

**CONFIDENTIAL**



**NIMMUNE**  
**B I O P H A R M A**

**COMPANY PRESENTATION | March 2023**



# Precision Immunology Therapeutics for Human Diseases



## Precision Immunology-Focused Platform

- Precision Immunology-focused immunoregulatory therapeutics for autoimmune diseases
- Newly discovered and validated immunological targets
- Gastrointestinal, rheumatic and cutaneous autoimmune indications with large unmet clinical needs
- The leading immunoregulatory medicines company



## Highly Experienced Biotech Team

- The team has an IP track record of about 200 patents and over 300 publications in immunology
- Previous experience in \$20M in non-dilutive rounds, \$170M in equity financing, IPO and \$218M in business development deals
- Developed a 17-product pipeline including a Phase 3-ready UC drug, a Phase 2-ready UC drug, and cleared 8 INDs in less than 4 years



## High-Impact Therapeutic Assets

- Omilancor, Phase 3-ready lead product candidate targeting LANCL2, is an orally active, once-daily, gut-restricted, first-in-class therapeutic for UC and pivotal studies planned for 2023
- NIM-1324, an orally active, once-daily, systemically distributed drug targeting LANCL2 in lupus; completed Phase 1 testing in 2022
- De-risking, cost-efficiency, and accelerated path to market



## Transformative Drug Development Pipeline

- Franchise of first-in-class oral small-molecule therapeutics targeting new and validated immunological pathways
- Clinical indications targeting GI and rheumatology
- Opportunity to license and partner some programs while advancing our core programs along critical value-accruing clinical milestones to commercialization



# Nimmune Leadership Team

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## **Dr. Josep Bassaganya-Riera**

*Executive Chairman of the Board, President, and CEO*

Biotech entrepreneur and innovator with 25 years of scientific innovation in immunology, drug development, business development and biotech fundraising experience. Founded Landos Biopharma, Inc.



## **Dr. Raquel Hontecillas**

*Chief Scientific Officer*

25 years of translational experience in immunology, drug development, and the biotech industry focusing on infectious, autoimmune, and metabolic diseases. Former CSO at Landos.



## **Jennifer Collette, MSA, CPA**

*Chief Accounting Officer & Controller*

15 years of experience in accounting and financial systems. Expertise in technical & project accounting, budget planning, controls, and financial reporting. Former Head of Finance at Landos.



## **Dr. Andrew Leber**

*Chief Development Officer*

Expertise spans immunology and A.I.-based drug development for autoimmune disease with specific focus on CD, UC, RA, and lupus. Former VP of Scientific & Product Development at Landos.



## **Marek Ciszewski, JD**

*Chief Financial Officer*

25 years of biopharma and financial industry expertise, encompassing investor relations and managing capital structures for biotech companies. Former VP of Financial Strategy and Investor Relations at Landos.



# Nimmune Board Members

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## Board of Directors

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### **Dr. Josep Bassaganya-Riera**

*Nimmune Executive Chairman of the Board,  
President and CEO*

### **Dr. Raquel Hontecillas**

*Nimmune Board Member and CSO*

## Clinical Advisory Board

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### **Jean-Frederic Colombel, MD**

*Director of the Helmsley IBD Center  
at Mount Sinai, NYC, NY*

### **Hans Herfarth, MD, PhD**

*Director of the UNC Multidisciplinary IBD  
Center, Chapel Hill, NC*

### **George Tsokos, MD**

*Chief Division of Rheumatology, Harvard  
Medical School, Beth Israel Deaconess  
Medical Center, Boston, MA*

### **Fabio Cominelli, MD, PhD**

*Director of the UH Case Medical Center,  
Cleveland, OH*

### **Francisco Sylvester, MD**

*Chief Division of Pediatric  
Gastroenterology, UNC Chapel Hill, NC*





# Omilancor Activates Novel Immunoregulatory Target LANCL2

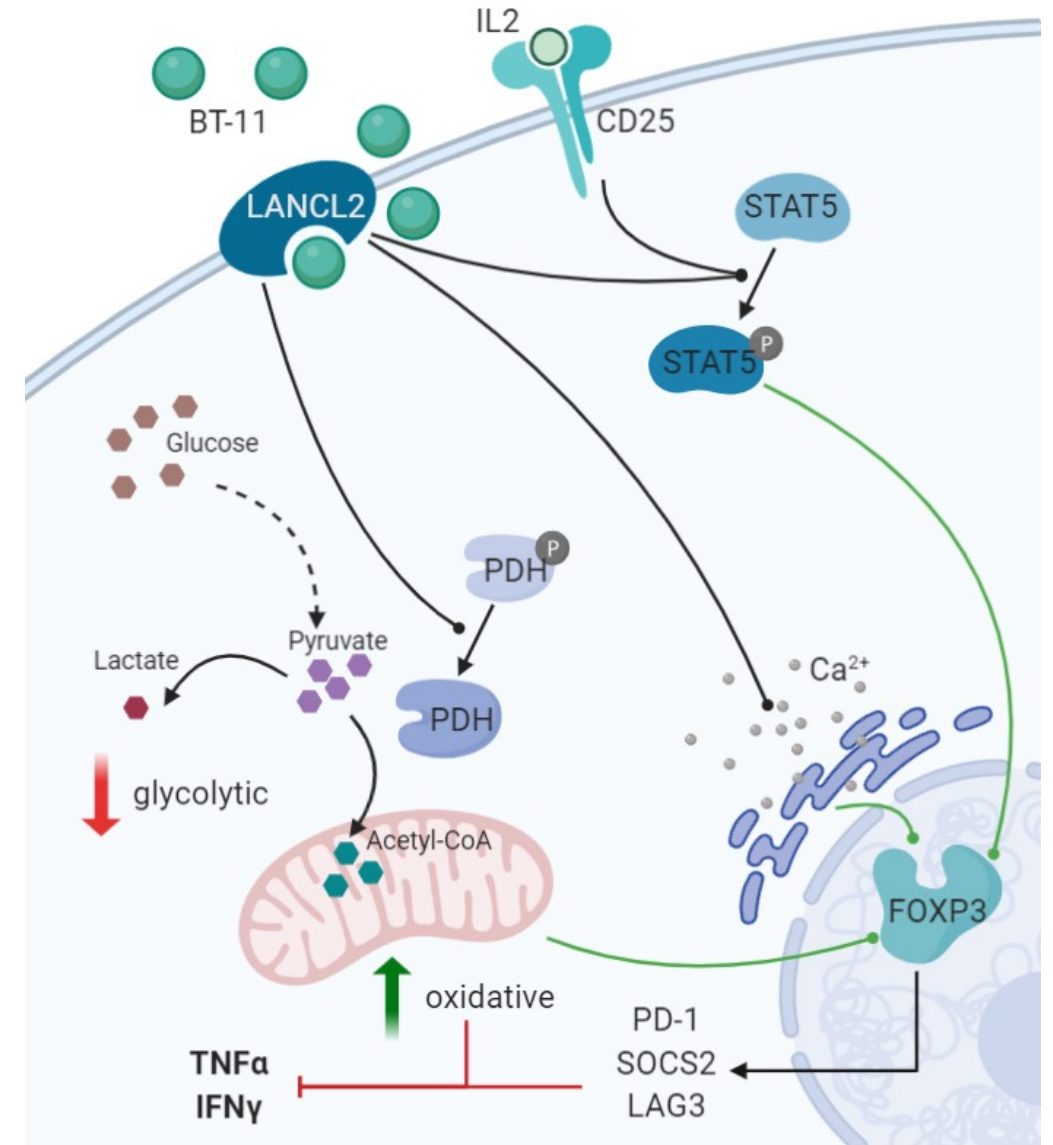
## Lanthionine Synthetase C-Like 2 (LANCL2):

- Multipronged mechanism of action targeting known immunological targets downstream tied to autoimmune diseases, including IBD

## Omilancor generates suppressive regulatory CD4+ T cells (Tregs) that restore and maintain immune tolerance in the GI tract:

- ✓ Enhances CD25/STAT5 signaling to support the stable differentiation of regulatory CD4+ T cells with greater anti-inflammatory functionality
- ✓ Increases PDH activity, resulting in increased oxidative metabolism supporting FOXP3 stability
- ✓ Increases suppressive effects of Tregs due to enhanced immune checkpoint surface markers (LAG3 and PD-1)

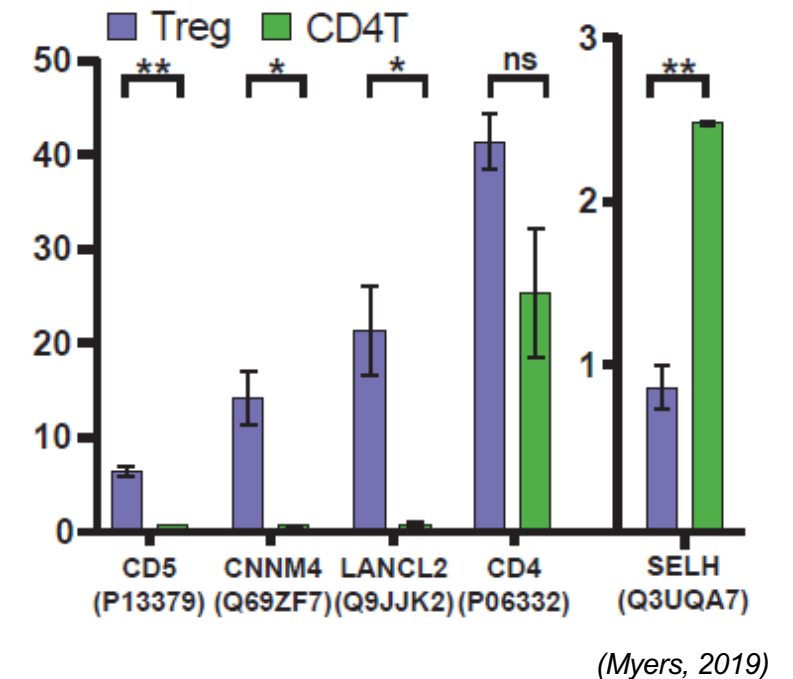
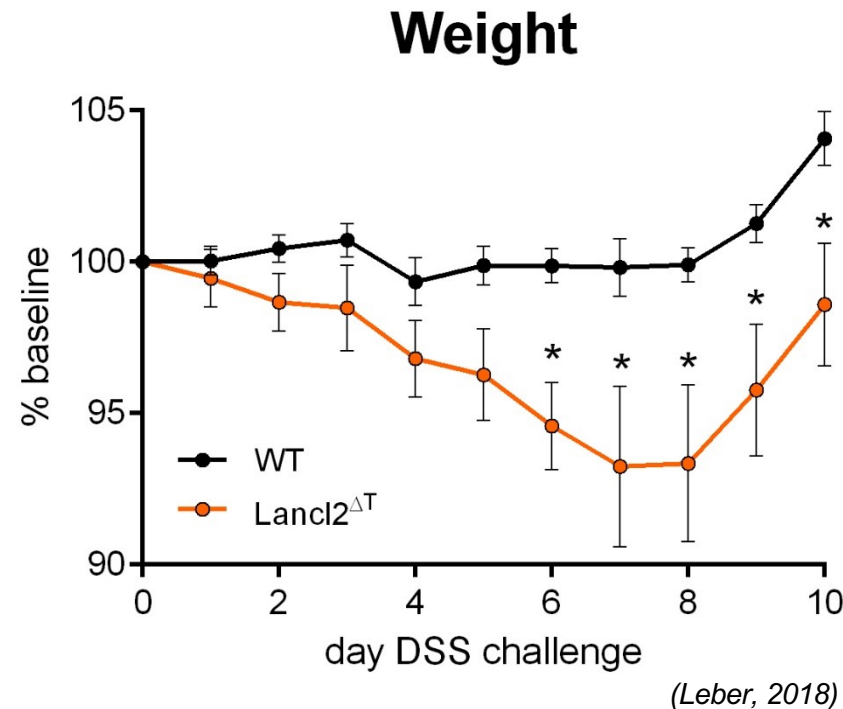
Leber, A., et al. *Inflammatory Bowel Diseases*. 2018 24:1978-1991.  
Carbo, A., et al. *J Med Chem*. 2016 Nov 23;59(22):10113-10126.  
Leber, A., et al. *J Immunol*, 2019.





