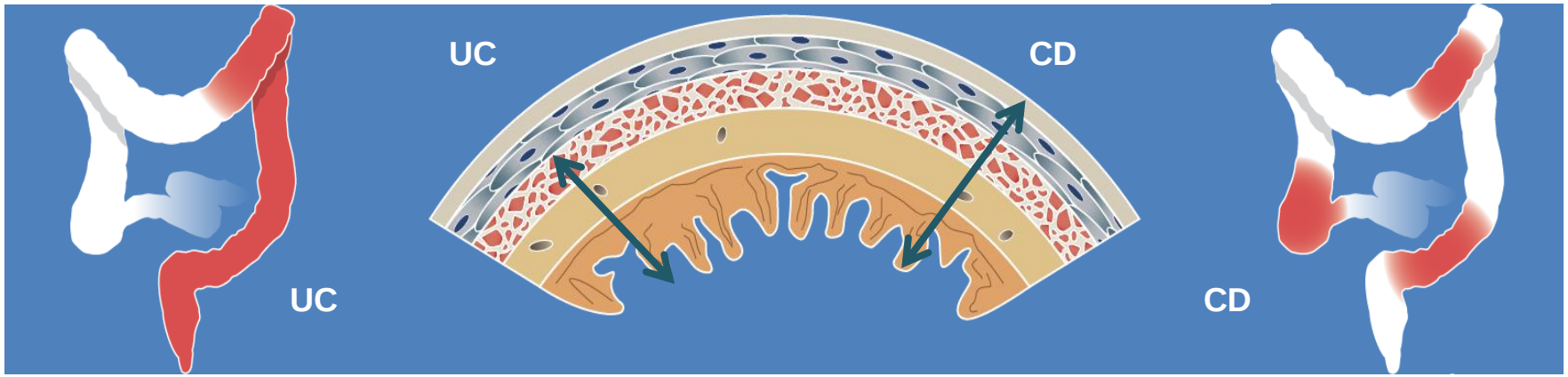
# Inflammatory Bowel Disease (IBD): Ulcerative Colitis and Crohn's Disease are Two Different Diseases

**Ulcerative colitis (UC)**
- Continuous inflammation
- Colon and rectum only
- Mucosal and sub-mucosal layers
- Risk of cancer
- Extra-intestinal manifestations
- Often debuts between 15-30 years of age

**Crohn's disease**
- Patchy inflammation
- Entire gastrointestinal (GI) tract
- All layers of GI wall (fistulas and strictures)
- Risk of cancer
- Extra-intestinal manifestations
- Often debuts between 15-30 years of age



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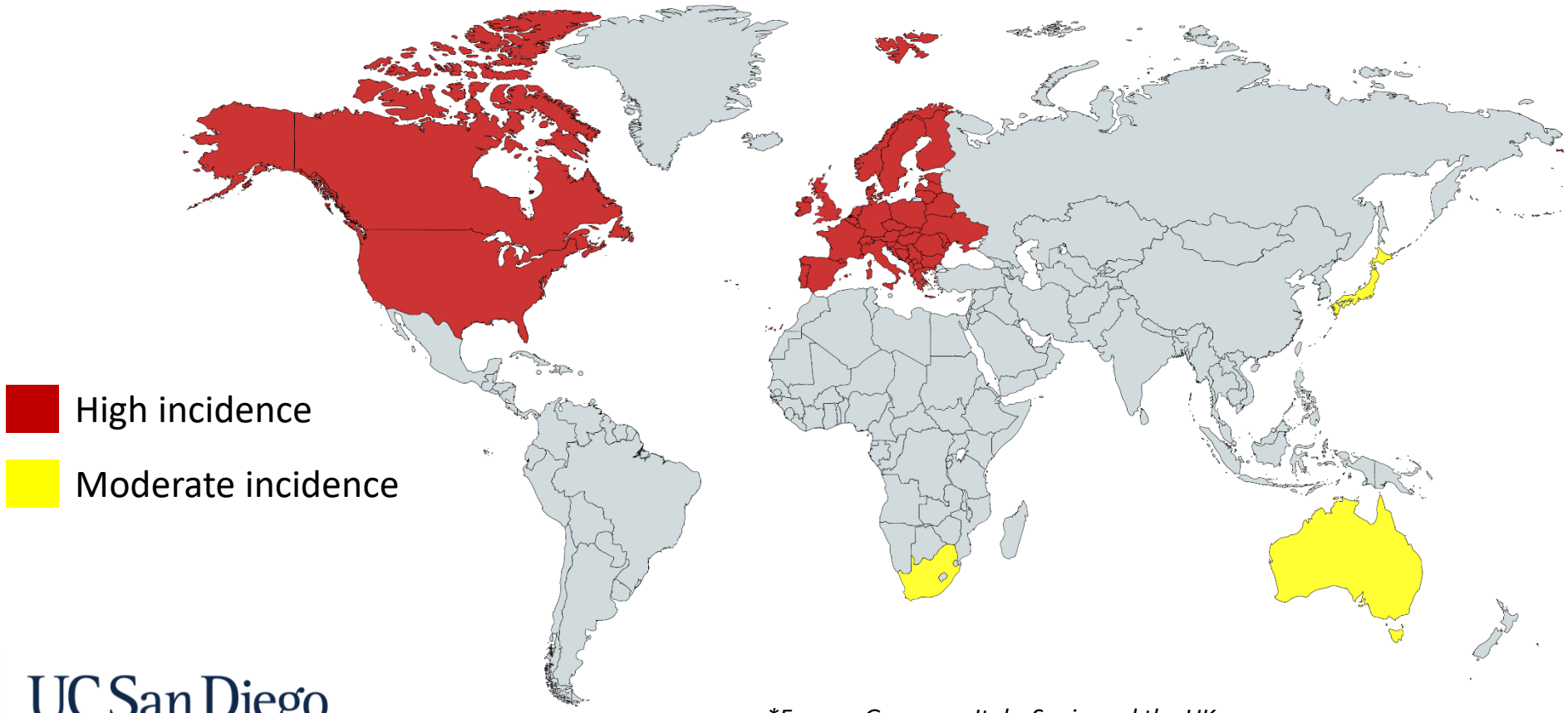
# Incidence of Ulcerative Colitis

- High incidence areas: US (approx. 1.1 million patients) and Europe (approx. 800 000 patients in EU5*)
- Incidence is rising in Asia




*France, Germany, Italy, Spain and the UK



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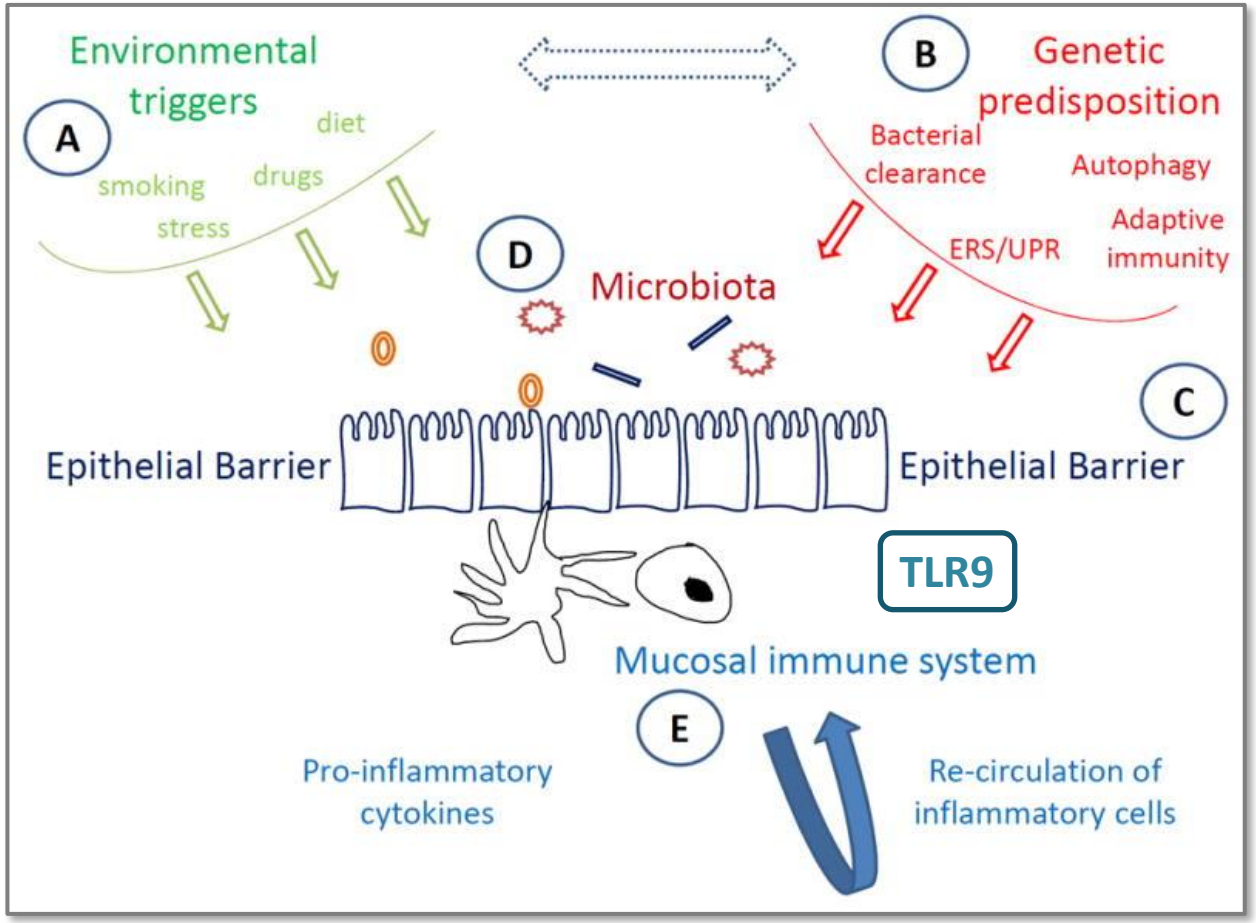
# Etiology of Ulcerative Colitis

- Multifactorial pathogenesis
  - Genetic, environmental, microbial
- Dysfunctional response from the innate and adaptive immune system
  - Multiple inflammatory cytokines are overexpressed
  - Amplification of immune responses lead to phenotypic expression of the disease and tissue destruction
  - Mediate dysfunctional cell-cell interactions in innate and adaptive immune pathways




Reprinted from *Translational Research*, Vol 167, Bamias G, Pizarro TT, Cominelli F, Pathway-based approaches to the treatment of inflammatory bowel disease, Pages 104-115, Copyright 2016, with permission from Elsevier.



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# Symptoms of Ulcerative Colitis

- Blood and mucus in stool
- Diarrhoea
- Bowel urgency
- Abdominal pain



- Weight loss
- Anemia
- Fever
- Loss of appetite



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# Complications of Ulcerative Colitis

- Extra-intestinal complications
    - Eye diseases, arthritis, skin conditions, mouth ulcers
- Toxic megacolon
- Colorectal cancer



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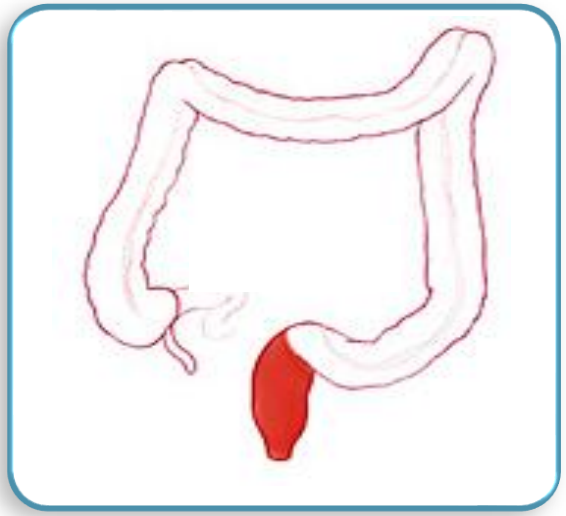
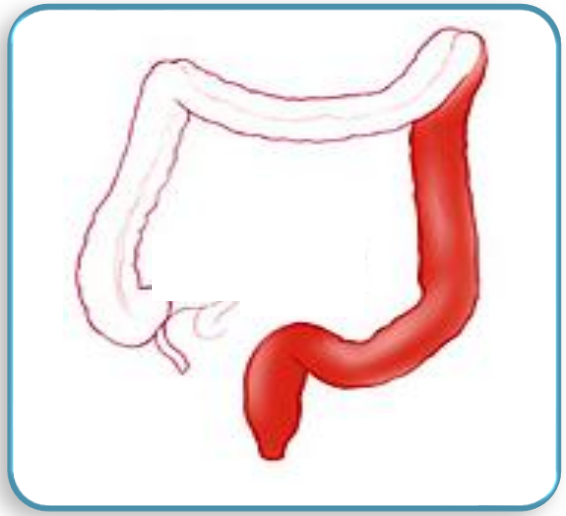
# UC Classification by Disease Extension

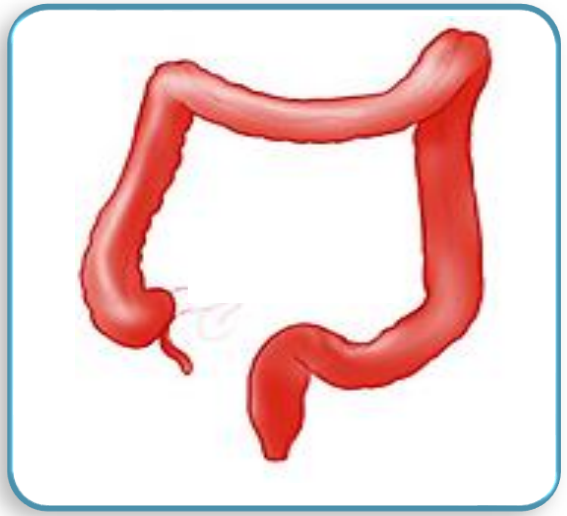
Proctitis



Left-sided colitis



Pancolitis



Dignass A, *et al. J Crohns Colitis* 2012;6:965–990;
http://www.hopkins-gi.org/GDL_disease.aspx?GDL_Disease_ID=2A4995B2-DFA5-4954-B770-F1F5BAFED033&GDL_DC_ID=D03119D7-57A3-4890-A717-CF1E7426C8BA



