

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT PURSUANT TO  
SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Date of Report: October 25, 2023  
(Date of earliest event reported)

ANAPTYSBIO, INC.  
(Exact Name of Registrant as Specified in Charter)

Delaware  
(State or Other Jurisdiction of Incorporation)

001-37985  
(Commission File Number)

20-3828755  
(IRS Employer Identification No.)

10770 Wateridge Circle, Suite 210,  
San Diego, CA 92121  
(Address of Principal Executive Offices, and Zip Code)

(858) 362-6295  
(Registrant's Telephone Number, Including Area Code)

Not Applicable  
(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

- Written communication pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communication pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communication pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value \$0.001 per share	ANAB	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (17 CFR §230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR §240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

**Item 7.01. Regulation FD.**

On October 25, 2023, AnaptysBio presented its PD-1 Agonist (Rosnilimab) R&D slide presentation, a full copy of which is attached hereto as Exhibit 99.1.

The information in this item 7.01, including Exhibit 99.1, shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference into any other filing under the Exchange Act or Securities Act of 1933, as amended, except as expressly set forth by specific reference in such a filing.

**Item 9.01. Financial Statements and Exhibits.**

(d) Exhibits

<b>Exhibit Number</b>	<b>Exhibit Title or Description</b>
<a href="#">99.1</a>	AnaptysBio PD-1 Agonist (Rosnilimab) R&D Slide Presentation October 2023.
104	Cover Page Interactive Data File (the cover page XBRL tags are embedded within the inline XBRL document).

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## SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Date: October 25, 2023

AnaptysBio, Inc.

By: /s/Dennis Mulroy

Name: Dennis Mulroy

Title: Chief Financial Officer

# **PD-1 Agonist (Rosnilimab) R&D Event**

**Wednesday, Oct. 25, 2023**

**1:15pm PT/4:15pm ET**



AnaptysBio 

## Forward looking statement

This presentation and any accompanying oral presentation contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995, including, but not limited to: the timing of initiation of the Company's clinical trials, including rosnilimab's clinical trial and in ulcerative colitis; the timing of the release of data from the Company's clinical trials, including rosnilimab's Phase 2b clinical trial in rheumatoid arthritis and rosnilimab's Phase 2 clinical trial in ulcerative colitis; the timing of ANB033's IND filing; whether any of the Company's product candidates will be best in class or are optimized; the potential to receive any additional royalties from the GSK collaboration; the Company's ability to find a licensing partner for imsidolimab or etokimab and the timing of any such transaction; and the Company's projected cash runway. Statements including words such as "plan," "continue," "expect," or "ongoing" and statements in the future tense are forward-looking statements. These forward-looking statements involve risks and uncertainties, as well as assumptions, which, if they do not fully materialize or prove incorrect, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Forward-looking statements are subject to risks and uncertainties that may cause the company's actual activities or results to differ significantly from those expressed in any forward-looking statement, including risks and uncertainties related to the company's ability to advance its product candidates, obtain regulatory approval of and ultimately commercialize its product candidates, the timing and results of preclinical and clinical trials, the company's ability to fund development activities and achieve development goals, the company's ability to protect intellectual property and other risks and uncertainties described under the heading "Risk Factors" in documents the company files from time to time with the Securities and Exchange Commission. These forward-looking statements speak only as of the date of this presentation, and the company undertakes no obligation to revise or update any forward-looking statements to reflect events or circumstances after the date hereof.

Certain information contained in this presentation may be derived from information provided by industry sources. The Company believes such information is accurate and that the sources from which it has been obtained are reliable. However, the Company cannot guarantee the accuracy of, and has not independently verified, such information.

The trademarks included herein are the property of the owners thereof and are used for reference purposes only. Such use should not be construed as an endorsement of such products.

## Agenda

TOPIC	SPEAKER
<b>Rosnilimab: a best-in-class PD-1 agonist</b>	<b>Dan Faga Chief Executive Officer</b>
MOA and differentiation	Martin Dahl, Ph.D. Senior Vice President, Research
<i>Rosnilimab in RA</i>	
Unmet patient needs and opportunity for PD-1 agonists	Jonathan Graf, M.D. Professor, Medicine University of California, San Francisco
Targeting RA with rosnilimab and translational data	Cailin Sibley, M.D., MHS, FACR Vice President, Translational Medicine
<i>Rosnilimab in UC</i>	
Unmet patient needs, disease biology, and rationale for PD-1 agonist in UC	Bruce Sands, M.D., M.S. Professor and Chief, Gastroenterology Icahn School of Medicine, Mount Sinai
Targeting UC with rosnilimab and translational data	Martin Dahl, Ph.D.
PD-1 safety data and Phase 2 development plans in RA and UC	Paul Lizzul, M.D., Ph.D. Chief Medical Officer
Market opportunity and closing remarks	Dan Faga
Q&A	AnaptysBio



## Developing best-in-class immune cell modulators to restore immune balance across autoimmune & inflammatory diseases

Immune Cell Modulators			Cytokine Antagonists (legacy programs for out-licensing)
<p><b>Rosnilimab</b> (PD-1 agonist)</p> <p>P2b in Rheumatoid Arthritis</p> <p>P2 in Ulcerative Colitis</p>	<p><b>ANB032</b> (BTLA agonist)</p> <p>P2b in Atopic Dermatitis</p>	<p><b>ANB033</b> (CD122 antagonist)</p> <p>IND-enabling</p>	<p><b>Imsidolimab</b> (IL-36R)</p> <p>P3 in GPP</p> <hr/> <p><b>Etokimab</b> (IL-33)</p> <p>P2b/3-ready in Epithelial-driven diseases</p>
<p>Potential development in additional diseases areas across dermatology, gastroenterology and rheumatology</p>			

<p><b>Research-driven</b></p> <p>Preclinical pipeline of immunology targets</p>	<p><b>Strong capital position</b></p> <p>Cash runway to YE 2026</p>	<p><b>GSK immuno-oncology financial collaboration</b></p> <p>Significant royalty potential</p>
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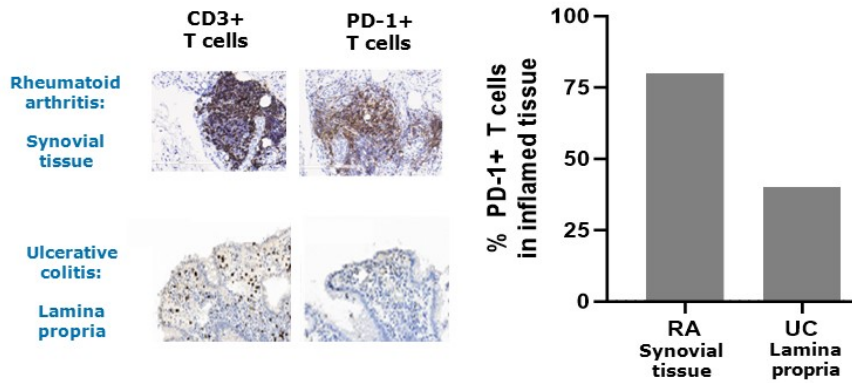


## Immune cell modulator development plan: initiation of three P2 trials across three therapeutic areas

Antibody Program	Therapeutic Indication	Development Stage and Anticipated Milestones				
		Lead Optimization	IND Enabling	Phase 1	Phase 2	Phase 3
<b>Rosnilimab</b> (PD-1 agonist)	<b>Rheumatoid Arthritis</b>	[Lead Optimization, IND Enabling, Phase 1]			P2b initiated Q3 2023 Top-line data mid 2025	
	<b>Ulcerative Colitis</b>	[Lead Optimization, IND Enabling, Phase 1]			Ph2 initiation Q4 2023 Top-line data H1 2026	
<b>ANB032</b> (BTLA agonist)	<b>Atopic Dermatitis</b>	[Lead Optimization, IND Enabling, Phase 1]			P2b initiated Q2 2023 Top-line data YE 2024	
<b>ANB033</b> (CD122 antagonist)	<b>Inflammatory Diseases</b>	[Lead Optimization]	IND submission H1 2024			



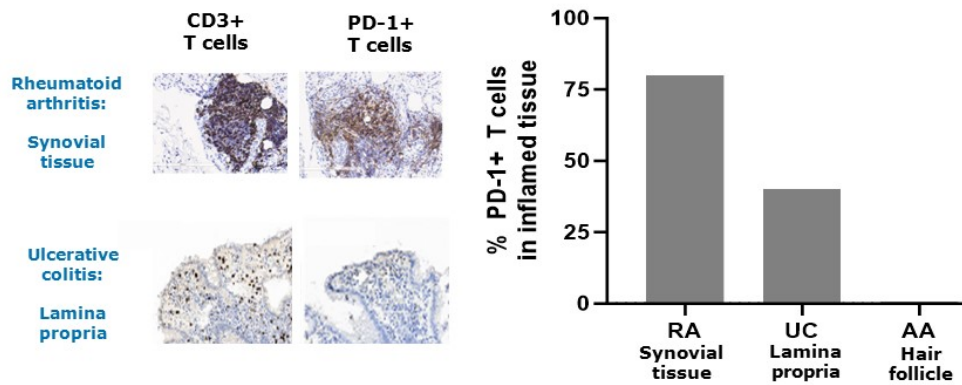
## PD-1+ T cells are prevalent in inflamed tissue and periphery in RA and UC



In systemic inflammatory diseases, a **multiple fold increase of PD-1+ T cells** is observed in periphery compared to healthy controls<sup>1</sup>

- **~1.5x in RA**
- **~2x in UC**

## PD-1+ T cells are prevalent in inflamed tissue and periphery in RA and UC, but lacking in AA

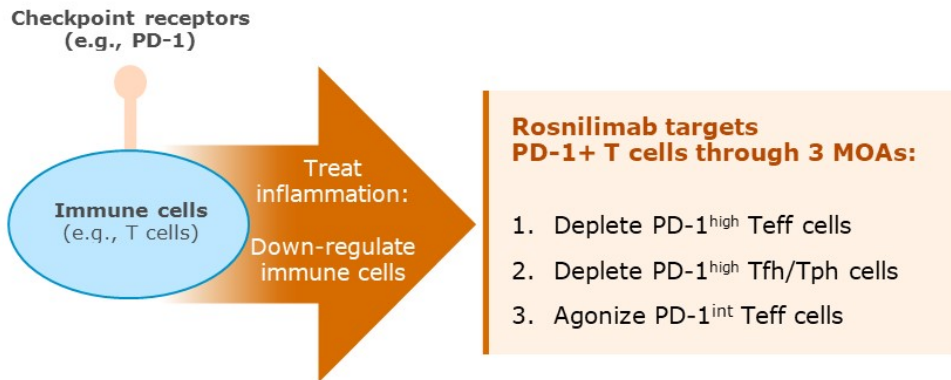


In systemic inflammatory diseases, a **multiple fold increase of PD-1+ T cells** is observed in periphery compared to healthy controls<sup>1</sup>

- **~1.5x in RA**
- **~2x in UC**
- **Not increased in AA**

Adapted from Nguyen et al, Human Pathology (2022) 126, 19e27; Guo et al, PLoS One 2018; 13(2): e0192704. Shi et al. (2023), PeerJ, DOI 10.7717/peerj.15481. 1. Murray-Brown et al, RMC Open, 2022, Shi et al. (2023), PeerJ, DOI 10.7717/peerj.15481.

## Checkpoint agonists “hit the brakes” to restore immune balance

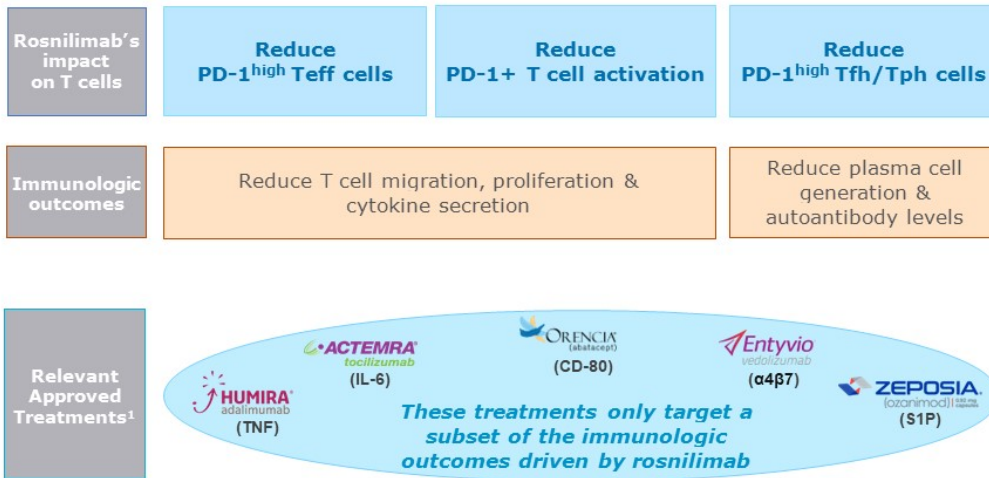


**Rosnilimab's membrane-proximal binding epitope results in best-in-class potency vs. Lilly's PD-1 agonist**

Teff=T effector cells; Tph cells=Peripheral helper cells; Tfh cells=Follicular helper cells.



