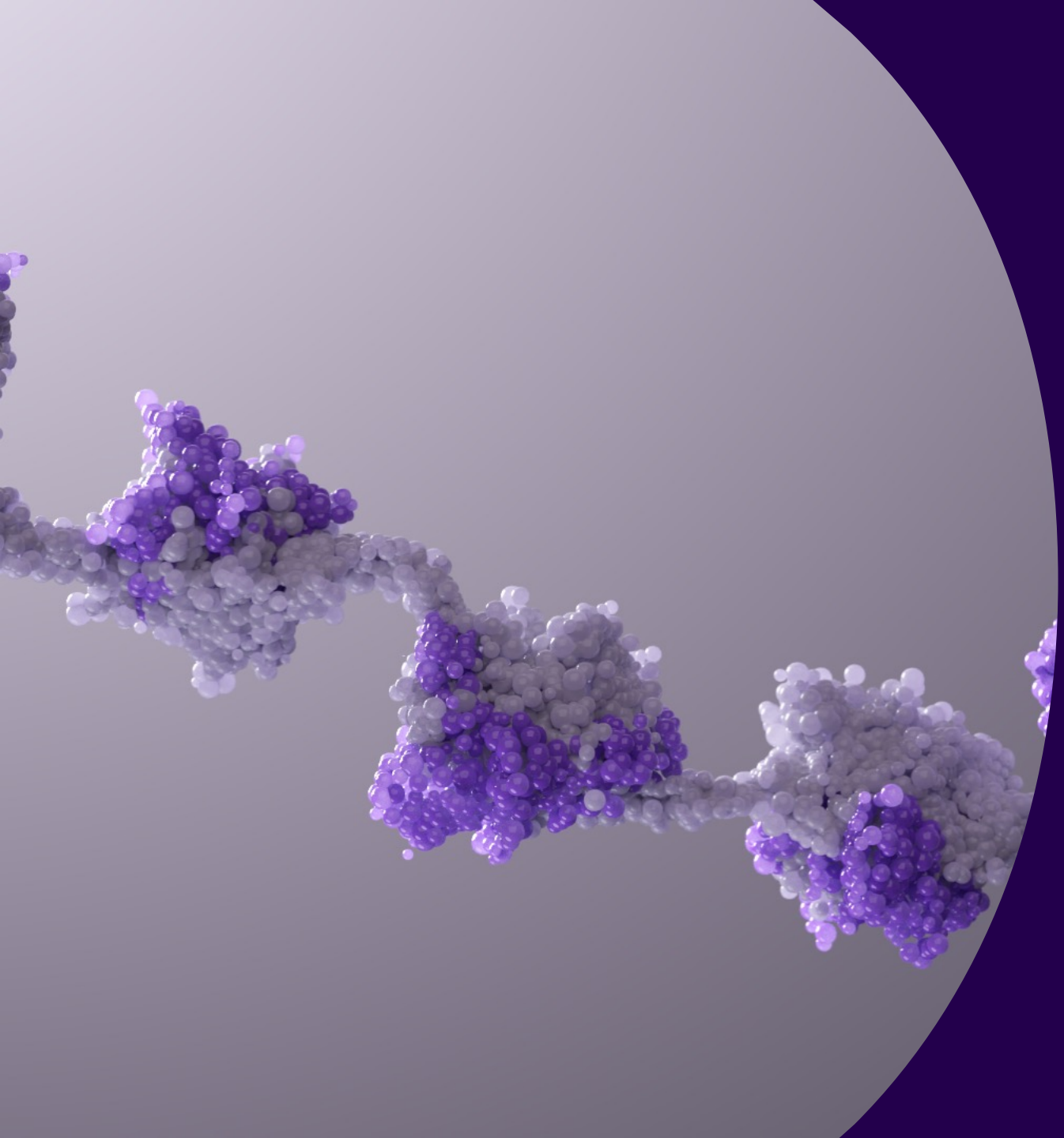

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R&D Day

Play to Win

New York, NY

December 7, 2023

Forward-looking statements

This document contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. These statements include projections and estimates and their underlying assumptions, statements regarding plans, business transformations, objectives, intentions and expectations with respect to future financial results, events, operations, services, product development and potential, and statements regarding future performance. Forward-looking statements are generally identified by the words "expects", "anticipates", "believes", "intends", "estimates", "plans", "potential", "outlook", "guidance" and similar expressions. Although Sanofi's management believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Sanofi, that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include among other things, the uncertainties inherent in research and development, future clinical data and analysis, including post marketing, decisions by regulatory authorities, such as the FDA or the EMA, regarding whether and when to approve any drug, device or biological application that may be filed for any such product candidates as well as their decisions regarding labelling and other matters that could affect the availability or commercial potential of such product candidates, the fact that product candidates if approved may not be commercially successful, the future approval and commercial success of therapeutic alternatives, Sanofi's ability to benefit from external growth opportunities, to complete capital markets or other transactions and/or obtain regulatory clearances, risks associated with developing standalone businesses, risks associated with intellectual property and any related pending or future litigation and the ultimate outcome of such litigation, trends in exchange rates and prevailing interest rates, volatile economic and capital market conditions, cost containment initiatives and subsequent changes thereto, and the impact that pandemics, political disruption or armed conflicts or other global crises may have on us, our customers, suppliers, vendors, and other business partners, and the financial condition of any one of them, as well as on our employees and on the global economy as a whole. The risks and uncertainties also include the uncertainties discussed or identified in the public filings with the SEC and the AMF made by Sanofi, including those listed under "Risk Factors" and "Cautionary Statement Regarding Forward-Looking Statements" in Sanofi's annual report on Form 20-F for the year ended December 31, 2022. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

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Agenda

R&D Day – December 7th

8:30-8:35 Introduction
Eva Schaefer-Jansen

8:35-9:00 Play to Win - Next Chapter of Growth
Leveraging innovation to drive growth
Paul Hudson
Transforming R&D to become an Immunology powerhouse
Houman Ashrafian

9:00-9:40 Unlocking the full value of Sanofi Immunology (Part 1)
Addressing key pathways in Immuno-Inflammation to transform the practice of medicine
Naimish Patel
Multi-indication assets to drive future growth
Shaju Backer

9:40-10:00 Q&A

10:00-10:15 Break

10:15-10:45 Unlocking the full value of Sanofi Immunology (Part 2)
Physician perspective on MS
Sharon Stoll
Addressing high unmet needs in neuro-inflammation through innovative mechanisms
Erik Wallstroem

10:45-11:15 Transforming COPD treatment paradigm
Expanding leadership in respiratory
Manuela Buxo
Physician perspective on COPD
MeiLan Han, Elizabeth Laws, Brian Foard

11:15-11:30 Q&A

11:30-11:45 Break

11:45-12:20 Charging our R&D engine to step-up productivity
Leading in Immunology Research
Frank Nestle
Advancing a productive and maturing development pipeline
Dietmar Berger
Employing AI to increase R&D productivity
Helen Merianos

12:20-12:25 Concluding remarks
Houman Ashrafian

12:25-12:45 Q&A

12:45-14:00 Lunch with Sanofi senior management

14:00-15:50 Scientific deep-dive sessions
Immunology and Neurology discussions with R&D leadership

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Leveraging innovation to drive growth

Paul Hudson

Chief Executive Officer

Topics for discussion today

1. Greater insight into our *pipeline priorities and growth drivers*
2. Data that underpin our decision to *invest strategically in R&D*
3. Actions we are taking to *improve R&D productivity*
4. Progress towards our ambition to become the first pharma company *powered by AI at scale*

We are a *development-driven*, *tech-powered* biopharma company committed to *serving patients* and *accelerating growth*.

Looking back at *Play to Win 2019* priority assets

	Planned submission as shown in CMD 2019	Status
BIVV001 (ALTUVIIIO)	**2022e**	Approved on time
fitusiran	**2021e**	Potential U.S. submission in 2024
SERD (amcenestrant)	**2021e**	*Stopped early*
venglustat	**2022e**	*Stopped early (ADPKD)*
nirsevimab (Beyfortus)	**2023e**	Approved on time
BTKi (tolebrutinib)	**2024e**	Phase 3 on-going

Strategic R&D portfolio transformation propelling an industry-leading immunology pipeline

Immunology & Inflammation

Atopic dermatitis
- amlitelimab
- IRAK4 degrader
- lunsekimig

HS
- amlitelimab
- IRAK4 degrader
- Anti TNFa/OX40L

Psoriasis
- Oral TNFR1si

PN/CSU
- Dupixent
- rilzabrutinib

Asthma
- amlitelimab
- lunsekimig
- rilzabrutinib

COPD
- Dupixent
- itepekimab
- lunsekimig

CRSwNP
- lunsekimig

IBD
- Dupixent
- Anti-TL1A
- eclitasertib
- Oral TNFR1si

RA
- Oral TNFR1si

SLE/Sjogren's
- frexalimab

Neuro-inflammation

Multiple Sclerosis
- tolebrutinib
- frexalimab
- SAR443820 (RIPK1i)

ALS
- SAR443820 (RIPK1i)

CIDP
- riliprubart

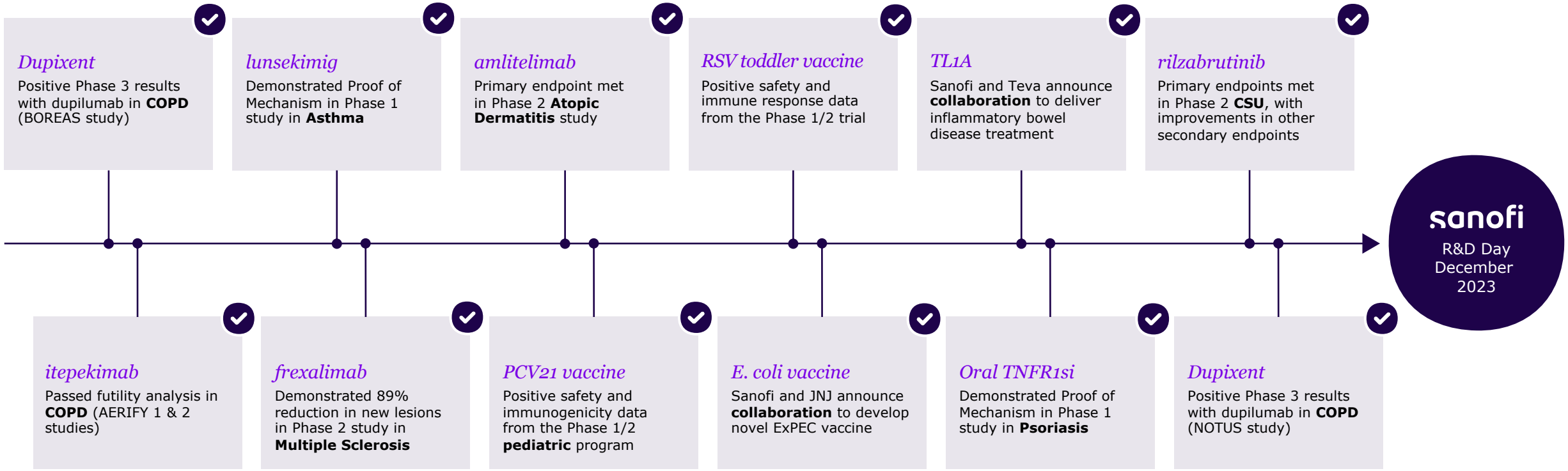
Transplant & Type 1 Diabetes

Transplant
- Rezurock
- riliprubart

Type 1 Diabetes
- Tzield
- frexalimab

Includes indications currently explored.