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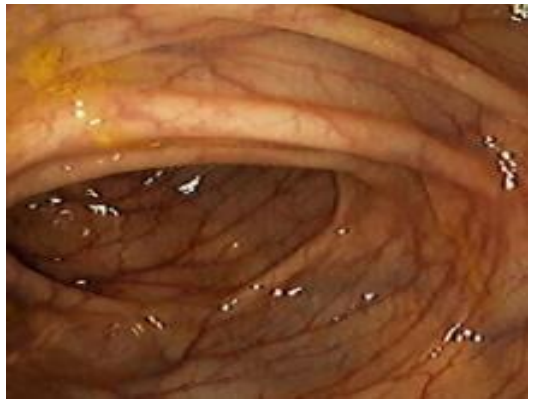
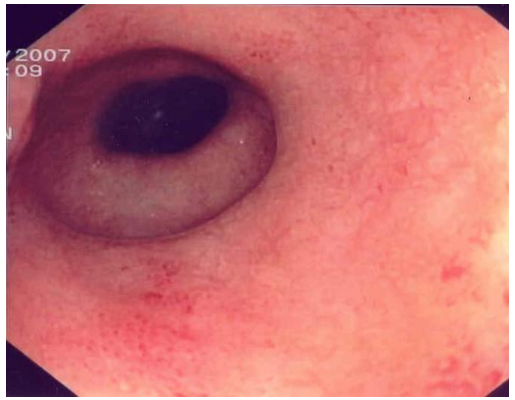
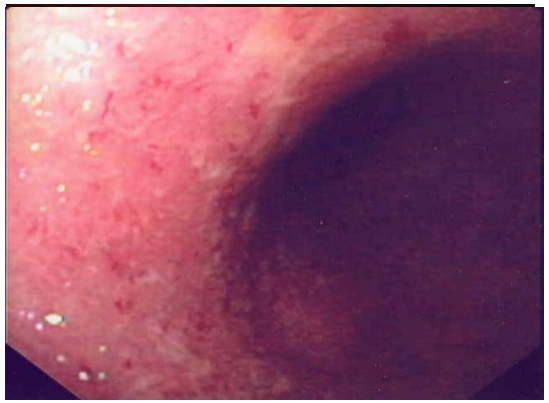
# UC Classification of Disease Severity by Endoscopic Findings



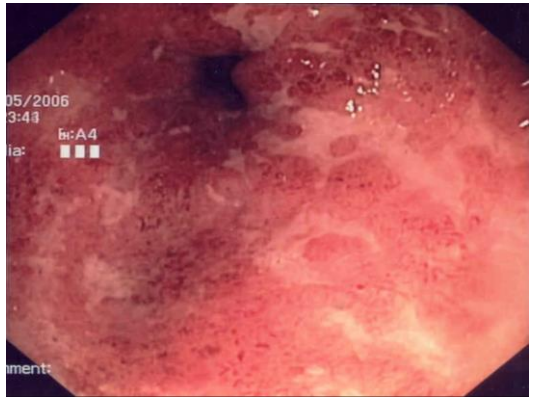
**Remission**



**Mild**
erythema, decreased vascular pattern



**Moderate**
marked erythema, absent vascular pattern, friability, erosions



**Severe**
spontaneous bleeding, ulceration



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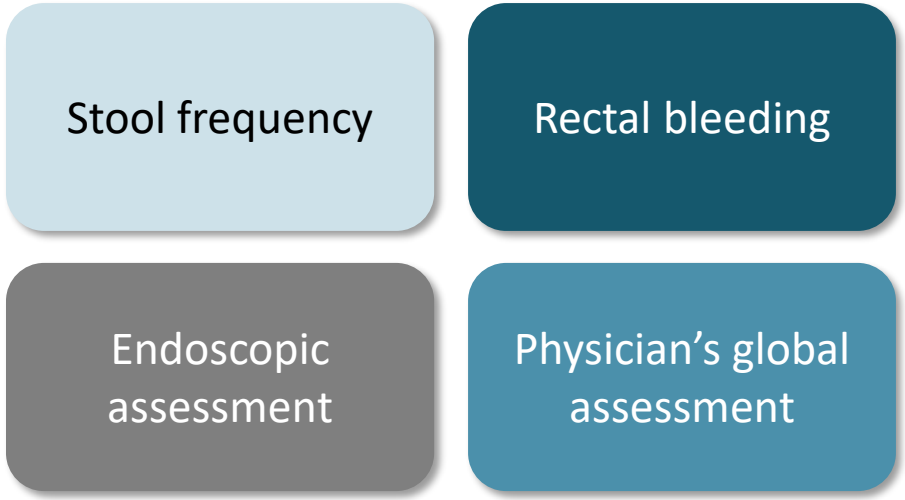
# Mayo Score for Measuring Disease Activity

- A numerical disease activity instrument
- It is the sum of scores from 4 components




- It is ranging from 0-12 with the higher total score indicating more severe disease
- 3-component Mayo score excluding the physician's global assessment is recommended for clinical trials



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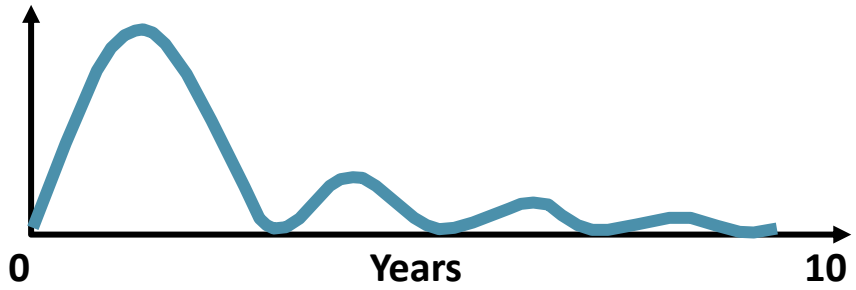
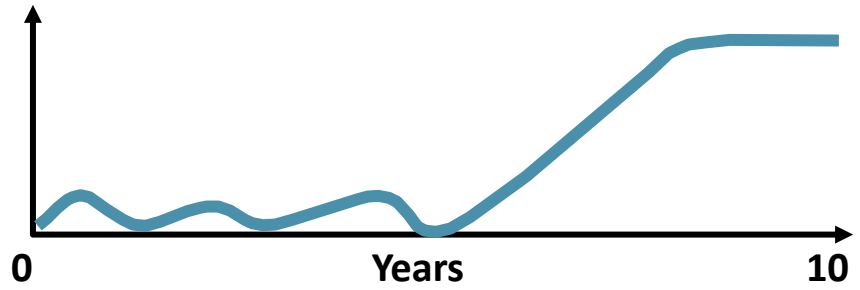
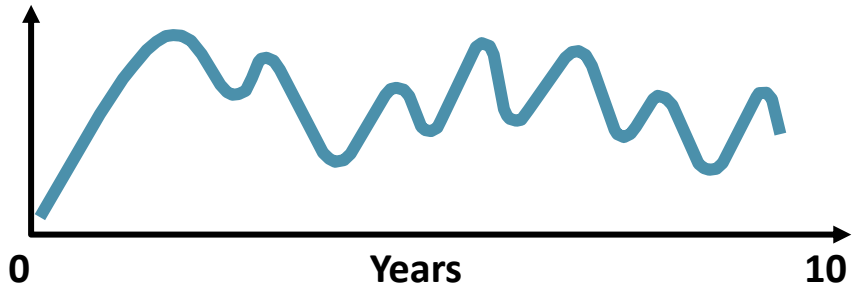
# Ulcerative Colitis is a Remitting and Relapsing Disease



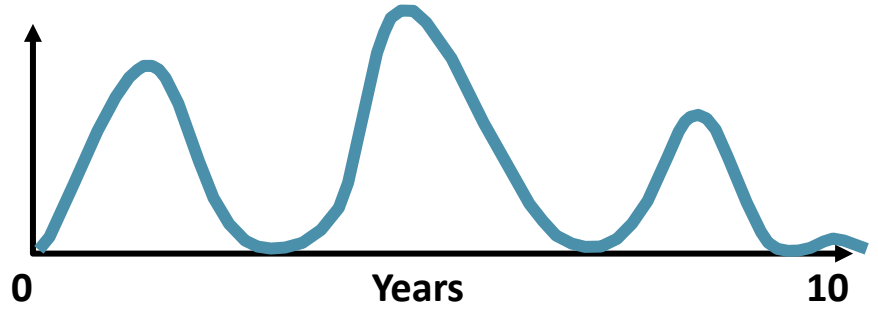

**Curve 1:** Remission or mild severity of intestinal symptoms after initial high activity




**Curve 2:** Increase in the severity of intestinal symptoms after initial low activity




**Curve 3:** Chronic continuous symptoms




**Curve 4:** Chronic intermittent symptoms



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*Solberg IC, et al. Scan J Gastroenterol 2009;44(4):431–440*

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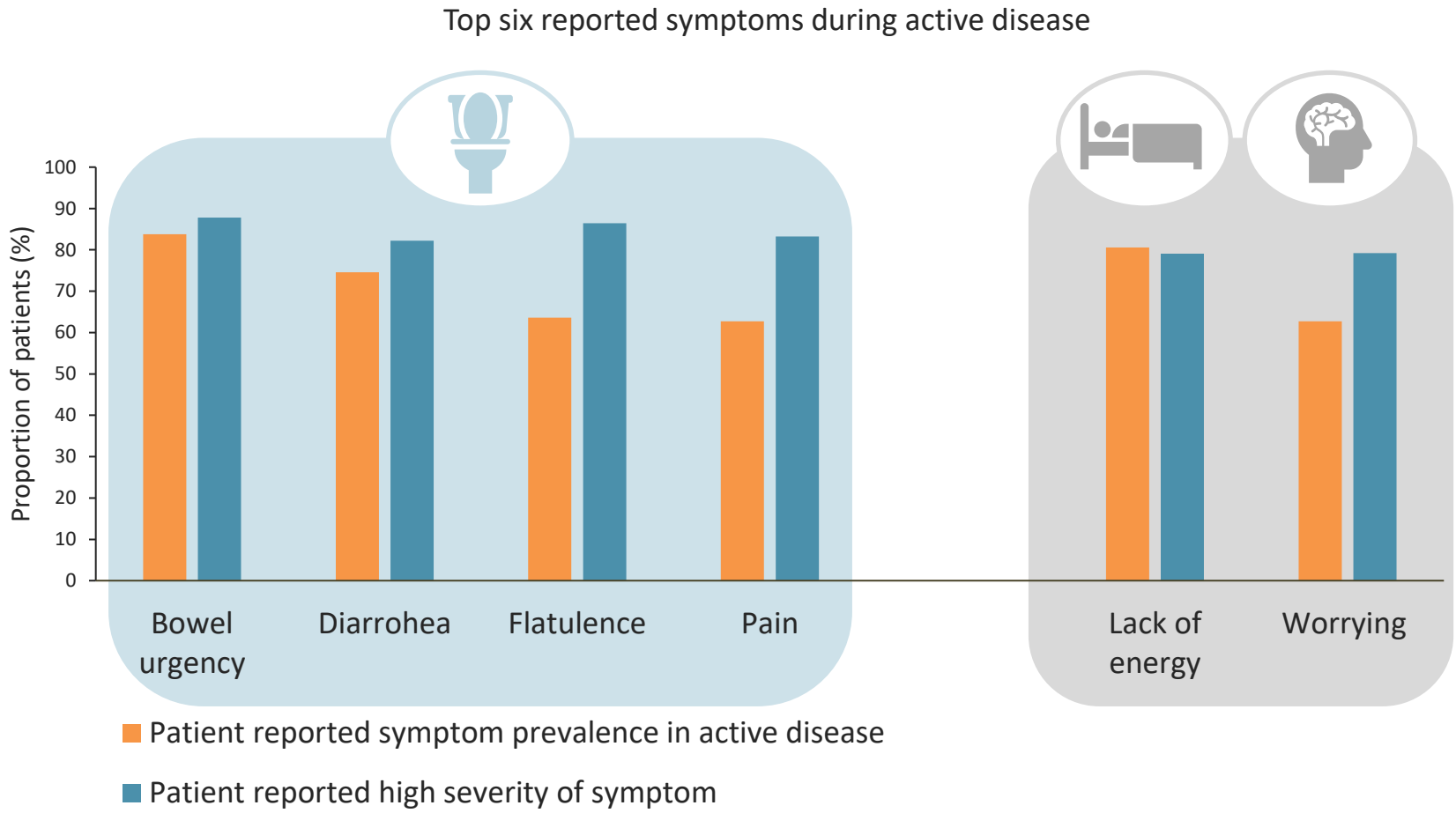
# IBD Causes Severe Physical and Psychological Disease Burden




Farrell D et al. Journal of Crohn's and Colitis, 2016, 315–322



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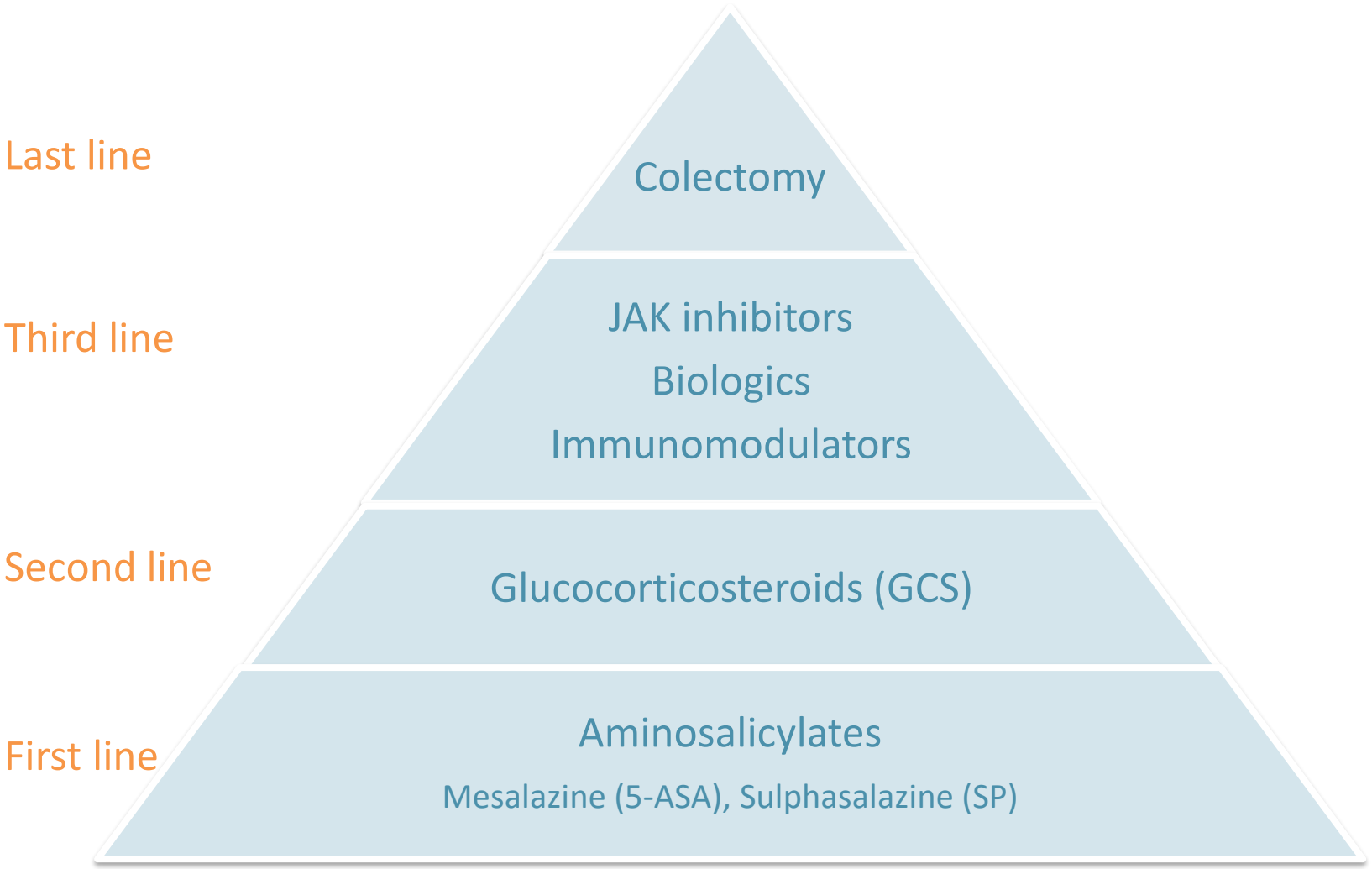
# Current Treatment Algorithm of Ulcerative Colitis