# LANCL2 is a novel Treg associated receptor relevant to IBD

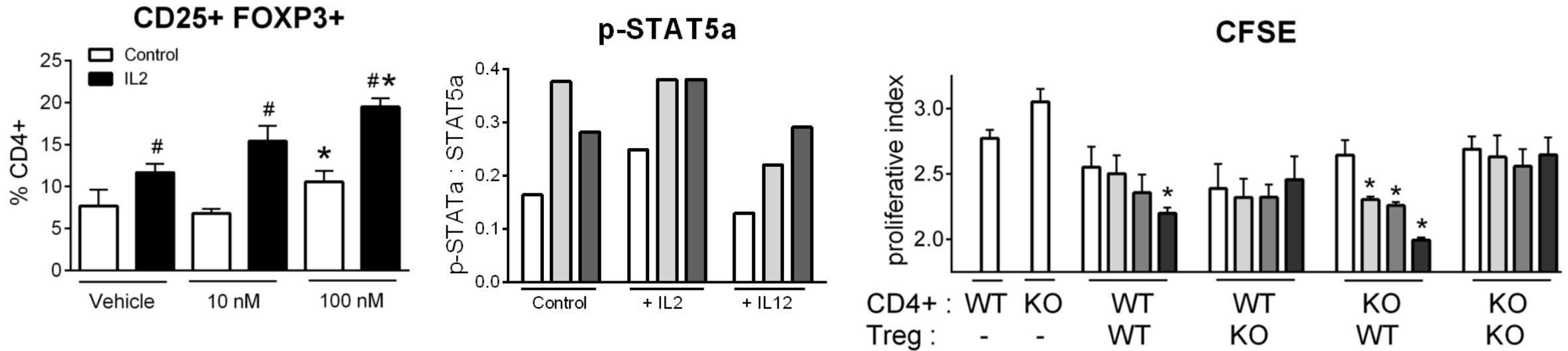
- *LANCL2<sup>-/-</sup> mice have been characterized in multiple autoimmune conditions*
- *The loss of LANCL2 in CD4<sup>+</sup> T cells results in worsening of disease severity and Treg defects in a DSS model of colitis*
- *LANCL2 was identified to be one of the three most differentially expressed proteins in Tregs relative to CD4<sup>+</sup> T cells as a whole*







# LANCL2 in Regulatory CD4+ T cells



*LANCL2 activation supports IL-2 induced CD25+ Treg differentiation and capacity to suppress proliferation*

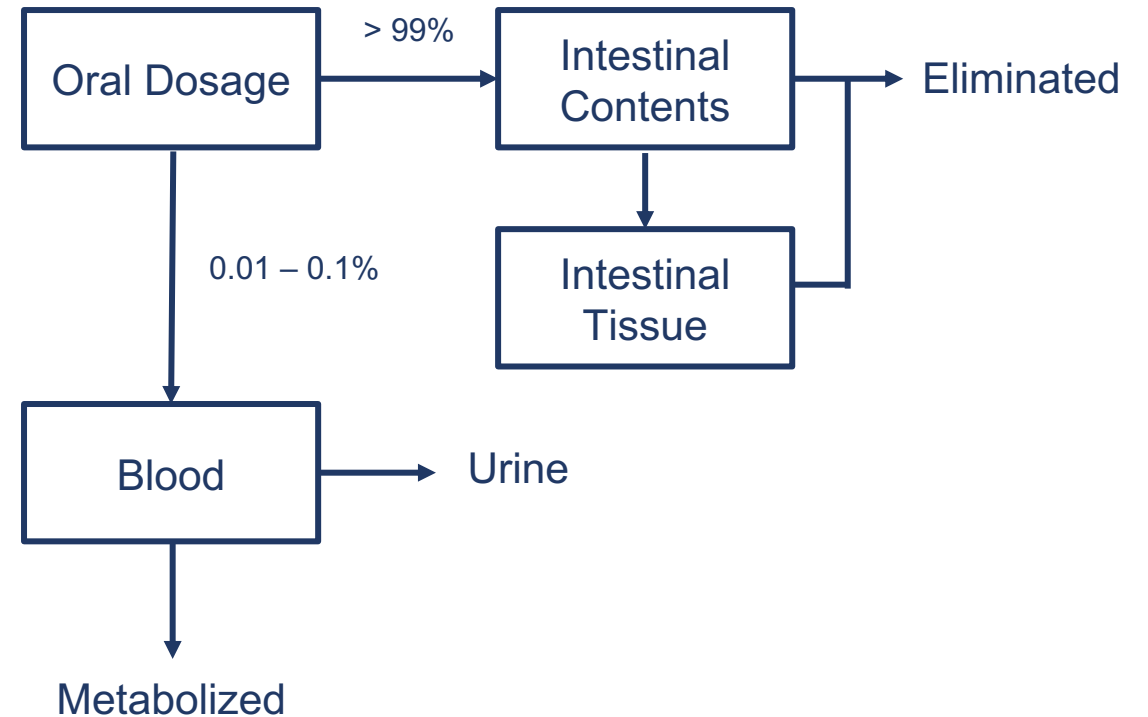
LANCL2 can serve as a target to reverse the diminished CD25+ expression in regulatory CD4+ T cells that occurs during autoimmune disease, rescue compromised IL-2 signaling and restore suppressive capacity





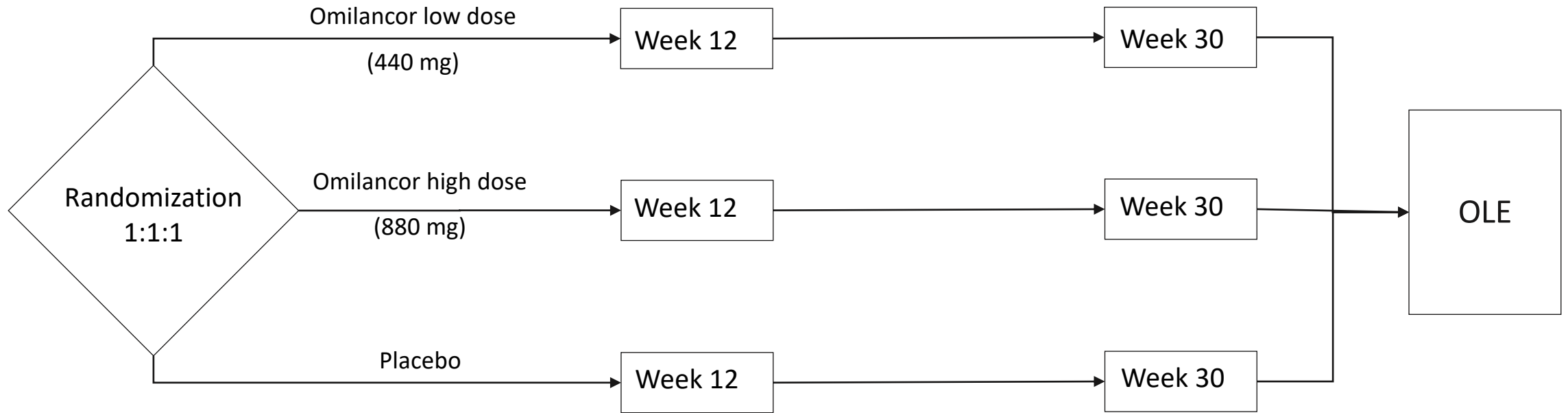
# Safety and Pharmacokinetics - Omilancor

- ✓ No adverse event trends or AEs of special interest at doses of up to 6600 mg for 7 days or 880 mg for over 1 year in humans
- ✓ NOAEL > 1000 mg/kg/d in pivotal 6-month rat and 9-month dog GLP toxicology studies
- ✓ No effects on carcinogenicity, genotoxicity or reproductive, cardiovascular, central nervous, and respiratory systems in targeted nonclinical studies
- ✓ No restrictions on ADME-based drug-drug interactions





# Completed First-in-Patient Study Design of Omilancor in Mild to Moderate UC

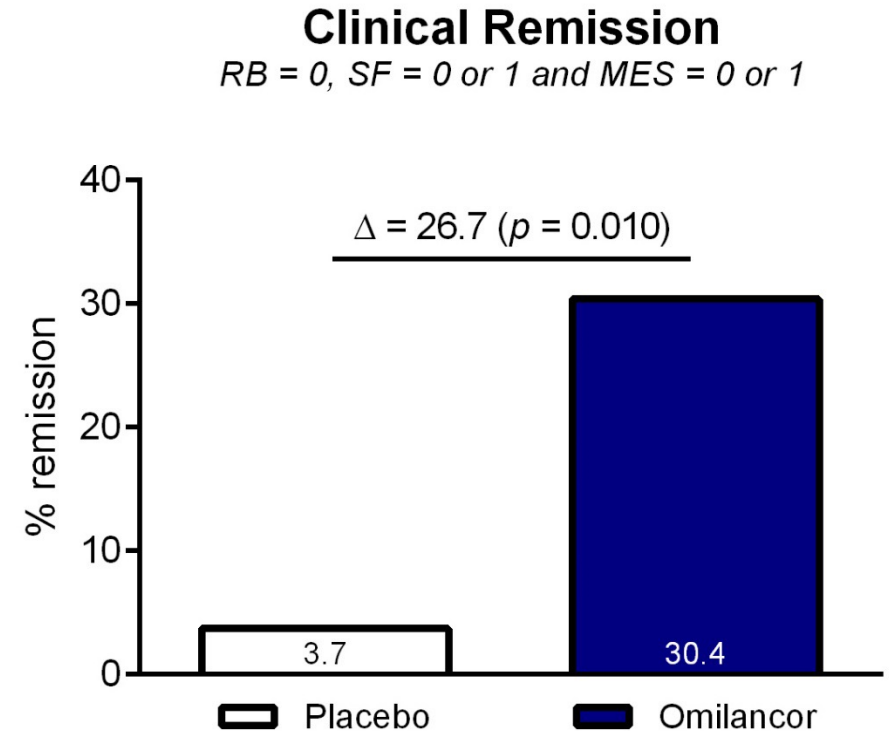


- Primary Objective
- The primary objective of this proof-of-concept study was to establish the efficacy of oral BT-11 in inducing clinical remission at Week 12 in subjects with mild to moderate ulcerative colitis (UC).
- Key Inclusion Criteria
- Male and female subjects with mild to moderate UC defined by a total Mayo Score of  $\geq 4$  with MES  $\geq 2$  (confirmed by central reader); 5-aminosalicylates (max 4.8 g/day) and oral corticosteroids (max 20 mg/day prednisone or equivalent) must be stable for the 12-week induction period.