Outstanding pipeline news flow in 2023



Unprecedented pipeline of *blockbuster opportunities*

Potential pipeline-in-a-product

€2-5bn peak sales potential each

Pipeline asset	Indication(s)	Expected first submission
tolebrutinib *(BTKi)*	Full spectrum of MS - *Ph. 3*	2024
rilzabrutinib *(BTKi)*	ITP - *Ph. 3* Asthma - *Ph. 2*	2024 *(ITP)*
itepekimab *(Anti-IL-33)*	COPD former smokers - *Ph. 3*	2025
lunsekimig *(Anti-IL13/TSLP)*	Asthma - *Ph. 2b*	2027+
IRAK4 degrader	AD, HS - *Ph. 2*	2027+
Anti-TL1A	IBD - *Ph. 2*	2027+

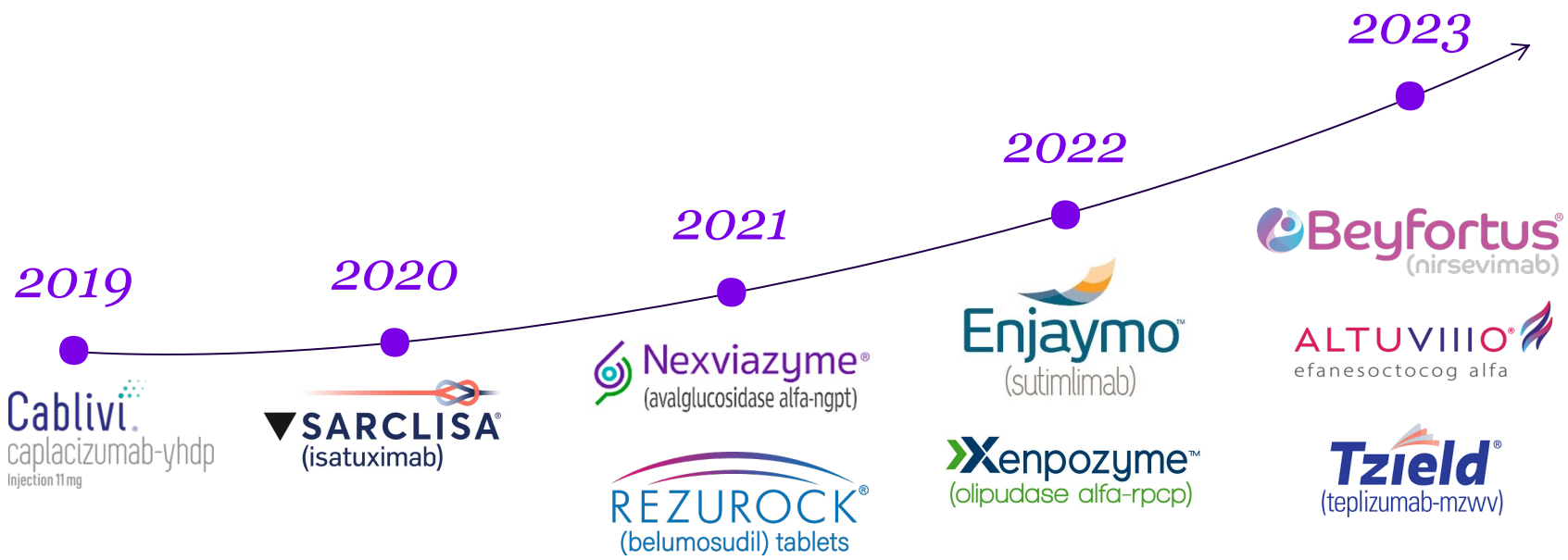
Pipeline asset	Expected submission
ExPEC vaccine - *Ph. 3*	2027+
RSV mRNA OA combo vaccine - *Ph. 1/2*	2027+
Acne mRNA vaccine - *Ph. 1/2*	2027+

€5bn+ peak sales potential each

Pipeline asset	Main indications	Expected first submission
amlitelimab *(Anti-OX40L)*	Atopic dermatitis - *Ph. 3*	2027
	Asthma - *Ph. 2b*	
frexalimab *(Anti-CD40L)*	RMS, SPMS - *Ph. 3*	2027 *(RMS)*
	Type 1 Diabetes - *Ph. 2b*	
SAR441566 *(Oral TNFR1si)*	Rheumatoid arthritis, Psoriasis - *Ph. 2b*	2027+
	IBD	

Note: non-exhaustive, non-risk-adjusted peak sales estimates, at CER, barring unforeseen events.

Steady stream of launches will drive sustained growth



Proven ability to accelerate and *execute on development* for internal & external assets

Leading commercial platform in immunology, vaccines and rare diseases to maximize opportunities & patient access

Building an *Immunology Powerhouse* driven by new launches, Dupixent and Vaccines

>€10bn

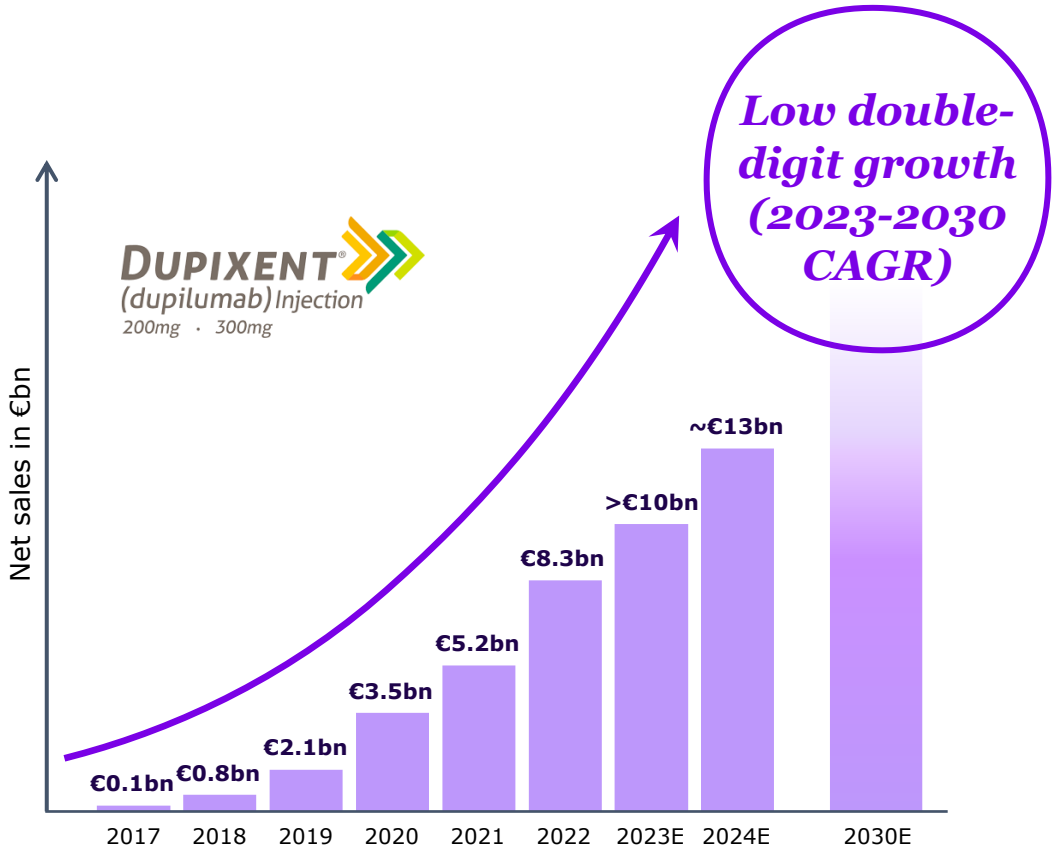
Sales contribution from Pharma launches by 2030[1]

Potential launches

tolebrutinib, itepekimab, amlitelimab, frexalimab, rilzabrutinib, lunsekimig, Oral TNFR1si

Already launched

ALTUVIIIO, TZIELD, Sarclisa, Nexviazyme, Rezurock



>€10bn

Sanofi Vaccines sales by 2030

Already launched

Beyfortus

Vaccines Investor Event, June 29, 2023

Barring unforeseen events. 1 Risk-adjusted net sales, at CER. Pharma already launched also includes net sales from Xenpozyme, Enjaymo, Cablivi.

A development-driven, tech-powered biopharma company committed to serving patients and *accelerating growth*

Execute Play to Win

Continue to deliver on *Dupixent*

Reducing our cost structure, plans to save up to €2bn for reallocation by end-2025

Pharma launches contributing *>€10bn sales*[1] by 2030

Industry-leading immunology pipeline

12 new molecular entities with €2-5bn or €5bn+ peak sales potential

Driving long-term value

Intention to *separate Consumer Healthcare* at the earliest Q4 2024

Strong EPS rebound expected in 2025

Disciplined *capital allocation* strategy

Barring unforeseen events 1. Risk-adjusted net sales, at CER.

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Transforming R&D to become an Immunology powerhouse

Houman Ashrafian
Head of Research and Development

Introducing the team

Houman Ashrafian

Head of R&D

Naimish Patel

Head of Global Development for I&I

Shaju Backer

Global Franchise Head of Immunology

Erik Wallstroem

Head of Development, Neurology

Manuela Buxo

Global Head of Dupixent Franchise

Frank Nestle

Global Head of Research, Chief Scientific Officer

Dietmar Berger

Global Head of Development, Chief Medical Officer

Helen Merianos

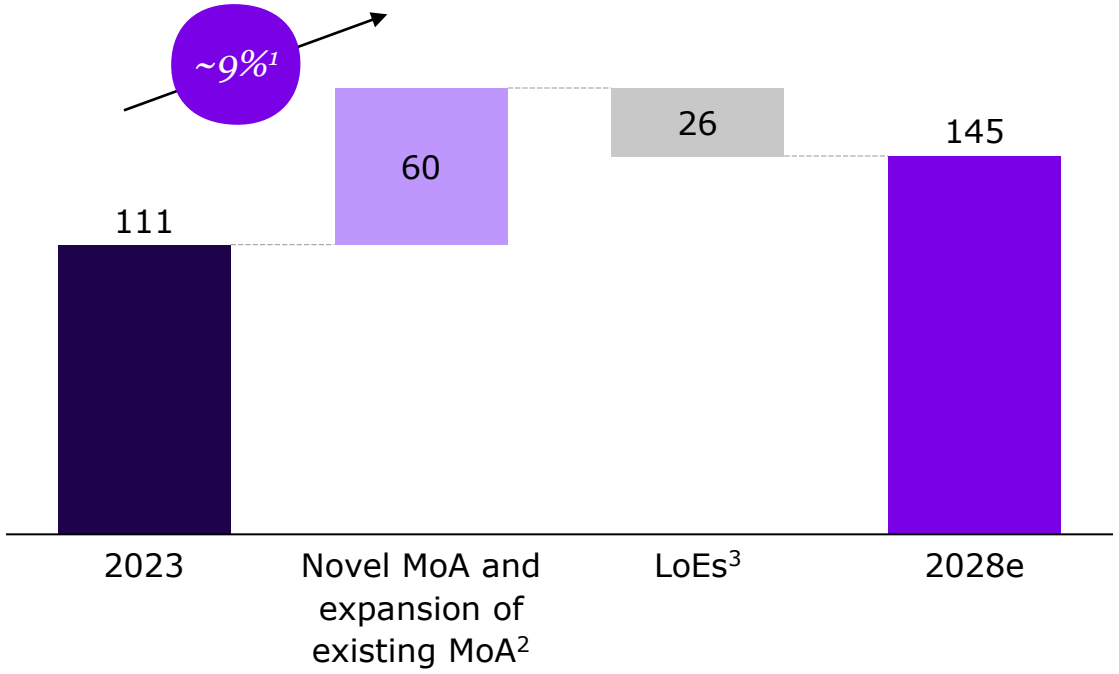
Global Head of R&D Portfolio Strategy

Impressions from my first months at Sanofi R&D

- *Exciting pipeline* with potential *FIC/BIC* late-stage assets, particularly building on our *I&I capabilities*
- Broad array of *leading-edge technology platforms* and deep understanding of *biological pathways*
- Proven track record in *combining internal and external innovation* with our leading *development capabilities*
- Early adopter of *Digital / AI at scale* across R&D value chain

We are uniquely positioned to win in the *I&I* market

Immunology & Inflammation market
(WW revenues – Advanced therapy $bn, 2023-2028e)



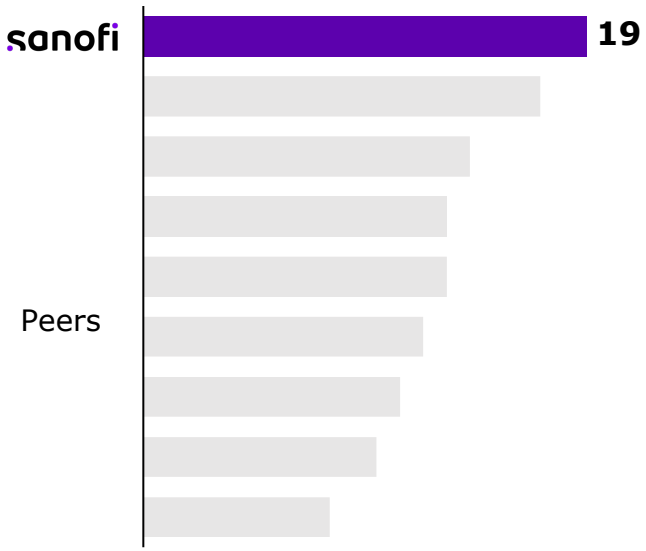
- *>70% of assets* achieve blockbuster status in large indications[4]
- *Multiple blockbusters* can coexist in the same indications
- Novel MoAs drive higher *biologics penetration*
- *Pipeline-in-a-product* opportunities

1. CAGR 2023-2028. 2. Novel MoAs: generate initial revenue in 2023+. 3. Declining revenue from 2023 to 2028. 4. Blockbuster is defined as an asset generating >$1bn revenue in a particular indication, only including assets that have launched by 10/24/2023 in the U.S. in specified indications. Indications surveyed: Rheumatoid arthritis, Psoriasis, Crohn's disease, Ulcerative colitis, Asthma, Atopic dermatitis. Note: advanced therapy only for traditional I&I markets (Rheumatology, Dermatology, Respiratory, Gastroenterology). Includes key biosimilar forecasts (TNF, IL-12/23, CD20, IL-6) from DataMonitor. Source: Evaluate Pharma consensus forecasts (as of October 2023), Datamonitor.