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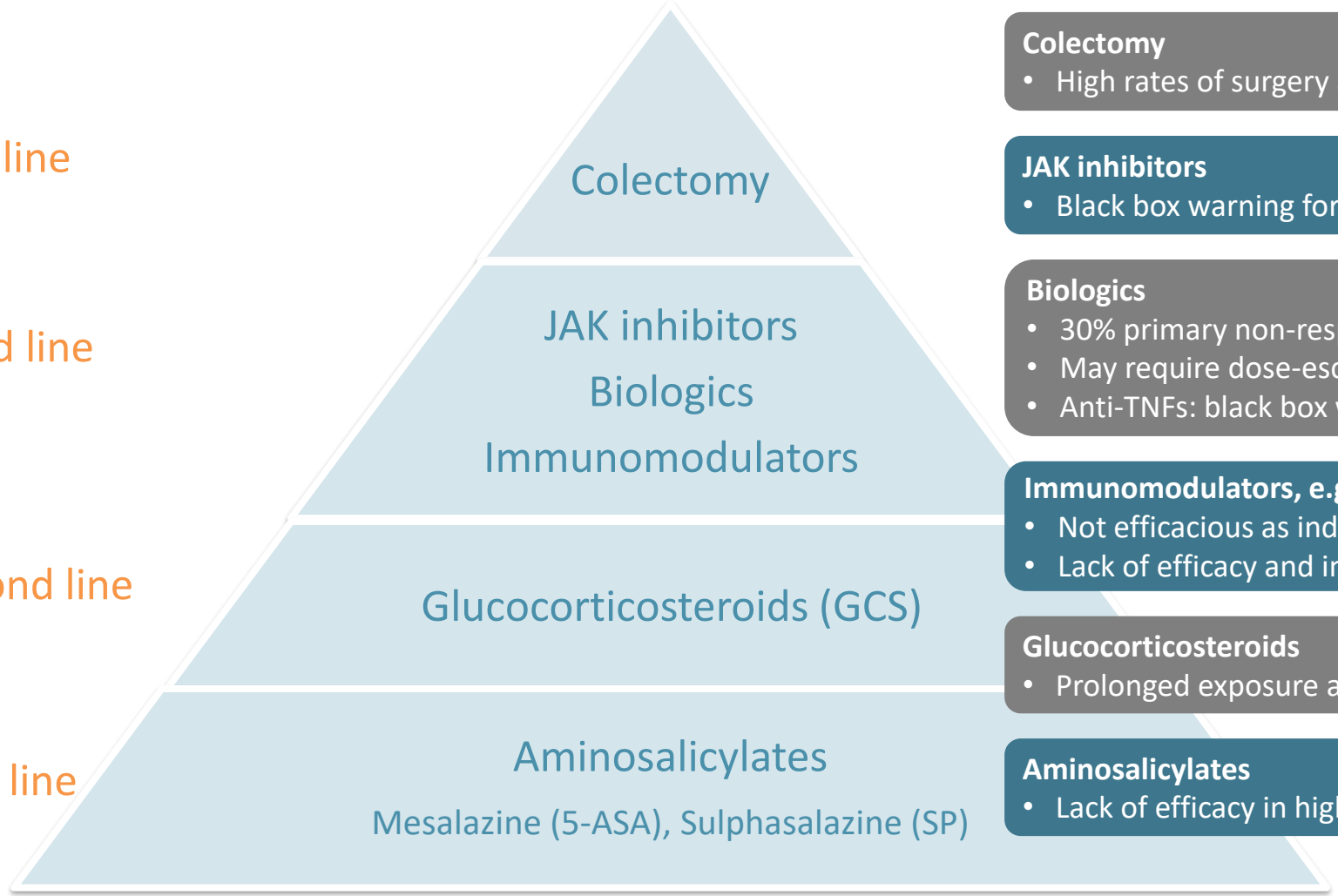
# New Approaches are Needed to Address Enduring Unmet Needs




**Colectomy**
- High rates of surgery and post-surgery complications[1]

**JAK inhibitors**
- Black box warning for serious infections, malignancies & thrombosis

**Biologics**
- 30% primary non-responders, 50% secondary loss of response[2]
- May require dose-escalation and monitoring
- Anti-TNFs: black box warnings for serious infections & malignancies

**Immunomodulators, e.g. thiopurines**
- Not efficacious as induction agents
- Lack of efficacy and intolerance in some patients

**Glucocorticosteroids**
- Prolonged exposure associated with side-effects

**Aminosalicylates**
- Lack of efficacy in high proportion of patients



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[1]*Peyrin-Biroulet L. Aliment Pharmacol Ther. 2016 Oct;44(8):807-16*
[2]*Danese S et al. Dig Dis 2019, 37:266*

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# What is Expected from New Drugs for IBD?

- Different Mechanism of Action
- Better rates of inducing clinical remission
- Less “loss of response” in responders
- Efficacy in primary/secondary non-responders to anti-TNF
- Evidence of efficacy and safety in combination therapy
- Less immunogenicity
- Less risk of infection
- Less risk of general immunosuppression
- Agents with limited ability to cross the placental barrier

*Source: D’Haens, UEGW 2014*



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# Late Stage Development Pipeline for Moderate to Severe UC

**Anti-integrin therapy**
Etrolizumab

**Anti-interleukin 23 (p19) therapy**
Mirikizumab

**Janus kinase (JAK) inhibitor therapy**
Filgotinib
Upadacitinib

**S1P1 modulator therapy**
Ozanimod
Etrasimod

**TLR9 agonist**
Cobitolimod

*Compounds in development with reported phase IIb or phase III data*



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# Local Delivery of Drugs to the GI Tract

**Small molecules**
Mesalamine – market
Budesonide – market
TD-1473 – phase IIb
GB004 – phase II
ST-0529 – phase II
MORF-057 – phase I

**TLR9 agonist**
Cobitolimod – phase III

**Antibodies**
V565 – phase I
TP10 – preclinial

**Peptides**
PTG-200 – phase II
PN943 – phase II
ZP10000 – preclinical



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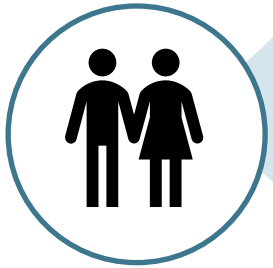
# Summary

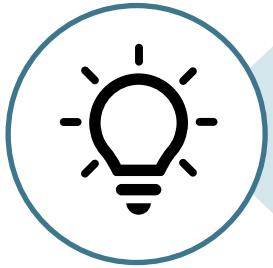


**ULCERATIVE COLITIS IS A DEBILITATING DISEASE**

- Patients suffer physical and psychological impacts from UC
- UC and its management impact work productivity for patients

**ENDURING UNMET MEDICAL NEED**

- Current treatments are effective for some patients, however substantial failure rates remain
- Safety and tolerability issues limit use of some treatments
- Topical therapies have been long ignored



**COBITOLIMOD - A PROMISING CANDIDATE FOR MODERATE TO SEVERE LEFT-SIDED UC**

- Cobitolimod has a novel mechanism of action, and based on the available data, a compelling safety profile, while delivering clinically relevant efficacy with an infrequent dosage regimen



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# Ulcerative Colitis – the Patient Perspective

Jonas Eriksson
Mag- och tarmförbundet

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# Cobitolimod

## A Late Stage, First-in-Class Immunotherapeutic

Professor Raja Atreya
University of Erlangen-Nürnberg

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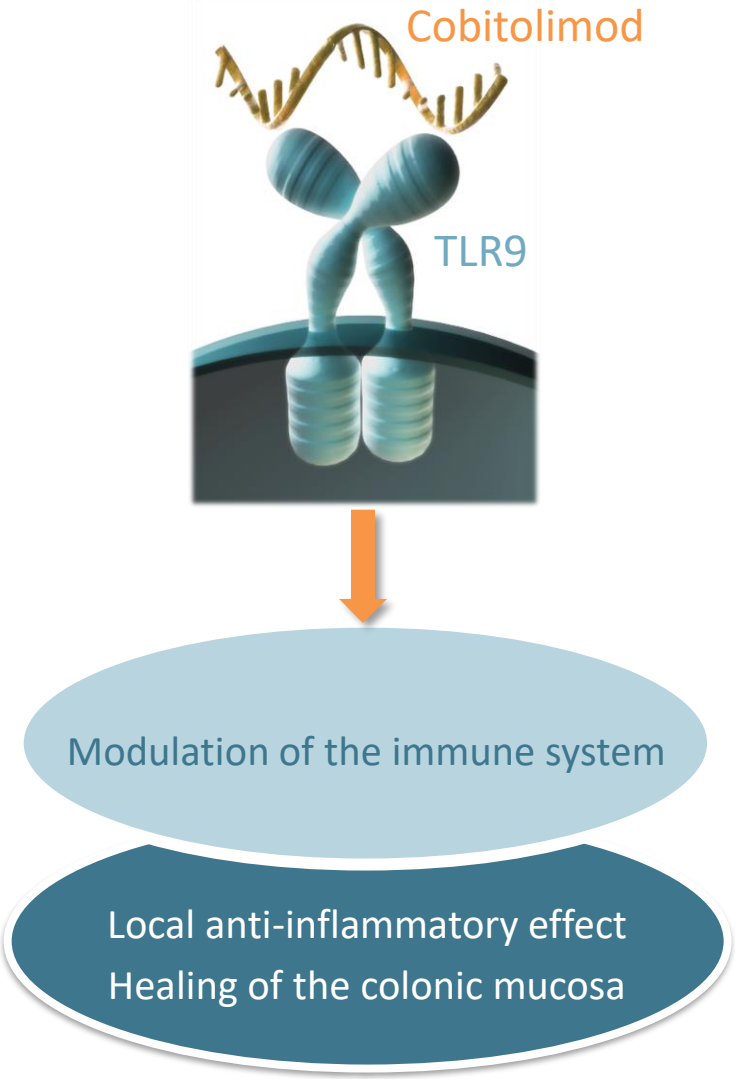
# Cobitolimod is a First-in-Class TLR9 Agonist

- Cobitolimod is an oligonucleotide which activates Toll Like Receptor 9 (TLR9) by mimicking microbial DNA
- Cobitolimod modifies the dysregulated mucosal cytokine balance in intestinal inflammation
- Cobitolimod is administered rectally as a 50 ml solution



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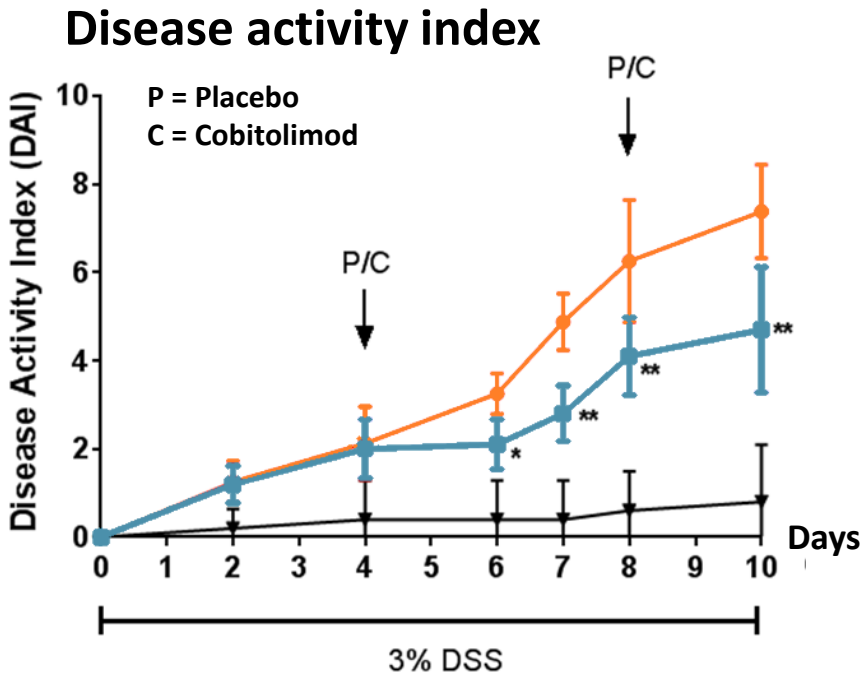
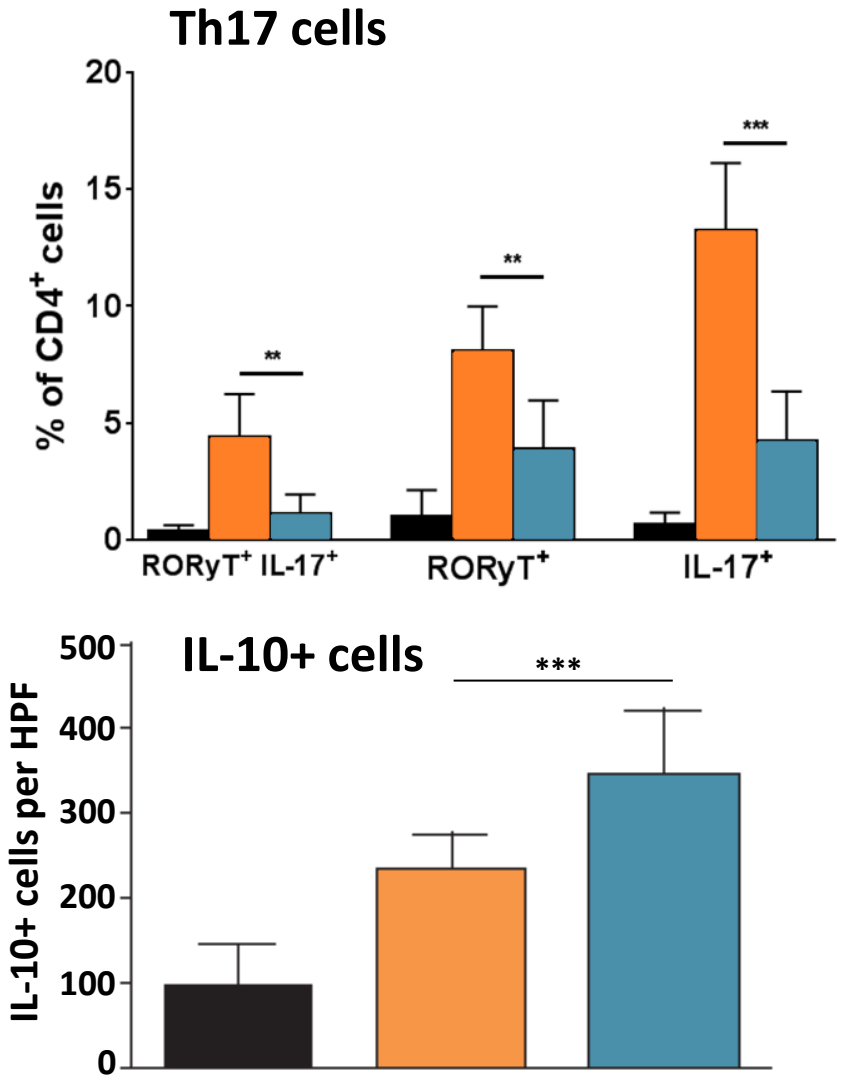
# Cobitolimod Ameliorates Experimental Colitis Models