## Rosnilimab's impact in inflamed tissue and periphery has potential to deliver differentiated efficacy and safety



<sup>1</sup>Other efficacious treatments have less specific MOAs causing safety liabilities, including Rinvoq (JAKs), Rituxan (broad B cell depleter), Lemtrada (broad lymphocyte depleter)

## Rosnilimab has potential to treat wide range of systemic inflammatory diseases, including RA and UC

### Rheumatoid arthritis:

**~500,000 patients**  
**>\$10bn U.S. sales** in "post TNF" market<sup>1</sup>

**20-25% cycle**  
all treatment classes  
**not achieving** low disease activity<sup>2</sup>

### Large commercial markets

- Biologic experienced patients

### Standard of care is insufficient

- RA (Post TNF): ~20-35% ACR50
- UC: ~25-30% clinical remission induction

### Ulcerative colitis:

**~100,000 patients**  
**>\$6.5bn U.S. sales**, excluding TNF, market<sup>3</sup>

**1/3 to 1/2 relapse**  
**within 1 year** following  
remission on induction therapy<sup>4</sup>

### Significant room to differentiate

- Drive deeper responses across broader patient population
- Restore immune balance

1. Expected by 2028 (Evaluate 29 Nov 2022); 2. Market research conducted by Ambit in 2022; 3. Expected by 2028 (Evaluate 21 Aug 2023); 4. Phase 3 registrational data from product labels

## Rosnilimab targets PD-1+ T cells broadly impacting pathogenic drivers of autoimmune & inflammatory diseases

PD-1 agonists deplete and agonize PD-1+ T cells, in both inflamed tissue and the periphery

Rosnilimab, a best-in-class PD-1 agonist, reduces T cell migration, proliferation & cytokine secretion and reduces plasma cell generation & autoantibody levels



Translational and clinical data support Rosnilimab's potential for deep responses across heterogenous patient populations while restoring immune balance in RA and UC

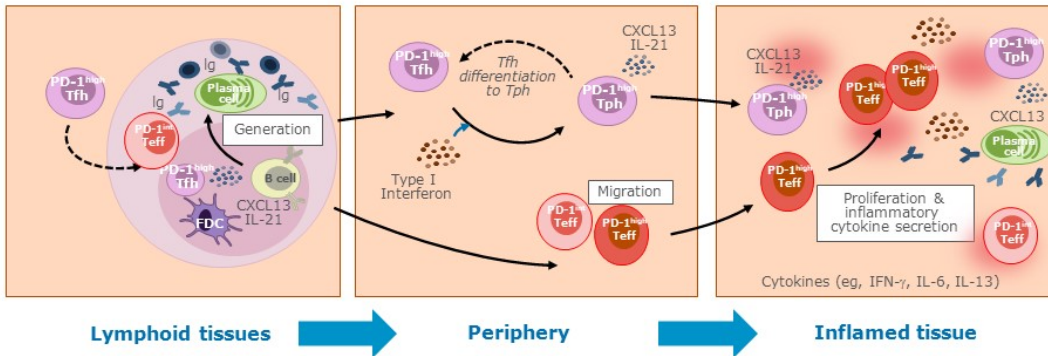
RA: global Phase 2b trial initiated Q3:23 with top-line data mid:25  
UC: global Phase 2 trial initiating Q4:23 with top-line data H1:26

## Agenda

TOPIC	SPEAKER
Rosnilimab: a best-in-class PD-1 agonist	Dan Faga Chief Executive Officer
<b>MOA and differentiation</b>	<b>Martin Dahl, Ph.D.</b> <b>Senior Vice President, Research</b>
<i>Rosnilimab in RA</i>	
Unmet patient needs and opportunity for PD-1 agonists	Jonathan Graf, M.D. Professor, Medicine University of California, San Francisco
Targeting RA with rosnilimab and translational data	Cailin Sibley, M.D., MHS, FACR Vice President, Translational Medicine
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## PD-1 expressed preferentially on activated Teff and Tfh/Tph cells mediating autoimmune pathology

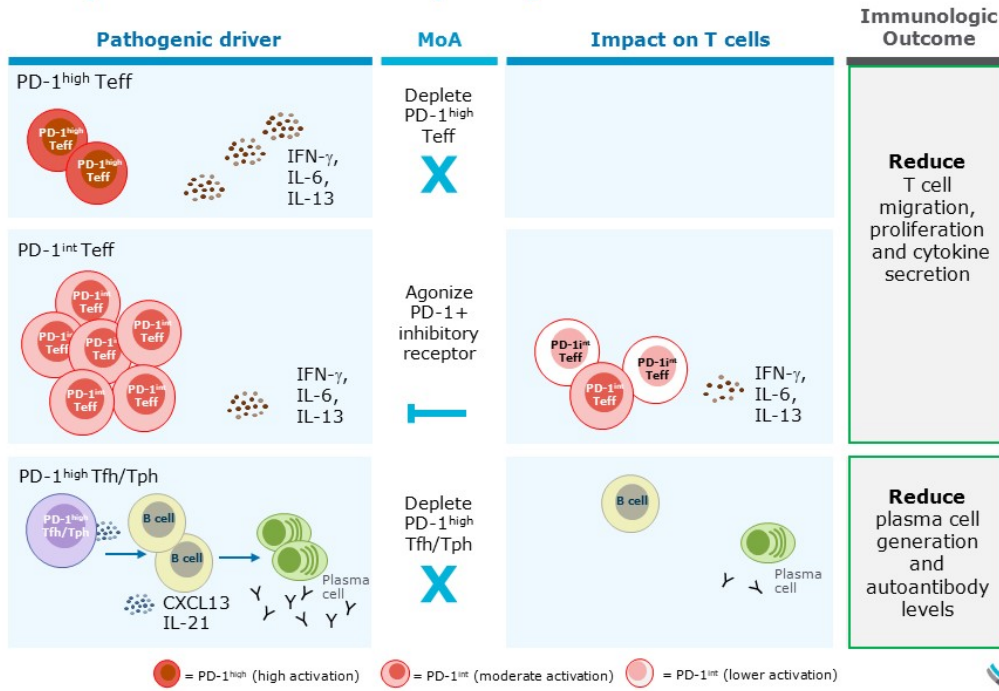
	<p><b>Teff (effector)</b></p>	<ul style="list-style-type: none"> <li>• In response to stimulation, become highly activated (PD-1<sup>high</sup>) or moderately activated (PD-1<sup>int</sup>)</li> <li>• Secrete inflammatory cytokines, cause tissue damage and perpetuate inflammatory cycle</li> </ul>
	<p><b>Tfh (follicular helper) Tph (peripheral helper)</b></p>	<ul style="list-style-type: none"> <li>• Secrete CXCL13 and IL-21 which recruit and mature B cells into "autoantibody secreting" plasma cells</li> <li>• Are PD-1<sup>high</sup></li> </ul>



Adapted from Akiyama et al, Ann Rheum Dis, 2023.



## Rosnilimab depletes and agonizes PD-1+ T cells targeting multiple drivers of disease pathogenesis



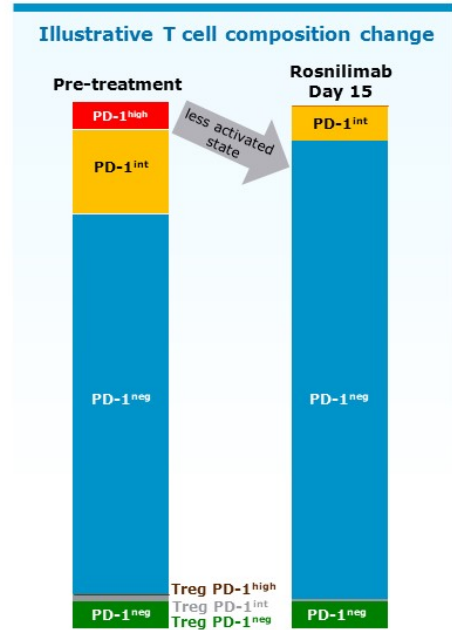
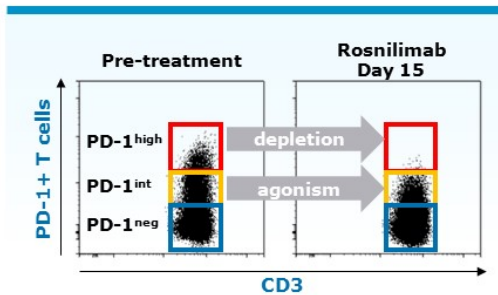
## Rosnilimab restores immune balance bringing T cell composition to a less activated state

PD-1 expression on both CD4 and CD8 T cells correlates with activation state

Rosnilimab targets only a small proportion of T cells

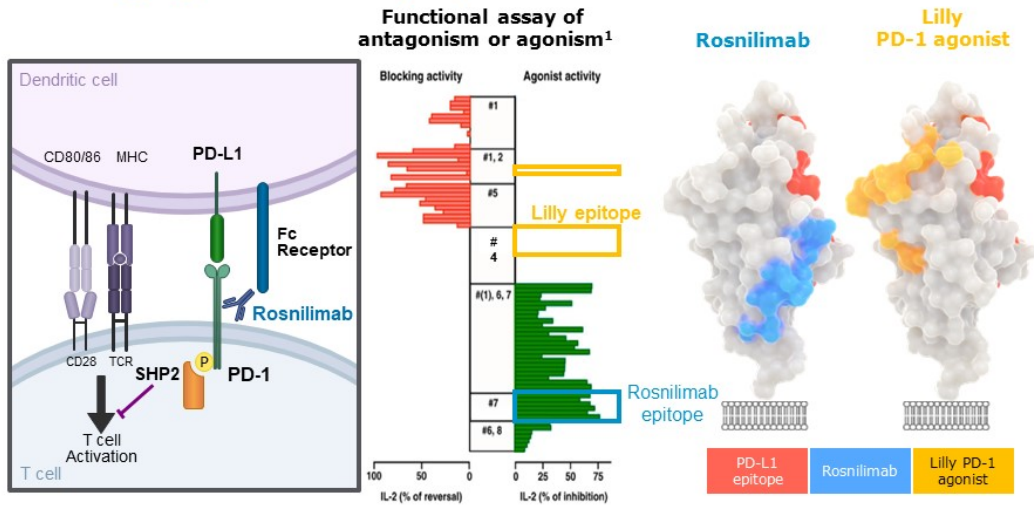
In healthy volunteers:

- Deplete PD-1<sup>high</sup> T cells: ~5-8% of total T cells
- Agonize remaining PD-1<sup>int</sup> T cells: ~15% of total T cells



Data illustrative, based on Phase 1 data from healthy volunteer study. Data on file with Anaptys.

## Rosnilimab optimizes PD-1+ T cell inhibitory signaling by enabling tight immune synapse formation




**“A shared feature of agonist mAbs is recognition of the membrane-proximal extracellular region...” and “...activity depends on Fc receptor-supported crosslinking”**

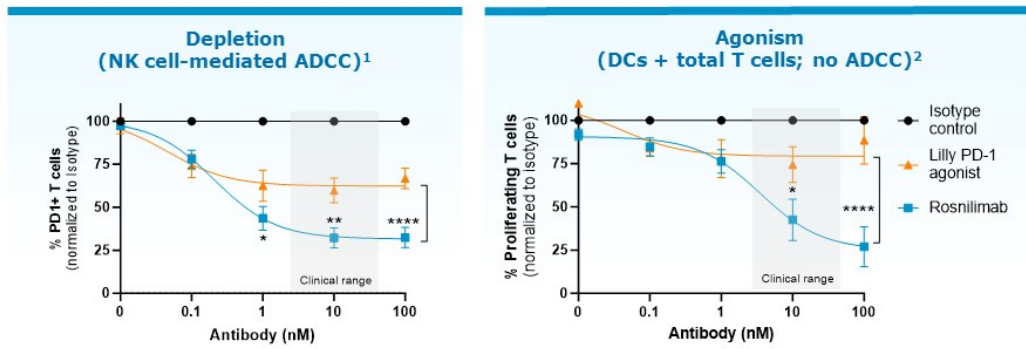
Suzuki, et al. 2023

1. Adapted from Suzuki et al., Sci. Immunol. 8, eadd4947 (2023).

## Rosnilimab's membrane-proximal binding epitope results in best-in-class potency vs. Lilly's PD-1 agonist

		Rosnilimab (IgG1k Fc)	Lilly (IgG1k Fc)
<b>Structural characteristics</b>	Membrane-proximal epitope	✓	
	PD-1 binding properties	✓	✓
	Fc receptor binding affinity	✓	✓
<b>Functional outputs</b>	Depletion (PD-1 <sup>high</sup> )	✓	Decreased
	Agonism (PD-1 <sup>int</sup> )	✓	Decreased

## Rosnilimab demonstrates potent depletion and agonism at clinically relevant concentrations



<sup>1</sup> Healthy donor T cells + NK cells (1:5 ratio) + antibody in in-vitro ADCC assay, representative data from N=5 donors.