Sanofi portfolio positioned as *leading* I&I franchise

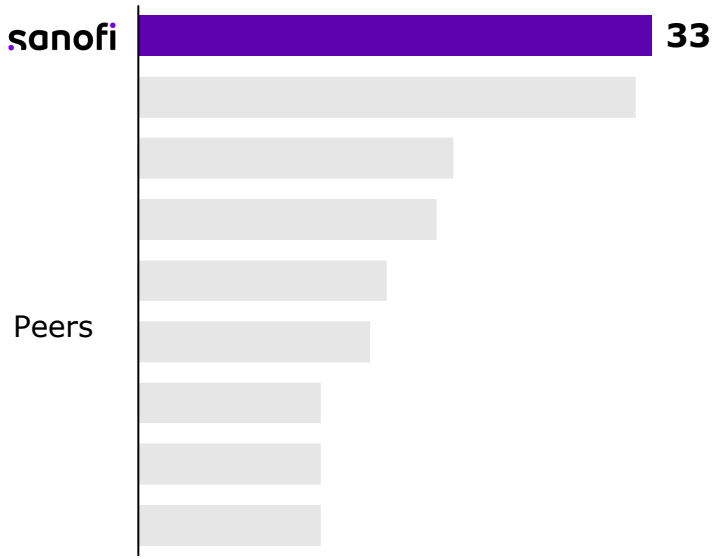
#1 *Total I&I assets*

Total I&I assets
Pipeline and commercial



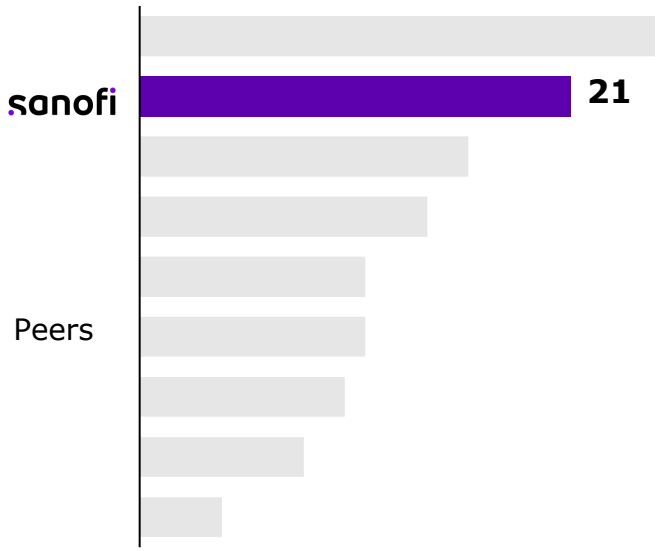
#1 *Asset-indication density*

Number of asset-indication pairs[1]
Pipeline



#2 *First-in-class assets*

Number of potential FIC asset-indication pairs[1]
Pipeline



1. Counting asset-indication pairs (an individual asset may be counted multiple times) and includes FIC in LCM (asset-indication pair is only counted if mechanism and indication are publicly known and that asset is the latest in development in that mechanism-disease); I&I indications include those within Dermatology, Respiratory, Rheumatology, GI and close adjacency disease areas. Source: L.E.K. analysis based on company publicly disclosed pipelines on website or investor materials.

We are *all-in on* Immunology, across therapeutic areas

I&I	Vaccines	Neuro-inflammation	Transplant & Type 1 Diabetes	Oncology	Rare Diseases	Other immune–mediated diseases
Sustain leadership in I&I and Vaccines		*Build up scale* in areas where we can leverage our I&I strengths			*Pursue opportunistically* building upon existing strength & capabilities	Potential *expansion* where *biologically & commercially* relevant, predominantly leveraging our *internal pipeline*

~80% of late-stage assets[1]

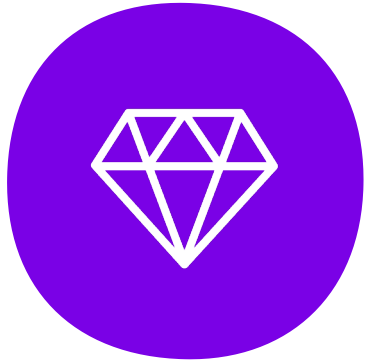
Focus on *FIC / BIC*

1. With at least one indication in I&I, Vaccines, Neuro-inflammation.

Key topics to prepare for the *future*

Peak investment

Multiple Phase 3 trials launching in parallel



Focus

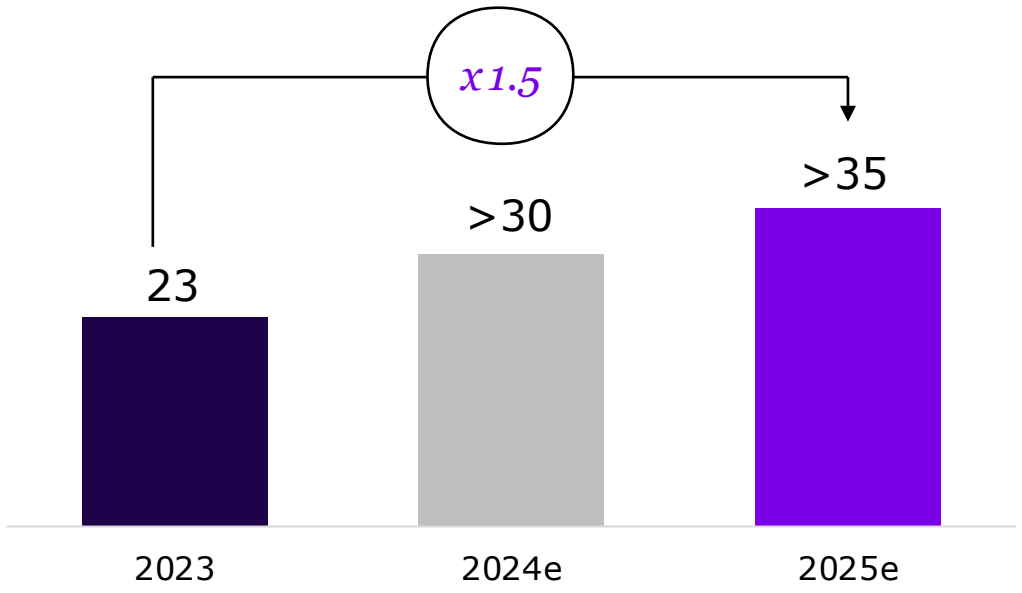
Breadth of platforms, sites and therapeutic areas

Pipeline sustainability

Fueled by in house research and external innovation

Launching *multiple Phase 3* trials in Immunology

Phase 3 projects[1]



Planned Phase 3 studies starts in 2024[2]

Name	Description	Indication
amlitelimab	Anti-OX40L mAb	AD
rilzabrutinib	BTKi	PN
rilzabrutinib	BTKi	CSU
frexalimab	Anti-CD40L mAb	RMS
frexalimab	Anti-CD40L mAb	nrSPMS
riliprubart	C1s inhibitor	CIDP
riliprubart	C1s inhibitor	CIDP – IVIg
SP0202	Next Generation Conjugate Vaccine	PCV21
SP0125	Live Attenuated Virus Vaccine	RSV toddler
SP0282[3]	Bioconjugate Vaccine	ExPEC

Barring unforeseen events. 1. A project can consist of 2 or several trials. 2. Study start defined as First Patient In. 3. Phase 3 costs to start in 2024 due to partnership closing in Q4 2023.

First impression where Sanofi oncology has a *right to win*

Our strategy in Oncology

Highest unmet needs of patients

Immune–mediated MoAs

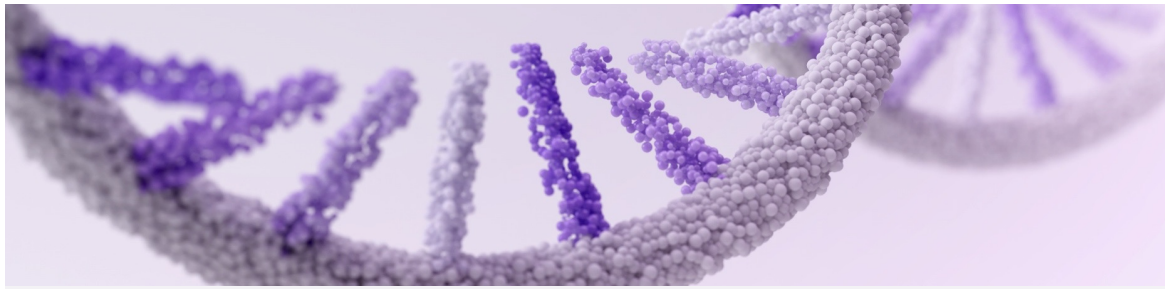
New & differentiated platforms

Select examples

- *Sarclisa:* Building a pipeline in Multiple Myeloma
- *NK cell engagers:* Harnessing the power of immune-mediated MoA (e.g., CD123 NKCE)
- *Differentiated ADCs:* Expanding our presence in GI and Lung (e.g., CEACAM5-TOPO1)

Sanofi to present clinical data at ASH 2023

Sustainable pipeline fueled by *in house research* and *external innovation*



- *Differentiated technology platforms*
  From small molecules to antibodies, mRNA, genomic medicine
- *First-in-class target combinations*
  Hitting multiple core pathways
- *Deep understanding of pathway biology*
  Strength in target identification and Precision Medicine

- *Strong track record in sourcing and launching external innovation*
  E.g., ALTUVIIIO, amlitelimab, Beyfortus, Rezurock, Tzield
- *Deeply rooted in the innovative healthcare ecosystem within France and across Europe*
  E.g., Strategic partnerships and academic alliances

Continued pipeline momentum driven by Immunology

	2024			2025		
Key pivotal readouts	*tolebrutinib*	Brain-penetrant BTKi for full spectrum of MS	RMS, nrSPMS	*itepekimab*	First-in-class IL-33 in COPD former smokers	COPD
Pipeline-in-a product Phase 2 readouts	*amlitelimab* (Anti-OX40L)	Durable disease modification in I&I diseases	Asthma	*SAR441566* (Oral TNFR1si)	Potential foundational oral regimen in I&I diseases	Psoriasis RA
				amlitelimab (Anti-OX40L)	Durable disease modification in I&I diseases	HS
Key Phase 2 readouts	*rilzabrutinib*	Asthma (HD)		*IRAK4 degrader*	AD, HS	
	Anti-TL1A	IBD (IA)		*Anti-TNFα/OX40L*	HS	

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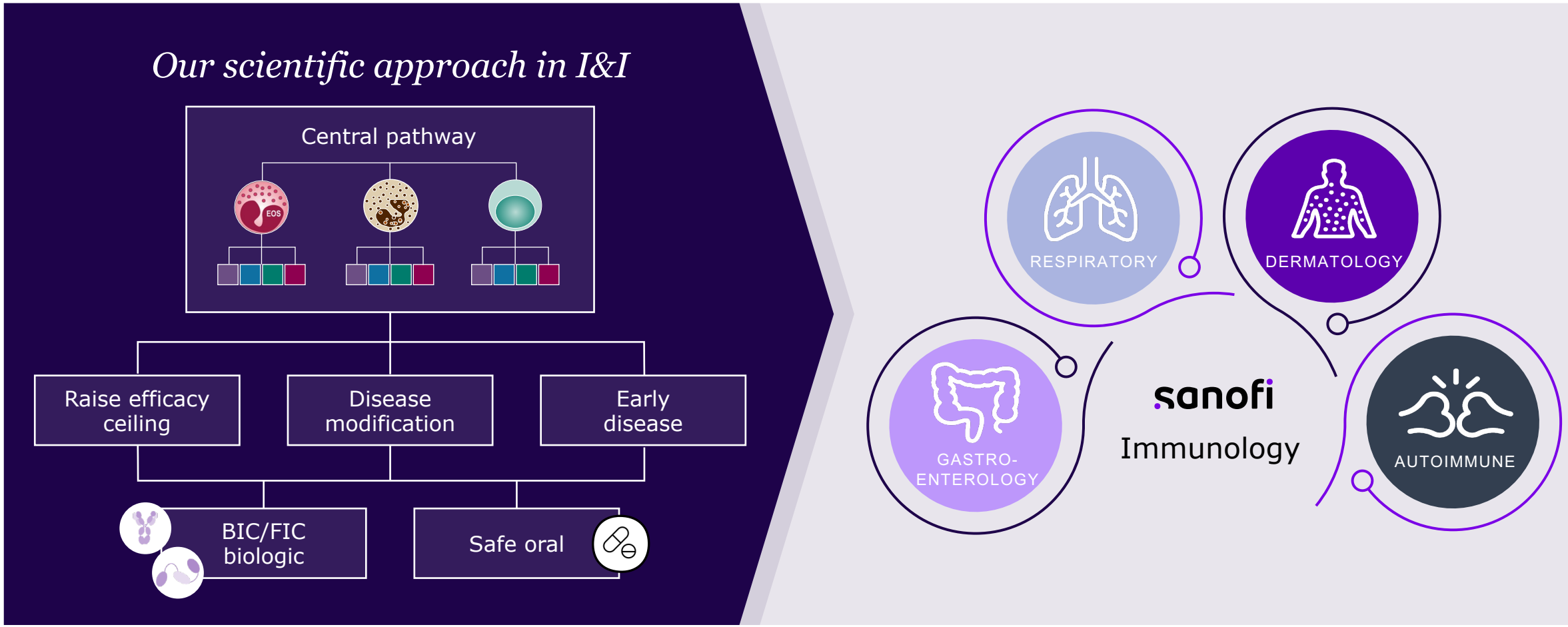
Addressing key pathways in Immuno-Inflammation to transform the practice of medicine