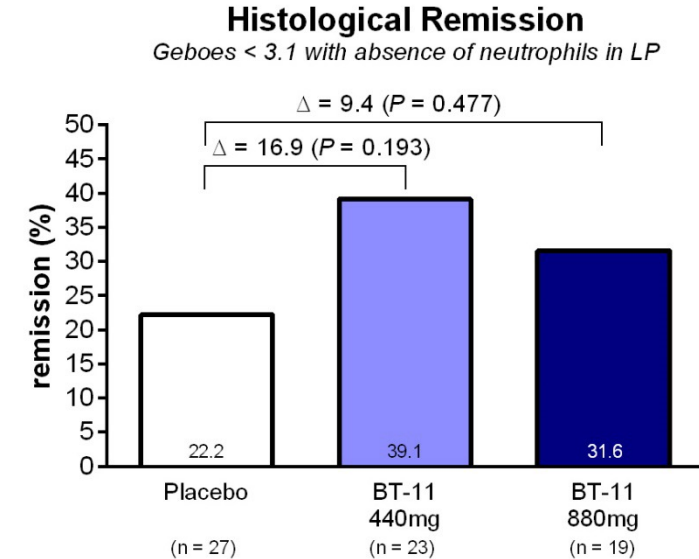
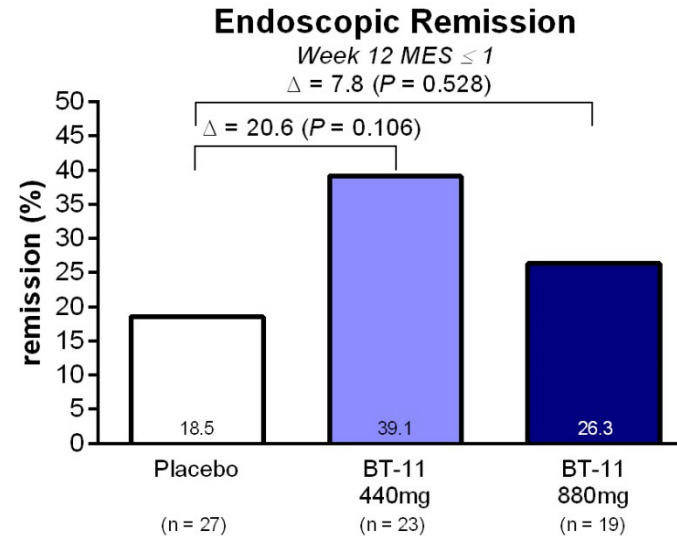
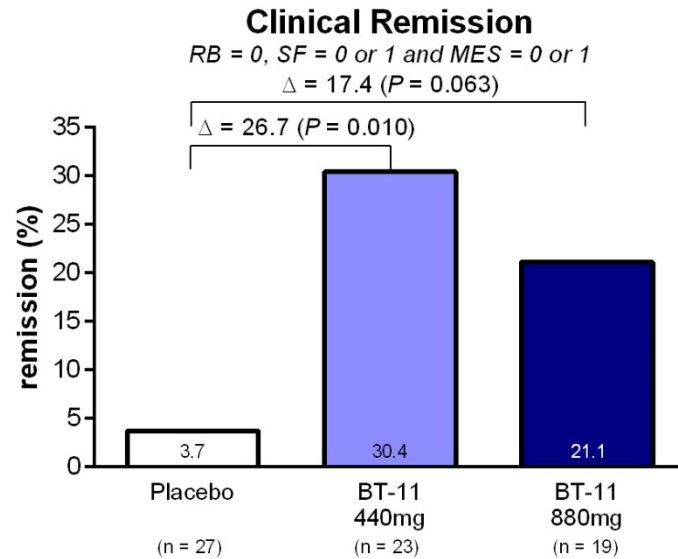
# Positive Clinical Remission Rates

<b>Primary endpoint definition</b>	Clinical remission at Week 12 as defined by stool frequency of 0 or 1, rectal bleeding of 0 and Mayo endoscopic subscore of 0 or 1
<b>Analysis population</b>	Subjects with rectal bleeding greater than 0, histological activity and elevated fecal calprotectin at baseline
<b>Analysis method</b>	Stratified Cochran-Mantel-Haenszel Method
<b>Stratifications</b>	Previous biologic usage Corticosteroid use at baseline





# Statistically Significant Approvable Primary Endpoint

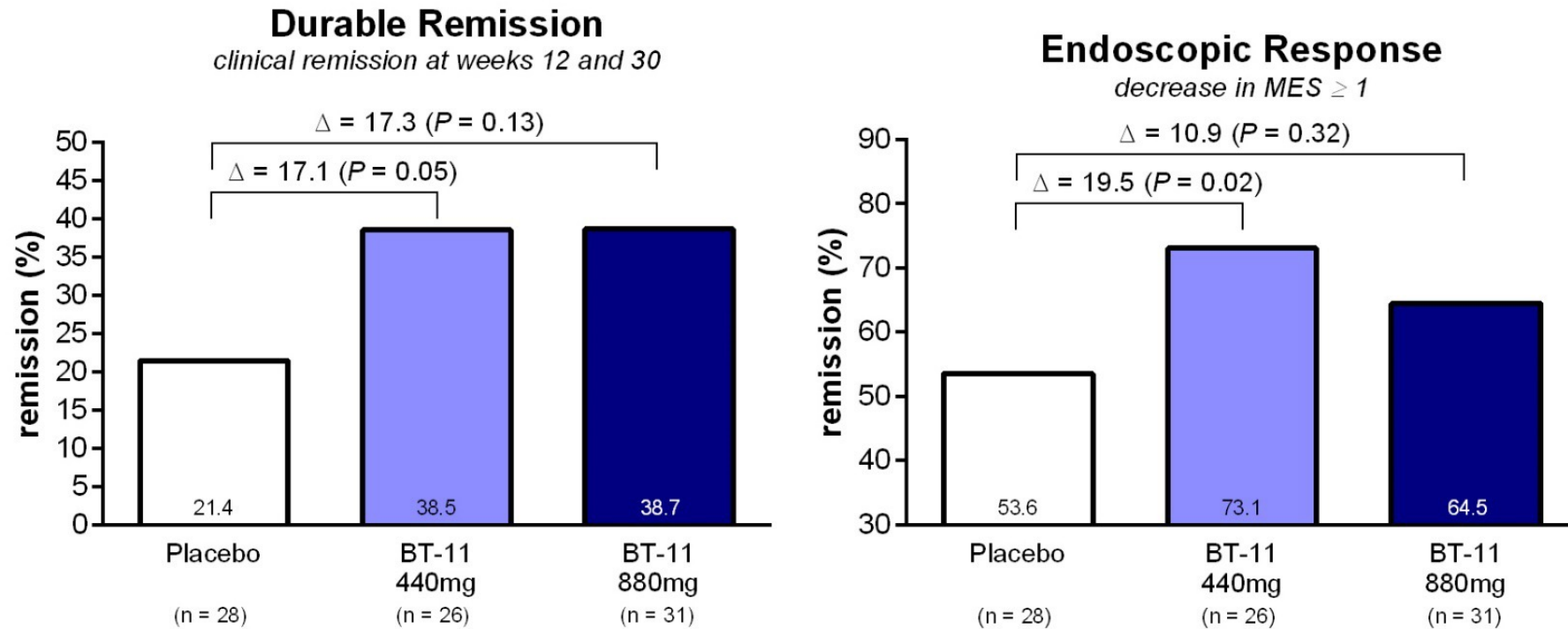


Population excludes patients with rectal bleeding = 0, Geboes histological score of 0, or fecal calprotectin < 250 ug/g at baseline

*In patients with clinically, endoscopically and histologically active UC at baseline, 440 mg omilancor outperforms placebo for the induction of clinical remission.*



# Clinical remission to omilancor is maintained through week 30



Population is the induction responder set, the primary analysis set for the maintenance period

Responses observed endoscopically and clinically with omilancor are maintained after 30 weeks of treatment.



# Displayed Biologic-like Efficacy with Improved Safety Profile

	Trial Name	Remission Rate	Placebo Adjusted Rate	Endpoint	Safety
<b>Omilancor</b>	<b>BT-11-201</b>	<b>30.4</b>	<b>26.7</b>	3-component remission	No identified trends in AE profiles

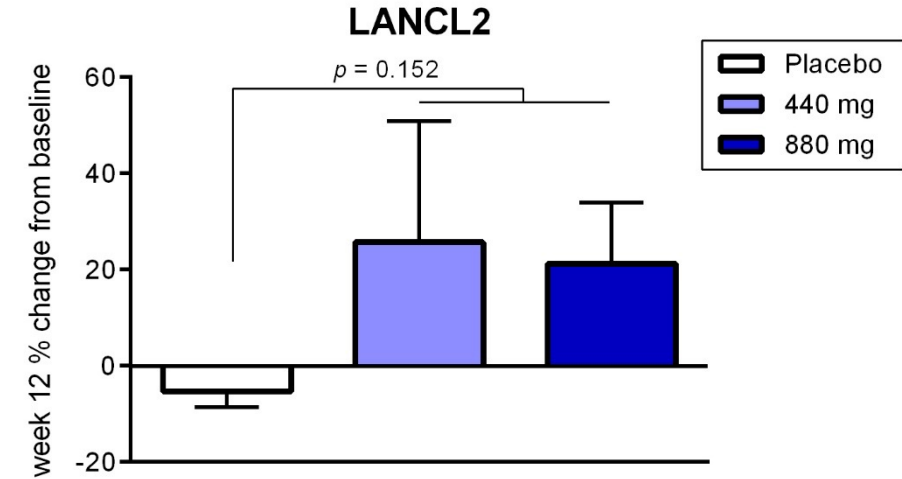
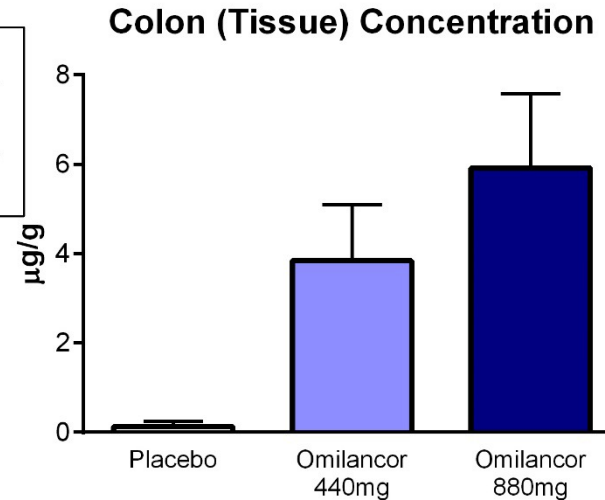
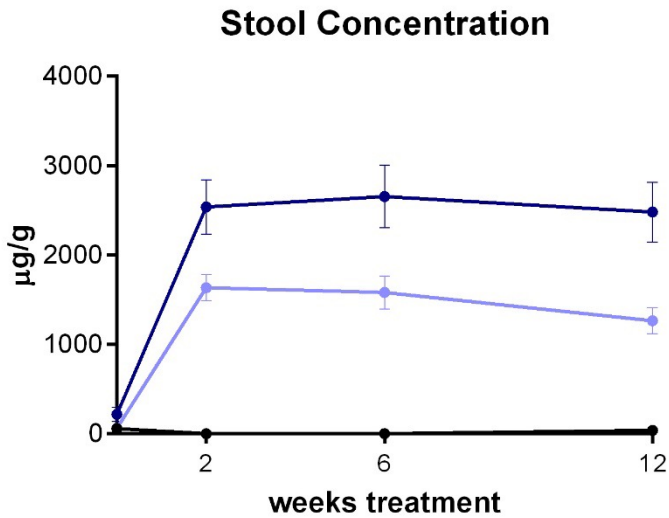
	Trial Name	Remission Rate	Placebo Adjusted Rate	Endpoint	Safety
<b>Filgotinib</b>	Selection	26.1 (biologic naïve) 11.5 (experienced)	10.8 (biologic naïve) 7.3 (experienced)	3-component remission	Class warnings for thrombosis, Herpes zoster and serious infection. Leukopenia
<b>Ozanimod</b>	True North	18.4	12.4	3-component remission	CV risk, macular edema, LFT elevations
<b>Vedolizumab (ENTYVIO)</b>	Gemini 1	16.9	11.5	Total Mayo score ≤ 2	Slightly increased risk of infection. Severe hepatitis in small numbers of patients
<b>Adalimumab (HUMIRA)</b>	Ultra 1	18.5	9.3	Total Mayo score ≤ 2	Increased risk for cancers and infections.
<b>Tofacitinib (XELJANZ)</b>	Octave 1	18.5	10.3	Total Mayo score ≤ 2	Class warnings for thrombosis, Herpes zoster and serious infection. Leukopenia

*Filgotinib (Gilead press release May 2020); Ozanimod (Sandborn, W., et al. 2016); Vedolizumab (Feagan, B., et al. 2013); Adalimumab (Reinisch, W., et al. 2011, Sandborn, W., et al. 2012); Tofacitinib (Sandborn, W., et al. 2017, D'Amico, F., et al. 2019)*