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*Schmitt et al., J Crohns Colitis. 2020; 14,4: 508-524.*

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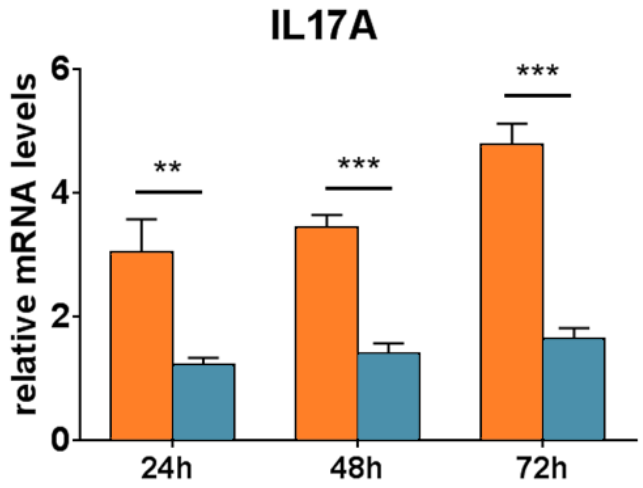
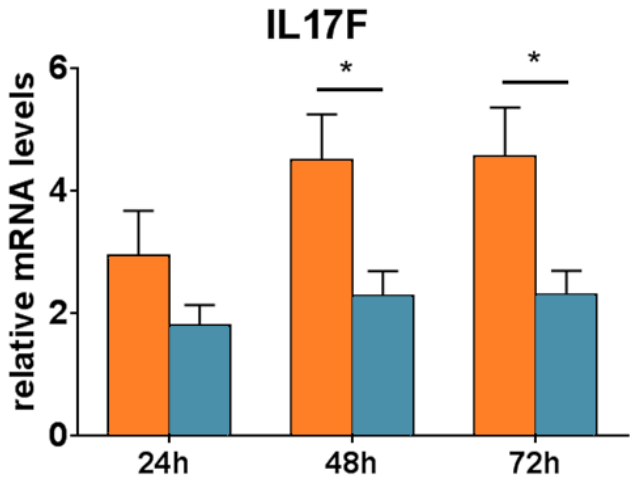
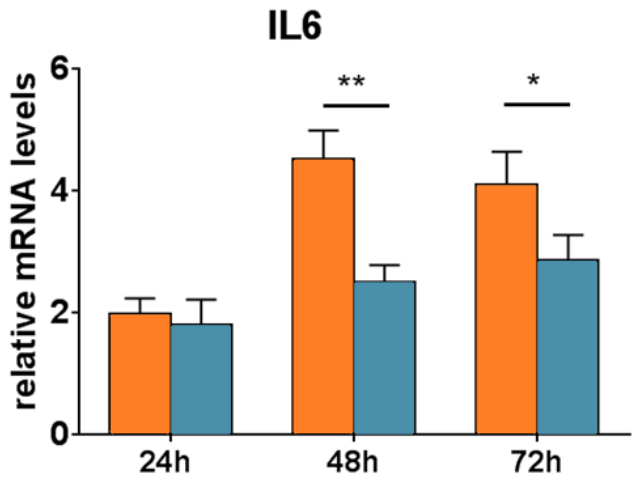
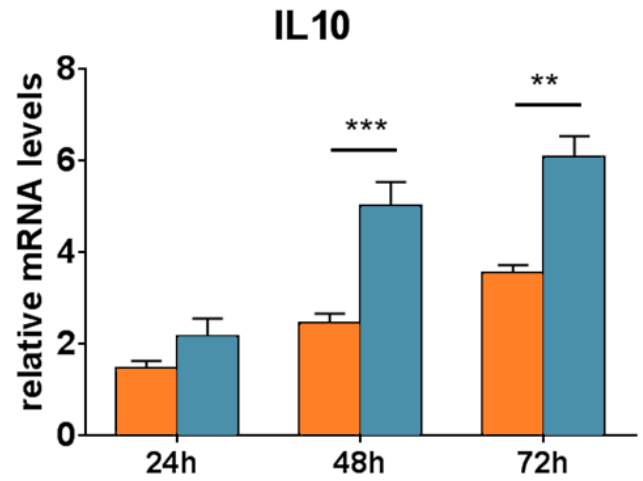
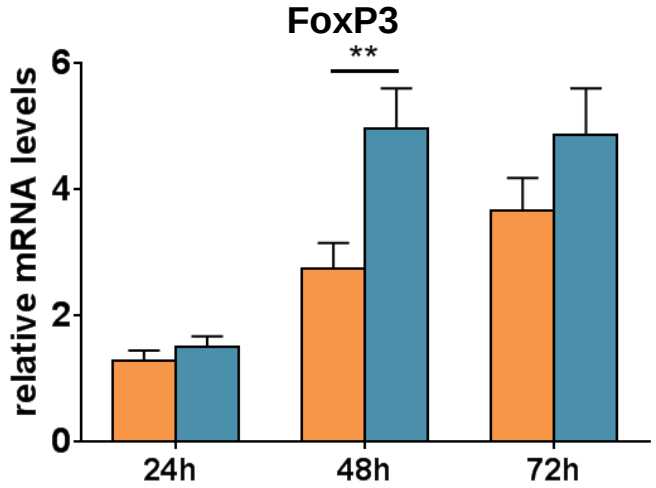
# Cobitolimod Decreases IL17 & IL6 & Increases IL10 Production in Cultured Mucosal Cells of UC Patients




LPS (n=9)

LPS + cobit. (n=9)

*Expression of different cytokines in LPMCs from UC patients stimulated with LPS in vitro with or without cobitolimod, *p≤0.05, **p ≤0.01, ***p ≤0.001*

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*Schmitt et al., J Crohns Colitis. 2020; 14,4: 508-524.*

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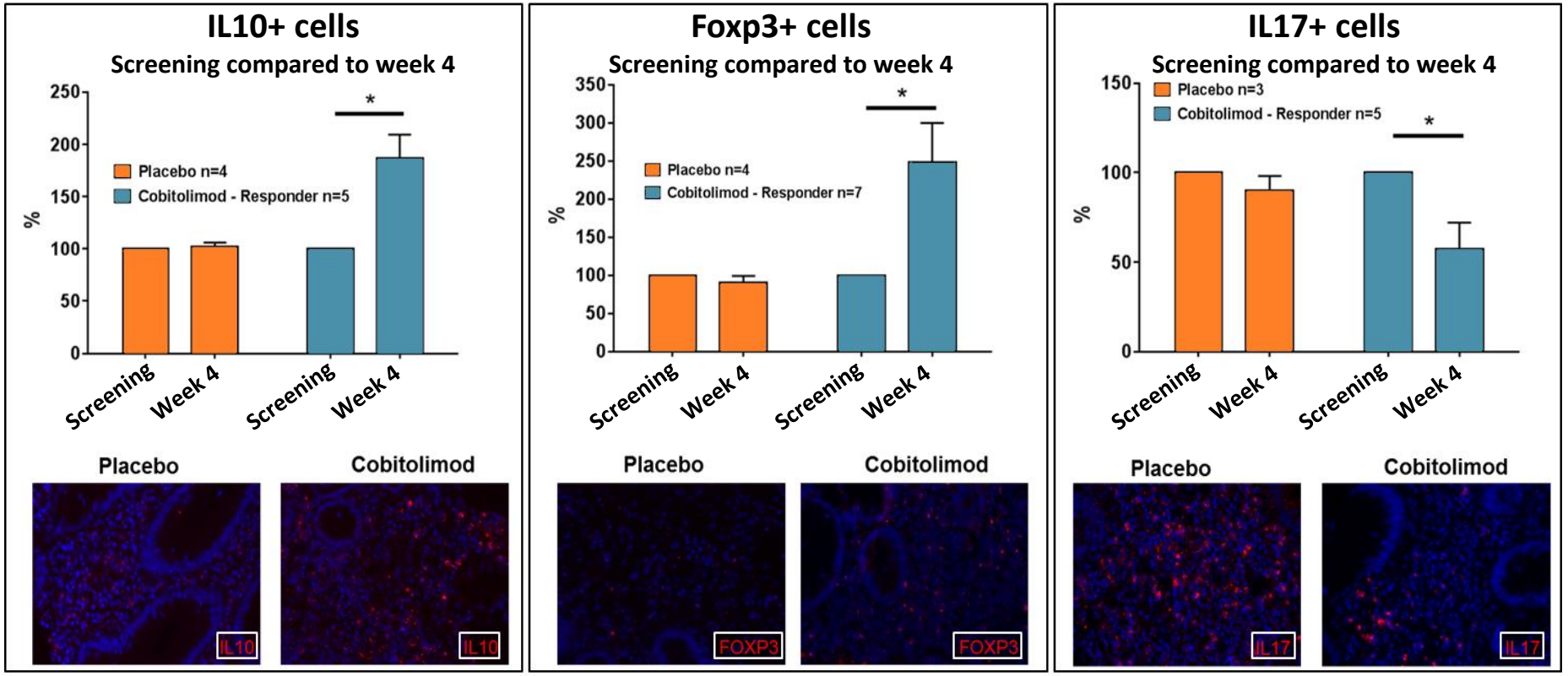
# Cobitolimod Increases IL10+ and FOXP3+ and Decreases IL17+ Intestinal Cells in UC Patients




*Immunohistochemistry analysis of colonic biopsis from UC patients at screening or 4 weeks after receiving one single rectal dose of 30 mg cobitolimod or placebo.*p<0.05*



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*Schmitt et al., J Crohns Colitis. 2020; 14,4: 508-524.*

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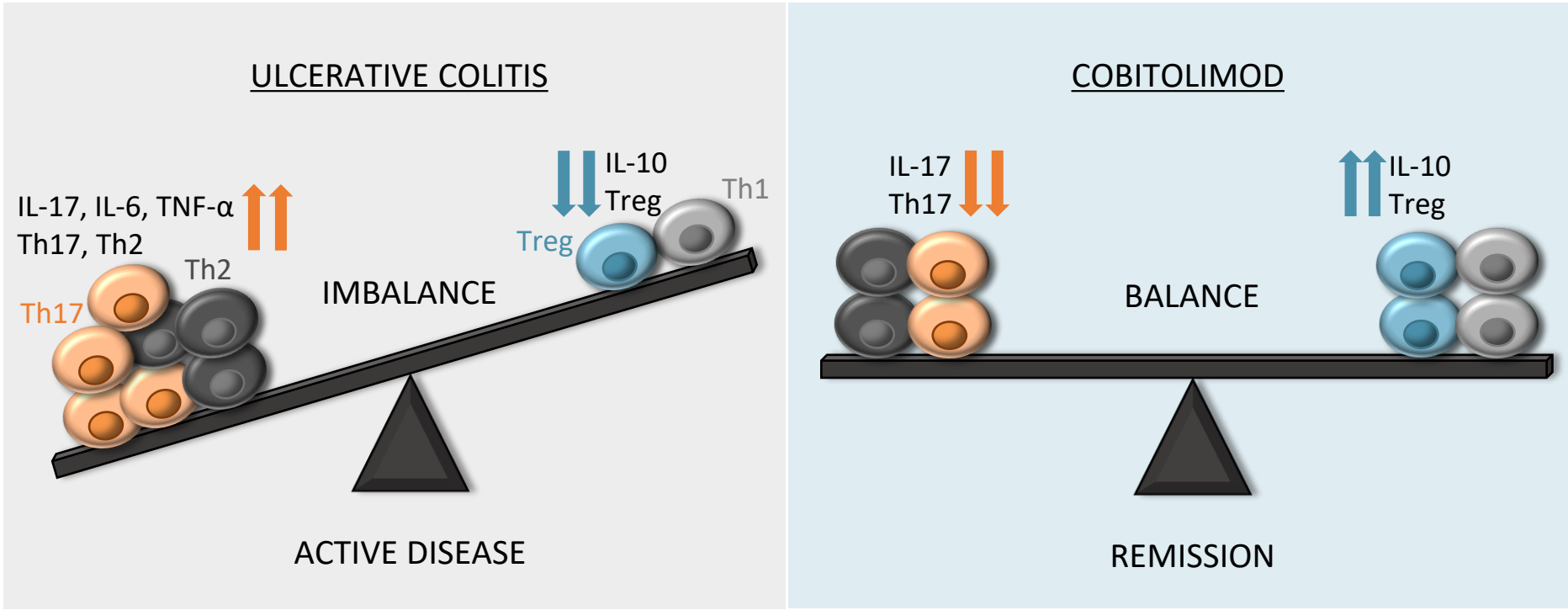
# Cobitolimod Induces Anti-Inflammatory Effects that Balance the Immune System in UC