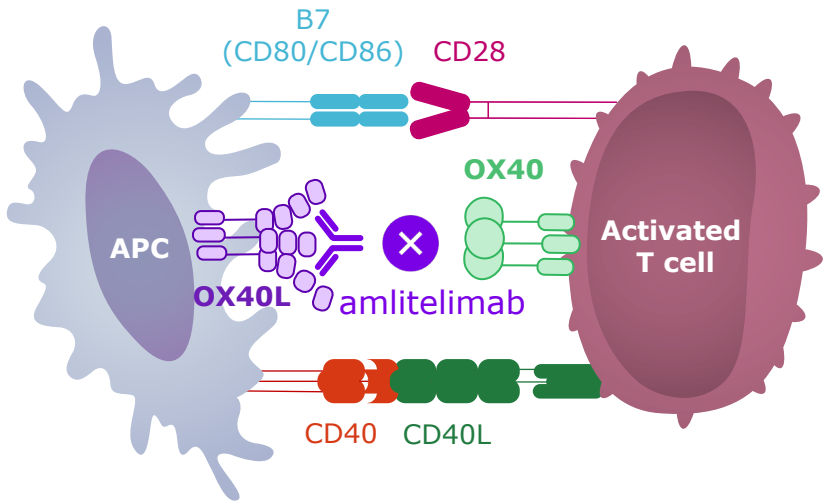
Naimish Patel

Global Head of Development
for Immunology and Inflammation

Unlocking the full value of Sanofi Immunology



Amlitelimab: Potential *best-in-class* OX40L pathway blockade, a key pathway in immune diseases



Blocking OX40L on antigen presenting cells, inhibits T-cell dependent inflammation *without immunosuppressive cell depletion*

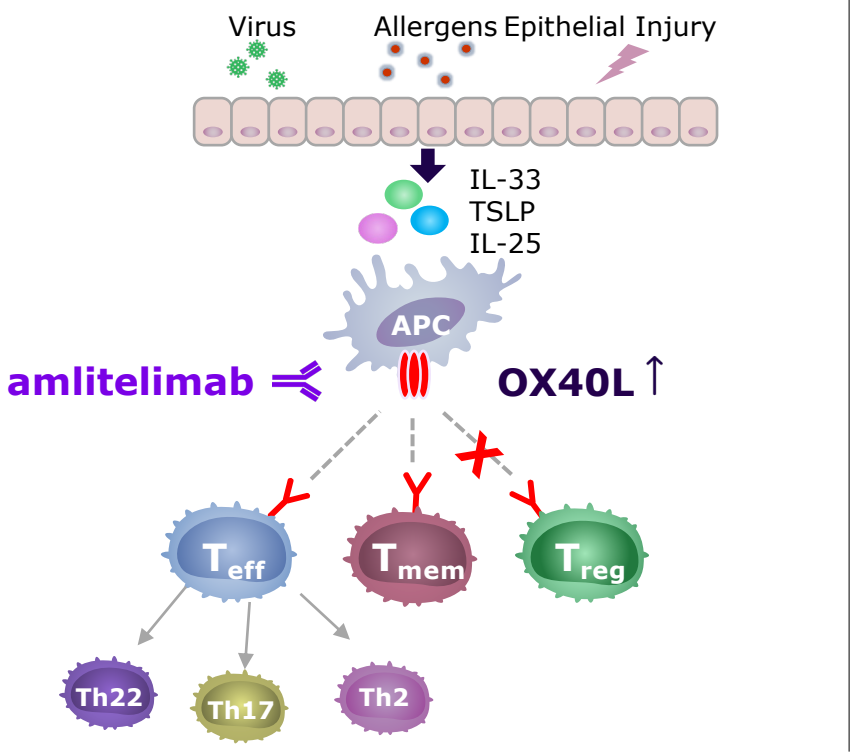
Efficacy across both Type 2 and non-Type 2 pathways, *broadly* eligible population

Pursuing durable *disease modification and long-term control* for best-in-disease Q12W dosing in AD

Central controller of inflammation, with potential for pipeline-in-a-product, leading to a *€5bn+ peak sales potential*

Amlitelimab is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

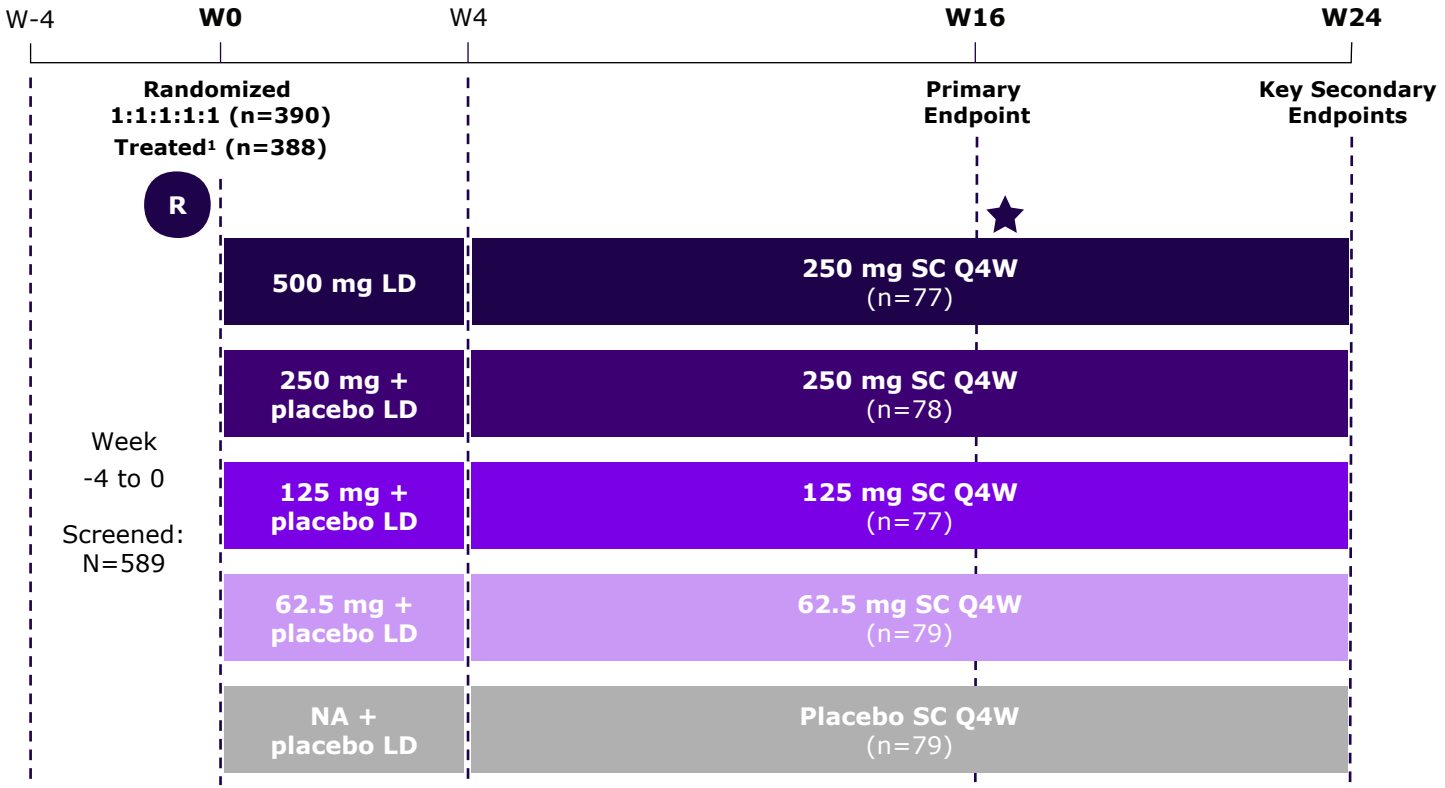
Amlitelimab: *Unique MoA* of blocking OX40L has clear advantages versus blocking OX40



- Anti-OX40L on APC, rebalancing the immune system without *target cell depletion*
- Targets Th2/Th17/Th22 for *broad indication* profile
- *OX40L blockade advantages over OX40 depletion*
  - OX40L expression limited to sites of inflammation,
  - Preserves T_{eff}, T_{mem} cells,
  - Preserves and activates T_{reg},
  - Avoids cytokine release (fever, chills).

Amlitelimab is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Comprehensive amlitelimab Phase 2b trial design in AD



STREAM-AD (NCT05131477). 1. Two patients found to be not eligible after randomization.
Amlitelimab is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Primary endpoint

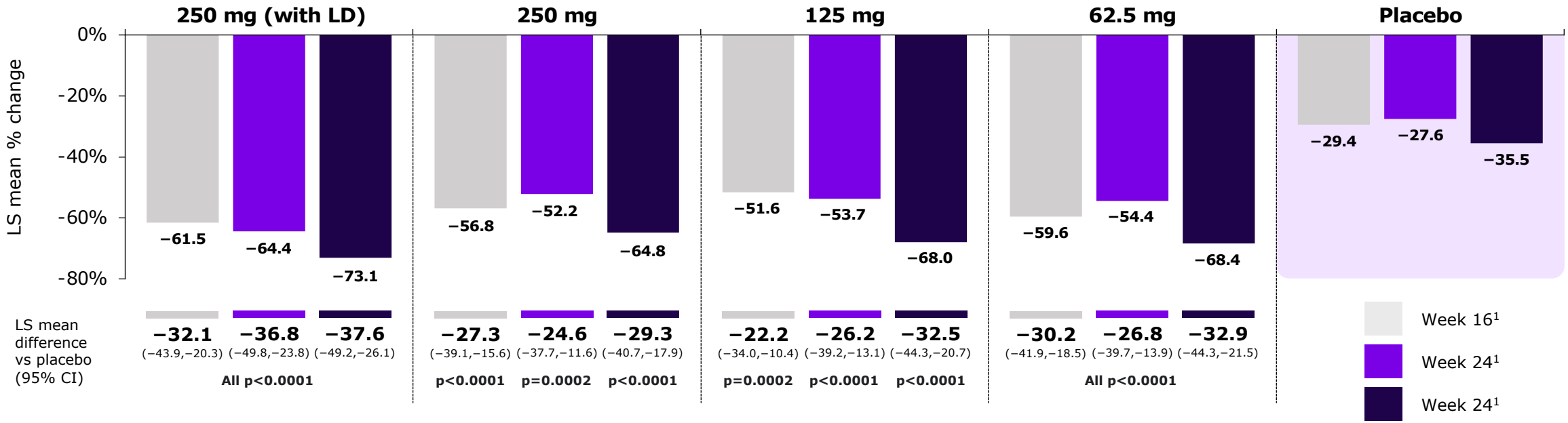
Percentage change in EASI from baseline to Week 16

Secondary endpoints include

- Percentage change in EASI from baseline to Week 24
- Percentage of patients with EASI-75 at Week 16/24
- Percentage of patients with IGA 0/1 at Week 16/24
- Incidence of TEAEs
- Change in soluble protein blood biomarkers
- ADA titers and incidence

Amlitelimab: Significant *efficacy* across doses, suggesting target saturation and potential for durable response

Percentage Change in EASI From Baseline at Weeks 16 and 24



- Study met primary and key secondary endpoints (percentage change in EASI), regardless of how rescue treatment was statistically handled and with the largest placebo-adjusted difference demonstrated using 'treatment policy' data across all doses
- 250 mg Q4W with LD dose showed greatest placebo-adjusted difference at Week 16, that continued to improve through Week 24

1. Week 16 and Week 24 data collected after early treatment discontinuation due to reasons other than lack of efficacy prior to endpoint timepoint are included. Data on or after rescue medication or prohibited medications impacting efficacy start date or after the date of treatment discontinuation due to lack of efficacy prior to endpoint timepoint, were set to missing and imputed by WOCF. Any other unobserved values or other missing data are imputed by multiple imputation. Data using treatment policy: all data are used for analysis, regardless of treatment discontinuation, regardless of rescue/prohibited concomitant medications use. Missing data are imputed by multiple imputation based on all patient's data.
Amlitelimab is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Generally *well-tolerated* across all dose arms

TEAEs through Week 24	amlitelimab pooled dose groups	Placebo
Number (%) unique patients (N=388)	**N=310**	**N=78**
Any TEAEs	209 (67.4%)	47 (60.3%)
Deaths	0	0
Any TEAE leading to treatment discontinuation	14 (4.5%)	5 (6.4%)

Most frequent TEAEs by PT through Week 24 (≥5% in pooled amlitelimab groups)	amlitelimab pooled dose groups	Placebo
Number (%) unique patients (N=388)	**N=310**	**N=78**
Worsening AD	53 (17.1%)	30 (38.5%)
Nasopharyngitis	34 (11.0%)	7 (9.0%)
COVID-19	24 (7.7%)	5 (6.4%)
Headache	19 (6.1%)	2 (2.6%)

1. Pooled PTs of "oral herpes", "herpes simplex reactivation", "herpes dermatitis" and "eczema herpeticum". 2. Including PTs of "conjunctivitis allergic", "conjunctivitis", "conjunctivitis bacterial". Amlitelimab is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Of patients who reported a TEAE: in the pooled amlitelimab groups 196 (93.8%) were mild or moderate, and in the placebo group 44 (93.6%) were mild or moderate