From 2021 Landos non-confidential slide deck and CCFA abstract



# PK/PD results validate sufficient target engagement at both doses



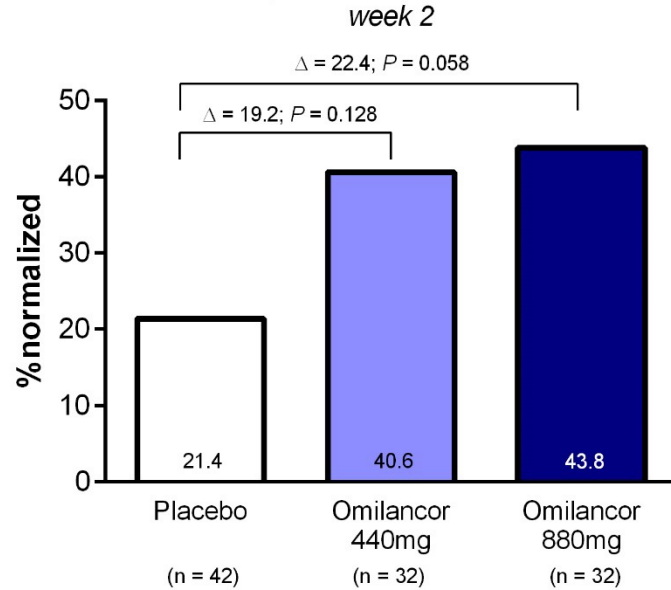
- Omilancor stool concentrations stable between 2 and 12 weeks of dosing
- No significant difference in stool concentrations between UC patients after 12 weeks and healthy volunteers after 7 days
- Stool and tissue concentration scale in a near dose-proportional manner
- 440 and 880 mg doses effectively clear therapeutic threshold, engage LANCL2, and increase LANCL2 expression in the colon



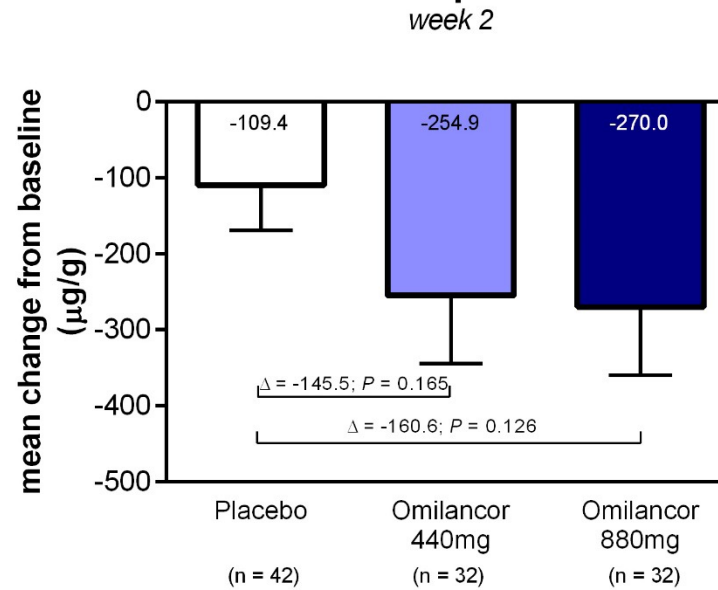


# Biomarker Response After 2 Weeks of Treatment

## Fecal Calprotectin Normalization



## Fecal Calprotectin



Fecal calprotectin considered normalized at < 250 ug/g  
 Inclusive of subjects with abnormal levels at baseline

	Rate	Placebo Adjusted
<i>Normalization &lt; 250 ug/g</i>		
<b>Omilancor (440 mg)</b> Week 2	40.6	19.2
<b>Tofacitinib</b> Week 12	29.0	N/A
<b>Ustekinumab</b> Week 8	30.3	8.5
<i>Normalization &lt; 150 ug/g</i>		
<b>Omilancor (440 mg)</b> Week 2	33.3	15.1
<b>Vedolizumab</b> Week 6	29.3	12.5



## No Emergent Trends in AE Profiles in UC Patients Relative to Placebo

	Placebo (n = 66)	Omilancor 440 mg (n = 66)	Omilancor 880 mg (n = 66)
<b>Subjects reporting <math>\geq 1</math> AE – no. (%)</b>	20 (30.3%)	18 (27.3%)	20 (30.3%)
<b>Total AEs – possibly related or higher</b>	10	16	11
<b>Total AEs – definitely related</b>	0	0	0
<b>Infections and Infestations</b>	5 (7.6%)	4 (6.1%)	5 (7.6%)
<b>Lymphopenia</b>	1 (1.5%)	0 (0%)	0 (0%)
<b>AEs experienced in <math>\geq 5\%</math> of subjects</b>			
<i>Ulcerative colitis worsening</i>	5 (7.6%)	7 (10.6%)	7 (10.6%)

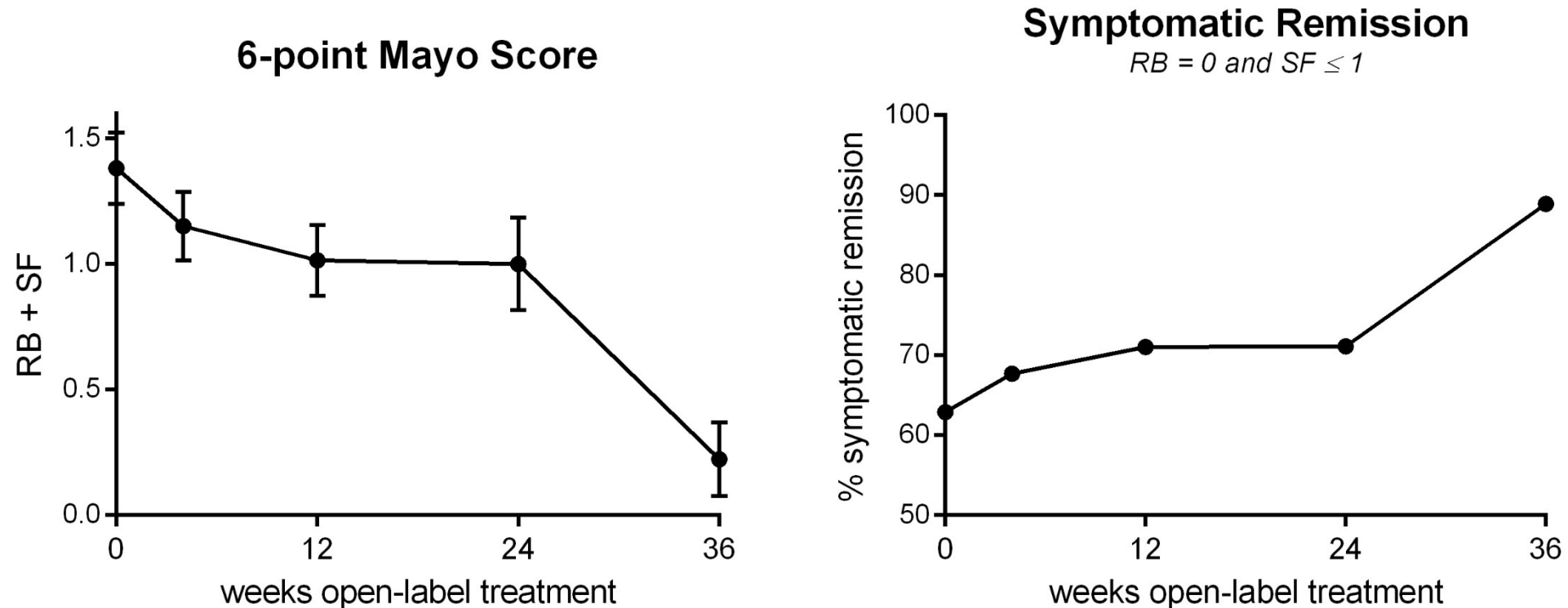
**4 SAEs were reported during the induction phase. All were judged to be not related to study treatment:**

- Worsening of UC (2)
- Calcaneus fracture
- Amoebiasis

**No Inhibition of the JAK Pathway by omilancor**



## Patients Treated with Omilancor Maintain low Mayo Scores and UC Symptoms beyond 1 year of Treatment



- Nearly 90% of patients achieving remission thresholds in stool frequency and rectal bleeding after 36 weeks of open-label treatment.
- Clinical remission (based on 3-component Mayo) was observed in 36.1% ( $\Delta = 16.7\%$ ) of the omilancor 880 mg group and 35.5% ( $\Delta = 16.1\%$ ) of the omilancor 440 mg group during the blinded maintenance phase.



## Clinical Plans for Omilancor in UC

### Positive Outcome from End-of-Phase 2 meeting with FDA

- Gained FDA agreement on key elements of pivotal global Phase 3 program that are necessary to prepare for regulatory approval

### Phase 3 Design

- Total of 1,378 patients with active UC across two trials
- Trials will evaluate one dose (440 mg) versus placebo
- Primary endpoints include:
  - Clinical remission at Week 12
  - Clinical remission at Week 52
- Mucosal healing rate at Week 12 defined by endoscopic subscore of 0 or 1 with Geboes histologic index  $< 3.1$  (label: mucosal healing)