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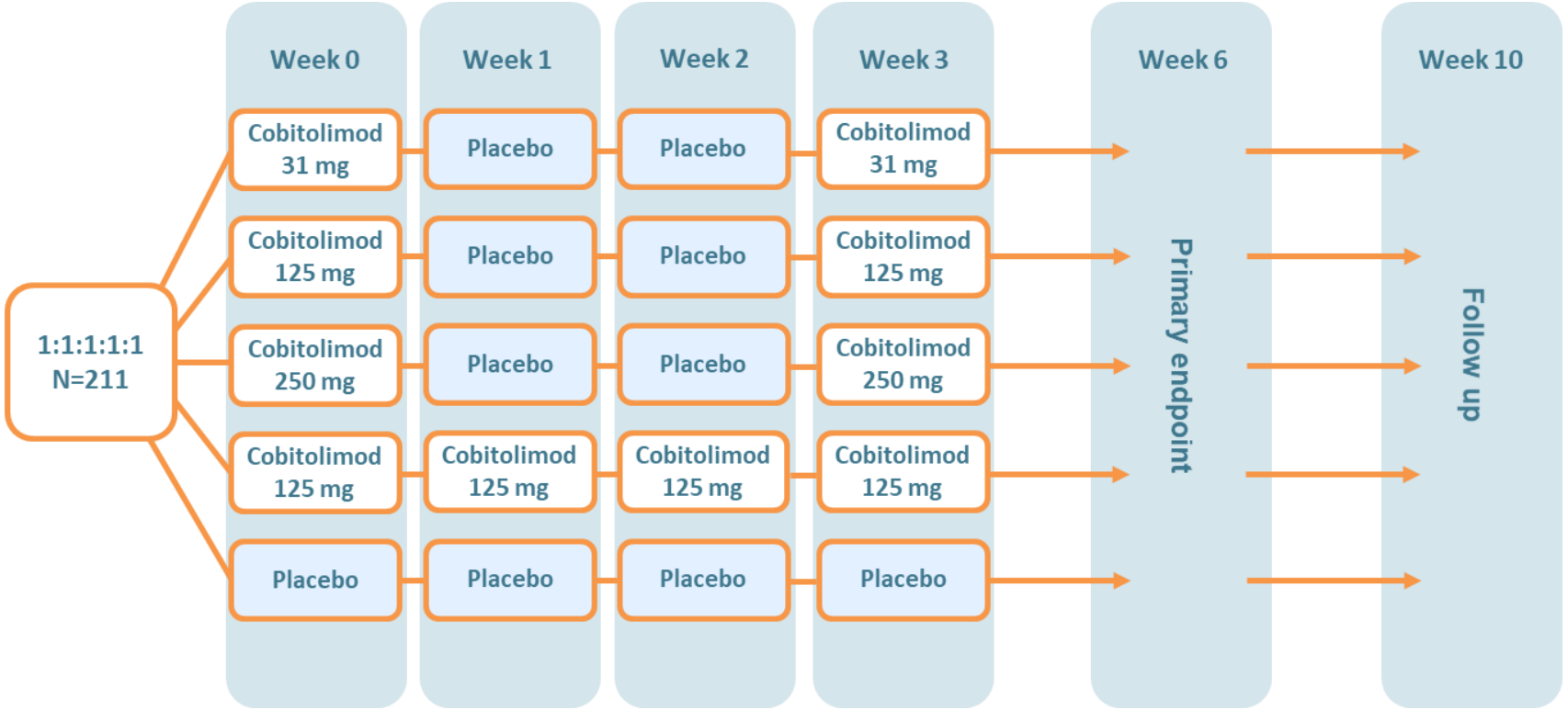
# Phase IIb CONDUCT Study Design

## Primary objective

To evaluate the efficacy of cobitolimod treatment at different dose levels and frequencies compared to placebo with regard to clinical remission 6 weeks after first treatment, in patients with moderate-to-severe ulcerative colitis




## Main inclusion criteria

- Moderate-to-severe, left-sided UC (centrally read)
- Current use, dependency, refractoriness or intolerance to glucocorticosteroids
- Failed immunomodulators and/or biologics
- No concomitant biologics



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# Primary Endpoint and Statistical Design

**Primary endpoint**

Clinical Remission at week 6 defined by Modified Mayo sub scores:

i) Rectal bleeding of 0
ii) Stool frequency of 0 or 1
(with at least one point decrease from Baseline), and
iii) Endoscopy score of 0 or 1 (excluding friability), centrally read

**Statistical design**

One-sided test of the null hypothesis, that there is no difference in the primary endpoint between each active treatment arm and placebo, with a type I error rate of 0.10. Appropriate to provide high statistical power to detect a clinically meaningful effect while maintaining an acceptable sample size.

# Patient Demographics at Baseline

| | COBITOLIMOD | | | | PLACEBO (n=44) | OVERALL (n=211) |
|---|---|---|---|---|---|---|
| | 31 mg x 2 (n=40) | 125 mg x 2 (n=43) | 125 mg x 4 (n=42) | 250 mg x 2 (n=42) | | |
| Age<br>Mean year (SD) | 47.4 (16.4) | 47.0 (16.9) | 47.2 (14.9) | 46.2 (14.0) | 45.5 (15.2) | 46.6 (15.4) |
| Gender<br>female % | 35.0 | 53.5 | 42.9 | 38.1 | 25.0 | 38.9 |
| UC duration<br>Mean year (SD) | 7.88 (6.48) | 8.46 (7.43) | 8.14 (6.77) | 7.89 (6.83) | 7.36 (7.28) | 7.94 (6.92) |
| Full Mayo score<br>Mean (SD) | 8.5 (1.2) | 8.0 (1.8) | 8.3 (1.7) | 8.5 (1.3) | 8.3 (1.6) | 8.3 (1.5) |
| Mayo endoscopic score<br>Mean (SD) | 2.6 (0.5) | 2.6 (0.5) | 2.5 (0.5) | 2.6 (0.5) | 2.5 (0.5) | 2.6 (0.5) |
| Rectosigmoid colon disease extent<br>descending colon endoscopic score = 0, % | 57.5 | 51.2 | 54.8 | 45.2 | 47.7 | 51.2 |
| Descending colon disease extent<br>descending colon endoscopic score ≥1, % | 42.5 | 48.8 | 45.2 | 54.8 | 52.3 | 48.8 |

*Full analysis set*



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# Concomitant and Prior Medication

| | COBITOLIMOD | | | | PLACEBO (n=44) | OVERALL (n=211) |
|---|---|---|---|---|---|---|
| | 30 mg x 2 (n=40) | 125 mg x 2 (n=43) | 125 mg x 4 (n=42) | 250 mg x 2 (n=42) | | |
| Concomitant glucocorticosteroids % | 45.0 | 30.2 | 33.3 | 40.5 | 38.6 | 37.4 |
| Dose prednisolone, mg/day Mean (SD) | 15.7 (5.3) | 15.0 (4.6) | 15.0 (6.2) | 12.5 (4.5) | 14.8 (5.6) | 14.6 (5.2) |
| Concomitant 5-ASA % | 87.5 | 88.4 | 78.6 | 78.6 | 88.6 | 84.4 |
| Concomitant AZA/6-MP % | 22.5 | 13.9 | 23.8 | 21.4 | 15.9 | 19.4 |
| Prior use of TNF-α inhibitor % | 22.5 | 23.3 | 28.6 | 21.4 | 18.2 | 22.7 |
| Prior use of vedolizumab % | 10.0 | 7.0 | 7.1 | 11.9 | 0 | 7.1 |

*Full analysis set*

# Primary Endpoint

| Clinical Remission at Week 6* | COBITOLIMOD | | | | PLACEBO (n=44) |
|---|---|---|---|---|---|
| | 30 mg x 2 (n=40) | 125 mg x 2 (n=43) | 125 mg x 4 (n=42) | **250 mg x 2 (n=42)** | |
| % of patients | 12.5 % | 4.7 % | 9.5 % | **21.4 %** | 6.8 % |
| Δ to placebo | 5.7 % | -2.1 % | 2.7 % | **14.6 %** | |
| Odds Ratio | 2.0 | 0.7 | 1.4 | **3.8** | |
| P-value one-sided test (pre-specified) | 0.1806 | 0.6649 | 0.3279 | **0.0247** | |
| P-value two-sided test | 0.3612 | 0.6701 | 0.6559 | **0.0495** | |

*Full analysis set, NRI *Primary Endpoint = Clinical Remission at Week 6 defined as Modified Mayo sub scores: i) rectal bleeding of 0, ii) stool frequency of 0 or 1 and iii) endoscopy score of 0 or 1 (excluding friability)*



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# Selection of Secondary Exploratory Endpoints

| Week 6 | COBITOLIMOD | | | | PLACEBO (n=44) |
|---|---|---|---|---|---|
| | 30 mg x 2 (n=40) | 125 mg x 2 (n=43) | 125 mg x 4 (n=42) | **250 mg x 2 (n=42)** | |
| Clinical remission, full Mayo Score % | 15.2 | 2.4 | 7.7 | **20.0*** | 7.7 |
| Symptomatic remission % | 27.0 | 26.2 | 25.0 | **35.1*** | 20.9 |
| Endoscopic improvement % | 20.6 | 12.2 | 25.6 | **40.5** | 30.0 |
| Clinical response % | 51.5 | 43.9 | 38.5 | **57.1** | 51.3 |
| Normalization (<250 mg/kg)# of faecal calprotectin % | 21.4 | 23.5 | 20.6 | **15.2** | 6.7 |

*One-sided p-value (pre-specified with cut-off <0.10), *p<0.1.*
*Clinical remission, full Mayo score: i) rectal bleeding subscore of 0, ii) stool frequency subscore of 0 or 1 (with at least one point decrease from baseline), iii) centrally read endoscopy score of 0 or 1 and iiii) PGA score of 0 or 1. Symptomatic remission: Mayo subscores i) rectal bleeding of 0, ii) stool frequency of 0 or 1 (with at least one point decrease from baseline). Endoscopic improvement: Mayo endoscopic subscore of 0 or 1. Clinical response: three point and ≥30% decrease from baseline in the sum of the full Mayo score.*
*#Normalization of faecal calprotectin to <250 mg/kg in patients with faecal calprotectin >250 mg/kg at baseline*

*Full analysis set, observed data*



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# Safety

| Treatment Emergent Adverse Events<br><br>No of patients (%) | COBITOLIMOD | | | | PLACEBO (n=44) |
|---|---|---|---|---|---|
| | 30 mg x 2 (n=40) | 125 mg x 2 (n=43) | 125 mg x 4 (n=42) | 250 mg x 2 (n=42) | |
| Patients with AEs | 10 (25.0%) | 17 (39.5%) | 15 (35.7%) | 18 (42.9%) | 21 (47.7%) |
| Patients with Serious AEs | 2 (5.0%) | 0 | 2 (4.8%) | 4 (9.5%) | 2 (4.5%) |
| Deaths | 0 | 0 | 0 | 0 | 1 (2.3%) |

*Safety analysis set, some patients have reported several adverse events*

# Cobitolimod - A Promising Novel Therapy in UC

- Cobitolimod is a potential new medication for left-sided moderate to severe ulcerative colitis
- Cobitolimod has a novel and unique mechanism of action
- Met the primary endpoint in the phase IIb study CONDUCT
- Supportive findings in secondary endpoints
- Cobitolimod was well tolerated and no safety signals were detected
- TLR9 activation is a promising novel therapeutic option in UC patients and is planned to be confirmed in an upcoming phase III program

# CONDUCT Results Published in the Lancet Gastroenterology and Hepatology

Cobitolimod for moderate-to-severe, left-sided ulcerative colitis (CONDUCT): a phase 2b randomised, double-blind, placebo-controlled, dose-ranging induction trial

Harnessing localised delivery of gut-selective therapy for ulcerative colitis

Comment

*Atreya et al Lancet Gastroenterol Hepatol. 2020 Dec;5(12):1063-1075*



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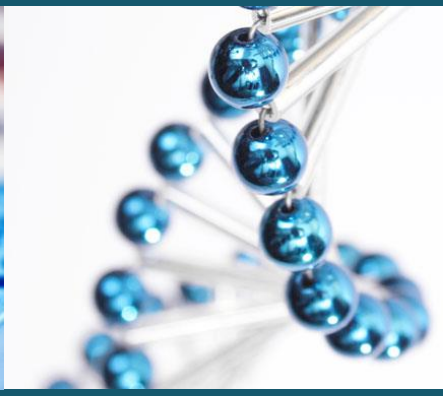