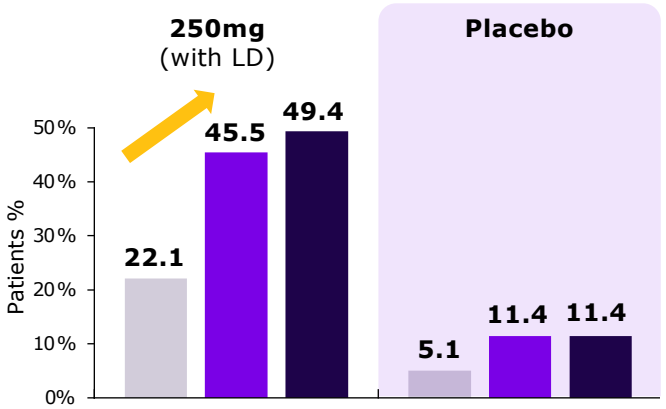
No reports of serious infections[1], severe injection site reactions or aphthous ulcers. No chills, pyrexia or influenza/influenza-like illness within 72 hours of injection

Low incidence of conjunctivitis[2], balanced across treatment arms

Anti-drug antibodies levels were generally low and not found to impact the PK of amlitelimab

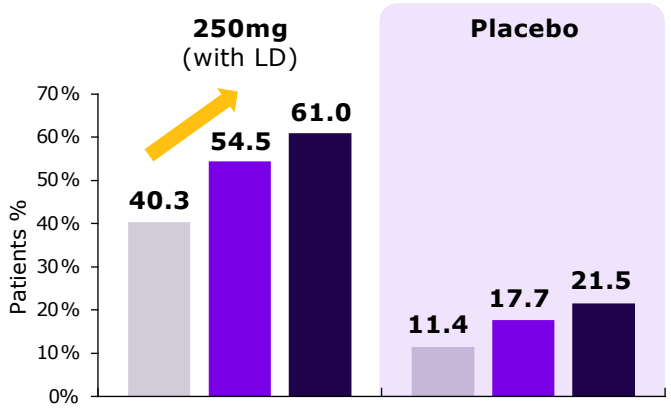
Amlitelimab shows significant *improvements* in signs and symptoms of atopic dermatitis

Percentage of patients achieving *IGA 0/1 at Weeks 16 and 24*



Proportion difference vs. placebo (95% CI)	250mg (with LD)		Placebo
	17 (6,27)	34 (21,47)	38 (25,51)
	p=0.0022	p<0.0001	p<0.0001

Percentage of patients achieving *EASI-75 at Weeks 16 and 24*



Proportion difference vs. placebo (95% CI)	250mg (with LD)		Placebo
	29 (16,42)	36 (23,50)	39 (25,53)
		All p<0.0001	

Week 16[1] Week 24[1] Week 24[2]

Results support the clinically *meaningful efficacy* with regards to regulatory accepted endpoints

Best efficacy observed in high dose regimen with loading dose, showing progressive improvements to Week 24

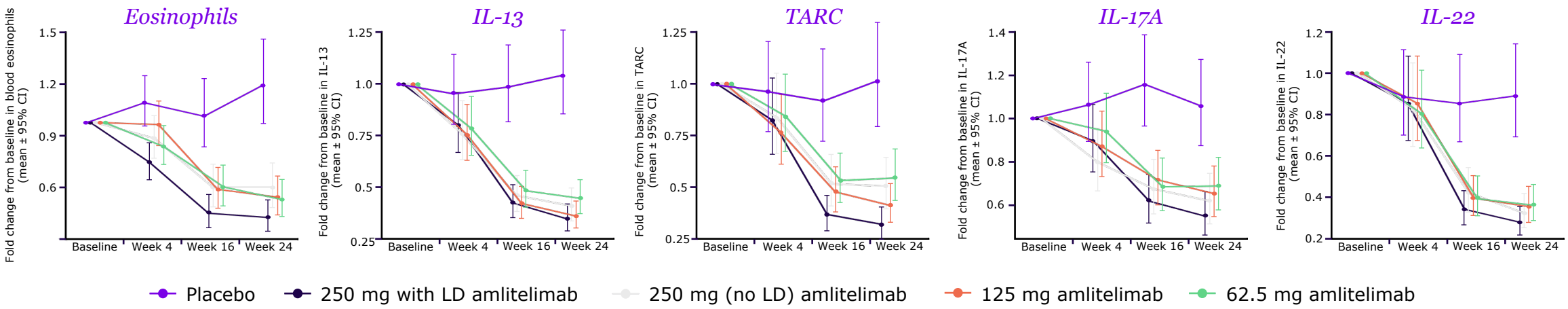
Opportunity for *reducing treatment dosing frequency*

1. Data collected after early treatment discontinuation due to reasons other than lack of efficacy prior to endpoint timepoint are included. Data on or after rescue medication or prohibited medications impacting efficacy start date or after the date of treatment discontinuation due to lack of efficacy prior to endpoint timepoint, were considered as non-responders. Any other unobserved values or other missing data are considered as non-responders at Week 16 and Week 24. 2. All data are used for analysis regardless of treatment discontinuation, regardless of rescue/prohibited concomitant medications use. Missing data are considered as non-responders at Week 16/Week 24.
Amlitelimab is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Amlitelimab demonstrates a *potent* effect on key biomarkers elevated in atopic dermatitis

- Amlitelimab treatment reduced biomarkers elevated in AD including Th2-related IL-13 and TARC, Th17/Th22-related IL-17A and IL-22 and notably led to decreased eosinophil counts
- Amlitelimab treatment substantially reduced these biomarkers across all doses at Weeks 16 and 24
- Greatest observed reduction in the 250 mg with LD arm, with consistent dose-dependent trend, and a substantial decrease in eosinophils as early as Week 4

Fold-change from Baseline to Week 24

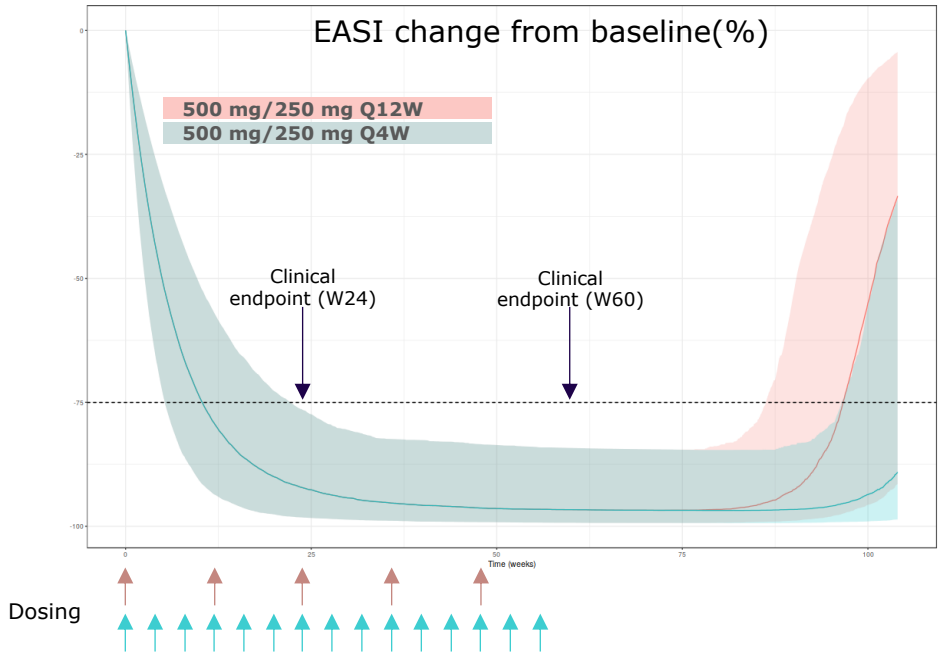


Amlitelimab is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Amlitelimab: Durable disease control with potential for *best-in-disease* dosing at Q12W

Best-in-disease dosing with Q12W:
Q12W efficacy predicted equivalence to Q4W

Population Pharmacokinetic/EASI model



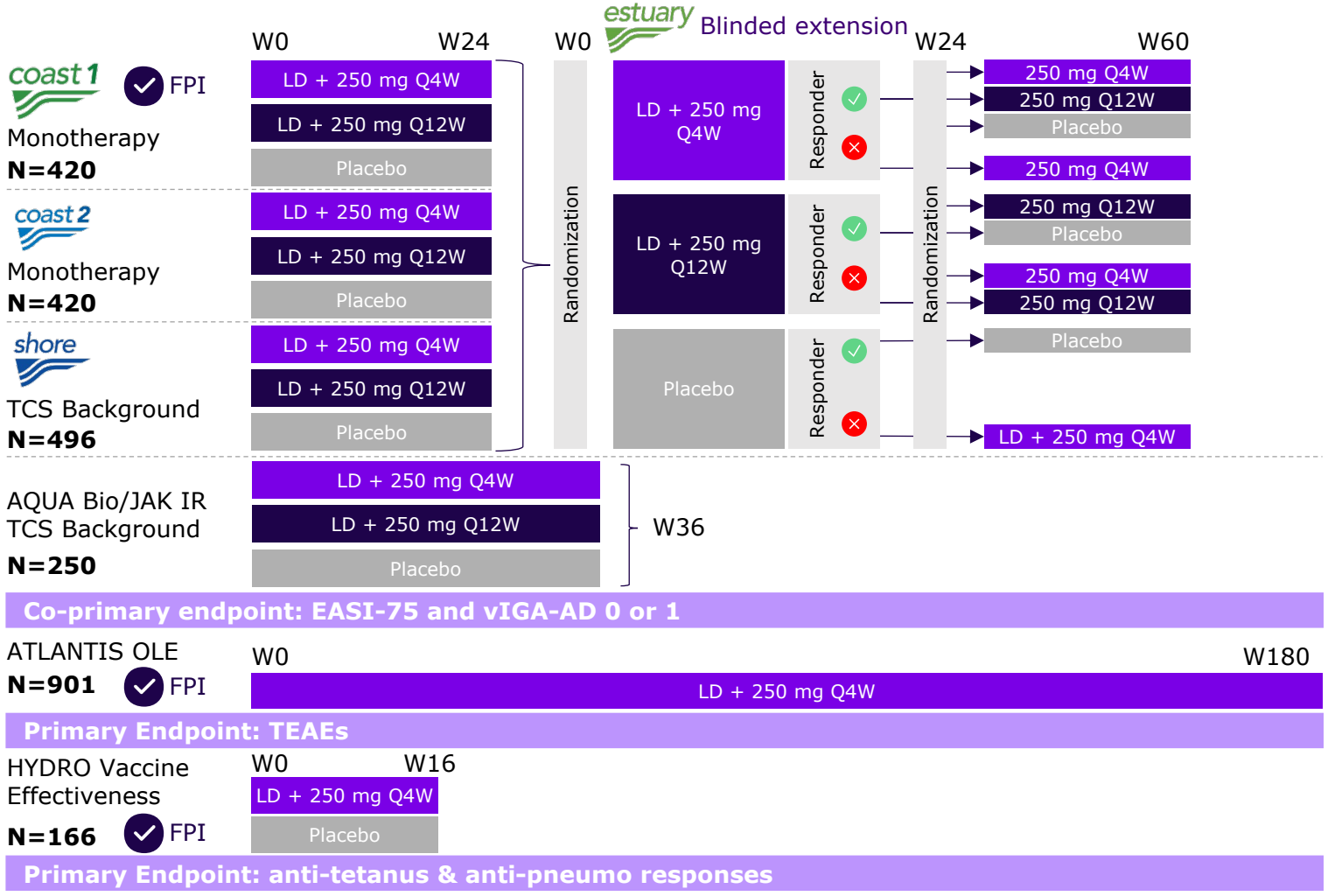
Additional data from Part B follow-up predicts *sustained effect* when dosing is stopped

Pharmacokinetic/Pharmacodynamic modeling suggests the highest dose plus loading dose followed by Q12W dosing will give *equivalent efficacy* to the highest dose given Q4W

PK/PD modeling also predicts *sustained effect* when dosing is stopped suggesting potential for durable disease control

Amlitelimab is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Amlitelimab: Comprehensive AD development program ensures *robust data package* at launch



- Unprecedented *Q12W extended* interval dosing from initiation & as maintenance therapy
- Dedicated study in *Bio- or -JAKi-IR patients*
- Combined investigation in *adults & adolescents*
- Most *extensive biomarker* plan in AD
- Up to *5-year safety* data at launch

Amlitelimab is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Amlitelimab: Potential *Pipeline-in-a-product* targeting core central pathway

Indication	Status	Clinical evidence	Eligible population	Next milestone
AD	Phase 3	Statistically significant improvements in overall efficacy on EASI and IGA scores at 24w	**3.0M**	Phase 3 data in 2026 Submission in 2027
Asthma	Phase 2b	Effect on T2 and non-T2 biomarkers in AD	**1.9M**	Phase 2b data in H2 2024
HS[1]	Phase 2	Target residual B-cell signature[2] after TNF	**0.4M**	Phase 2 data in 2025