January  
2021

✓ Initial Phase 2 data announced

May  
2021

✓ Provided follow-up Phase 2 data

June  
2021

✓ EoP2 meeting with FDA

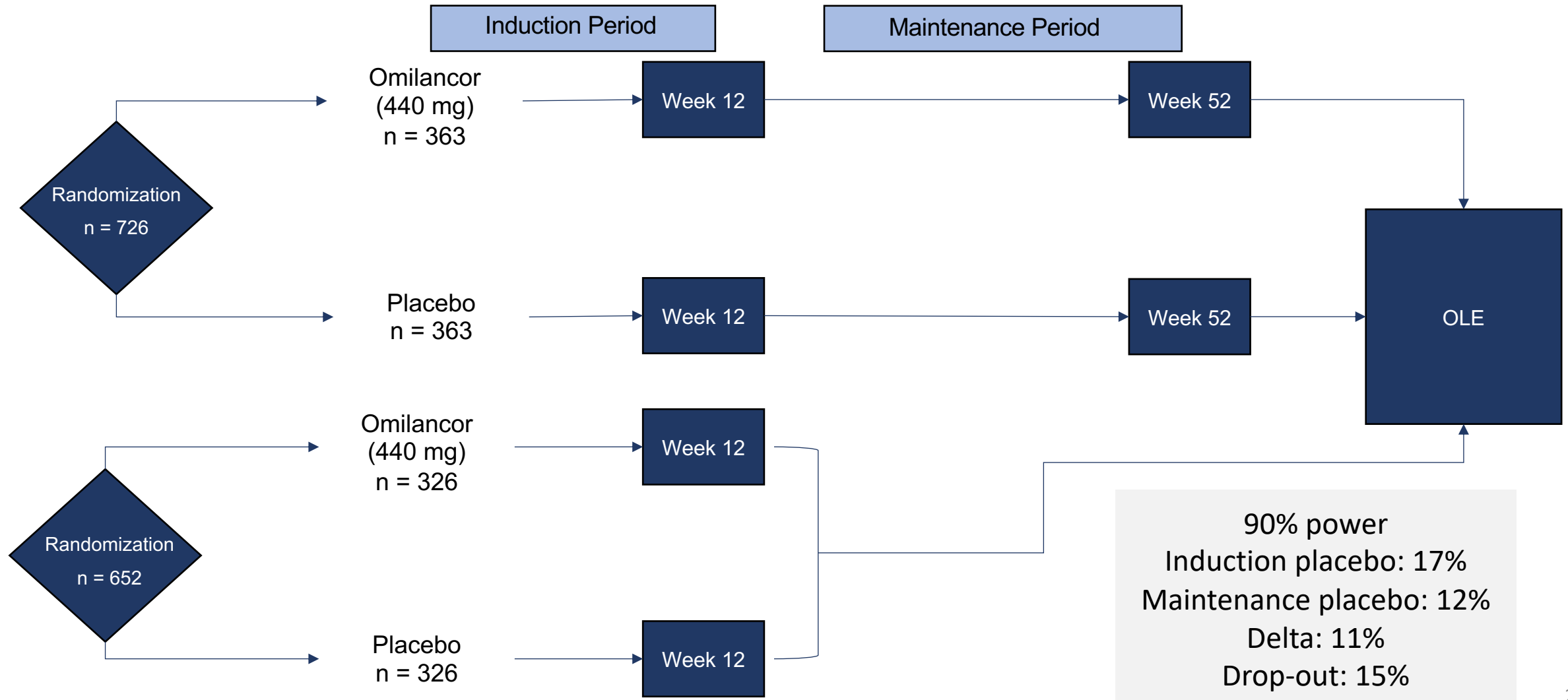
2023

Initiate registrational Phase 3 trial



# Phase 3 Pivotal Study Design of Omilancor in UC

*Aim to enroll a total of 1,378 patients*





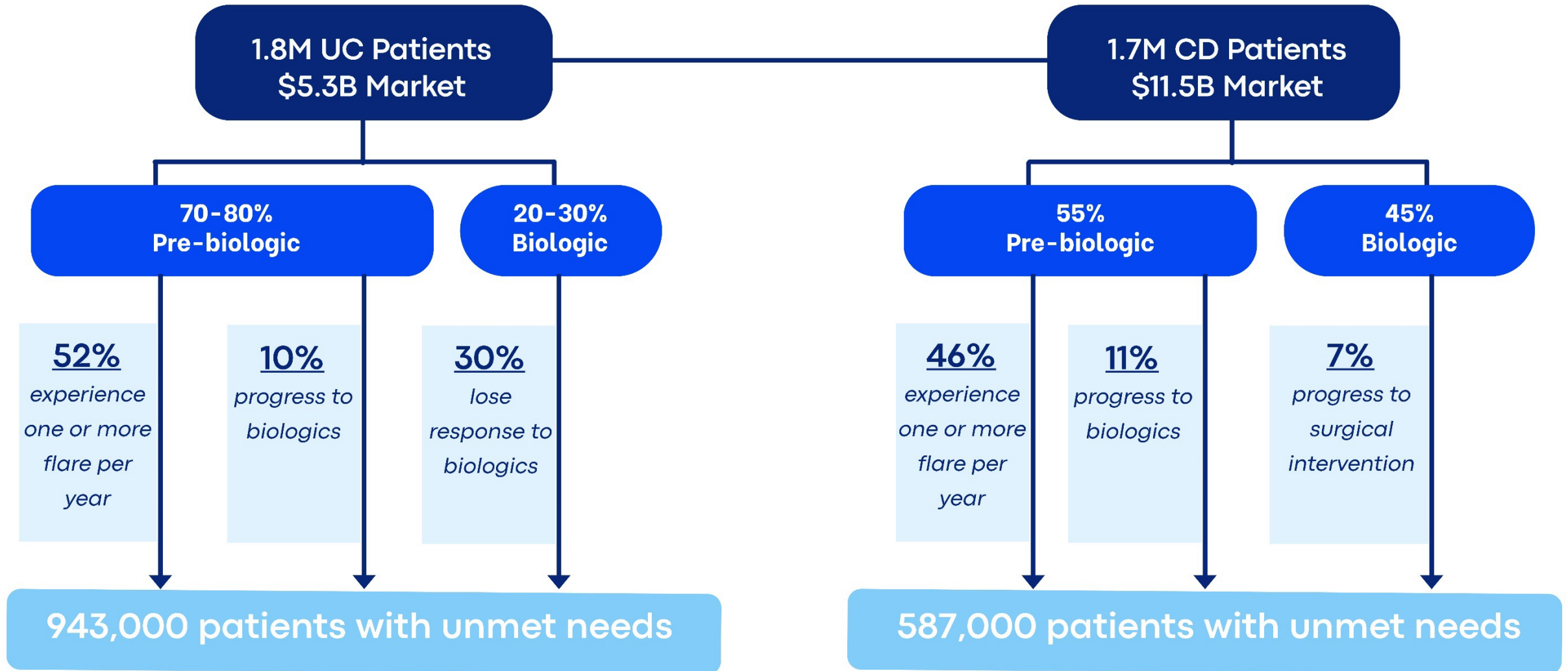
## Omilancor Meets the Approvable Primary Endpoint of Clinical Remission

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- ✓ Upon discussions with the FDA on design of our Phase 3 clinical trials, we agreed on an approvable population of active UC patients for the upcoming Phase 3 trials
- ✓ Analysis of our Phase 2 data using the same population that will be enrolled in our Phase 3 trials demonstrated **statistically significant approvable primary endpoint for clinical remission**
- ✓ Statistical significance of the primary endpoint in the induction and maintenance phases of the trial correlated with changes in predictive biomarkers of response to treatment such as FCP
- ✓ Statistically significant clinical remission with omilancor in our Phase 2 trial helps predict an 80% success rate for our Phase 3 trial meeting its primary endpoint and sets a robust regulatory path to NDA and commercialization



# Well-Positioned to Address Unmet Need in a Large Segment of IBD Treatment Paradigm

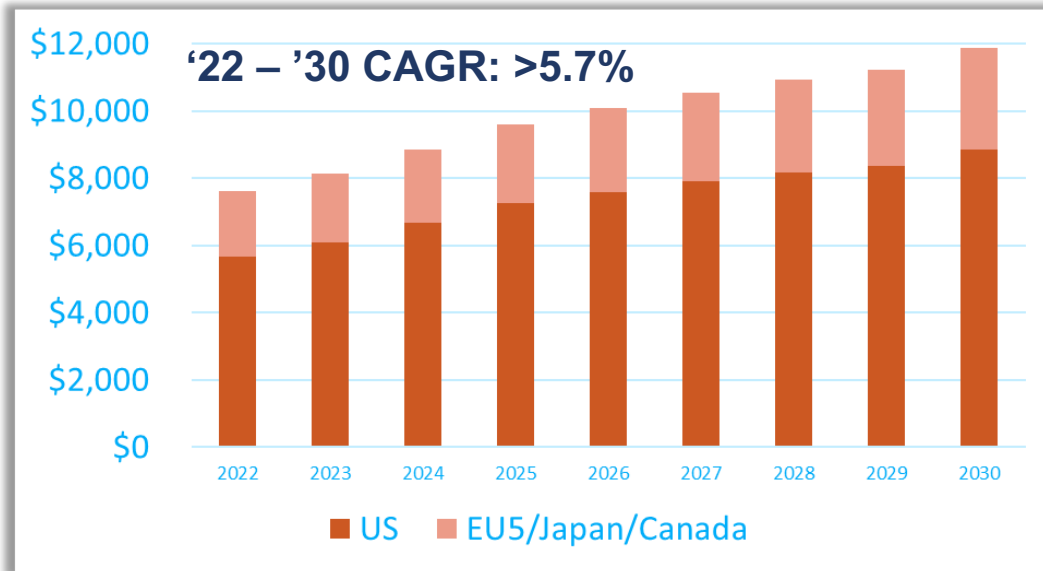






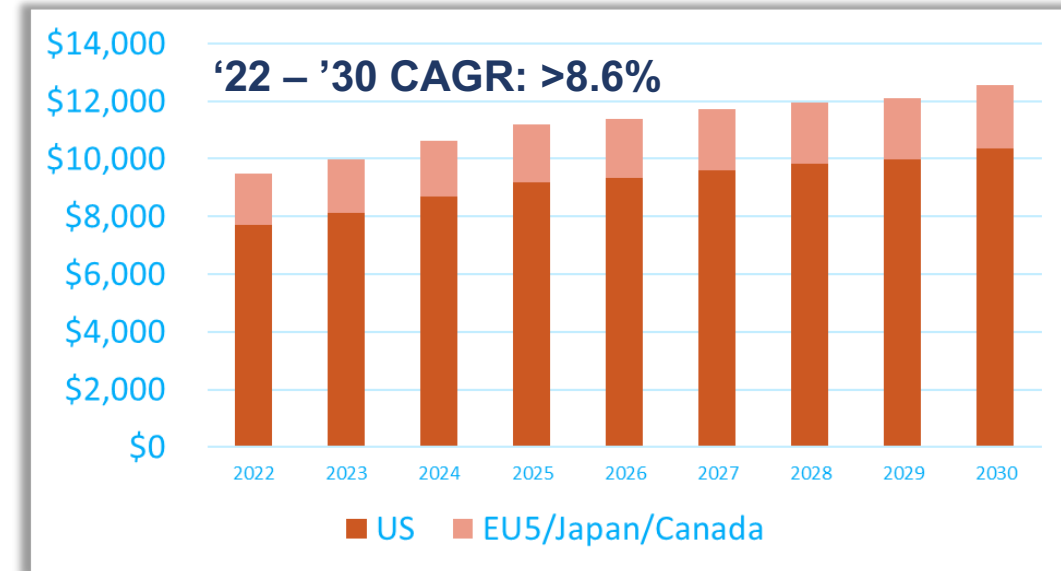
# Clearly Defined Commercial Opportunity

## Ulcerative Colitis Market – Projected Annual Sales



Source: DRG/Clarivate

## Crohn's Disease Market – Projected Annual Sales



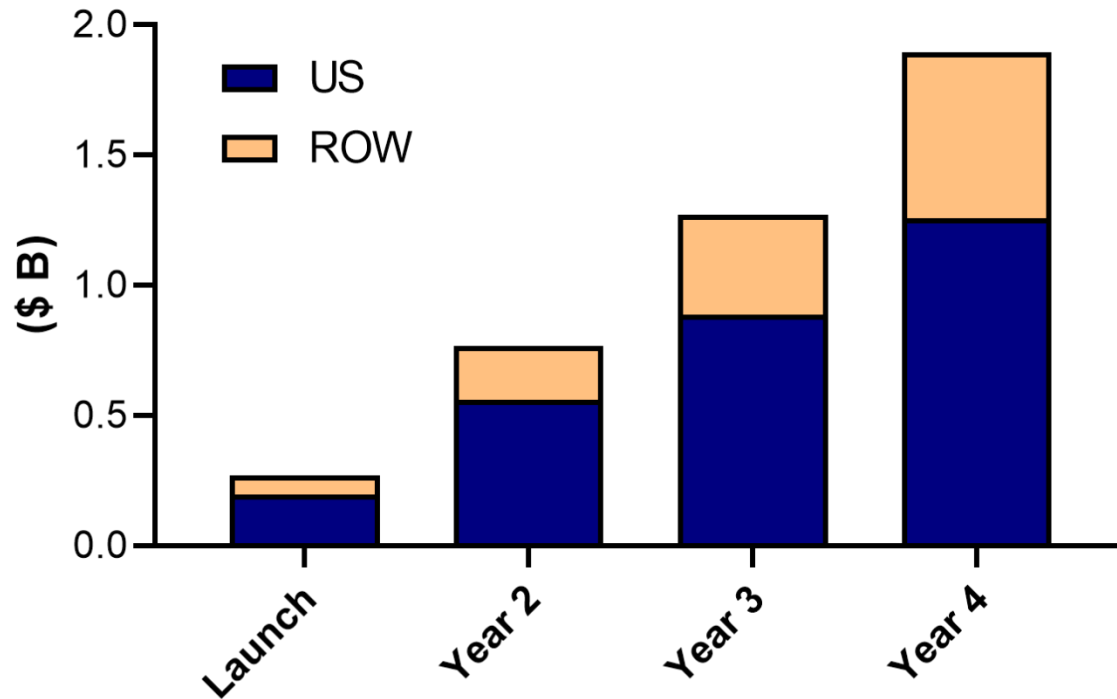
Source: DRG/Clarivate

**Massive market opportunities for Omilancor as the first AND best in class oral therapy with unblemished safety profile**