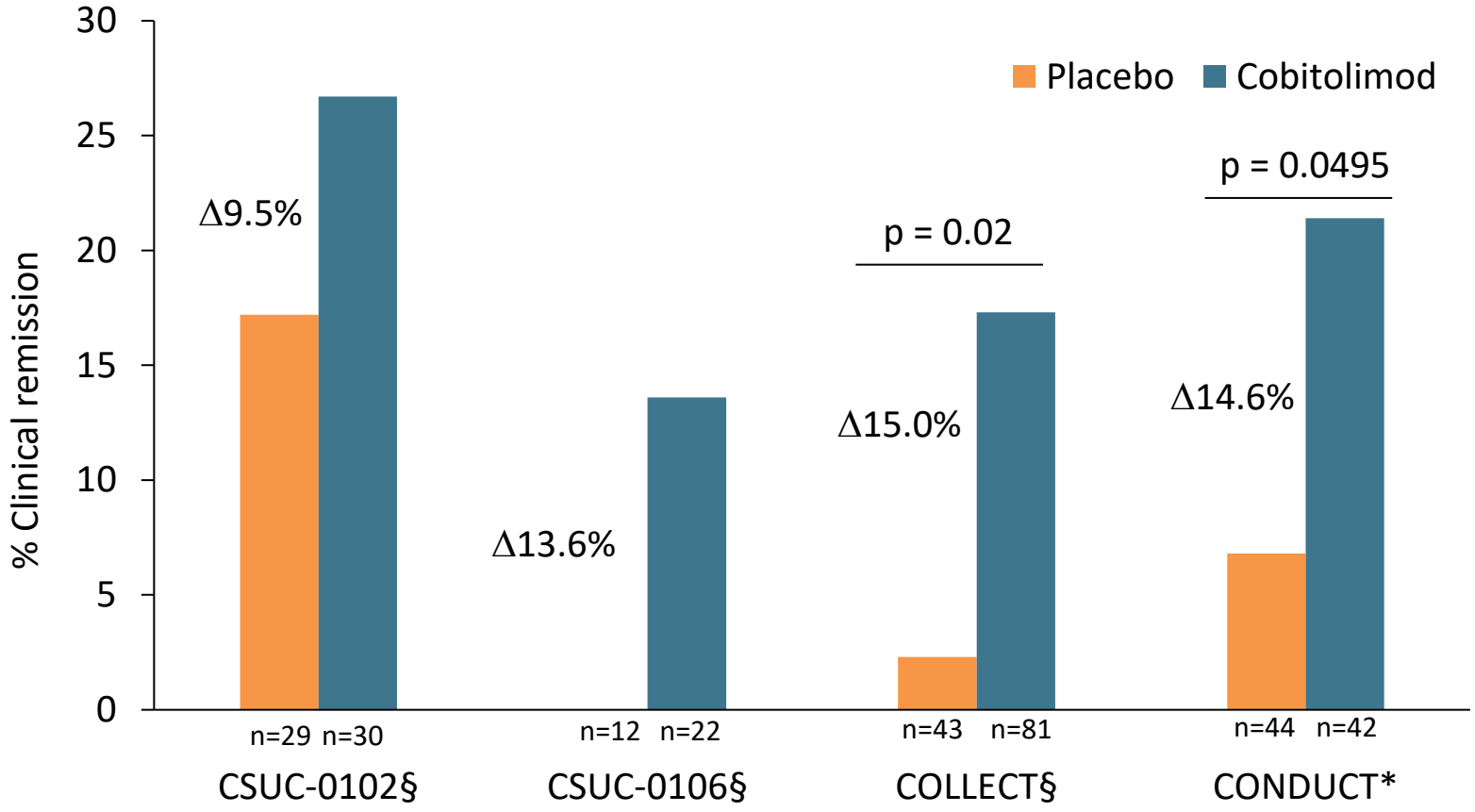

# InDex Pharmaceuticals
## R&D day

## Planned phase III program with cobitolimod

Thomas Knittel, CMO & Pernilla Sandwall, COO

*December 8, 2020*

# Supportive Findings in Previous Clinical Studies with Cobitolimod




*§ Clinical Remission defined as Full Mayo score (or converted CAI for COLLECT) ≤2 with no subscore exceeding 1, 4 weeks after one dose of 30 mg cobitolimod*
**Clinical Remission defined as Modified Mayo sub scores: i) rectal bleeding of 0, ii) stool frequency of 0 or 1 and iii) endoscopy score of 0 or 1 (excluding friability) at week 6 after two doses of 250 mg cobitolimod. Caution advised when comparing data across clinical studies*



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# European Key Opinion Leaders

- **Raja Atreya**, Prof., MD, Department of Medicine, University of Erlangen-Nürnberg, Erlangen, Germany
- **Walter Reinisch**, Prof., MD, Division of Gastroenterology & Hepatology, Medical University of Vienna, Austria
- **Laurent Peyrin-Biroulet**, Prof., MD, Nancy University Hospital, Nancy, France
- **Antonio Gasbarrini**, Prof., MD, Catholic University of Rome, Internal Medicine Depart./Gastroent. Division, Rome, Italy
- **Markus Neurath**, Prof., MD, Department of Medicine, University of Erlangen, Erlangen, Germany
- **Geert D'Haens**, Prof., MD, Amsterdam University Medical Center, Amsterdam, the Netherlands
- **Jonas Halfvarsson,** Prof., MD, Department of Gastroenterology, Faculty of Medicine and Health, Örebro University, Sweden



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# Advisory Board North America

- **Chaired by William Sandborn**, Prof., MD, Division of Gastroent., IBD Center, UC San Diego Health, USA
- **Brian Feagan**, Prof., MD, Senior Scientific Director of Robarts Clinical Trials at Western University, Ontario, Canada
- **David Rubin**, Prof., MD, Section of Gastroenterology, Hepatology & Nutrition at UChicago Medicine, Chicago, USA
- **Bruce Sands**, Prof., MD, Division of Gastroenterology, Icahn School of Medicine at Mount Sinai, New York, USA
- **Christina Ha**, Ass. Prof., MD, Department of Gastroenterology and IBD, Cedars-Sinai, Los Angeles, USA
- **Florian Rieder**, Ass. Prof., MD, Department of Gastroenterology, Hepatology and Nutrition, Cleveland Clinic, Cleveland, USA



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# Successful FDA & EMA Interactions Regarding Phase III

- Presentation of CONDUCT data to the agencies and outline of the phase III program
- Both FDA and EMA endorse the advancement of cobitolimod into phase III studies in patients with moderate to severe, left-sided ulcerative colitis
- The regulators agreed with InDex to:
  - Conduct the two induction studies sequentially
  - Include a higher dose in addition to the 2×250 mg dose



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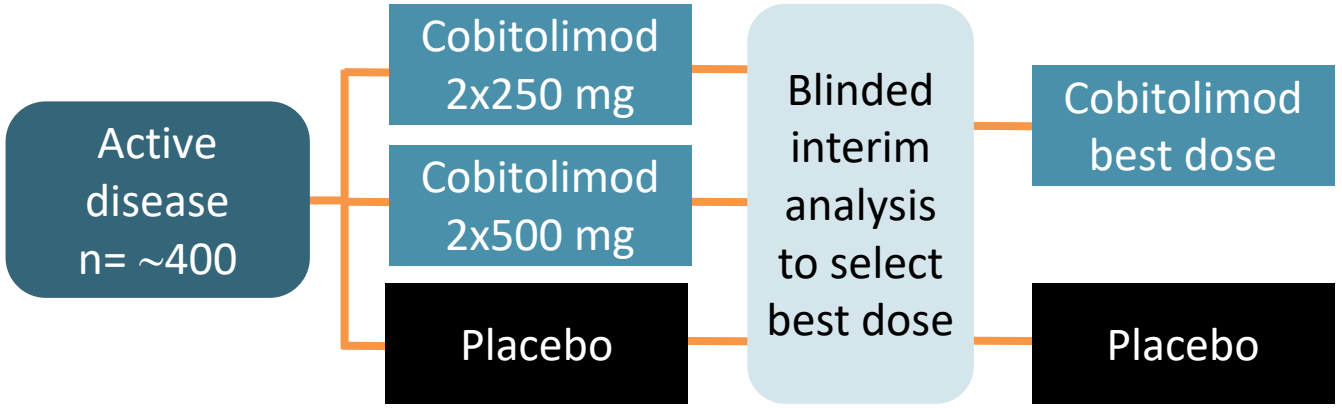
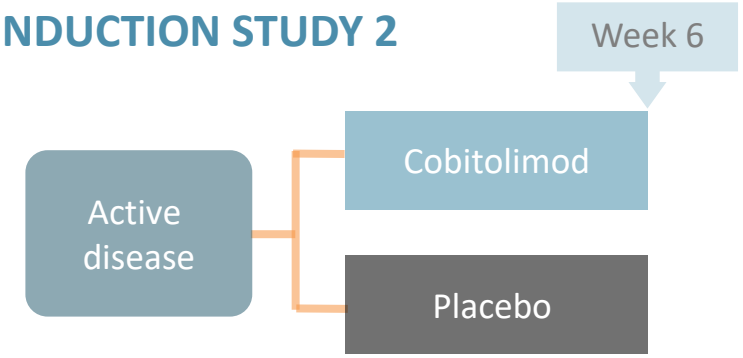
# Phase III Design

## INDUCTION STUDY 1 – ADAPTIVE DESIGN

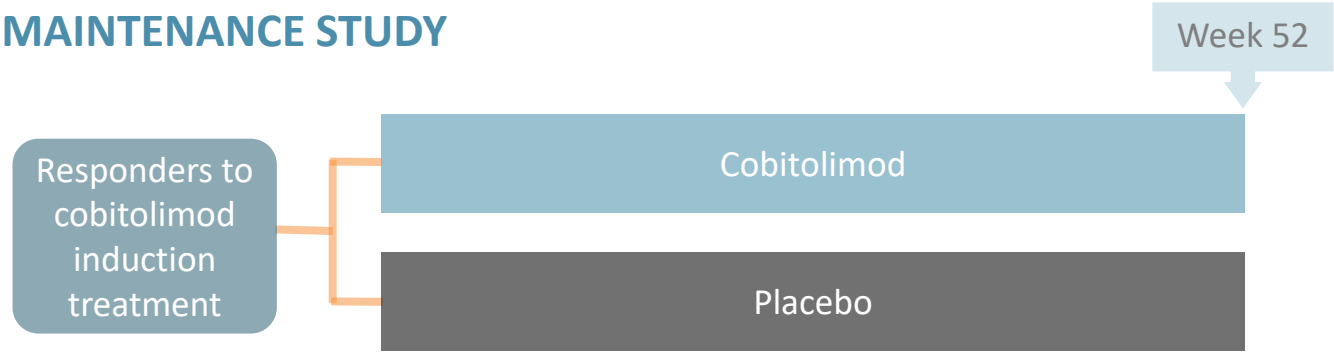



- Study design mimics CONDUCT study
- Moderate to severe, left-sided ulcerative colitis
- Patients failed conventional treatment and/or biologics/JAK inhibitor
- Dosing at week 0 and 3
- Primary endpoint clinical remission at week 6

## INDUCTION STUDY 2




## MAINTENANCE STUDY



# Phase III Considerations

- Study design based on the successful CONDUCT study
- Higher dose can increase efficacy further
- Adaptive design in first induction study provides cost and time efficiencies
- Sequential program allows optimization of second induction study



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# Phase III Execution

- Start planned for Q2 2021, subject to covid-19
- 18-24 months to complete first induction study from initiation
- Global study including a few hundred sites
- Will use leading global CRO
- Apply successful model from CONDUCT to build direct relationships with sites



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# CONDUCT Study Execution

- 91 clinics in 12 European countries
- Parexel as CRO
- Professor Raja Atreya, University of Erlangen-Nürnberg as Coordinating Investigator
- Competitive recruitment rate
  - 0.1 patient/site/month in line with concurrent phase III studies in UC

# Phase III Preparations

## COMPLETED ACTIVITIES

- Analyze full CONDUCT data set – √
- Regulatory interactions – √
- Market research – √
- Advisory Board North America – √
- CRO selection – √
- Study drug manufacturing – √
- Additional tox studies - √
- Presentation of the CONDUCT results at leading medical conferences - √
- Publication of the CONDUCT results in a scientific journal - √
- Phase III design - √

## ONGOING ACTIVITIES

- Finalize agreement with CRO
- Finalize study protocol and submit clinical trial applications

→ Start of phase III planned for Q2 2021, subject to covid-19



InDex Pharmaceuticals

APEX
HEALTHCARE CONSULTING

# InDex Pharmaceuticals R&D Day Presentation

## Feedback from IBD specialists and payers on cobitolimod through primary market research




**8th Dec 2020**

# Introduction

- InDex Pharmaceuticals commissioned Apex Healthcare Consulting (AHC) to conduct physician and payer market research to understand the clinical opportunity and pricing potential for their lead asset, cobitolimod, for the treatment of moderate to severe ulcerative colitis (UC). A high quality group of respondents were recruited.

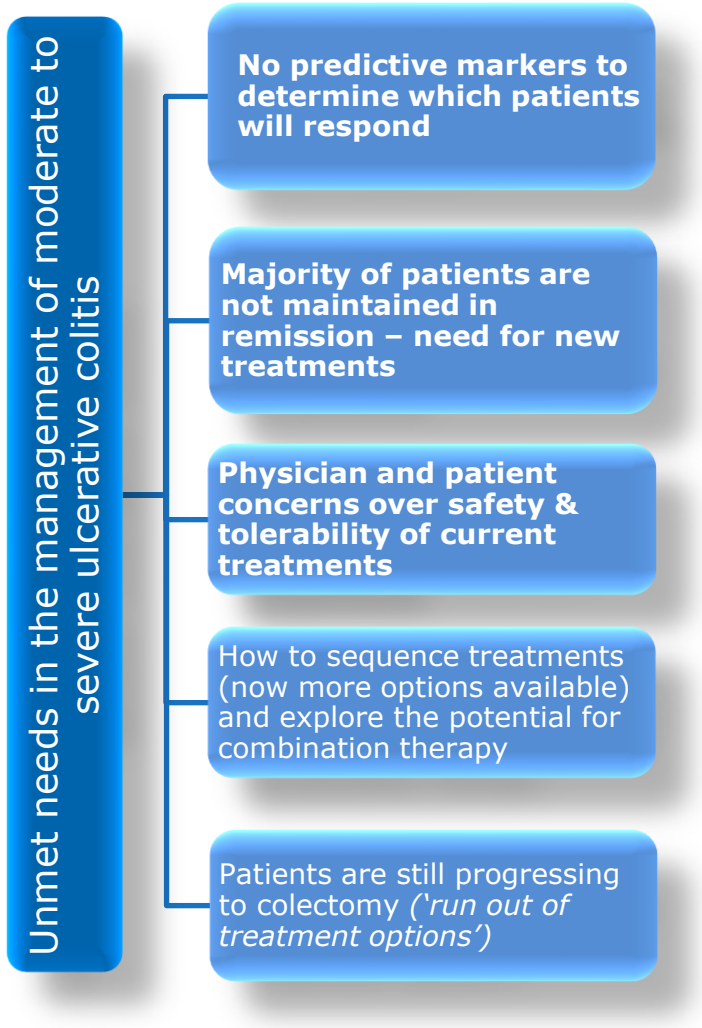
- Physician research was conducted with senior level gastroenterologists with a high caseload of UC patients. The recruited respondents were knowledgeable of the late-stage pipeline products in UC and ~60% (N=23/40) of respondents are or have been clinical trial investigators

| Physician Research | US | FR | DE | UK | TOTAL |
|---|---|---|---|---|---|
| *Gastroenterologists* | 16 | 8 | 8 | 8 | **40** |

- For the Payer research, interviews were conducted with respondents who had been involved in the evaluation of recent UC market entrants:
  - USA: Medical Directors or Pharmacy Directors from 2 national plans, 2 regional plans and one PBM
  - France: 2 recent members of the Commission de la Transparence (TC)
  - Germany: 1 G-BA advisor and two Statutory Health Insurance (SHI) representatives
  - UK: Ex-NICE advisor and two regional payers – Regional commissioner and Chief Pharmacy Director (who has advised NICE)

| Payer Research | US | FR | DE | UK | TOTAL |
|---|---|---|---|---|---|
| *National and Regional Payers* | 5 | 2 | 3 | 3 | **13** |