More than 5.3M eligible patients

Other indications currently explored adding potentially *another ~1.0M*

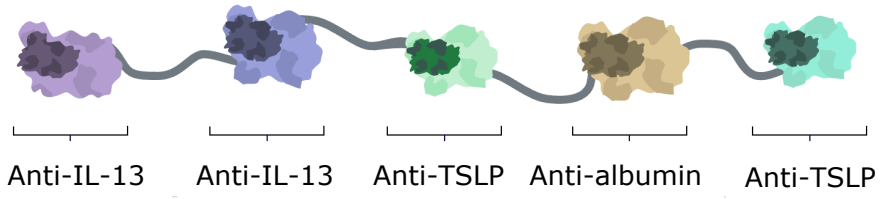
Indication	Preliminary evidence	Eligible population	Next milestone
Alopecia Areata	↑ Expression correlated with AA severity (SALT)	**0.6M**	Phase 2 start **in 2024**
Celiac disease	Potential to modulate gluten-specific CD4 T cells	**0.2M**	
Systemic Sclerosis	↑ Soluble Ox40L predictive of pulmonary worsening	**0.2M**	

- ✓ Strong science with potential for best-in-class efficacy
- ✓ Fully owned
- ✓ Potential pipeline-in-a-product

>€5bn peak sales potential

Advanced therapy eligible patients across U.S., EU5 (France, Germany, UK, Spain, Italy) and Japan. Additional details in Epidemiology Appendix. 1. Moderate to severe patients. 2. https://pubmed.ncbi.nlm.nih.gov/36689500/.
Amlitelimab is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Lunsekimig: Anti-IL-13/TSLP Nanobody® VHH shows potential to break *efficacy ceilings* in type 2 inflammation and beyond



Combining both mechanisms could potentially lead to *synergistic effects*

Exploring *multiple* respiratory indications and beyond

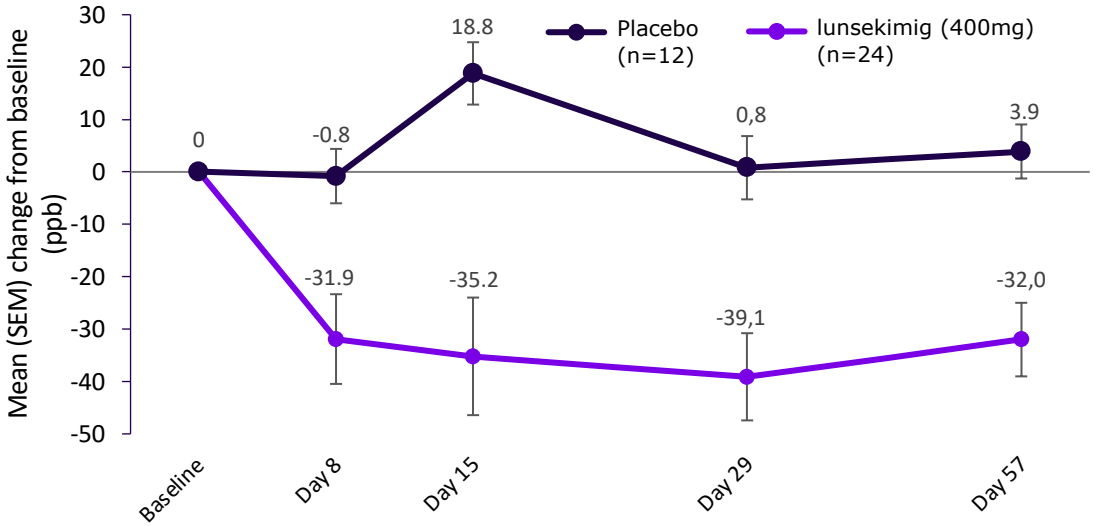
Potential to suppress airway inflammation and preserve airway function in asthma

Best-in-disease potential with *€2-5bn peak sales*

Lunsekimig is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

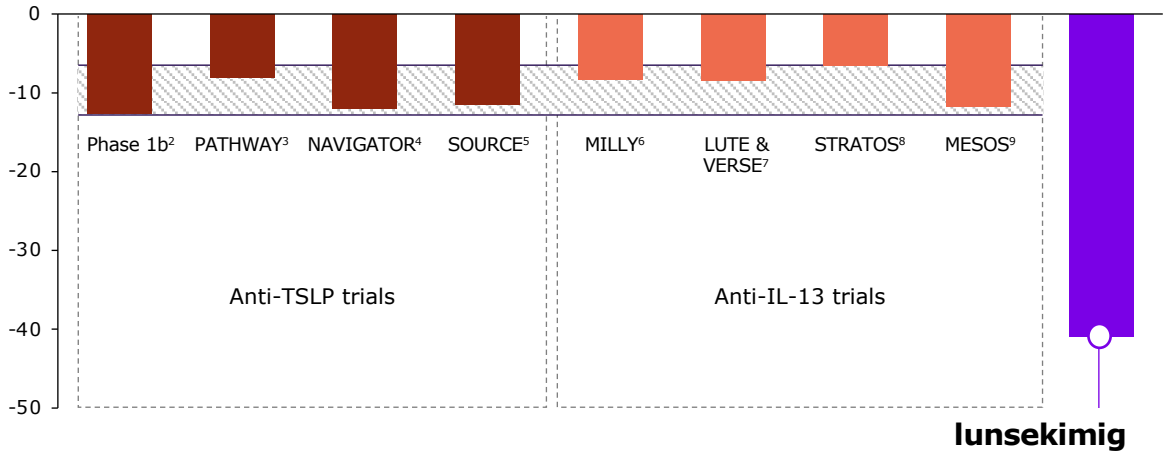
Lunsekimig: Phase 1b data in asthma supports potential *best-in-class* profile in airways diseases

FeNO change from baseline to Day 57



Confirmed improvement in FeNO, clinically relevant biomarker for type 2 airway inflammation[1]

Results of lunsekimig on FeNO suggest a synergistic effect of combining TSLP or IL13[2-10]



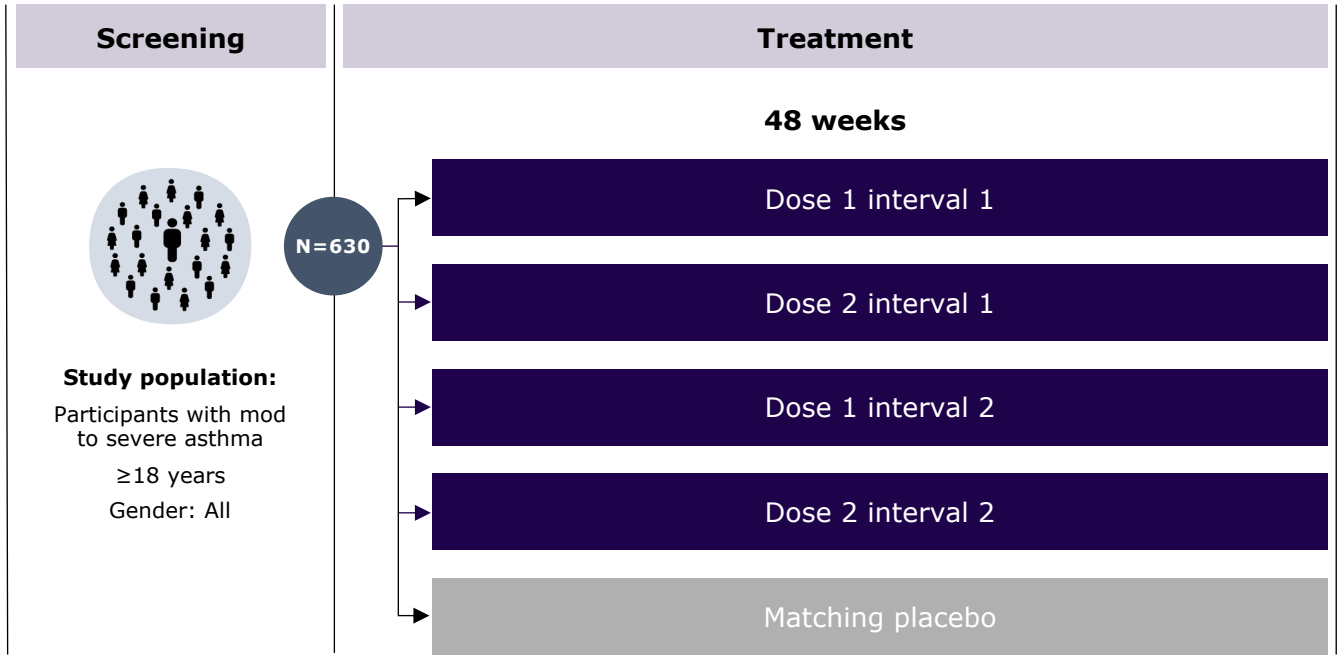
–40.9 ppb (90% CI: –55.4 to –26.4)[11]

Reductions in FeNO far greater than what has been observed in trials of anti-IL13 or anti-TSLP alone in asthma[12]

1. Raw data of FeNO change from baseline. 2. Gavreau GM, et al NEJM. 2014;370:2102-10. 3. Corren JC, et al. NEJM. 2017;377:936. 4. Menzies-Gow A, et al. NEJM. 2021;384:1800-09. 5. Weschler M, et al. Lancet Respir Med. 2022;10:650-60. 6.Corren JC, et al. NEJM. 2011;365:1088-98. 7. Austin CD, et al. Clin Exp Allergy. 2020;50:1342-51. 8. Hanania NA, et al. Thorax. 2015;70:748-56. 9. Panettieri RA, et al. Lancet Respir Med. 2018;6:511-25. 10. Russell RJ, et al. Lancet Respir Med. 2018;6:499-510. 11. Difference vs. placebo estimate from a mixed-effects model over time taking into account baseline FeNO and sex as co-variates. 12. The clinical significance of FeNO is under investigation. Not head-to-head comparisons, patient populations and baseline characteristics may differ between studies. Estimates of FeNO change from baseline versus placebo derived from published data.
Lunsekimig is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Lunsekimig: Asthma Phase 2b *first-patient-in achieved*, with data expected in 2026

Phase 2b, double-blind, placebo-controlled, parallel-group, 5-arm study AIRCULES



AIRCULES (NCT06102005). ACQ-5 is Asthma control questionnaire assessing symptoms, with lower score shows better asthma control.
Lunsekimig is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Primary endpoint

Annualized rate of asthma exacerbation events from baseline to Week 48

Secondary endpoints include

- Change from baseline in pre- and post-bronchodilator FEV1 from baseline to Week 48
- The absolute change in the percent predicted FEV1 from baseline (pre-BD and post-BD)
- Change from baseline in FeNO
- Annualized rate of loss of asthma control events (LOAC) events
- Proportion of participants with ≥ 0.5-point reduction in ACQ-5 score
- Monitoring of serum concentrations and Anti-drug antibodies

Lunsekimig: Strong science suggests *best-in-disease efficacy* for respiratory conditions

Indication	Status	Clinical data	Eligible population	Next milestone
Asthma	Phase 2b	–40.9 ppb FeNO reduction, best-in-disease data	**1.9M+**	Phase 2b data **in 2026**
High risk asthma	Phase 2			Study initiation **in 2024**
CRSwNP	Phase 2a	Tissue evidence of elevated TSLP and IL13 activity in nasal polyps[1]	**0.2M**	Study initiation **in 2024**

More than 2M eligible patients

Other indications currently explored adding potentially *another ~5M*

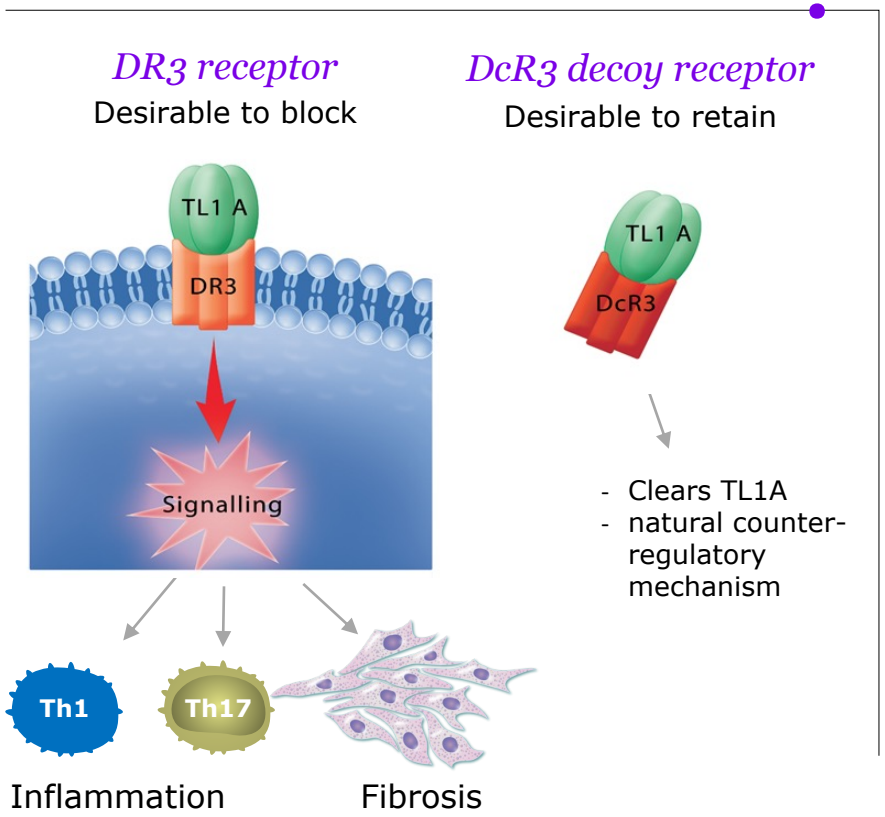
Indication	Eligible population	Next milestone
COPD[2]	**1.7M**	Phase 2b Asthma dose data to trigger COPD program
AD	**3.0M**	Phase 2b to start **in H2 2024**