# Novel mechanisms with good safety profile can achieve fast uptake in IBD

## Vedolizumab Sales



*Achieved **21%** market penetration in 3 years*

*Post 3-year average annual growth rate: **8%***

Omilancor is a first-in-class candidate with no safety concerns and can address a wider patient population



# NIM-1324 Overview



## Indications

- Systemic Lupus Erythematosus (SLE)
- Rheumatoid Arthritis (RA)
- Other indications may be explored based on clinical and translational findings



## Mechanism of Action

- Activates LANCL2 pathway, a membrane receptor that has been shown to modulate immunological mechanisms
- Same MoA as omilancor
- Former Landos LABP-104 asset



## Drug Profile

- Orally active with systemic distribution
- Once daily dosing



## Recent & Upcoming Milestones

- ✓ Cleared IND for SLE and RA
- ✓ First dosing in a Phase 1a NHV first in human study initiated in October 2021 and successfully completed in 2022
- ✓ Abstract of preclinical findings accepted for oral presentation at ACR Convergence 2021
- ✓ Phase 2-ready in 2023



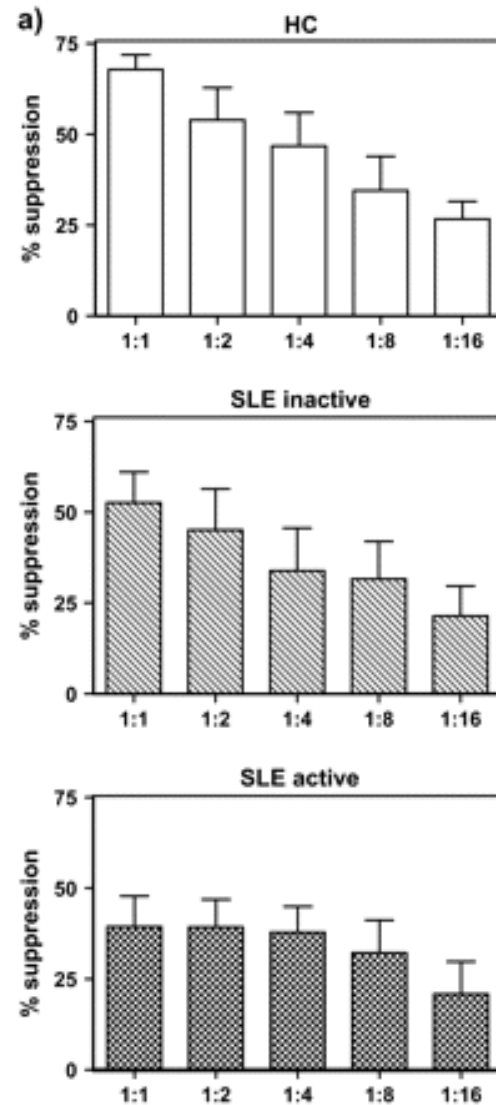
# Tregs in Lupus

## Regulatory CD4+ T cells are impaired in SLE:

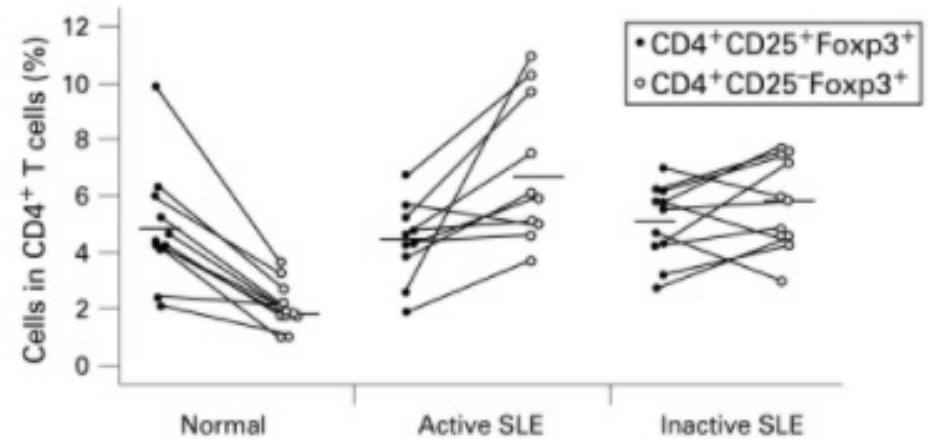
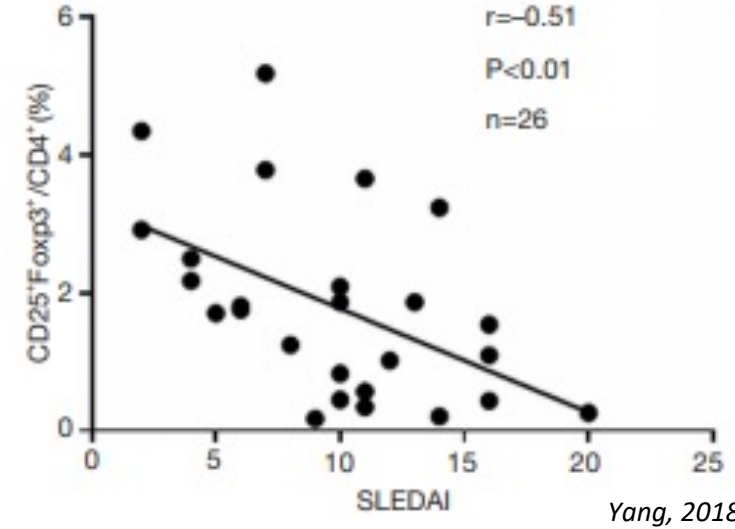
- High numbers of CD25- Tregs
- Low IL-2 levels
- Less suppressive and lower numbers of CD25+ FOXP3+ CD127 low Tregs

SLE patient Tregs show a reduced capacity to suppress proliferation of non-regulatory cells. CD25+ FOXP3+ are inversely proportional to SLEDAI score and CD25- FOXP3+ T cells are increased in patients with active disease

- LANCL2 enhances Treg function through synergism with IL-2/CD25 signaling and metabolic support of FOXP3 expression



Bonelli, 2008



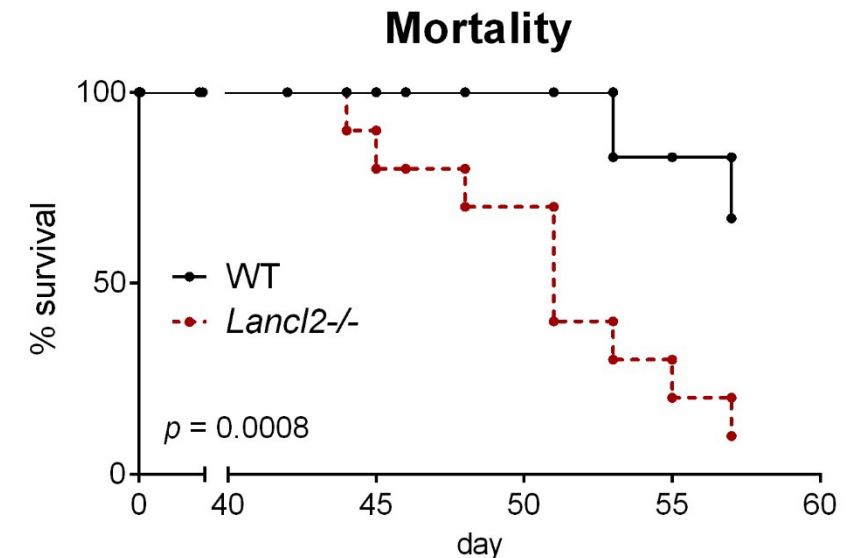
Zhang, 2008



# Comparison of the LANCL2 systemically and in the GI

	GI-Localized	Systemic
<b>Receptor localization</b>	Cell membrane	Cell membrane
<b>Site of action</b>	Epithelium and lamina propria	Lymphoid and metabolic tissues including the spleen, liver and lymphatic system.
<b>Effects on regulatory responses</b>	Ability to directly impact regulatory CD4+ T cells and indirectly through epithelial and dendritic cell interactions.	Ability to directly impact regulatory CD4+ T cells and indirectly through dendritic cell interactions.
<b>Metabolic effects</b>	Within immune cells and epithelial cells. No effects on macro-metabolism.	Within immune cells, adipocytes, muscle and liver. Effects on overall glucose and lipid homeostasis with select ligands.
<b>GI relevance</b>	High levels of luminal activators drives immune responses	Minor feedback on local GI responses from systemically distributed agonists
<b>Systemic relevance</b>	May provide mild benefits systemically through Treg re-circulation and microbiome effects	Can directly modulate the systemic immune system and modulate levels of macro-nutrients that activate the immune system
<b>Negative impacts on systemic immunosuppression or susceptibility to infection</b>	None	None

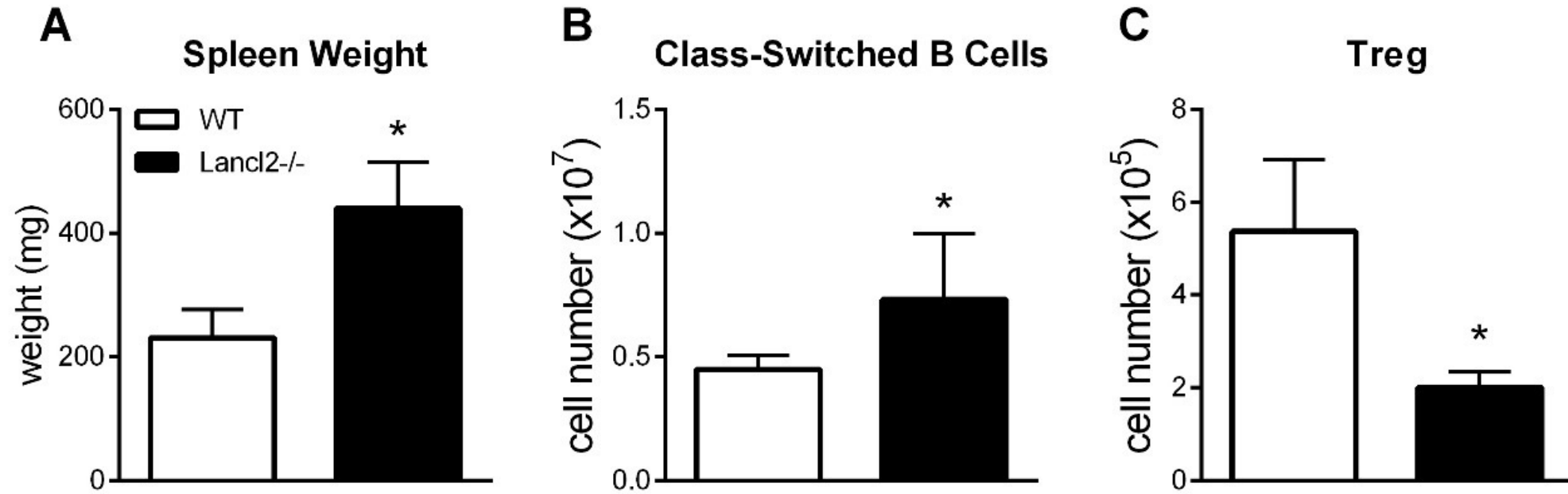
- Loss of LANCL2 increases mortality, spleen size and autoantibody production in TLR7-induced model of SLE (presented AAI 2019)
- LANCL2 and markers of downstream metabolic events are downregulated in SLE patient PBMCs



*Lancl2-/- mice experience accelerated and increased mortality in an R848 induced model of lupus and TLR activation*