# There is a desire for new effective and safe treatments for moderate to severe UC

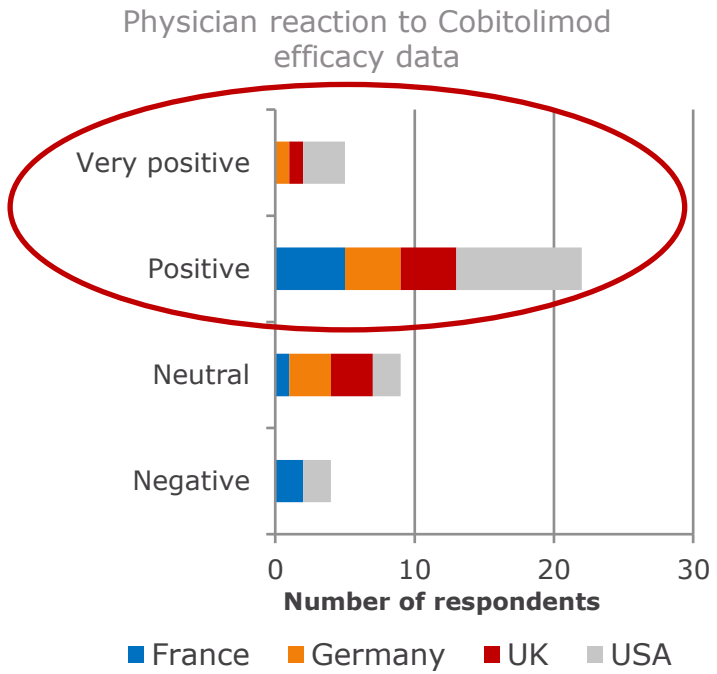



- New oral therapies are considered the most promising pipeline products for UC
- More selective JAK-1 inhibitors could have a role in UC, but ONLY if they show a superior side-effect profile to Xeljanz
- Mirikizumab is unlikely to demonstrate superior efficacy or safety to Stelara
- Etrolizumab is perceived as a potentially improved version of Entyvio
- If no safety signals, S1PR modulators could have potential as an earlier treatment or in combination with biologics

- Gastroenterologists consider the majority of the late-stage UC pipeline as successors to existing treatments with potentially minor improvements - they '*don't see any game changers right now'*

# Cobitolimod Profile Review

- The cobitolimod product profile, which was based on the CONDUCT Study results, tested well as a novel induction & maintenance treatment for moderately to severely active left-sided ulcerative colitis
  - 70% [N=28/40] gastroenterologists reacted positively to the product profile
- For gastroenterologists, cobitolimod has equivalent efficacy to current-biologic standard of care (TNFα inhibitors) with superior safety
  - The efficacy/safety ratio is considered unsurpassable
- When specifically asked to describe the efficacy of cobitolimod (from very negative to very positive), the majority (~70%) of gastroenterologists viewed the efficacy as positive or very positive
- Cobitolimod addresses the unmet need for a safe and effective treatment for moderate to severe UC



# Rectal administration is not unappealing to the majority of gastroenterologists

- The interviewed gastroenterologists believe that patients willing to be prescribed cobitolimod will be compliant with two enemas in 3 weeks during an acute flare, provided the product is easy to apply
  - Having to lie down for 30min afterwards is not an issue, as this is standard practice for currently used enemas
  - Patients typically take current enemas last thing in the evening before retiring to bed
  - Patients can choose a convenient time (e.g. weekends) for administration

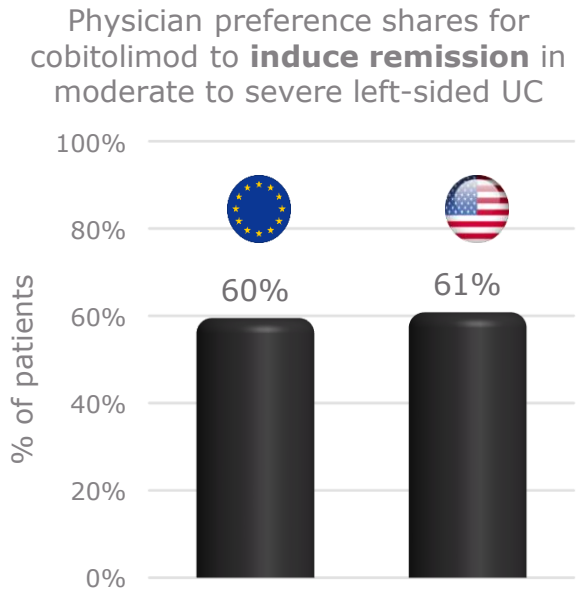
- Approximately monthly maintenance dosing is acceptable to physicians, and patients should be compliant, but there is a danger they could forget when it is due
  - Smartphone apps with reminders would be useful
  - Long term compliance could drop off after 12 months, if patients are asymptomatic – physicians believe that patients skip or forget doses of maintenance aminosalicylates

- The infrequent dosing schedule of cobitolimod is a key driver for acceptability of the rectal route of administration

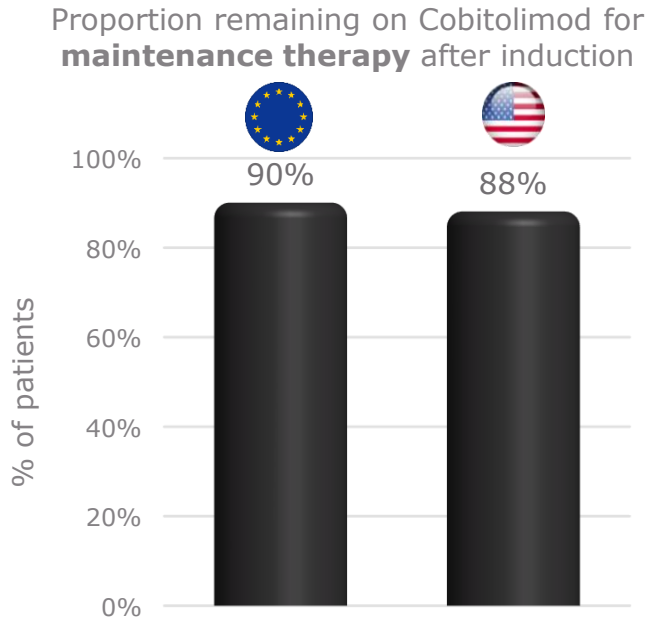
- Note that 95% of the gastroenterologists interviewed use rectal formulations for their UC patients

# Gastroenterologists are likely to prescribe cobitolimod to a significant proportion of their moderate to severe UC patients to induce and maintain remission

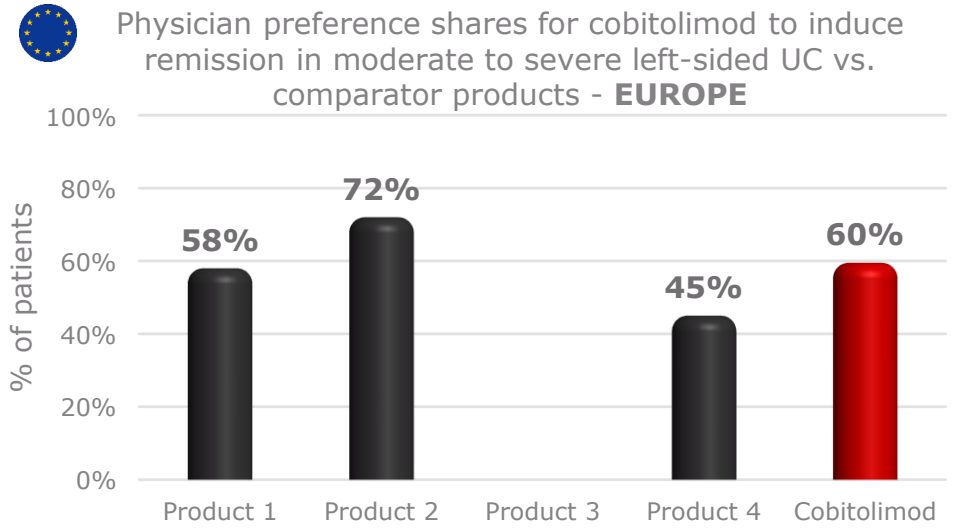
Left-sided UC

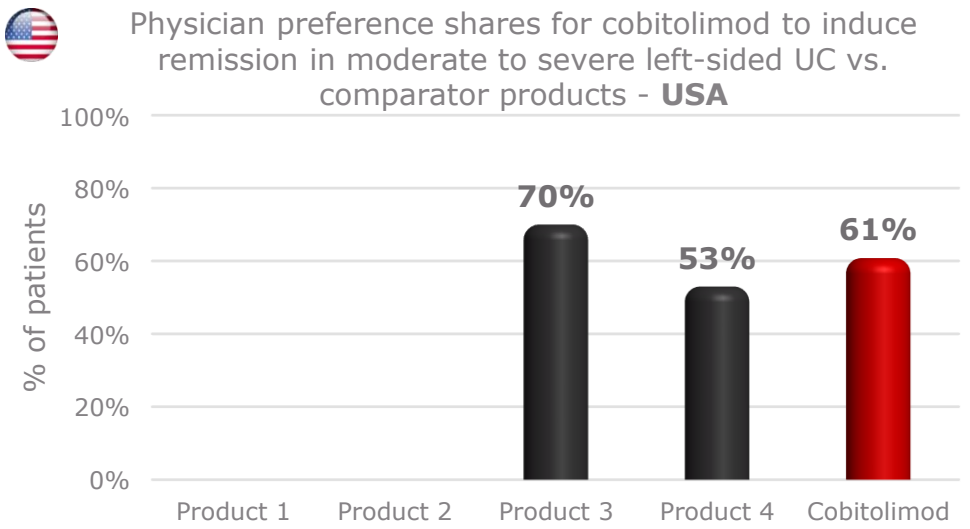



Of those patients who achieve remission



# Physician preference shares for cobitolimod compare favourably to other product profiles tested in market research




| Comparator | Indication | Geography |
|---|---|---|
| Product 1 (small molecule) | Chronic heart failure in children (0-4 years old) | Europe |
| Product 2 (small molecule) | Permanent Sensorineural Hearing loss (Age-Related) | Europe |
| Product 3 (small molecule) | Myasthenia Gravis | USA |
| Product 4 (Biologic) | Moderate to Severe Crohn's Disease | Europe and USA |

# Price Potential for cobitolimod

- Reflective of the market conditions, EU payers align with current EU prices for TNFα inhibitors (biosimilars) as the expected pricing strategy for cobitolimod
- An annual treatment price of €10,000 for cobitolimod approved for induction and maintenance therapy would be acceptable in France and Germany, as the price is at parity with TNFα inhibitors

| | €10,000 |
|---|---|
| France | Competitive with TNFα inhibitors |
| Germany | Realistic and acceptable |
| UK | Achievable, but likely to be positioned after TNFα inhibitors |

- Cobitolimod approved for induction and maintenance therapy could achieve an annual treatment price up to $45,000* – but payers may require step through one or more biologics before allowing access
- Prices lower than $30,000 could ensure placement before TNFα inhibitors, and are more attractive for consideration of cobitolimod used in a combination setting

| $35,000 | $45,000 |
|---|---|
| Payers may require step through one biologic before permitting use (or leave to physician choice)<br>Could be less attractive for combination use | Could be tiered as a co-preferred or nonpreferred option<br>Payers may require step through one or more biologics, although some will still allow physician choice |

* Annual treatment prices of $25K, $35K, $45K and $55K tested

# Conclusions

1. There is a desire for new effective and safe treatments for moderate to severe UC ✓
2. Topical delivery ensuring ‘minimal systemic exposure’ and ‘superior safety’ are perceived to be key clinical benefits of cobitolimod ✓
3. Cobitolimod has an acceptable dosing schedule ✓
4. Gastroenterologists are highly likely to prescribe cobitolimod, and it could be the product of choice for left-sided UC ✓
5. Cobitolimod addresses the unmet need for a safe and effective treatment ✓

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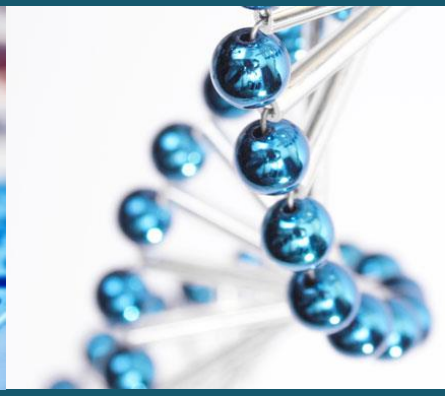


# InDex Pharmaceuticals
## R&D day

## The commercial potential of cobitolimod

Peter Zerhouni, CEO

*December 8, 2020*

# Cobitolimod – A Late Stage, First-in-Class Immunotherapeutic

- Cobitolimod is a potential new medication for moderate to severe ulcerative colitis
- Primary endpoint met in phase IIb study CONDUCT with an excellent safety profile
- 4 previous completed clinical studies support efficacy and safety demonstrated in CONDUCT
- Phase III to start Q2, 2021 – subject to covid-19

- Competitive efficacy
- Superior safety profile
- Local treatment, provides rapid onset
- Novel mechanism of action
- Potential for combination therapy

Cobitolimod has blockbuster potential with an outstanding combination of efficacy and safety



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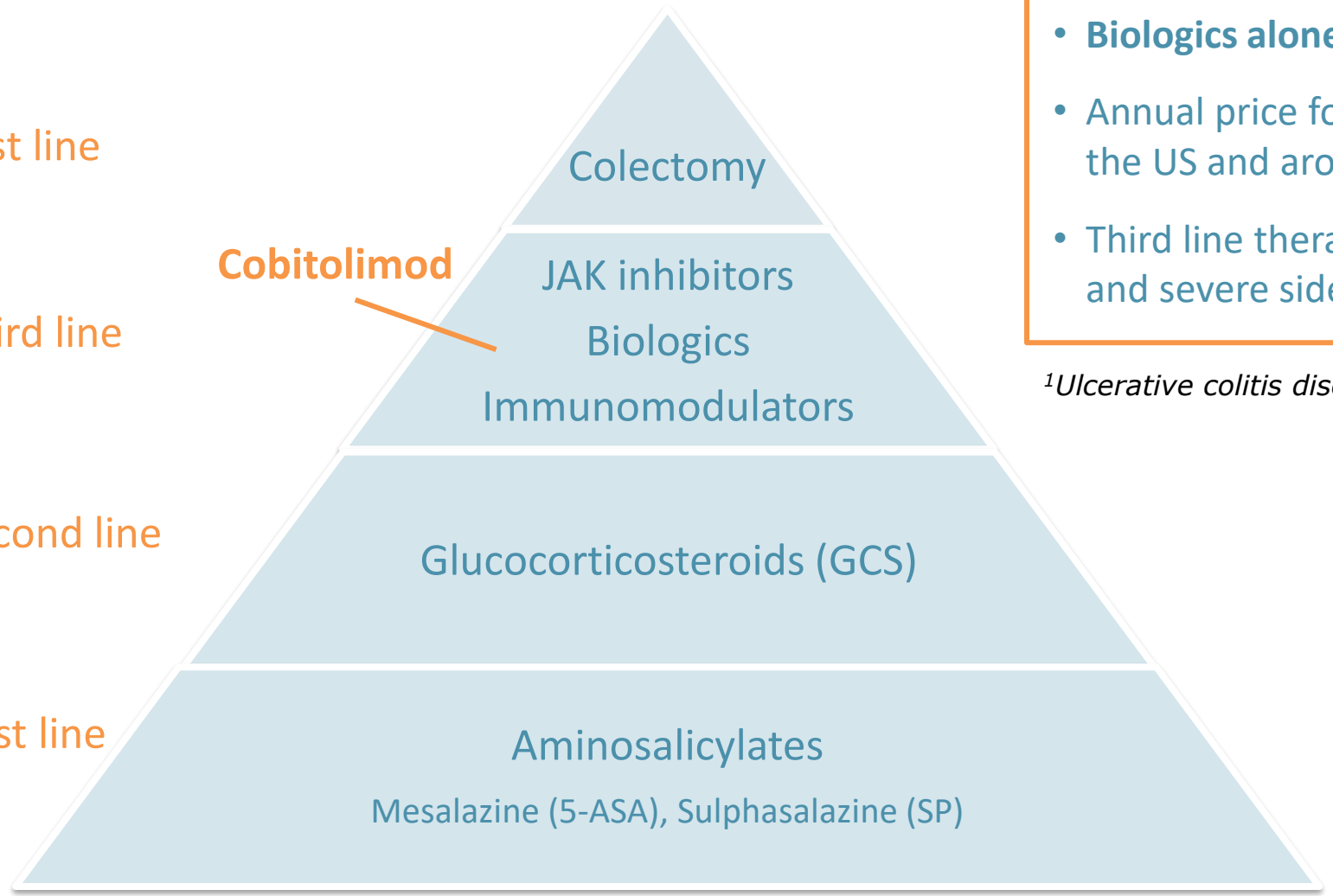
# Moderate to Severe UC Is a High Value Market