- ✓ Leveraging proprietary Nanobody® platform to combine proven pathways
- ✓ Synergistic effect observed in Phase 1
- ✓ Fully owned
- ✓ Potential to work across respiratory diseases

€2-5bn peak sales potential

Advanced therapy eligible patients across U.S., EU5 (France, Germany, UK, Spain, Italy) and Japan. Additional details in Epidemiology Appendix. 1. https://www.jaci-global.org/article/S2772-8293(23)00048-6/pdf. 2. Biologics eligible regardless of phenotype. Lunsekimig is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Potential *best-in-class* anti-TL1A profile with differentiated antibody design



TL1A blockade is an emerging MOA in IBD and beyond with anti-inflammatory and anti-fibrotic activity

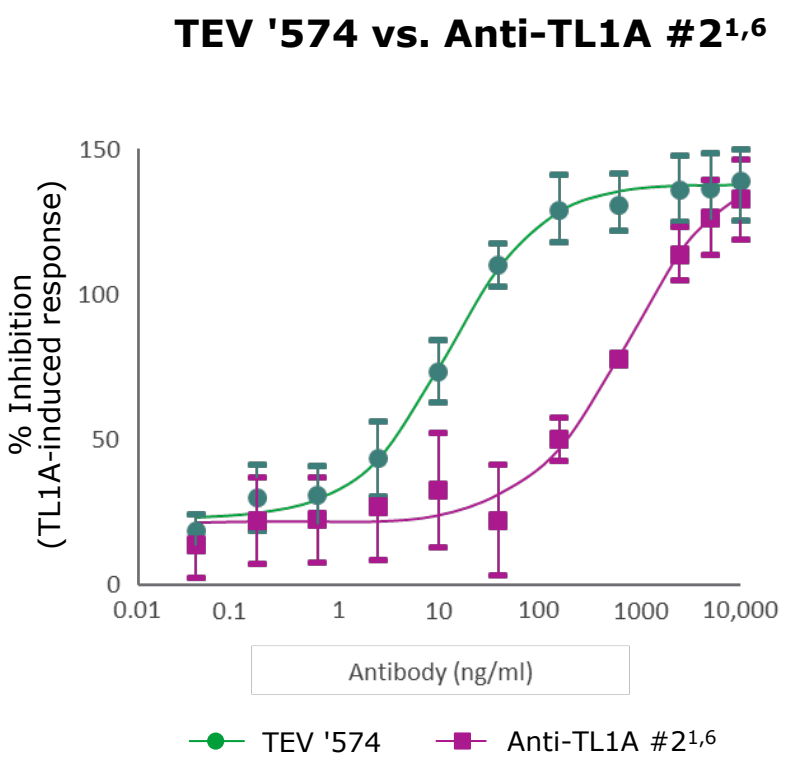
BIC potential due to greater in vitro potency and selectivity for DR3 receptor

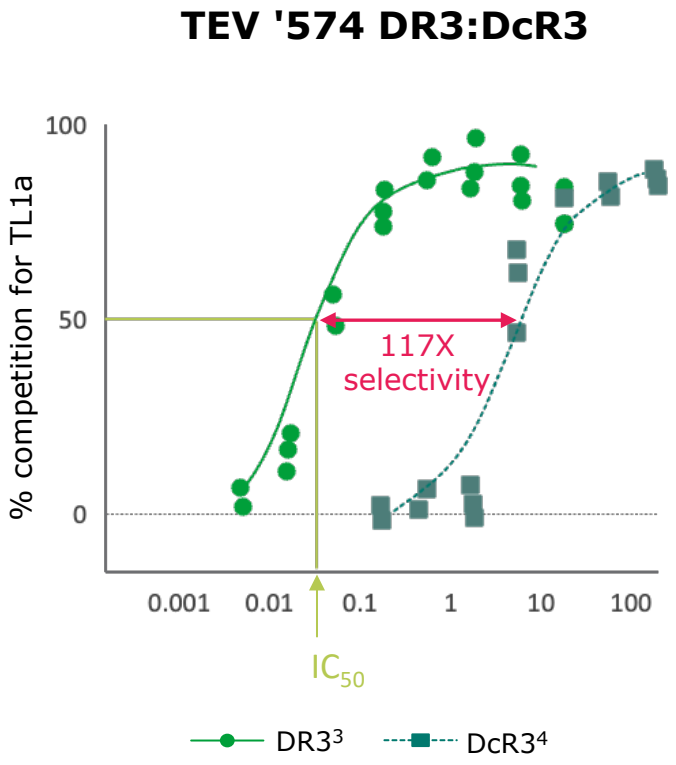
Favorable safety and tolerability profile, with low anti-drug antibody

Collaboration with Teva[1] Pharmaceuticals

1. Presentation available here https://s24.q4cdn.com/720828402/files/doc_presentations/2023/10/TL1A-Teva-Presentation-2023-10-04-website.pdf.
The Anti-TL1A is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Greater in vitro *potency and selectivity* for DR3 receptor





Higher *potency*[1,5] and *selectivity*[1,2] compared to competitors

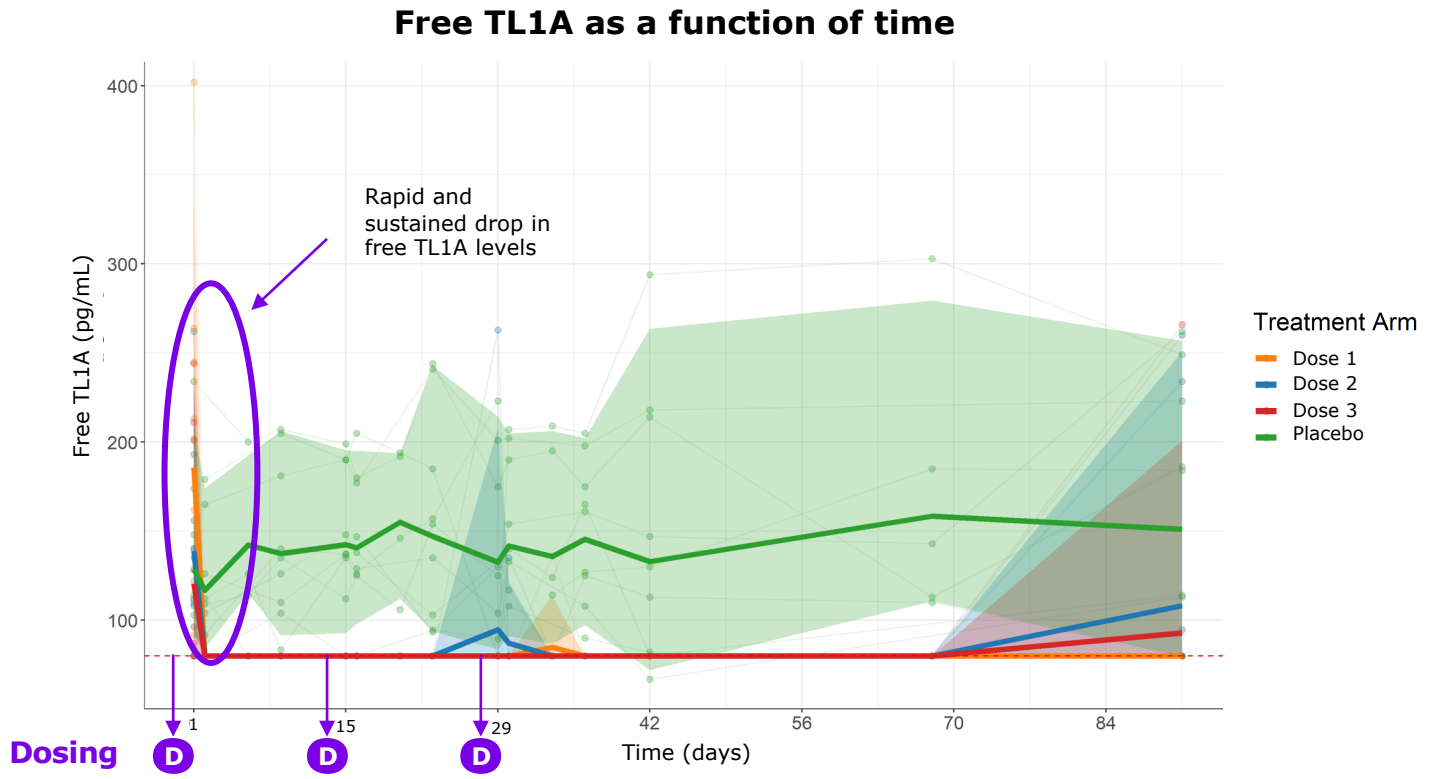
Provides potential for *potent* anti-inflammatory effect with competitive dosing regimen

1. Comparative reagents generated from sequences in publicly available patent publications, in in-house experimental comparison. 2. DR3:DcR3 selectivity (functional inhibition) in vitro. 3. DR3: pro-inflammatory signaling. 4. DcR3: natural TL1A antagonist (soluble decoy). 5. Inhibition of TL1A-induced apoptosis (TF-1 cells) in vitro. 6. Patent No. WO2021081365.
The Anti-TL1A is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Anti-TL1A: Potent *target engagement* demonstrated in a multi-ascending dose study in asthma patients

Significantly low concentration of Free TL1A at all dose levels, including ~40 days after last dose

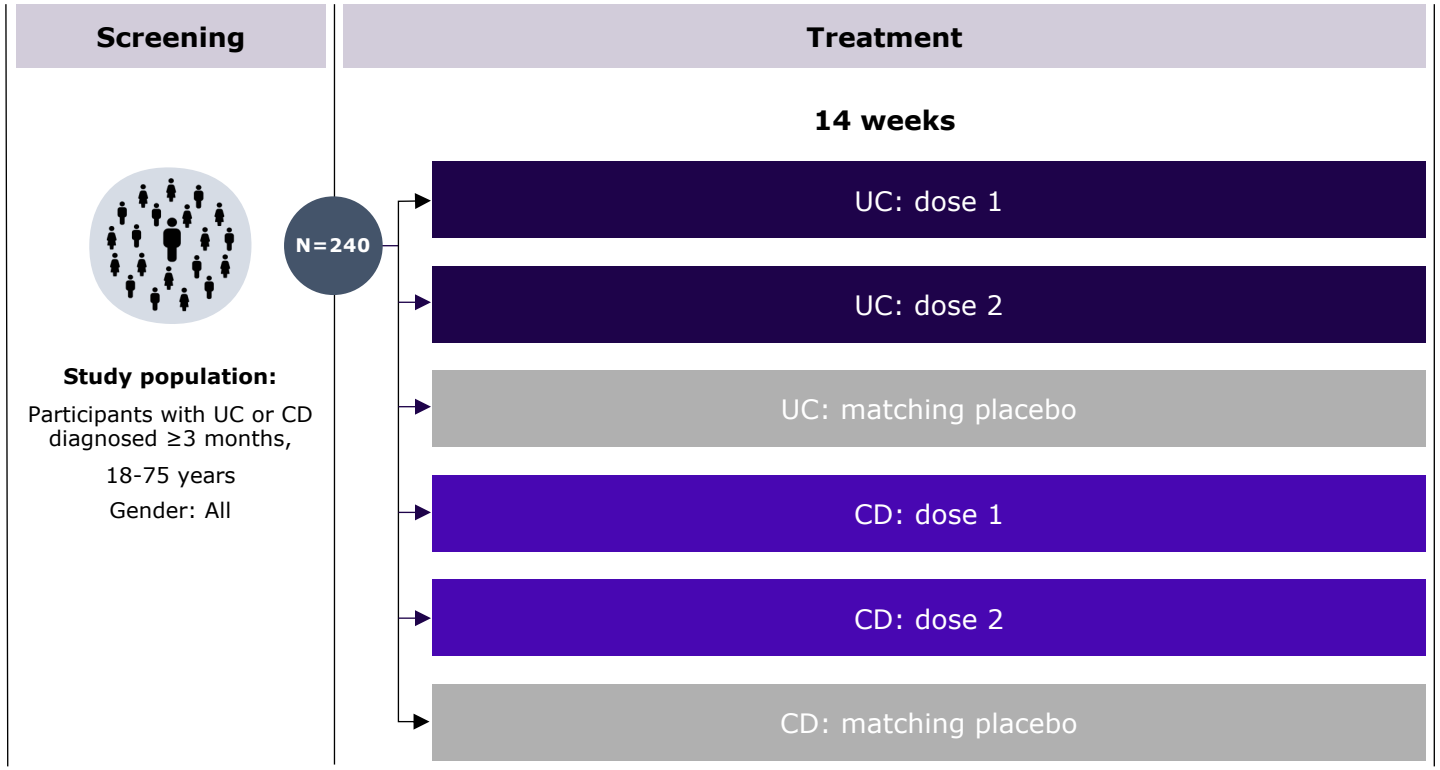
- MAD study mild asthmatic patients, with potent target engagement
- TEV'574 dosing: days **1, 15, 29**



Simoa-based assay method was concluded as fit for purpose for target engagement. The method showed BLLQ of 80 pg/mL and some matrix interference. New assay developed with BLLQ of 2pg/mL. Assay is ongoing validation. Thick lines represent geometric mean. Shaded area represents 95% PI. Red dashed line represents LLOQ= 80 pg/mL.