# LANCL2<sup>-/-</sup> mice have greater disease severity in a bm12 transfer model

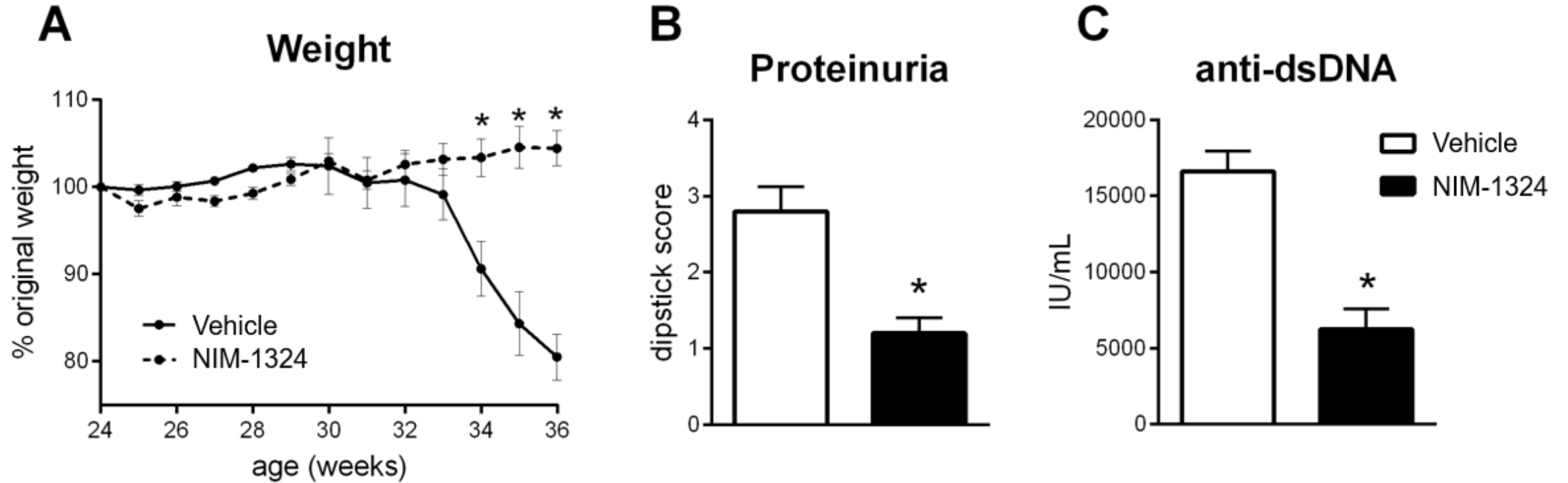


WT and Lancl2<sup>-/-</sup> mice were transferred  $2 \times 10^7$  splenocytes from bm12 donors. Spleens were harvested 2 weeks post-transfer ( $n = 8$ ).

Loss of LANCL2 results in increased spleen size along with abnormalities in B cell development and activation. LANCL2<sup>-/-</sup> mice also possess lower numbers of regulatory CD4<sup>+</sup> T cells in the spleen.



# NIM-1324 protects against markers of disease in an NZB/W F1 model



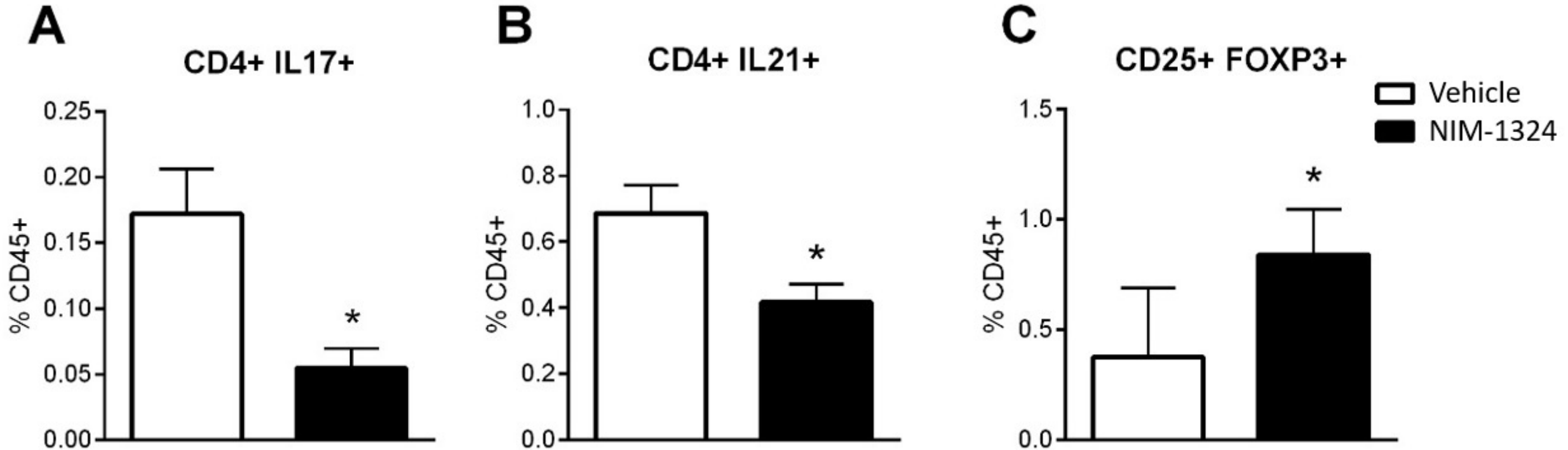
24-week-old NZB/W F1 mice with grade 2 or higher proteinuria were treated with vehicle or NIM-1324 (20 mg/kg) for 12 weeks (n = 10).

Oral NIM-1324 treatment protects against weight loss and reduces serum anti-dsDNA antibodies in an NZB/W F1 model. NIM-1324 reduces proteinuria grade and prevents worsening of proteinuria from baseline in 90% of mice.





# NIM-1324 displays consistent effects on splenic immune cells in 3 models of SLE-like disease

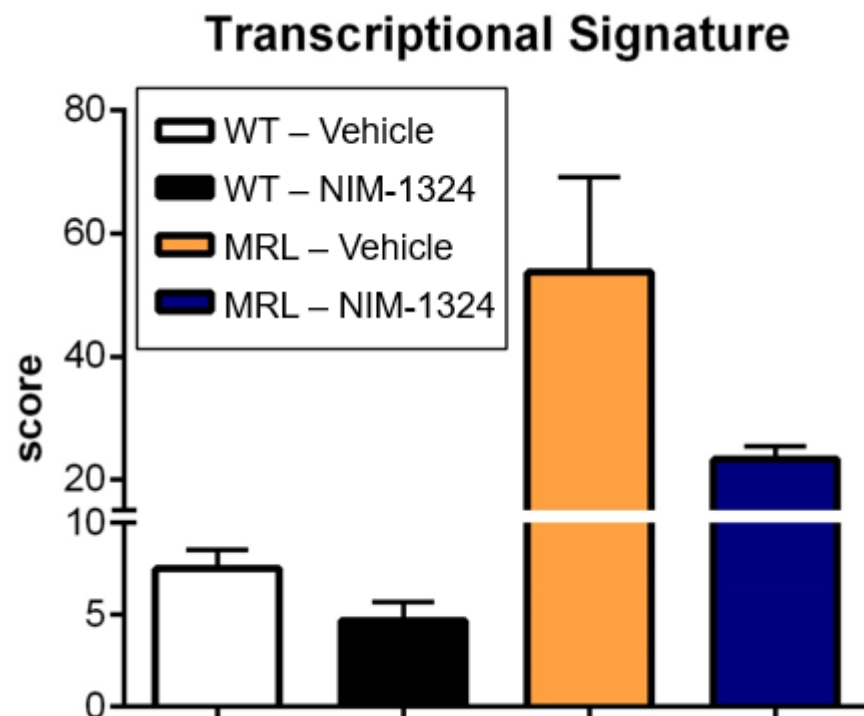


Data from an MRL/lpr model after 6 weeks of treatment (n = 10)

In NZB/W F1, MRL/lpr, and bm12 adoptive transfer models, oral NIM-1324 (20 mg/kg) consistently reduces IL17+ and IL21+ CD4+ T cells in the spleen while providing an increased proportion of regulatory CD25+ FOXP3+ CD4+ T cells.



## NIM-1324 is associated with a transcriptional signature in whole blood



*WT mice were treated with oral NIM-1324 for 7 days and MRL/lpr mice were treated with NIM-1324 for 4 weeks beginning at 14 weeks of age after which whole blood was collected for gene expression analysis (n = 5).*

In WT and MRL/lpr mice, a transcriptional signature of 15 genes differentiates NIM-1324 treated mice from vehicle treated mice and is predictive of response to therapy.

The 15 genes are representative markers for functional effects of NIM-1324 including:

- Increased mitochondrial metabolism
- Modulation of phagocytosis
- Decreased myeloid cell activation
- SLE-specific markers



## NIM-1324 reduces IFN $\alpha$ in patient PBMCs

### IFN $\alpha$ , % reduction from vehicle

Stimuli	50 nM NIM-1324	100 nM NIM-1324	200 nM NIM-1324
PMA + Ionomycin	51 *	54 *	70 *
Gardiquimod	42 *	90 *	92 *
ODN2395	33	46 *	59 *

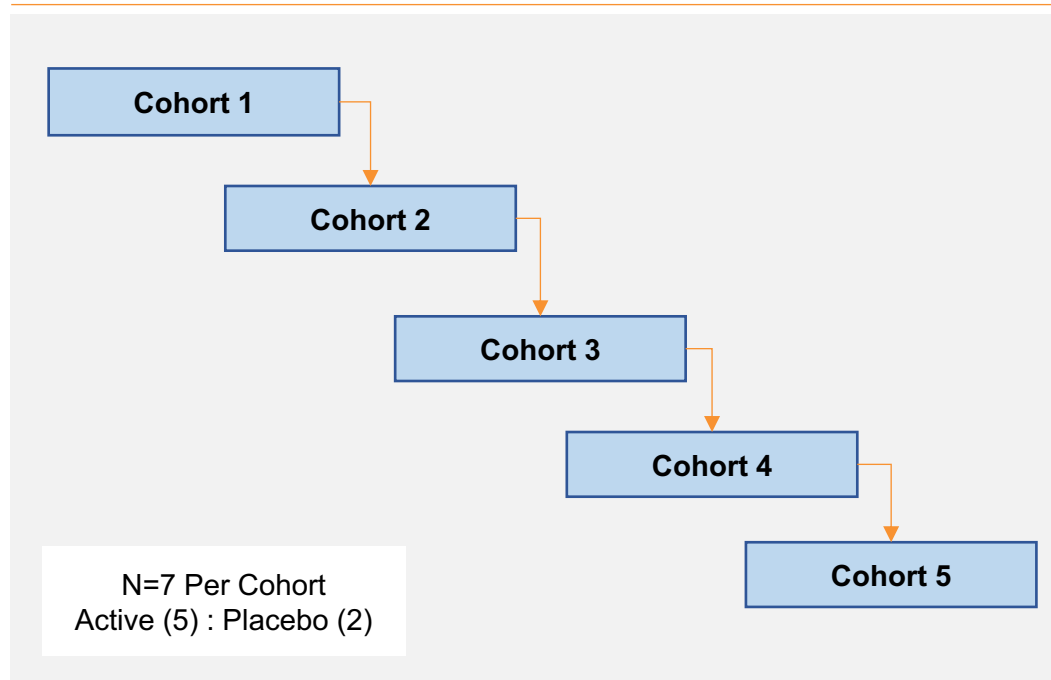
\*  $P \leq 0.05$

In SLE PBMCs treated with general, TLR7/8, and oligonucleotide stimuli, NIM-1324 reduces the production of type I interferon secreted by cells.