<sup>2</sup> Healthy donor purified DCs + autologous total T cells stimulated with anti-CD3, cultured for 3 days for assessment of T cell proliferation. Two-way ANOVA, Tukey's multiple comparison test. \*\*\*\*p<0.0001, \*\*\*p<0.001, \*\*p<0.01, \*p<0.05.

## Rosnilimab is optimized for two MOAs: depletion and agonism of PD-1+ T cells in both inflamed tissue and periphery

PD-1 expressed preferentially on activated Teff and Tfh/Tph cells mediating autoimmune and inflammatory pathology

Rosnilimab restores immune balance bringing T cell composition to a less activated state

Rosnilimab's membrane-proximal binding epitope and Fc receptor binding affinity enables formation of a tight immune synapse resulting in best-in-class potency

## Agenda

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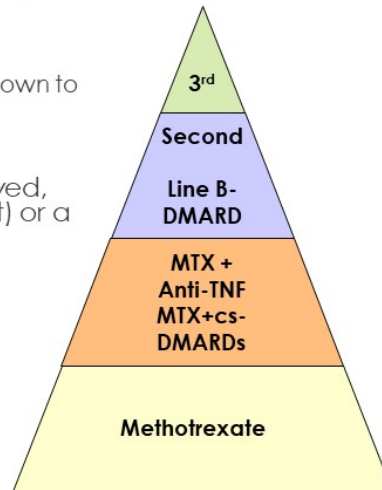
# RA Treatment Landscape 2023

JONATHAN GRAF, M.D.  
PROFESSOR OF MEDICINE, UCSF  
DIRECTOR, UCSF RA COHORT  
DIVISION OF RHEUMATOLOGY, ZUCKERBERG SAN FRANCISCO GENERAL



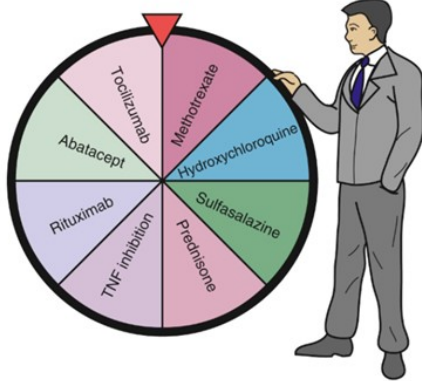
## Treat to target approach for early RA: 2023

- ▶ Start methotrexate
  - ▶ Initiate long term therapy with an agent shown to retard radiographic progression
- ▶ If low disease activity target is not achieved, add an b-DMARD (usually anti-TNF agent) or a combination of cs-DMARDs
- ▶ If disease remains active, ascend the pyramid of therapies until at disease activity target
- ▶ Even with T2T strategy, goal of remission is achieved in less than 60% of RA patients



## Choice of RA therapy: Not always obvious

THE RA WHEEL OF EMPIRIC THERAPY\*



RA is a heterogeneous disease

No standard biomarker to predict which therapy best for which patient

RA therapeutic landscape is often riddled with trial and error

Costly in terms of money, toxicity and delay in reaching T2T goals

*(Courtesy James O'Dell, MD)*

# Rheumatoid Arthritis: The ideal treatment landscape

Cs-DMARDs:  
MTX; LEFL

B-DMARDs:  
Anti-TNFs  
T-cell co-stim  
blockade  
Anti-IL6R

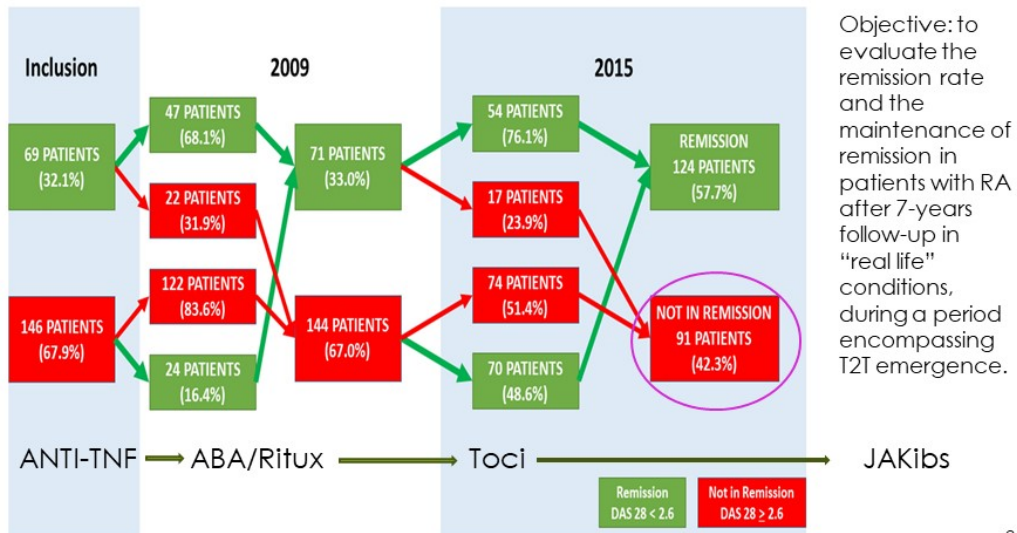


B-DMARDs:  
B-cell  
depleting  
therapies

Ts-DMARDs:  
JAKibs

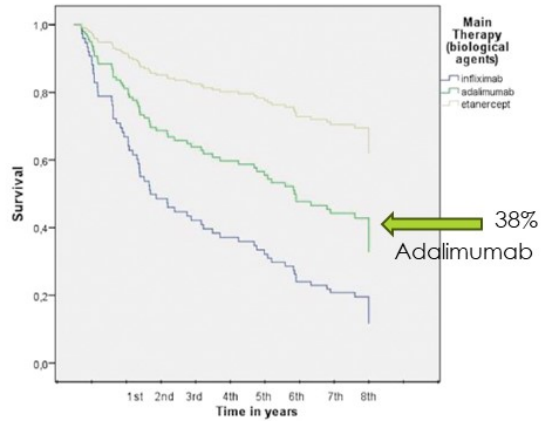
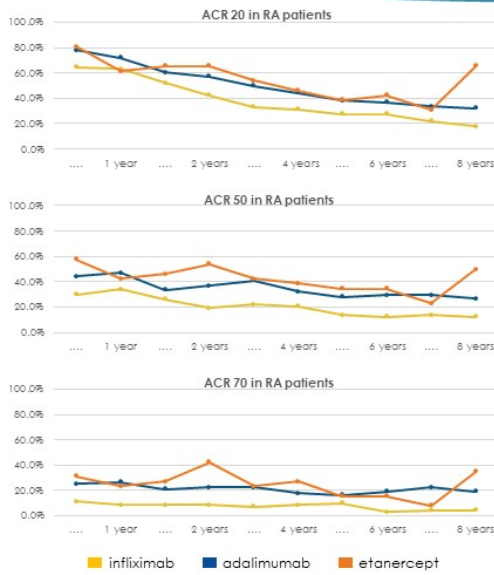
# Actual treatment landscape: State of RA treatment in real-world cohort: Poitiers, France 2007-2015

Larid et al. Sci Rep 12, 2563 (2022).



# Real world 8-year survival rates: Anti-TNF therapy 2000-2015

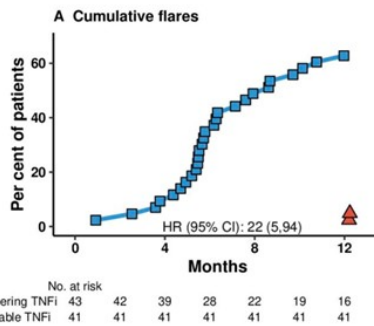
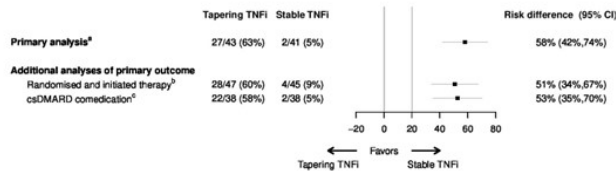
Papadopoulos et al. Rheumatology Advances in Practice, Volume 3, Issue 1, 2019



Real world is not a clinical trial:  
RA is a life-long disease

# Current B-DMARDs do not cure RA: Attempting to taper TNFis: The ARCTIC REWIND TNFi Trial

Lillegraven S, et al. Ann Rheum Dis 2023;0:1–10. doi:10.1136/ard-2023-224476



	No. at risk	0	4	8	12
Tapering TNFi	43	42	39	28	19
Stable TNFi	41	41	41	41	41

## Journal Series

Effect of tapered versus stable treatment with tumour necrosis factor inhibitors on disease flares in remission: a randomised, open label, non-inferiority trial

Siri Lillegårven, <sup>1</sup> Inga Paulsen, <sup>1</sup> Søren Højrup, <sup>1</sup> Anja Brügge Agø, <sup>1</sup> Joseph Jonson, <sup>1</sup> Inge Christoffer Olsen, <sup>2</sup> Jørn Støveland Landberg, <sup>3</sup> Tor Magne Midland, <sup>4</sup> Mathias Frøland, <sup>5</sup> Christian A. Hall, <sup>6</sup> Carsten Ballalund, <sup>7</sup> Cecilie Steink, <sup>8</sup> Hilde Haukeland, <sup>9</sup> Inger Myrnes Hansen, <sup>10</sup> Ellen Myhrvik, <sup>11</sup> Siri Uhlig, <sup>12</sup> Daniel H. Solomon, <sup>13</sup> Espen van der Heijde, <sup>14</sup> Tor K. Kvien, <sup>15</sup> Espen A. Haavardsholm, <sup>16</sup>

**ABSTRACT**

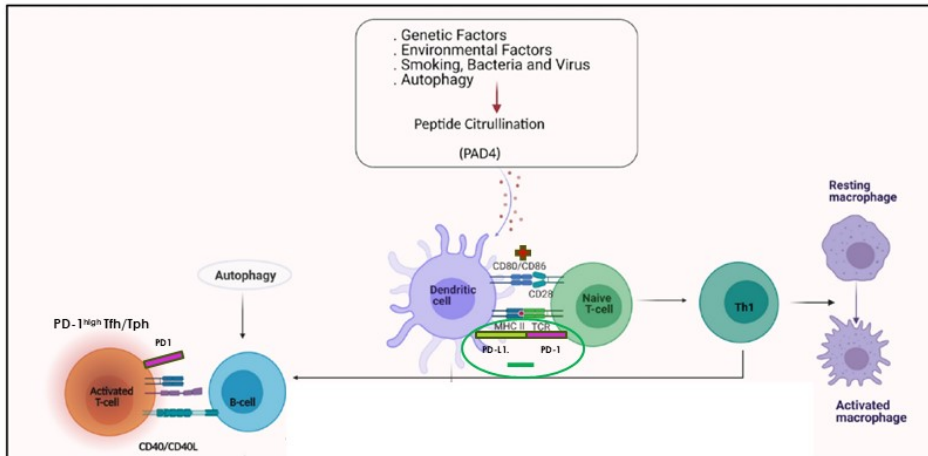
**Objective:** Many patients with rheumatoid arthritis (RA) remain treated with tumour necrosis factor (TNF) inhibitors (TNFi) for many years. It is unclear whether tapering of TNFi to discontinuation should be considered in remission. The aim of the ARCTIC REWIND TNFi trial was to assess the effect of tapering TNFi on remission compared with stable treatment in the risk of disease activity flare in patients with RA in remission.

**Method:** This randomised, open label, non-inferiority trial was conducted at the Norwegian Rheumatology Centre. Patients with RA in remission at baseline (DAS28-CRP < 2.6) were allocated to tapering TNFi or stable TNFi. Concomitant therapy, disease activity and functional disability were monitored. The primary endpoint was disease flare during the 12-month study period (intention-to-treat).

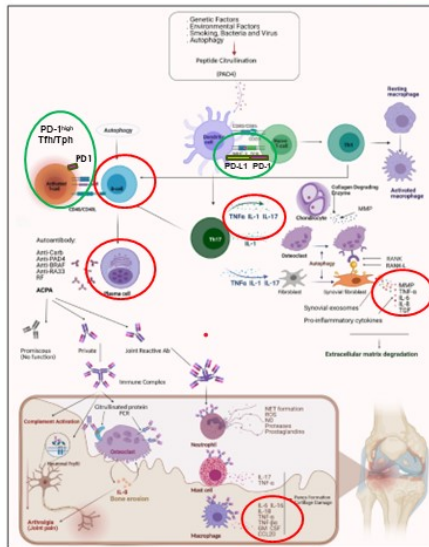
**Results:** Between June 2018 and January 2020, 88 patients were enrolled. 50 patients (57%) tapered TNFi to discontinuation. At baseline, 27 (30%) patients were on TNFi, 27 (30%) on TNFi and 34 (39%) on TNFi. The number of patients tapering TNFi to discontinuation was significantly higher (p < 0.001) compared with stable TNFi. The number of patients tapering TNFi to discontinuation was significantly higher (p < 0.001) compared with stable TNFi. The number of patients tapering TNFi to discontinuation was significantly higher (p < 0.001) compared with stable TNFi. The number of patients tapering TNFi to discontinuation was significantly higher (p < 0.001) compared with stable TNFi.