- **Biologics alone sell for >$5 Bn per year in UC[1]**
- Annual price for biologics is USD $30,000-80,000 in the US and around EUR 10,000 in EU
- Third line therapies have problems with tolerance and severe side effects

[1]*Ulcerative colitis disease coverage. Datamonitor Healthcare 2016*



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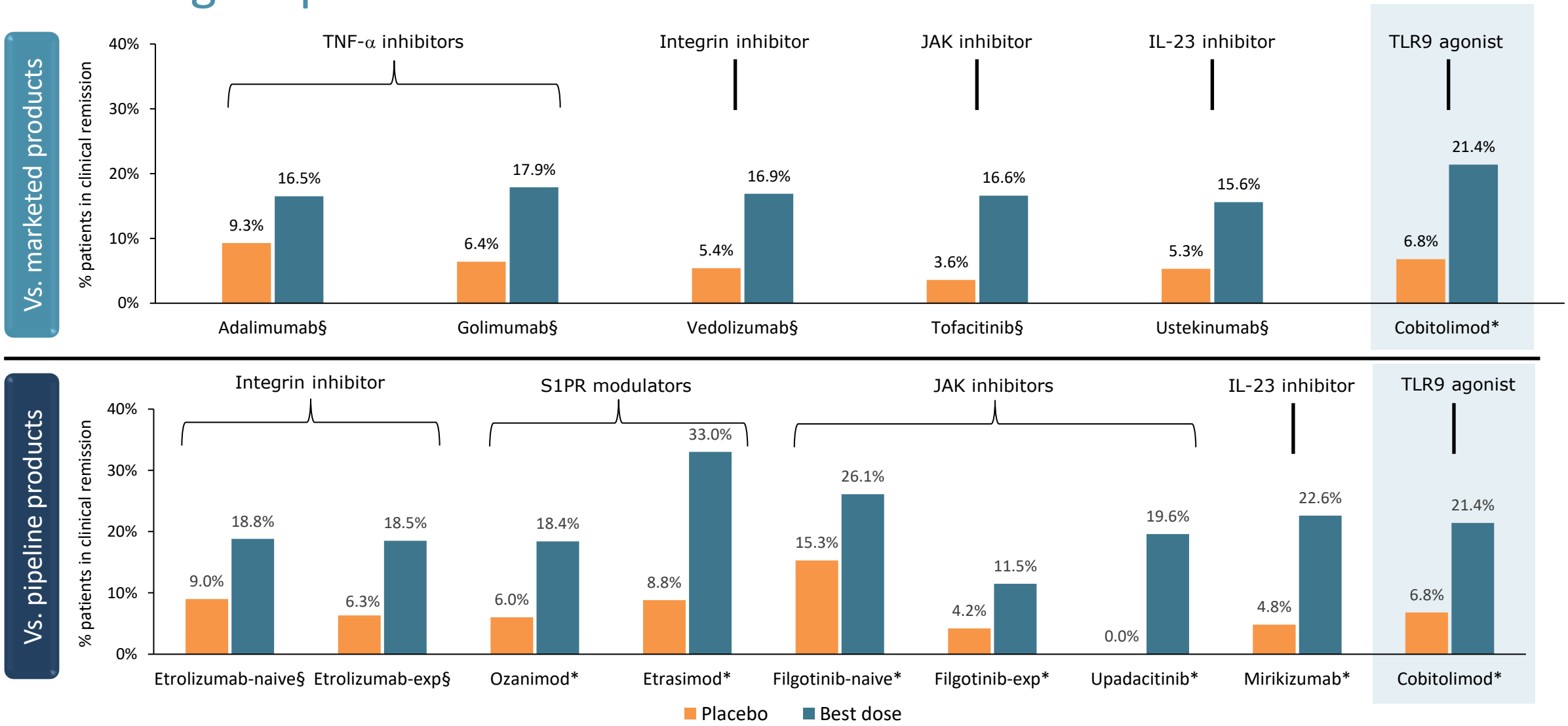
# Cobitolimod has Competitive Efficacy vs. Marketed Products and Late Stage Pipeline




§ Full Mayo Score ≤2, *3-component Mayo Score ≤2. Caution advised when comparing data across clinical studies. The patient population in the studies included a mix of biological naïve and biological experienced patients, except for etrolizumab and filgotinib where separate studies were performed. Infliximab excluded from comparison as not comparable phase III patient population.



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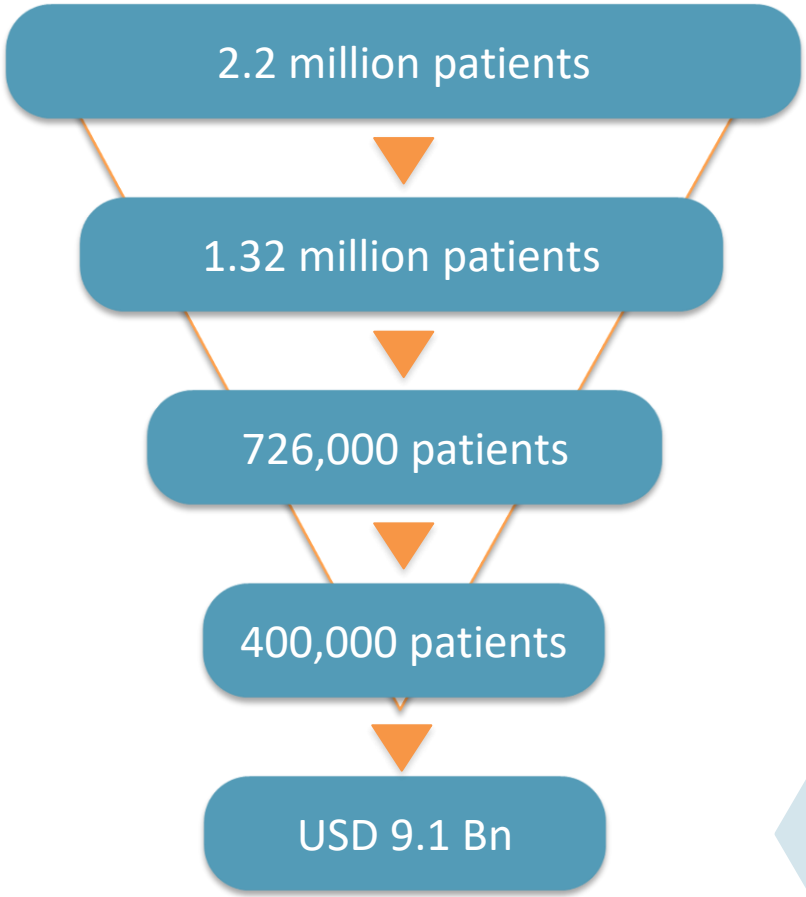
# Cobitolimod Addresses a USD >9 Bn Market




**UC population[1] in the US, EU-5[2] and Japan**
- US: 1,100,000, EU-5: 800,000 and Japan: 260,000 patients[3]

**Moderate to severe UC**
- ~60% of total UC population[4]

**Whereof left-sided UC**
- ~55% of moderate to severe UC population[5-11]

**Failing conventional therapy**
- ~55% of moderate to severe UC population[4]

**Assuming an annual price per patient of USD 35,000[4] in US and USD 11,000[4] in EU-5 and Japan**

Notes: 1) Above 18 years of age. 2) EU-5 countries (France, Germany, Italy, Spain and the UK). 3) Global Data Ulcerative Colitis prevalence. 4) Apex Market Research 2020 5) Rutgeerts et al. N Engl J Med 2005;353:2462-76, 6) Sandborn et al. Gastroenterology 2012;142:257–265, 7) Sandborn et al. Gastroenterology 2014;146:85–95, 8) Feagan et al. N Engl J Med 2013;369:699-710, 9) Sandborn et al .N Engl J Med 2017;376:1723-36, 10) Sandborn et al N Engl J Med 2019;381:1201-14, 11) Atreya et al. JCC 2016 Nov;10(11):1294-1302.



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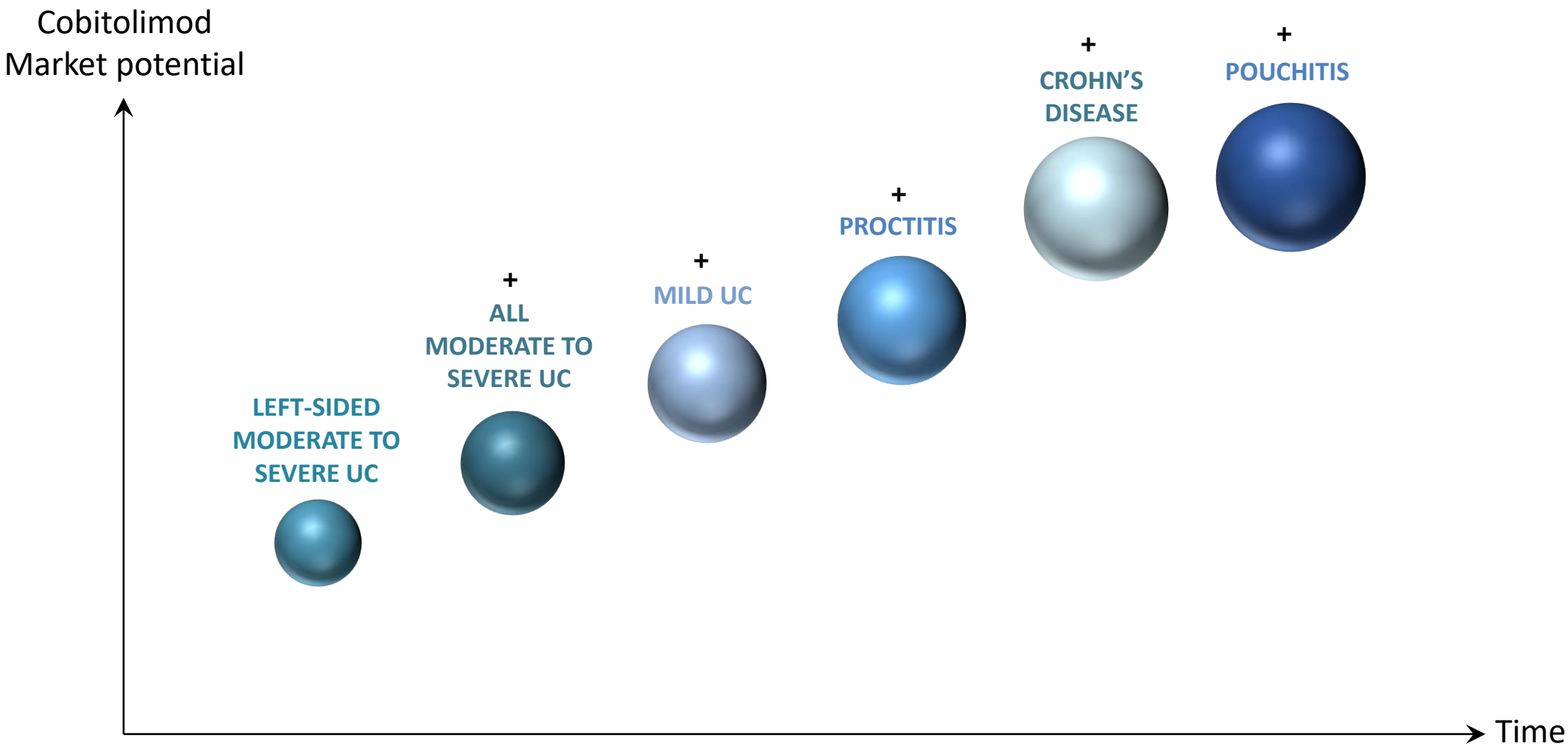
# High Market Potential with Market Expansion Possibilities



# Financing

- Intend to carry out a fully guaranteed rights issue of approximately SEK 500 million to fund phase III development of cobitolimod
- Subject to extraordinary general meeting scheduled to be held in January 2021
- Large existing shareholders Linc AB, Fourth AP Fund and SEB-Stiftelsen have expressed their interest to participate in the transaction
- Barclays Bank Ireland PLC and Carnegie Investment Bank AB have indicated their interest to underwrite part of the rights issue



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# Summary

## HIGH MARKET POTENTIAL

- Moderate to severe ulcerative colitis is a debilitating disease with enduring unmet medical need
- Cobitolimod's product profile validated with specialists and payers
- Cobitolimod has blockbuster potential with an outstanding combination of efficacy and safety and a new MoA

## LATE STAGE CLINICAL DEVELOPMENT

- Successful phase IIb study CONDUCT recently published in The Lancet Gastroenterology and Hepatology
- 4 previous completed clinical studies support efficacy and safety demonstrated in CONDUCT

## CLEAR PATHWAY FOR PHASE III INITIATION

- Start of phase III planned for Q2 2021, subject to covid-19
- Fully guaranteed rights issue underway



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# Q & A

**Questions**

E-mail to info@indexpharma.com

or write your question in the chat for the event



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