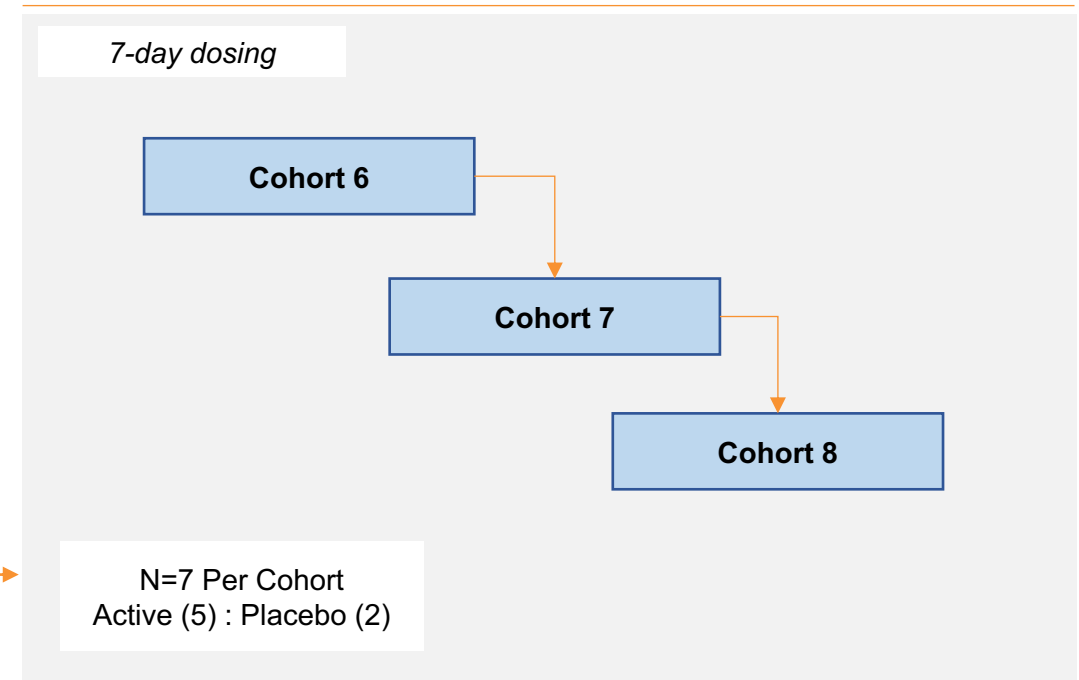


# NIM-1324 Phase I Clinical Trial Completed

## Single Ascending Dose



## Multiple Ascending Dose



- Monitoring of safety laboratory results, vital signs, AEs, and ECG
- Assessment of NIM-1324 transcriptional response profile in whole blood
- All primary and secondary endpoints of safety and tolerability were achieved
- No serious adverse events



## NIM-1324 Phase 1 results

<b>SAD</b>	<b>Placebo (n = 10)</b>	<b>Active (n = 25)</b>	<b>250 mg (n = 5)</b>	<b>500 mg (n = 5)</b>	<b>750 mg (n = 5)</b>	<b>1000 mg (n = 5)</b>	<b>1500 mg (n = 5)</b>
At least 1 TEAE	3 (30%)	6 (24%)	0	2 (40%)	3 (60%)	0	1 (20%)
At least 1 serious TEAE	0	0	0	0	0	0	0

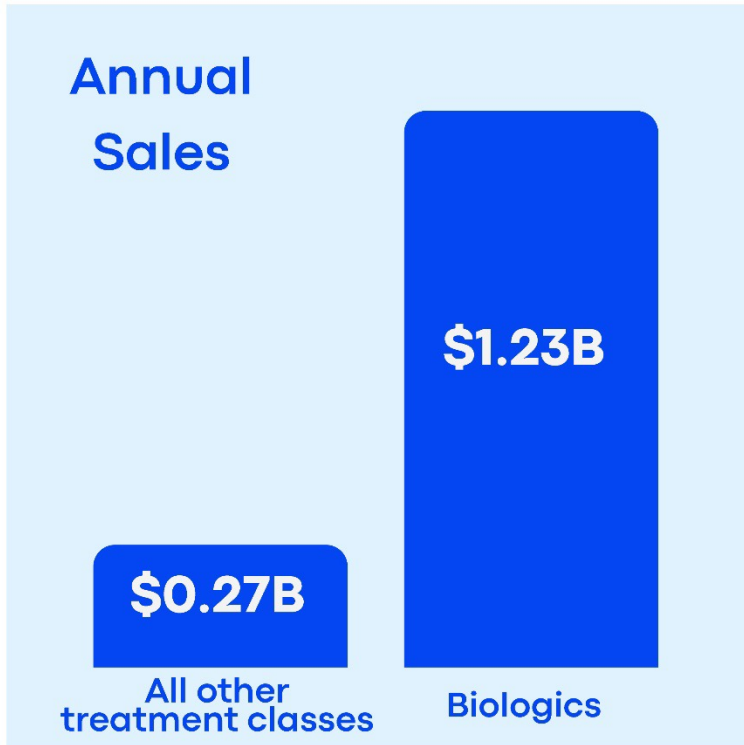
<b>MAD</b>	<b>Placebo (n = 7)</b>	<b>Active (n = 15)</b>	<b>250 mg (n = 5)</b>	<b>750 mg (n = 5)</b>	<b>1500 mg (n = 5)</b>
At least 1 TEAE	5 (71%)	10 (67%)	2 (40%)	5 (100%)	3 (60%)
At least 1 serious TEAE	0	0	0	0	0

- No AE trends relative to placebo
- No serious adverse events
- No discontinuations due to study drug

- Dose proportional change in plasma exposure within therapeutic range of 250 to 1000 mg with no increasing accumulation between day 2 and 7 of MAD pre-dose
- AEs were common Phase 1 AE attributed to on-site confinement (headache, fatigue, change in bowel habits)

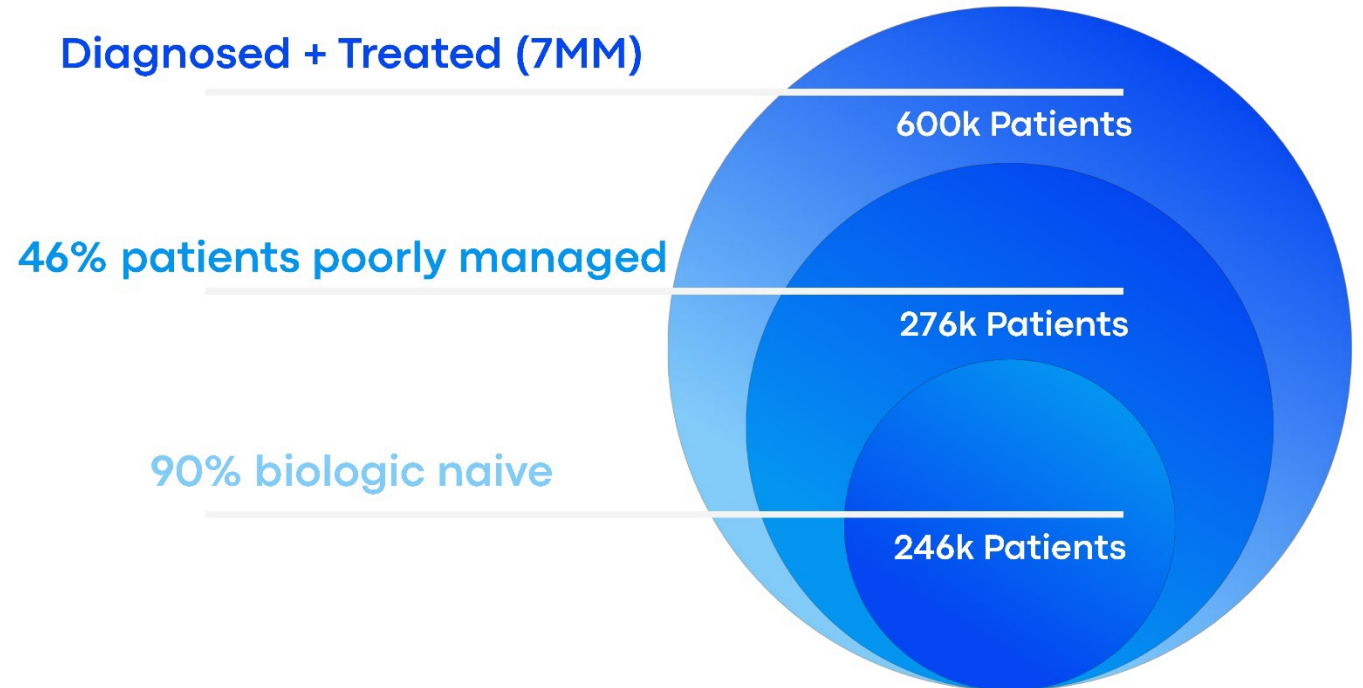


# Lupus Market Opportunity



82% of market value is biologics that treat only ~5% of patients

BENLYSTA estimated annual cost: \$42,000/patient

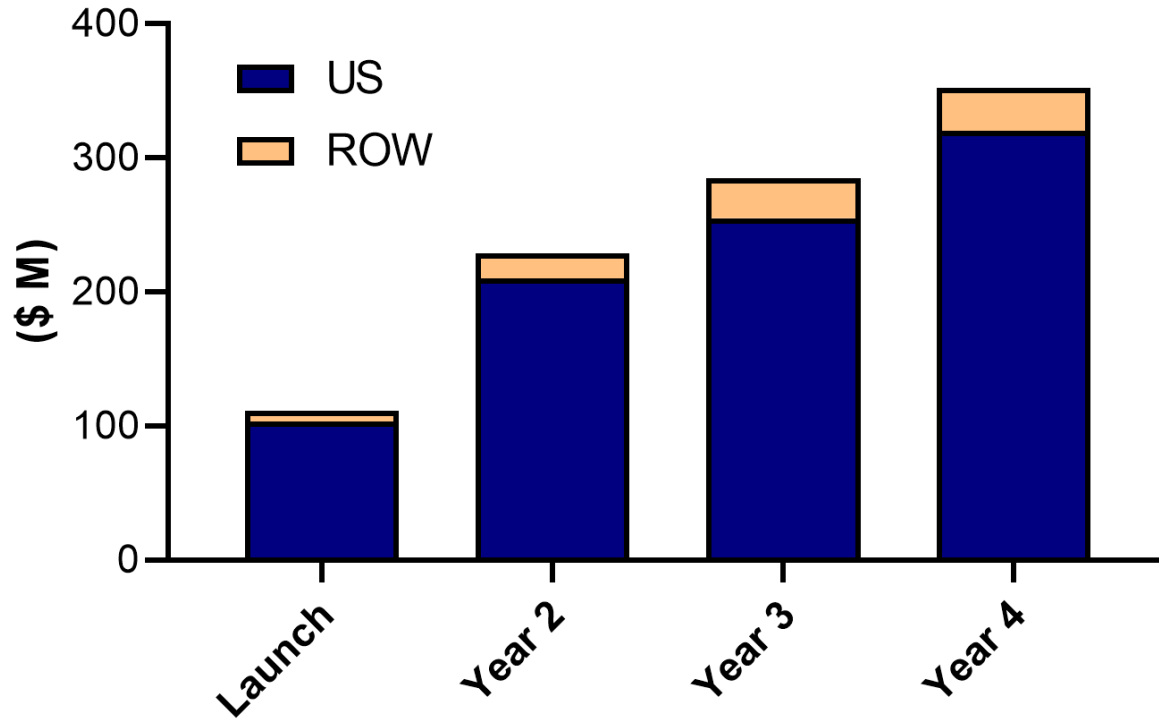


**Highly fractured pre-biologic market can lead to accelerate penetration**



# Lupus market in need of novel treatments to prevent disease progression

## Belimumab Sales



*Achieved **39%** market penetration in 3 years*

*Post 3-year average annual growth rate: **9%***

NIM-1324 is positioned to be a first-in-class therapy in lupus with no safety concerns targeting pre-biologic patients





## Summary and Conclusions



Nimmune is Phase 3-ready science-driven company well-positioned to develop a franchise of new first-in-class immunoregulatory therapeutics for GI and rheumatology.



Innovative Precision Immunology-focused drug discovery and development platform yielding novel targets, biomarkers, therapeutics and biomarker-driven drug development.



Extensive animal pharmacology, mechanism of action, toxicology, benign safety profile and clinical data on lead candidates (Phase 3-ready omilancor in UC; NIM-1324 for lupus).



Potential for first NDA for Omilancor in UC with multiple clinical data updates in 2023-2026.



Committed leadership team with immunology and biotech experience with a successful track record of 4 years from discovery of a new target to Phase 3-ready clinical testing in a cost-effective way.



Track record of significant shareholder value accretion.