**Conclusion:** In patients with RA in remission, tapering TNFi to discontinuation was significantly higher (p < 0.001) compared with stable TNFi. The number of patients tapering TNFi to discontinuation was significantly higher (p < 0.001) compared with stable TNFi.

# PD-L1 is a central nodal point regulating T cell activity



# Resetting the immunologic thermostat: Potential to down-regulate multiple pathways



Known targets of current therapeutics

TNF-α

IL-1

IL-6

B-cell activation

Plasma cell development

Other cytokines (GM-CSF) that use JAK-STAT signaling pathways

PD-1 agonist class has shown compelling POC





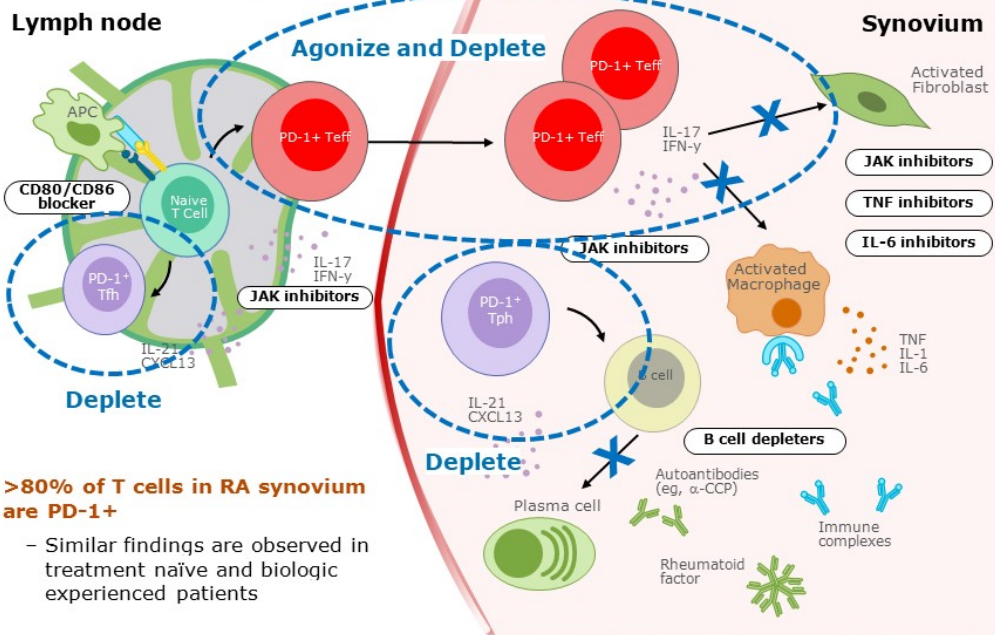
## What are the unmet needs in RA?

- ▶ Sizeable number of patients not at RA disease activity targets
  - ▶ Especially targets that achieve remission (or better)
- ▶ Need to reset the immune system environment so that:
  - ▶ Treatment efficacy doesn't wane
  - ▶ Therapy will work in ALL RA patients regardless of disease heterogeneity
- ▶ Analogy: Think about the environment in which one lives
  - ▶ Phoenix: Keep the air conditioning running all summer to keep house cool. But if air-conditioning stops working, you're in trouble.
  - ▶ Move to San Diego: the climate outside controls the climate inside. Electricity bills will be much less because you won't need air conditioning.

## Agenda

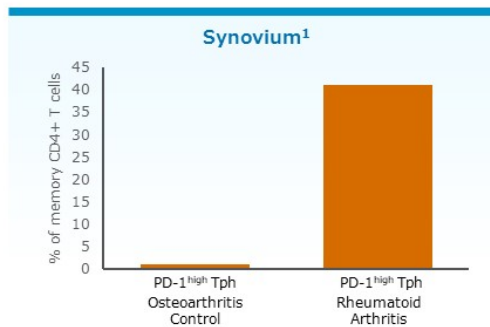
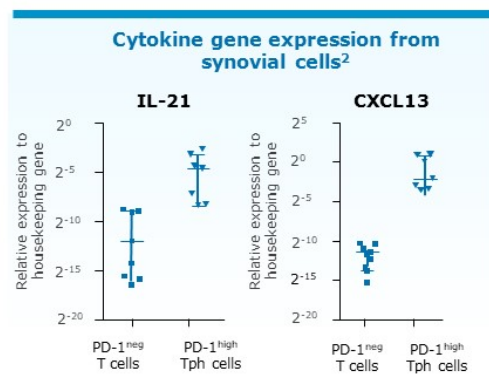
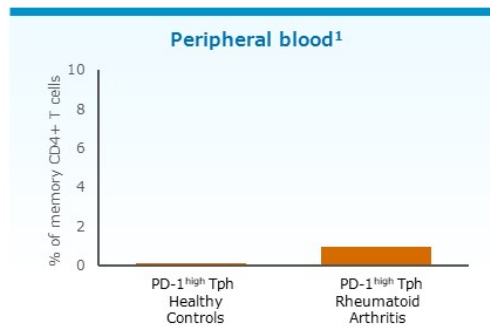
TOPIC	SPEAKER
Rosnilimab: a best-in-class PD-1 agonist	Dan Faga Chief Executive Officer
MOA and differentiation	Martin Dahl, Ph.D. Senior Vice President, Research
<i>Rosnilimab in RA</i>	
Unmet patient needs and opportunity for PD-1 agonists	Jonathan Graf, M.D. Professor, Medicine University of California, San Francisco
<b>Targeting RA with rosnilimab and translational data</b>	<b>Cailin Sibley, M.D., MHS, FACR</b> <b>Vice President, Translational Medicine</b>
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## PD-1+ T cells broadly impact multiple clinically validated drivers of RA pathogenesis



Adapted from Aletaha and Smolen, JAMA, 2018

## PD-1<sup>high</sup> Tph cells are elevated in RA synovium and secrete cytokines driving autoantibody production



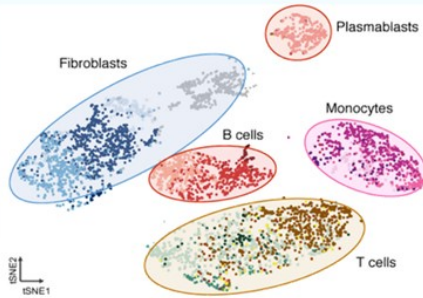
**Reduction of plasma cell generation results in reduced autoantibody levels which contribute to synovial inflammation and damage**

1. Adapted from Murray-Brown et al, RMC Open, 2022. 2. Adapted from Rao et al, Nature, 2017, p<0.001. RT-PCR data gene from isolated and sorted RA synovial cells normalized to RPL13A housekeeping gene

## PD-1 agonism overcomes synovial heterogeneity challenges given broad overlap with key disease subtypes

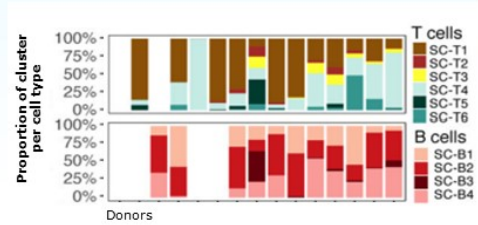
RA immune cells cluster into 18 different subtypes

Single cell RNA-Seq data from synovium



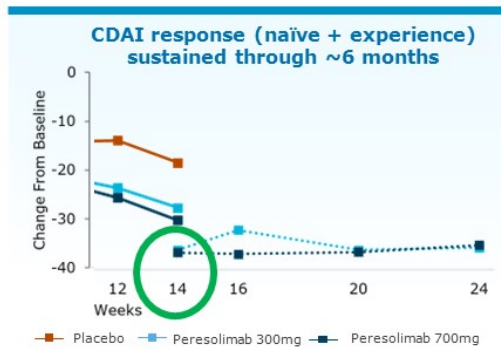
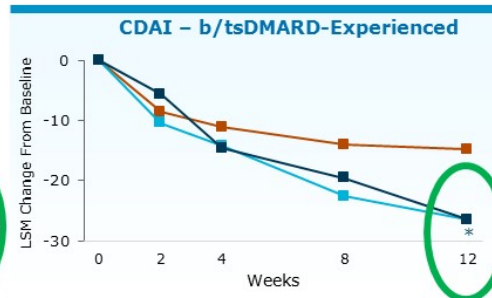
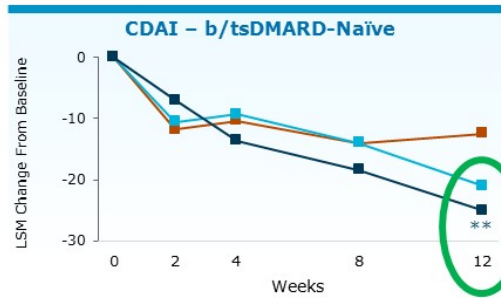
Individual patients differ in their composition of each cellular cluster

Leukocyte-rich RA



**Therapeutics with more narrow mechanisms of action would not target most disease subtypes**

## PD-1 agonist class is clinically validated in RA with compelling proof of mechanism

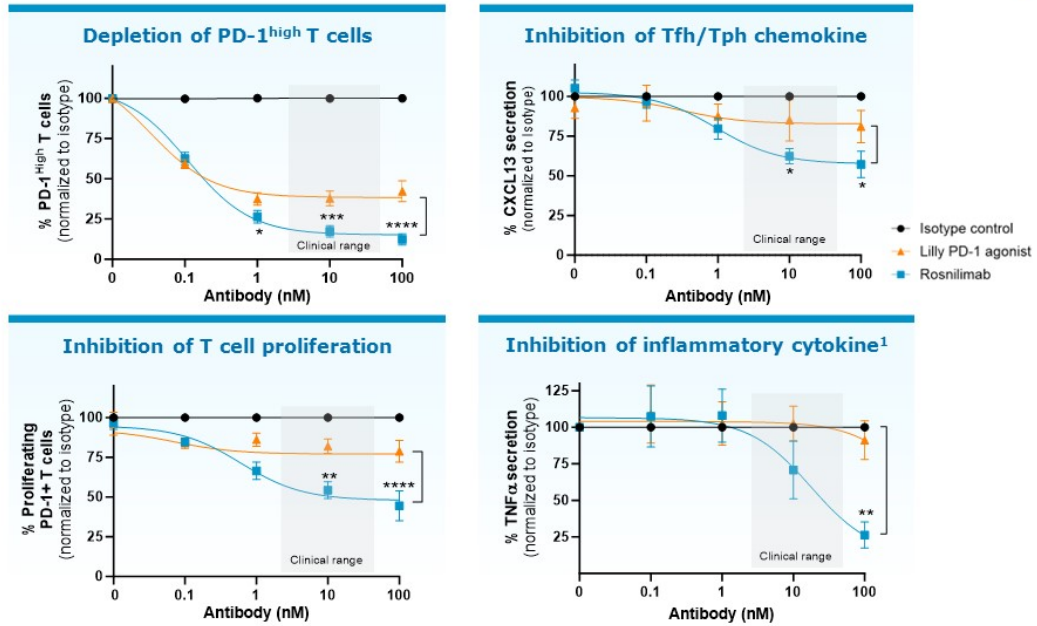


### PD-1 agonist emerging profile: Peresolimab 98 patient placebo-controlled P2a study

- No safety signal
- Consistent efficacy across biologic-naïve and biologic-experienced patients
- Week 14 efficacy sustained through 6 months

Tuttle, J. EULAR 2023, Week 14-Week 24 data estimated from peresolimab (PD-1 agonist) 2022 ACR presentation; CDAI=Clinical disease activity index. Sample size for top two charts: placebo n=24; peresolimab 300mg n=25 and peresolimab 700mg n=49. In bottom graph, placebo n=11, peresolimab 300mg n=12 and peresolimab 700mg n=18.

## Rosnilimab's potent depletion and agonism reduces T cell proliferation and inflammatory cytokines that cause joint damage



Anti-CD3+ anti-CD28 stimulation of RA patient PBMCs for assessment of depletion and agonism MOA, representative data from N=8 donors. Two-way ANOVA, Tukey's multiple comparison test. \*\*\*\*P<0.0001, \*\*\*p<0.001, \*\*p<0.01, \*p<0.05.  
<sup>1</sup>TNF $\alpha$  secretion measured in anti-CD3+ anti-CD28 stimulation of purified DC+T cells from N=4 healthy donors.

## Rosnilimab depletes and agonizes PD-1+ T cells broadly impacting multiple drivers of RA pathogenesis

PD-1 agonism overcomes synovial heterogeneity challenges given broad overlap with key disease subtypes

>80% of T cells in RA synovium are PD-1+, including PD-1<sup>high</sup> Tph cells which secrete cytokines driving autoantibody production

PD-1 agonist class is clinically validated in RA with consistent efficacy across biologic-naïve and biologic-experienced patients sustained over 6 months

Preclinical data support rosnilimab's potent immunologic outcomes



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<b>Unmet patient needs, disease biology, and rationale for PD-1 agonist in UC</b>	<b>Bruce Sands, M.D., M.S.</b> <b>Professor and Chief, Gastroenterology</b> <b>Icahn School of Medicine, Mount Sinai</b>
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# Ulcerative Colitis: Disease pathogenesis, treatment landscape, unmet need

Bruce E. Sands, MD, MS

Chief of the Dr. Henry D. Janowitz Division of Gastroenterology

Dr. Burrill B. Crohn Professor of Medicine

Icahn School of Medicine at Mount Sinai

Mount Sinai Hospital

Mount Sinai Health System

New York, USA



**Mount  
Sinai**

## Disclosure of potential conflicts of interest

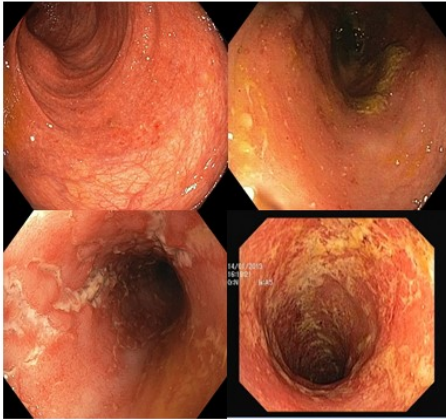
<b>Financial support for research</b>	Janssen
<b>Consultancy</b>	Abbvie, Abivax, Aclaris Therapeutics, Adiso Therapeutics, Agomab Therapeutics, Alfasigma, Alimentiv, Amgen, AMT, AnaptysBio, Arena Pharmaceuticals, Artizan Biosciences, Artugen Therapeutics, AstraZeneca, Bacainn Therapeutics, Boehringer-Ingelheim, Bristol Myers Squibb, Celltrion, Connect Biopharm, CytoKi Pharma, EcoR1 Capital, Eli Lilly and Company, Entera, Entera, Equilium, Ferring Pharmaceuticals, Fresenius Kabi, Galapagos, Genentech, Gilead Sciences, Glaxo SmithKline, GossamerBio, Imhotex, Immunic, Immunyx Pharma, Index Pharmaceuticals, Janssen, Johnson & Johnson, Kallyope, Kyowa Kirin, Lilly, Merck & Co., Microbiotica, Morphic Therapeutic, MRM Health, Pfizer, Progenity (Biora Therapeutics), Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Shire, Sun Pharma, Takeda, Target RWE, Teva Branded Pharmaceutical Products R&D, Theravance Biopharma, VectivBio, Ventyx Biosciences
<b>Stock and Stock Options</b>	Ventyx Biosciences

## Endoscopy findings of ulcerative colitis



Normal  
Colon

Total Mayo Clinic Score =  
SF + RB + MES + PGA



### Stool Frequency (SF)

0 = Normal for the patient  
1 = 1-2 stools/day in addition to the usual  
2 = 3-4 stools/day in addition to the usual  
3 = >5 stools/day beyond the usual

### Mayo Endoscopic Subscore (MES)

0 = Normal/inactive  
1 = Mild disease (erythema, decreased vascular pattern)  
2 = Moderate disease (marked erythema, loss of vascular pattern, erosions)  
3 = Severe disease (spontaneous bleeding, ulcerations)

### Rectal Bleeding (RB)

0 = No Blood  
1 = Blood streaks in less than half of evacuations  
2 = Evidence of fresh blood in most of the evacuations  
3 = Bowel movements with fresh blood

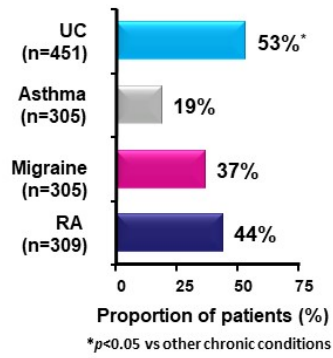
### Physician's Global Assessment (PGA)

0 = Normal  
1 = Mild disease  
2 = Moderate disease  
3 = Severe disease

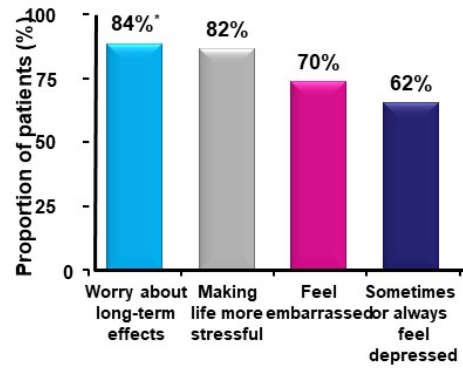
## UC has high impact on patient lives in U.S.

~1.5 million with UC in the U.S.

Proportion of patients who feel their condition was controlling their lives

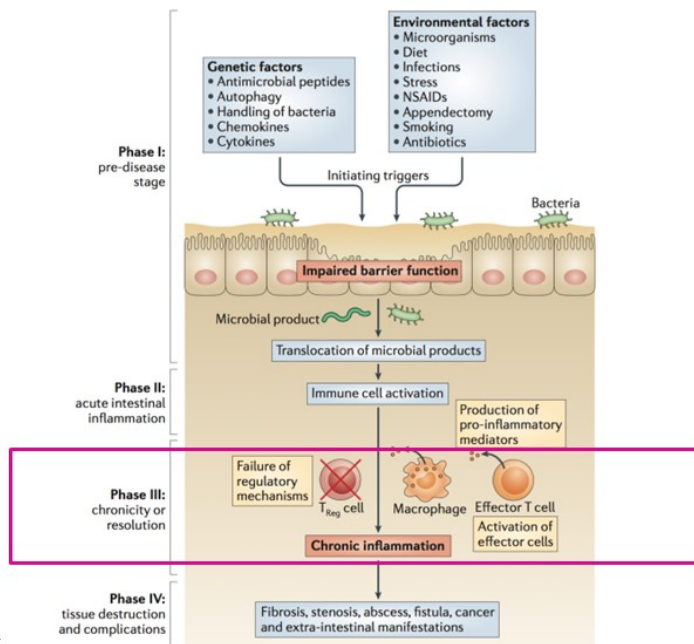


Psychological Impact of UC

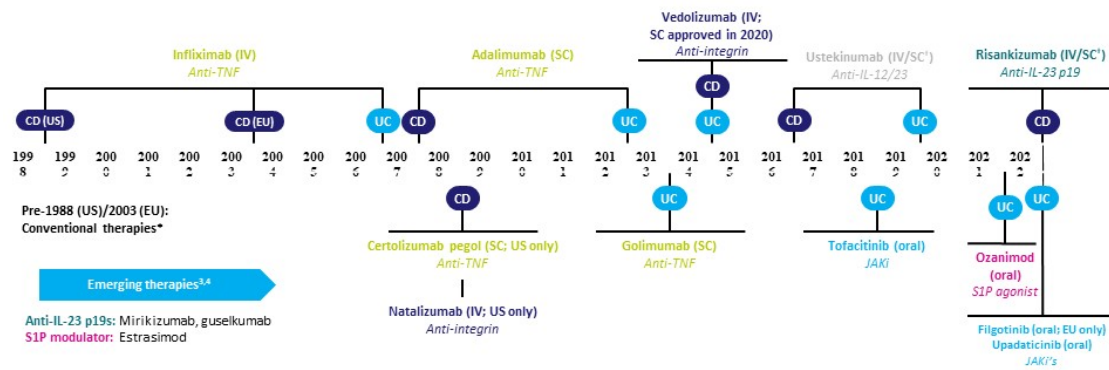


Internet survey designed to assess a variety of disease impact indices

## UC clinical presentation driven by activation of T effector cells, inflammatory cytokines and failure of regulatory mechanisms



## Increased understanding of IBD pathogenesis has led to the emergence of biologics and advanced therapies<sup>1,2</sup>



Last updated 16 December 2022. All approval dates reflect US Food and Drug Administration approval and European Medicines Agency/European Commission approval dates, unless otherwise stated.

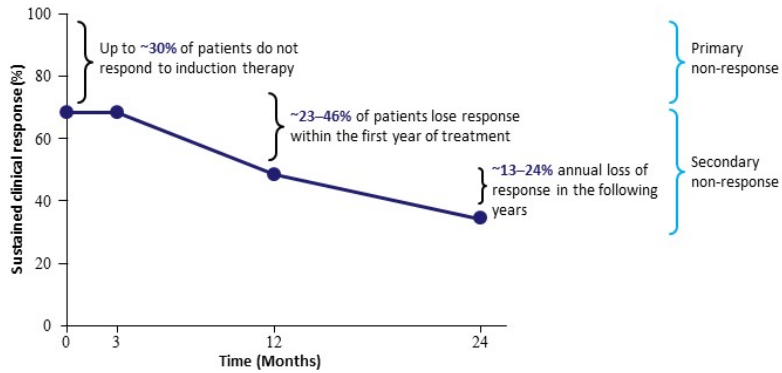
\*Conventional therapies include 5-aminosalicylic acid, steroids (prednisone/budesonide) and immunosuppressants; <sup>1</sup>IV induction and SC maintenance

CD, Crohn's disease; IBD, inflammatory bowel disease; IL, interleukin; IV, intravenous; JAKi, janus kinase inhibitor; S1P, sphingosine 1-phosphate; SC, subcutaneous; TNF, tumour necrosis factor; UC, ulcerative colitis

1. Adegboya SO, et al. *Int J Mol Sci* 2018;19:2244; 2. Jullerat P, et al. *Curr Res Pharmacol Drug Discov* 2022;3:100104; 3. Vieujean S, et al. *United European Gastroenterol J* 2022; online ahead of print (doi: 10.1002/ueg2.12305); 4. Grossberg LB, et al. *Aliment Pharmacol Ther* 2022;55:789-804; see slide notes for references supporting drug approval dates

## Anti-TNFs are considered the cornerstone of IBD treatment, including UC, but not all patients respond to treatment and many others lose response over time

### Treatment response rates with infliximab and adalimumab in CD<sup>1,2</sup>



Data more limited for UC; however, in Phase 3 trials, primary non-response rates with infliximab were ~30-40%, and more than half of initial responders lost response to treatment in the first year<sup>3</sup>

CD, Crohn's disease; IBD, inflammatory bowel disease; TNF, tumour necrosis factor; UC, ulcerative colitis

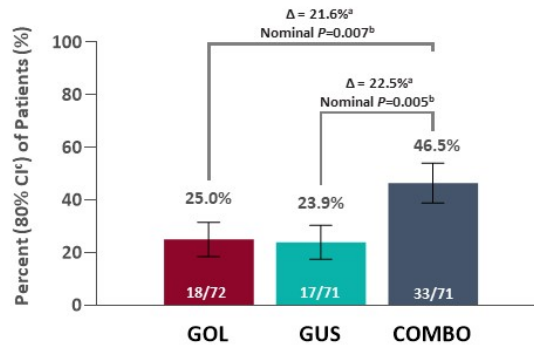
1. Roda G, et al. Clin Transl Gastroenterol 2016;7:e135; 2. Ben-Horin S, Chowers Y. Aliment Pharmacol Ther 2011;33:987-95; 3. Rutgeerts P, et al. N Engl J Med 2005;353:2462-77



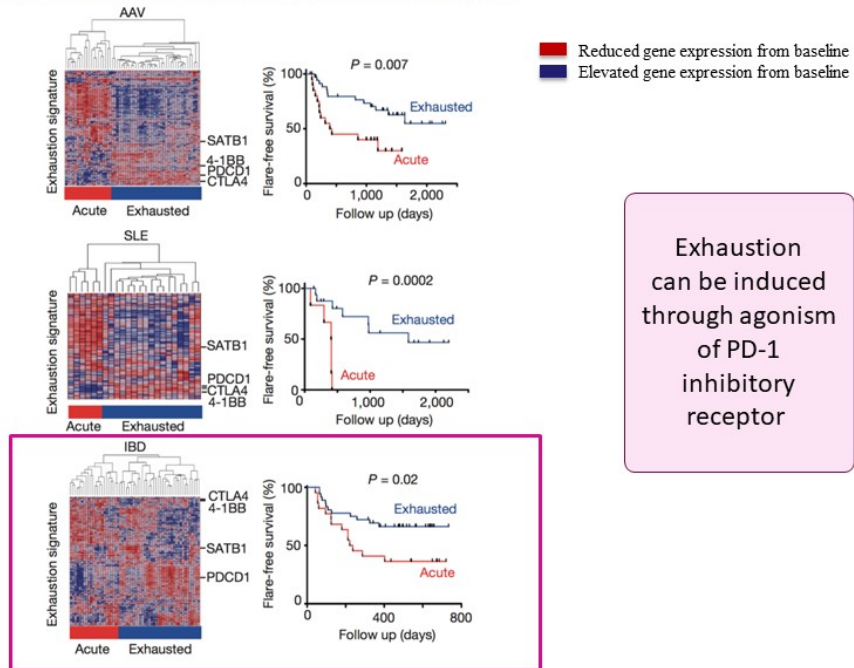
## Targeting multiple mechanisms provides opportunity to break through efficacy ceiling in moderate to severe UC

VEGA: Golimumab vs Guselkumab vs Combination

**Clinical remission at Week 12**  
Mayo Stool Frequency Subscore of 0 or 1 and Not Increased from Baseline,  
a Rectal Bleeding Subscore of 0, and an Endoscopy Subscore of 0 or 1 with  
No Friability Present on the Endoscopy



## PD-1 mediated T cell exhaustion is associated with reduced flares in numerous autoimmune diseases



Exhaustion can be induced through agonism of PD-1 inhibitory receptor

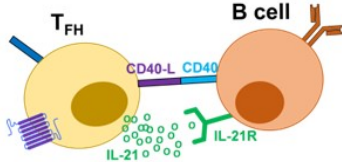
# Novel subset of T cells (T follicular helper cells) expanded in UC that may direct the B cell response

## Ulcerative colitis is characterized by a plasmablast-skewed humoral response associated with disease activity

Mathieu Uzzan<sup>1,2,3,4</sup>, Jerome C. Martin<sup>1,2,3,4,5</sup>, Luka Mesin<sup>6</sup>, Alexandra E. Livanos<sup>1,2</sup>, Tomas Castro-Dopico<sup>1,2,3</sup>, Ruiqi Huang<sup>1,2</sup>, Francesca Petralia<sup>1</sup>, Giuliana Magri<sup>1,2</sup>, Shashi Kumar<sup>1</sup>, Qing Zhao<sup>1</sup>, Adam K. Rosenzweig<sup>1,2</sup>, Minami Tokuyama<sup>1</sup>, Keshav Sharma<sup>1,2</sup>, Ryan Ungaro<sup>1</sup>, Roman Kosoy<sup>1,2</sup>, Dnyu Jha<sup>1,2</sup>, Jeremy Fischer<sup>1,2</sup>, Harpreet Singh<sup>1,2</sup>, Mary E. Keefe<sup>1,2</sup>, Nandhini Ramamoorthi<sup>1</sup>, William E. O'Gorman<sup>1</sup>, Benjamin L. Cohen<sup>1</sup>, Adebisi Rahman<sup>1,2,3</sup>, Francesca Cossarini<sup>1</sup>, Akihiro Seki<sup>1</sup>, Louise Leyre<sup>1,2</sup>, Sonia Tejedor Vazquez<sup>1,2</sup>, Saktesh Gurunathan<sup>1</sup>, Emilie K. Grasset<sup>1,2,3</sup>, Bojan Losic<sup>1,2</sup>, Maria Dubinsky<sup>1</sup>, Alexander J. Greenstein<sup>1</sup>, Zou Gottlieb<sup>1</sup>, Peter Legnani<sup>1</sup>, James George<sup>1</sup>, Haritz Iturr<sup>1</sup>, Aleksandar Stojimirovic<sup>1</sup>, Carrie Brodmerkel<sup>1</sup>, Andrew Kasarkas<sup>1,2,3</sup>, Bruce E. Sands<sup>1</sup>, Glauca Furtado<sup>1</sup>, Sergio A. Lira<sup>1,2</sup>, Zewen K. Tuong<sup>1,2</sup>, Hualbin M. Ko<sup>1,2</sup>, Andrea Cerutti<sup>1,2,3,4</sup>, Charles O. Elson<sup>1</sup>, Menna R. Clatworthy<sup>1,2</sup>, Miriam Merad<sup>1,2</sup>, Mayte Suarez-Farinas<sup>1,2</sup>, Carmen Argmann<sup>1,2,3</sup>, Jason A. Hackney<sup>1,2</sup>, Gabriel D. Victora<sup>1,2</sup>, Gwendalyn J. Randolph<sup>1,2</sup>, Ephraim Kenigsberg<sup>1,2</sup>, Jean-Frederic Colombel<sup>1</sup> and Saurabh Mehandru<sup>1,2,3,4</sup>

## A novel population of CXCL13+ Tfh-like cells is identified in the UC colon

A subset of T cells, T follicular helper cells (Tfh) 'help' with B cell responses



- Tfh/Tph cells significantly increased in active UC patients compared with stable remission UC patients and healthy controls
- Mayo Clinic Score, erythrocyte sedimentation rate, C-reactive protein all positively correlated with frequency of circulating Tfh cells in UC
- Tfh cells in germinal center increased in UC compared with controls
- Level of Tfh cells positively correlated with circulating new memory B cells, plasmablasts, serum IgG, IL-4, IL-21

**Tfh/Tph cells express programmed death 1 (PD-1), CXC chemokine receptor 5 (CXCR5), inducible costimulatory molecule (ICOS), and B cell lymphoma 6 (BCL-6) and produce IL-21**

Tfh/Tph = T follicular helper and T peripheral helper cells

## Summary: Ulcerative Colitis

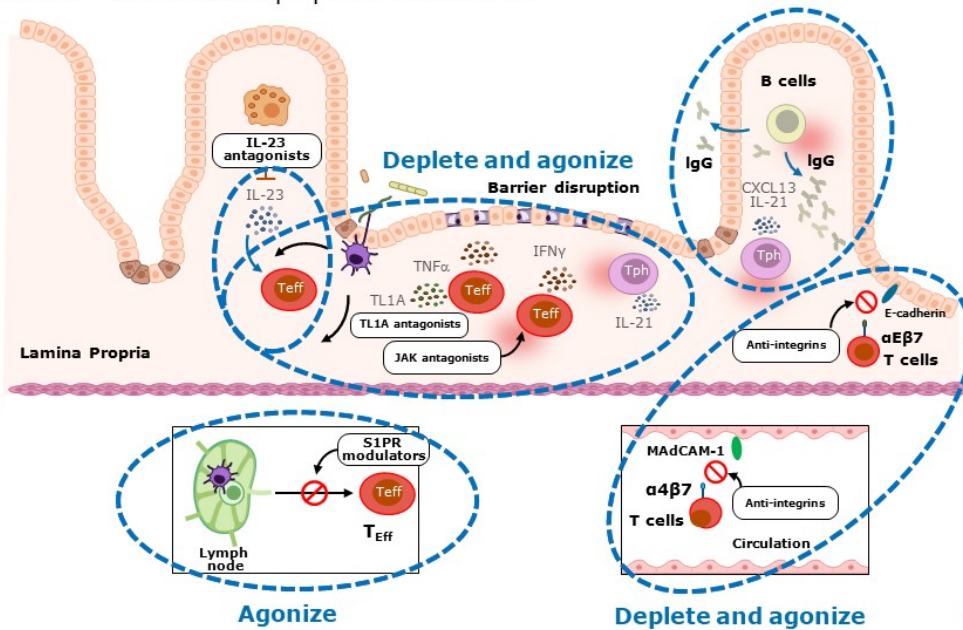
- High impact disease
  - High personal and economic impacts
  - Rising rates, globally
- Significant therapeutic limitations
  - Safety (anti-TNFs, JAK inhibitors)
  - Limited efficacy in achieving and maintaining remission
- Targeting multiple mechanisms provides opportunity to break through efficacy ceiling
- PD-1 pathway implicated in immune mediated disease, including UC
  - Therapies impacting T effector cells have been proven efficacious
  - PD-1+ Tfh/Tph cells expand in UC that may direct the B cell response
- PD-1 agonism has potential as a novel MOA for treatment of UC, with strong pre-clinical rationale

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Rosnilimab: a best-in-class PD-1 agonist	Dan Faga Chief Executive Officer
MOA and differentiation	Martin Dahl, Ph.D. Senior Vice President, Research
<i>Rosnilimab in RA</i>	
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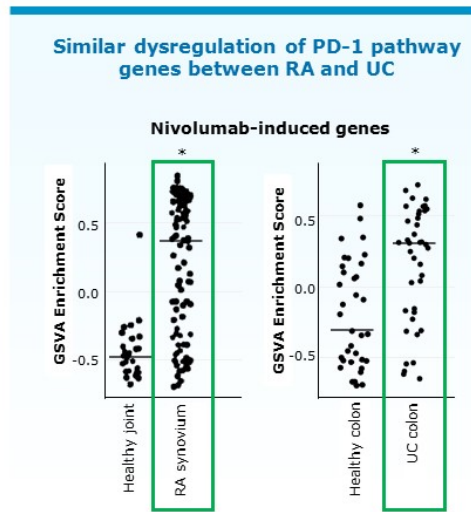
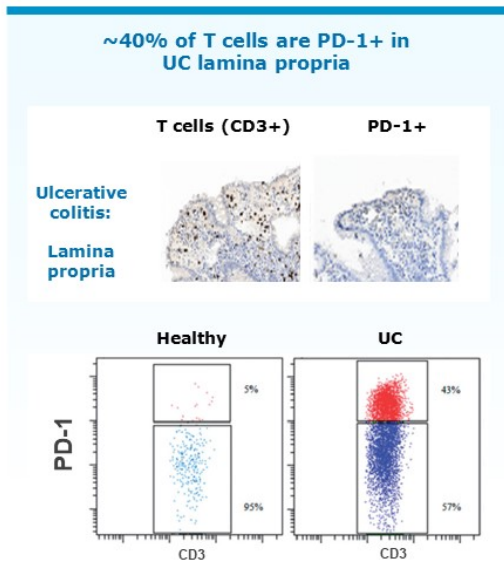
## PD-1+ T cell activation broadly impacts multiple clinically validated drivers of UC pathogenesis

>40% of T cells in lamina propria in UC are PD-1+



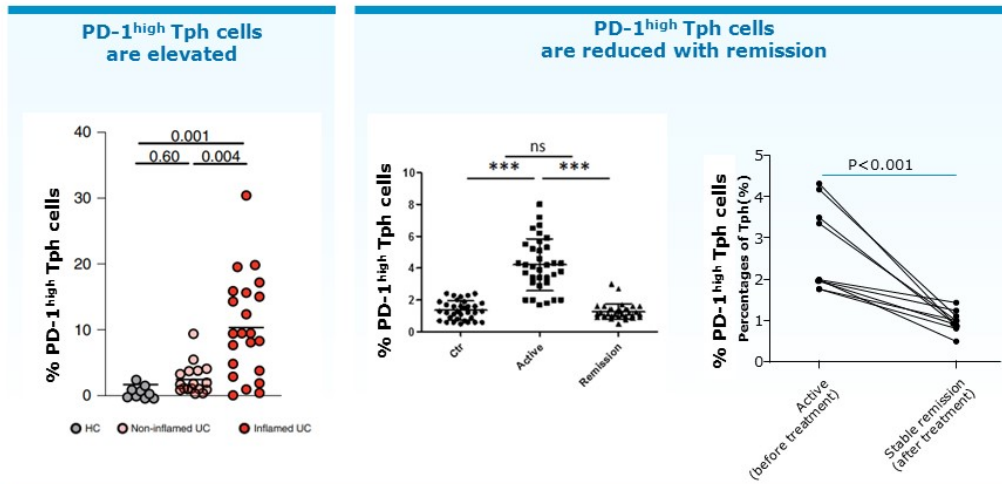
Adapted from Gastroenterology & Hepatology Volume 18, Issue 8 August 2022.

## PD-1+ T cells are elevated and dysregulated in UC



Guo et al, PLoS One, 2018; 13(2): e0192704; Nivolumab signature gene set containing ~100 genes induced by the anti-PD-1 antagonist therapeutic in TME of cancer patients was used for GSVAs (gene set variation analysis) in synovial tissue biopsy samples of patients with RA. We performed the same analysis from UC biopsy tissue by utilizing available published data. \* P<0.05

## Reduction of elevated PD-1<sup>high</sup> Tph cells in both UC colon and periphery correlates with remission



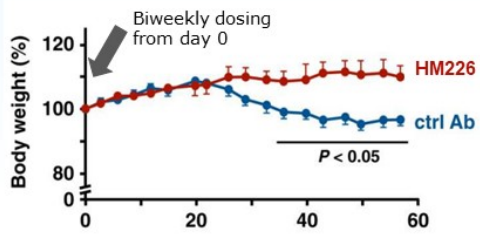
**Reduction of plasma cell generation & autoantibody levels, including anti-microbial IgG antibodies contributing to colonic inflammation and barrier disruption**

PD-1<sup>high</sup> Tph cells defined by CD3+CD4+CD45RA-PD-1+TIGIT+ICOS+CXCR5-. Long et al, Immunology Letters 233 (2021) 2-10., Rao et al, Nature, 2017, \*\*\* p<0.001

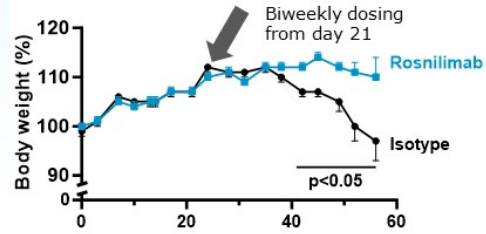


## Prophylactic or therapeutic dosing of PD-1 agonists induce and maintain remission in murine models

### Prophylactic dosing of HM226 PD-1 agonist induce and maintain remission from colitis

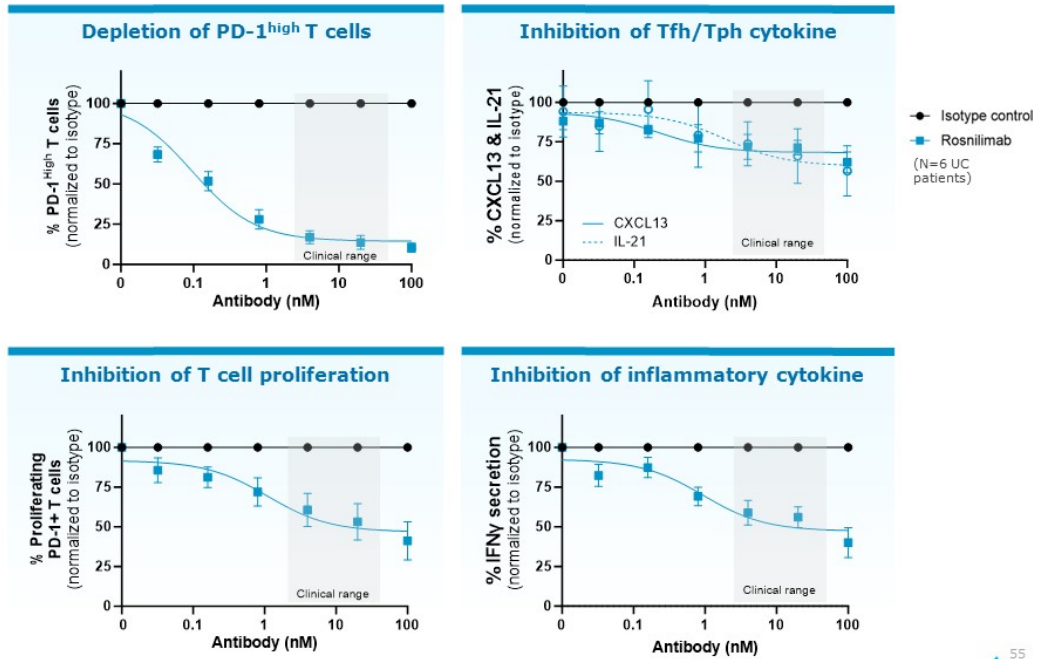


### Therapeutic dosing of rosnilimab induce and maintain remission from colitis



Rosnilimab and HM226 bind to the membrane proximal "epitope 7" of PD-1 that contributes to maximal PD-1 agonism. Rosnilimab formatted to mIgG2a to mediate effector function in mice. Suzuki et al., Sci. Immunol. 8, eadd4947 (2023).

## Rosnilimab's potent depletion and agonism reduces T cell proliferation and inflammatory cytokines that disrupt barrier function



Anti-CD3 + anti-CD28 stimulation of UC patient PBMCs for assessment of depletion and agonism MOA, representative data from N=6 donors.

## Rosnilimab depletes and agonizes PD-1+ T cells broadly impacting multiple drivers of UC pathogenesis

>40% of T cells in UC lamina propria are PD-1+, including PD-1<sup>high</sup> Tph cells which inversely correlate with disease remission

PD-1 agonists induce and maintain remission from colitis in murine models

Preclinical data support rosnilimab's potent immunologic outcomes

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## Rosnilimab, and overall PD-1 agonist class, well-tolerated with no dose limiting tox observed to date

### **Rosnilimab Phase 1: 144 healthy volunteers (HV) in SAD and MAD cohorts**

- Supports monthly SC dosing
- Favorable safety and tolerability
  - No SAEs related to rosnilimab<sup>1</sup>
  - No carcinogenic events observed
  - No infection risk signal

### **PD-1 agonist class: consistent tolerability profile to date**

- Competitor PD-1 programs no carcinogenic events or infection risk signal
- >100+ RA patients treated with Lilly PD-1 agonist (highest dose of 700 mg IV over 6 months) showed tolerable profile<sup>2</sup>

### **Abatacept, targeting all T cells, has not shown clinically relevant carcinogenic increases in decades of commercial use**

SAD=Single ascending dose; MAD=Multiple ascending doses; RO=Receptor occupancy; PK=Pharmacokinetics; SC = subcutaneous.

1. MAD cohort no SAEs; SAD cohorts 2 SAEs unrelated to rosnilimab as follows: Obstructive pancreatitis occurred in a placebo subject and Coronavirus infection occurred in drug 400 mg SC cohort on Day 24 until Day 31; participant recovered and discontinued from the study, and AE was deemed unrelated to rosnilimab.

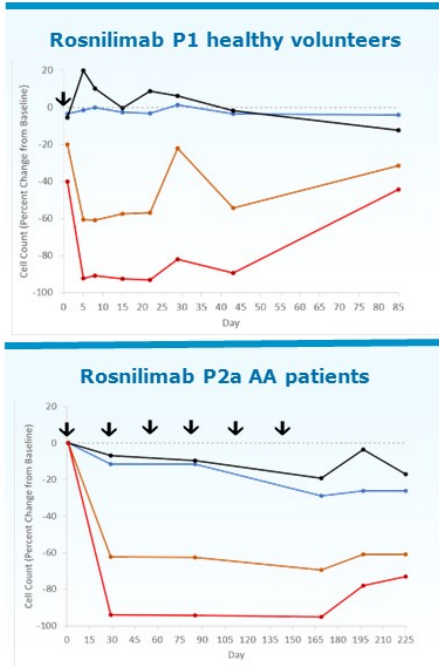
2. Lilly peresolimab Phase 2 data in RA, published in NEJM ([A Phase 2 Trial of Peresolimab for Adults with Rheumatoid Arthritis | NEJM](#)).

## Rosnilimab P2a in alopecia areata (AA) for Q4W SC dosing for 6 months was well tolerated with no significant safety signals

TEAE summary	Rosnilimab 400 mg (N=33)	Placebo (N=18)	All participants (N=51)
Participant with at least one TEAE	21 (63.6)	12 (66.7)	33 (64.7)
Related	6 (18.2)	3 (16.7)	9 (17.6)
Participant with at least one serious TEAE	1 (3.0)	1 (5.6)	2 (3.9)
Related	0	0	0
TEAE leading to treatment discontinuation	0	0	0
TEAE leading to study withdrawal	0	0	0
TEAE leading to death	0	0	0
Participant with at least one severe TEAE	1 (3.0)	0	1 (2.0)
Related	0	0	0
Top five TEAEs in more than 1 participant	Rosnilimab 400 mg (N=33)	Placebo (N=18)	All participants (N=51)
Infections (SOC)	12 (36.4)	11 (61.1)	23 (45.1)
COVID-19	7 (21.2)	2 (11.1)	9 (17.6)
Urinary tract infection	1 (3.0)	4 (22.2)	5 (9.8)
Arthralgia	2 (6.1)	1 (5.6)	3 (5.9)
Localized infection	1 (3.0)	2 (11.1)	3 (5.9)
Nasopharyngitis	1 (3.0)	2 (11.1)	3 (5.9)

TEAE=Treatment emergent adverse event, Serious TEAEs: SAE for Placebo (n=1) of intestinal obstruction (designated unrelated); SAE for Rosnilimab (n=1) patient reported an unconfirmed MI (designated unrelated) and same event was designated severe AE.

## Potent and sustained reduction in peripheral PD-1+ T cells for >30 days across P1 HV and P2a AA studies



### Consistent PD-1+ T cell effect

- >90% reduction of PD-1<sup>high</sup> T cells
- >50% reduction of PD-1+ T cells

### Overall T cell composition in less activated state

- Positive bias to Treg ratio

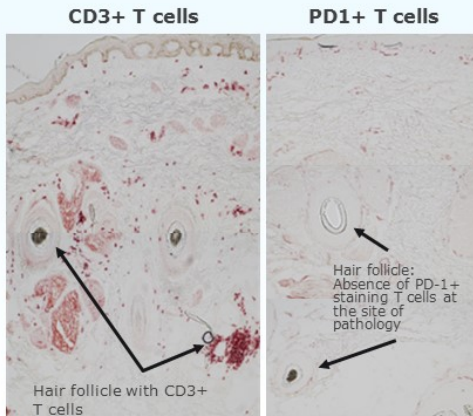
### AA patients are in a low systemic inflammatory state

- Represented by no significant increase in peripheral PD-1+ T cells relative to healthy controls

AA=Alopecia Areata; Results shown from 400mg subcutaneous dose (single dose in healthy and monthly dose in AA).

## PD-1 agonist MOA is not the right approach to treat AA given essentially undetectable PD-1+ cells at hair follicle

### Representative IHC staining of scalp biopsy samples at baseline<sup>1</sup>



### PD-1+ cells undetectable at hair follicle (site of clinical pathology)

- Only ~10-15% of T cells were PD-1+ in skin overall
- Non-localized and scattered throughout layers of skin

### Rosnilimab "proof of mechanism" observed in skin

- Reduction in PD-1+ T cells
- Reduction in T cell activation markers and increase in Tregs

### Targeting PD-1+ cells is not the right therapeutic approach for AA

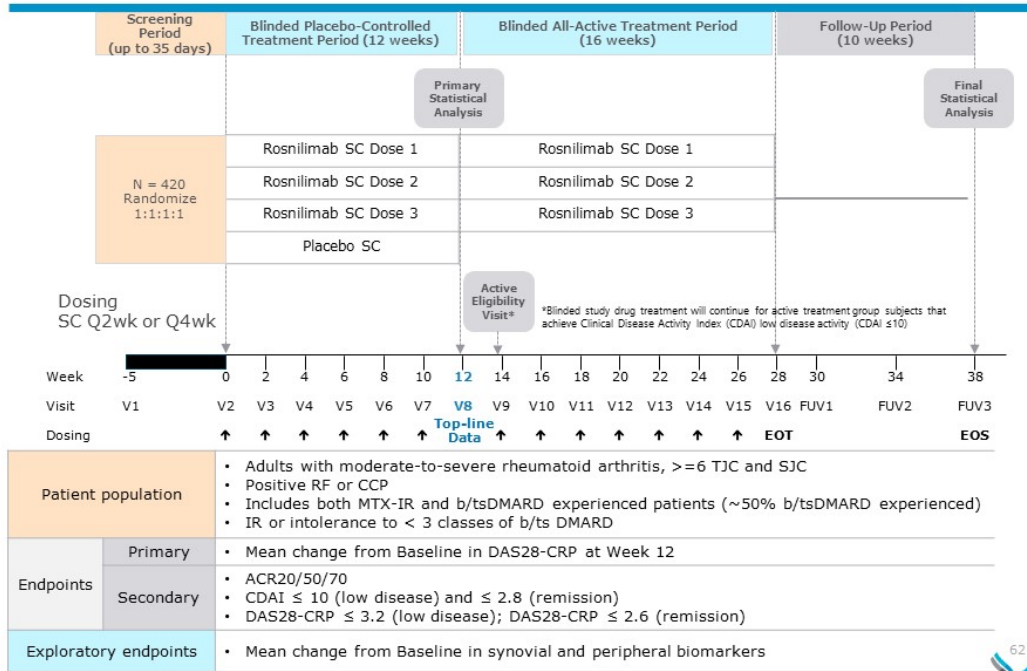
- Re-entry of hair into the anagen growth phase may also be independent of inflammation

1. Panels are generally representative of all biopsies. Red coloring represents CD3+ or PD-1+ T cells. While T cell infiltrate was seen at selected hair follicles, these cells were not PD-1+. When seen, the "rare" PD-1+ cells were scattered at dermal-epidermal junction away from site of disease pathology.



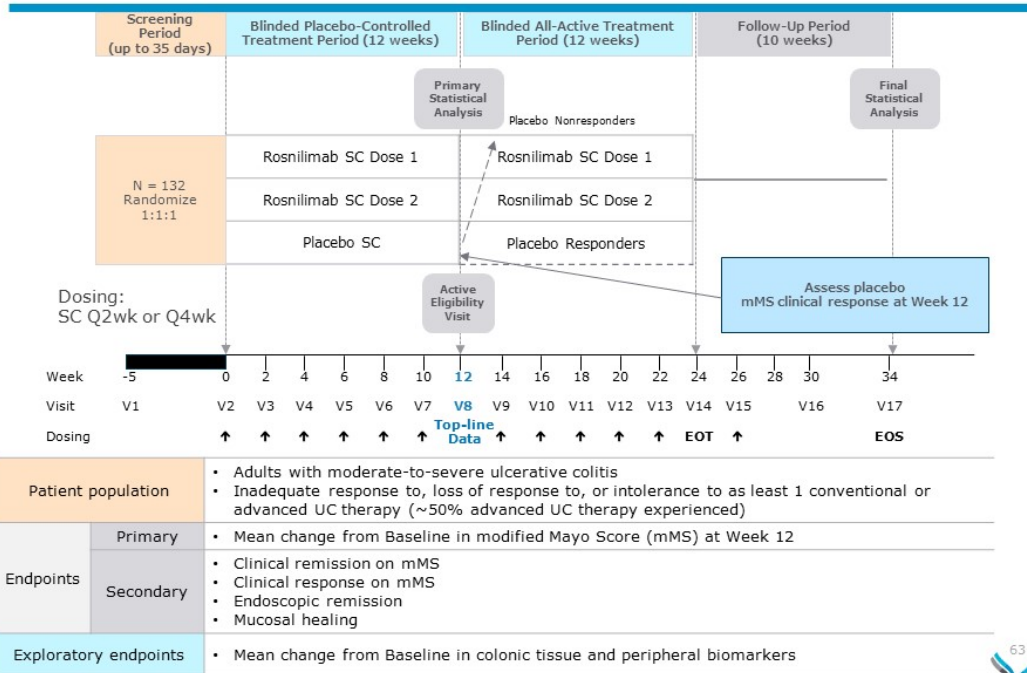
## Rosnilimab Phase 2b in moderate-to-severe RA

Initiated Q3 2023; Top-line data mid-2025

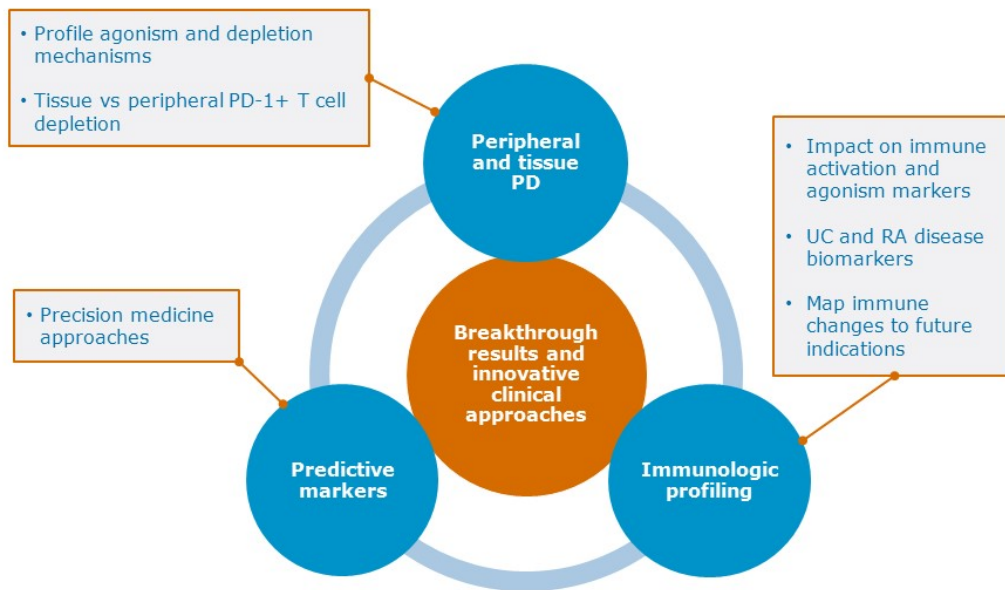


## Rosnilimab Phase 2 in moderate-to-severe UC

Initiating Q4 2023; Top-line data H1 2026



## Robust translational plans explore predictive markers of treatment response in RA and UC and inform future indications



## Rosnilimab is potential best-in-class in RA and first-in-class in UC

Rosnilimab was well tolerated in clinical studies with no significant safety signals while demonstrating potent and sustained reduction in peripheral PD-1+ T cells for >30 days

PD-1+ T cells are elevated in inflamed tissue and periphery in RA and UC

Global Phase 2b trial initiated in moderate-to-severe RA with top-line data expected mid:25

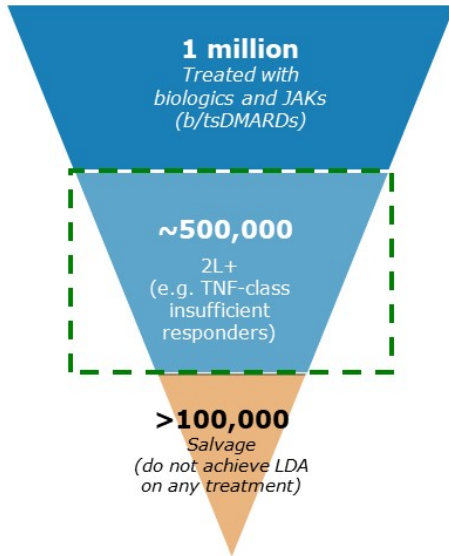
Global Phase 2 trial in moderate-to-severe UC initiating Q4:23 with top-line data expected 1H:26

## Agenda

TOPIC	SPEAKER
Rosnilimab: a best-in-class PD-1 agonist	Dan Faga Chief Executive Officer
MOA and differentiation	Martin Dahl, Ph.D. Senior Vice President, Research
<i>Rosnilimab in RA</i>	
Unmet patient needs and opportunity for PD-1 agonists	Jonathan Graf, M.D. Professor, Medicine University of California, San Francisco
Targeting RA with rosnilimab and translational data	Cailin Sibley, M.D., MHS, FACR Vice president, Translational Medicine
<i>Rosnilimab in UC</i>	
Unmet patient needs, disease biology, and rationale for PD-1 agonist in UC	Bruce Sands, M.D., M.S. Professor and Chief, Gastroenterology Icahn School of Medicine, Mount Sinai
Targeting UC with rosnilimab and translational data	Martin Dahl, Ph.D.
PD-1 safety data and Phase 2 development plans in RA and UC	Paul Lizzul, M.D., Ph.D. Chief Medical Officer
<b>Market opportunity and closing remarks</b>	<b>Dan Faga</b>
Q&A	AnaptysBio

## Substantial opportunity for new class of biologics with differentiated outcomes in RA

U.S. "biologic experienced" RA prevalence<sup>1,3,4</sup>



>\$10bn U.S. sales in "post TNF" market (2021)<sup>2</sup>

### Fragmented market

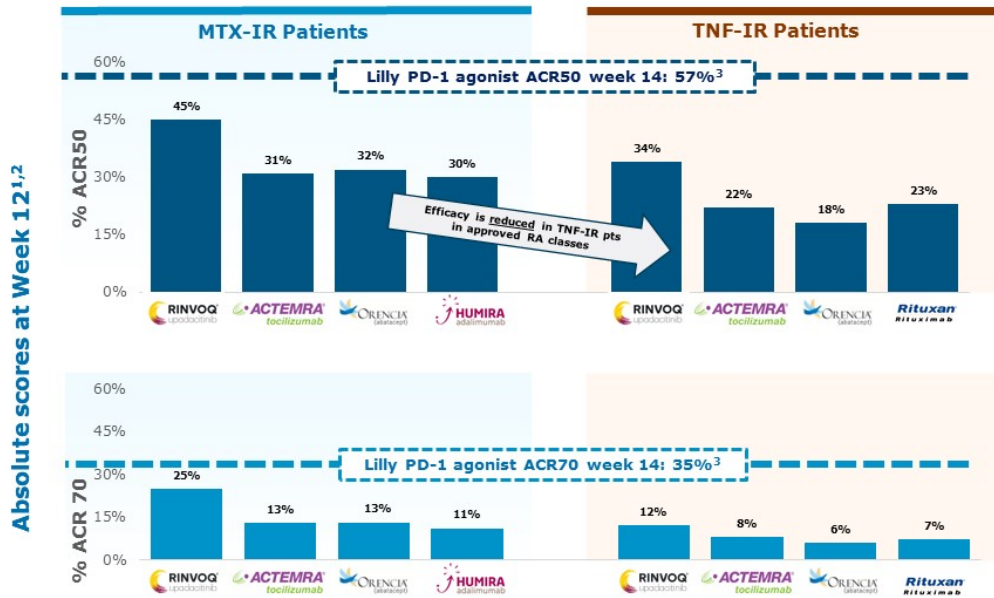
- Lack of established SOC
- No new therapeutic class launched since 2012 (*JAK inhibitors: Xeljanz*)

### PD-1 agonist: Significant potential to differentiate from insufficient SOC

- Deeper responses
- Broader patient population: consistent response across lines of therapy
- Restore immune balance
- Emerging profile allows potential for combinations in future

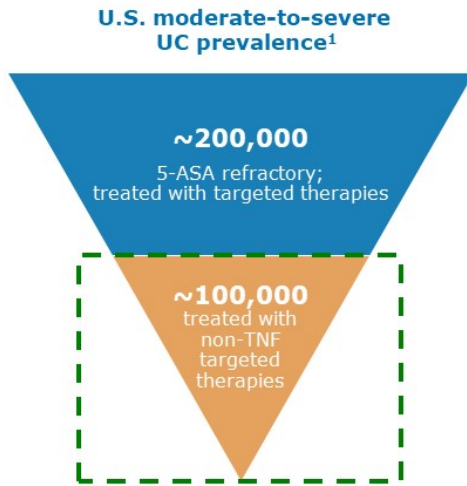
1. Claims analysis to determine market size based on 5 years of claims history; 2. Evaluate Pharma; 3. b/tsDMARD – biologic/targeted synthetic disease modifying antirheumatic drug, 2L – 2nd line; 4. Anaptys market research 2022

## PD-1 agonist class has shown commercially meaningful outcomes (ACR50 and ACR70) regardless of prior treatment



1. Phase 3 registrational data from product labels; 15mg dose for upadacitinib in STUDY V.2. Tocilizumab (8mg/kg dose); Smolen J (2008) The Lancet Vol 371: 987-997; Emery, P. (2008) ARD 67(11): 1516-1523; Adalimumab; Keystone E (2004) Arthritis & Rheumatism Vol 50 #5:1400-1411; Rituximab; Cohen S (2006) Arthritis & Rheumatism Vol 54 #9: 2793-2806 3. Tuttle, J. (2023) NEJM;388:1853-62. Note patient population is 63% MTX-IR, 37% b/tsDMARD-IR; Similar efficacy was observed regardless of prior b/tsDMARD use.

## Substantial opportunity for new class of biologics with differentiated outcomes in moderate and severe UC



**>\$6.5bn US sales in "non-TNF" market (2028)<sup>2</sup>**

- UC prevalence growing faster than population

### **Fragmented market**

- Severe: No clear choice after TNF failure
- Moderate: balance convenience and safety

### **PD-1 agonist: Significant potential to differentiate from insufficient SOC**

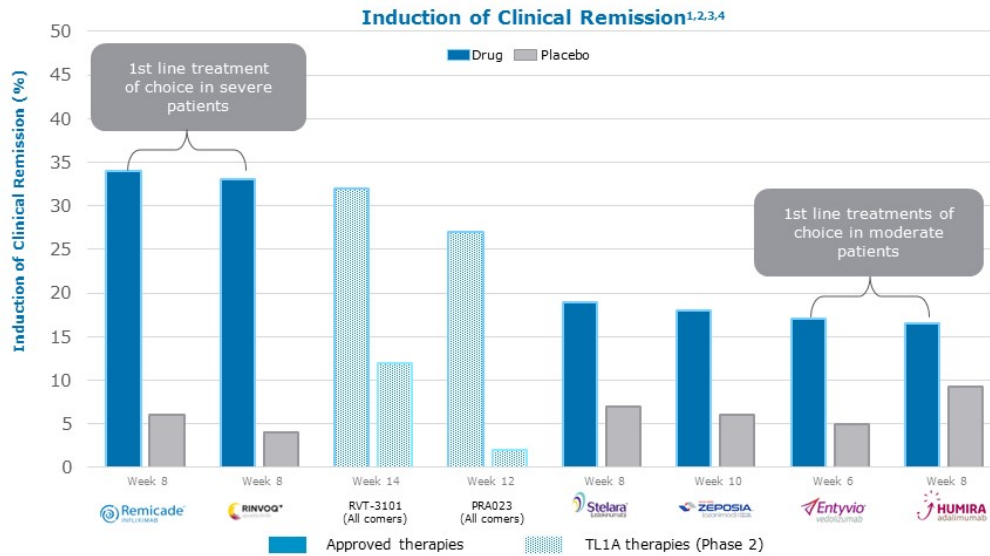
- Deeper responses: induction and/or maintenance
- Broader patient population: TNF-refractory
- Restore immune balance
- Emerging profile allows potential for combinations in future

1. Yu H (2018) Aliment Pharmacol Ther. 2018 Feb;47(3):364-370. doi: 10.1111/apt.14430; 2. Evaluate Pharma; Note: Targeted therapy – biologic/targeted small molecule drug, 2L – 2nd line



## UC lacks highly effective treatment options to induce and maintain clinical remission

Following remission on induction therapy, one third to one half of patients relapse within 1 year



1. Phase 3 registrational data from product labels; 2 Prometheus Bioscience corp. presentation Mar 2023; 3. Roivant corp presentation Jan 2023; 4. Remission measured using modified Mayo Score, except for Remicade, Humira and Entyvio which used full Mayo Score

## Rosnilimab targets PD-1+ T cells broadly impacting pathogenic drivers of autoimmune & inflammatory diseases

PD-1 agonists deplete and agonize PD-1+ T cells, in both inflamed tissue and the periphery

Rosnilimab, a best-in-class PD-1 agonist, reduces T cell migration, proliferation & cytokine secretion and reduces plasma cell generation & autoantibody levels

Translational and clinical data support rosnilimab's potential for deep responses across heterogenous patient populations while restoring immune balance in RA and UC

RA: global Phase 2b trial initiated Q3:23 with top-line data mid:25  
UC: global Phase 2 trial initiating Q4:23 with top-line data H1:26