Anti-TL1A: Phase 2b trial designed to address both *major IBD indications*

Phase 2b, randomized, double-blind, placebo-controlled, parallel-group study



Overall outcome measures

- UC: Number of participants who show clinical remission as defined by the Mayo score
- CD: number of participants who show response as defined by Simple Endoscopic Score for Crohn Disease (SES-CD)
- Safety

NCT05668013. The Anti-TL1A is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Potentially *best-in-class* profile in a highly promising class of innovative TL1A therapies

Indication	Status	Data	Eligible population	Next milestone
Crohn's Disease	Phase 2b	High selectivity to DR3 and high potency *in vitro*	**1.0M**	Phase 2b IA data **in H2 2024**
Ulcerative Colitis	Phase 2b		**1.3M**	Phase 2b IA data **in H2 2024**

Around 2.3M eligible patients

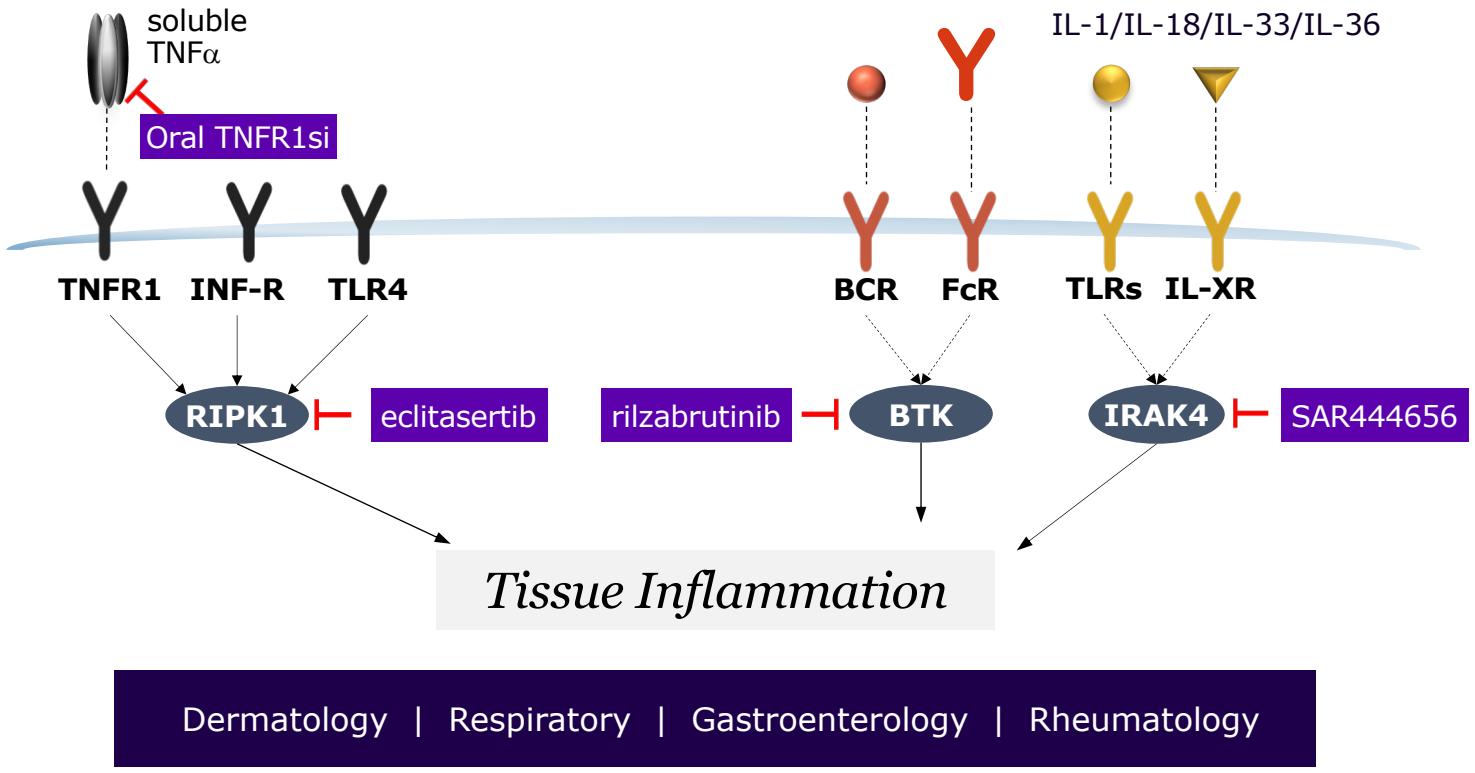
- ✓ Potential best-in-class efficacy
- ✓ Risk sharing
- ✓ Potentially addressing the $28bn+ WW IBD market[1]

€2-5bn peak sales potential

Advanced therapy eligible patients across U.S. and EU5 (France, Germany, UK, Spain, Italy). Additional details in Epidemiology Appendix.
The Anti-TL1A is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

1. Source: EvaluatePharma, does not include biosimilars.

Next-generation of *oral* pathway medicines



Antibody-like efficacy with oral convenience tackling core central pathway targets

- **Rilzabrutinib (BTKi covalent reversible)** targets a key step in B cell activation and in innate Type 2 cells
- **SAR444656 (IRAK4 Degrader)** blockade of kinase and scaffold function for maximal disease impact
- **SAR441566 (Oral TNFR1 Signaling Inhibitor)** selectively blocks TNFR1

Clear opportunity for oral therapies to move in front of biologics and significantly expand the number of treated patients

These products are currently under clinical investigation and their safety and efficacy have not been evaluated by any regulatory authority.

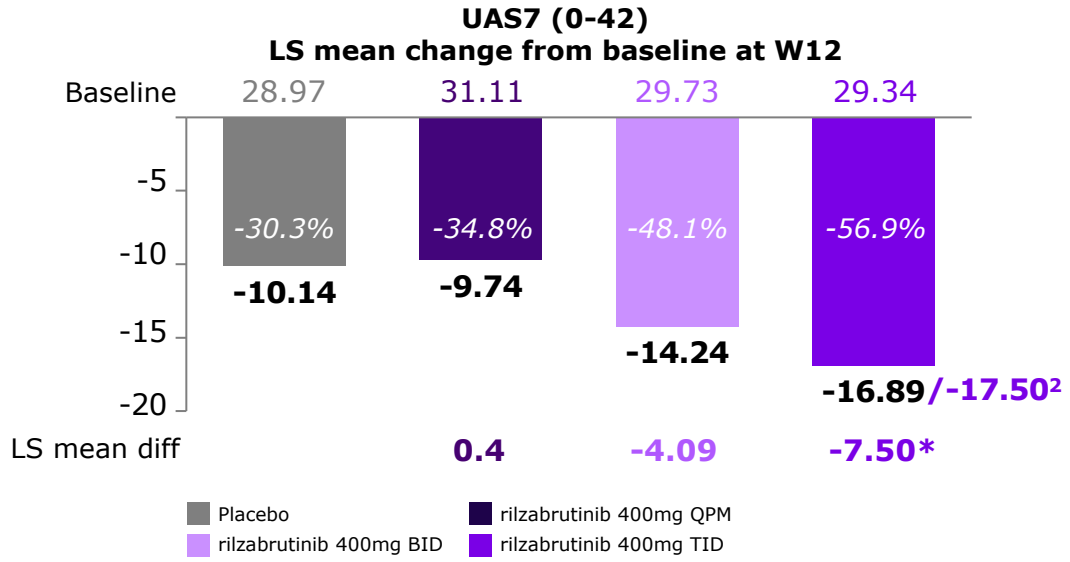
Rilzabrutinib is being evaluated in multiple Phase 2 clinical trials across a *range of indications*

	AD	CSU	Asthma	IgG4
Target Population	Inadequately controlled with topicals; adults 18 or older; moderate-severe	Moderate-severe disease; inadequate response to oral anti-H1	Add-on to ICS and second controller; adults 18-70 yrs, moderate-severe	Adult patients with IgG4-RD
Clinical Trial Design	- Placebo-controlled, 2 dose levels - N=120 - Primary efficacy evaluated at week 16	- Placebo-controlled, 3 dose levels - N=152 - Primary efficacy evaluated at week 12	- Placebo-controlled, 2 dose levels - N=192 - Primary efficacy at week 12	- 2 arms, open label - N=25 - Primary efficacy evaluated at week 12
Primary Endpoint	- Change in EASI Score	- ISS7/UAS7	- Loss of Asthma Control	- IgG4-RD RI
Status	**% change in EASI score not met, improvements in itch observed**	**Primary endpoints met, data to be presented**	**Interim results encouraging, final Ph2 H1 2024**	**Ph2 data in H2 2024**

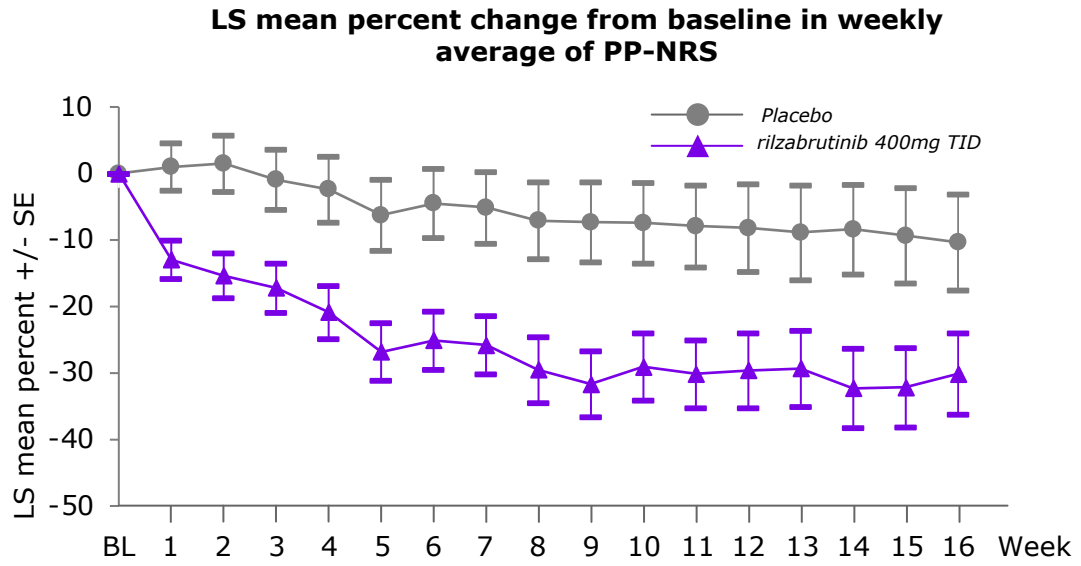
Rilzabrutinib is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Rilzabrutinib potentially first safe[1] oral to *rapidly control* recalcitrant itch

CSU: positive for all domains (itch, hives, urticaria) in Phase 2



AD: positive itch data in Phase 2



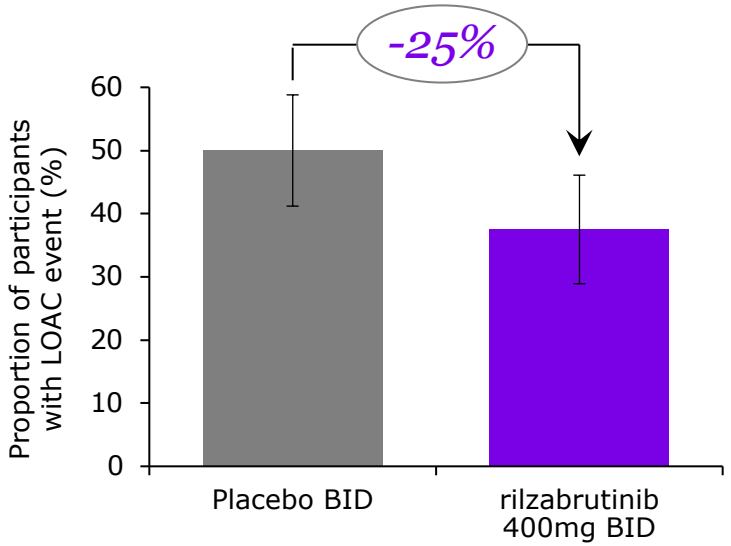
Failed primary endpoint of %EASI change

Potential to target neuroinflammatory axis in dermatology and respiratory

1. Well tolerated: no cytopenia, no bleeding/no petechiae, no cardio-vascular side effects. 2. p=0.0159/0.0079 (excluding outlier UAS7/ISS7=0 at baseline by error). Rilzabrutinib is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

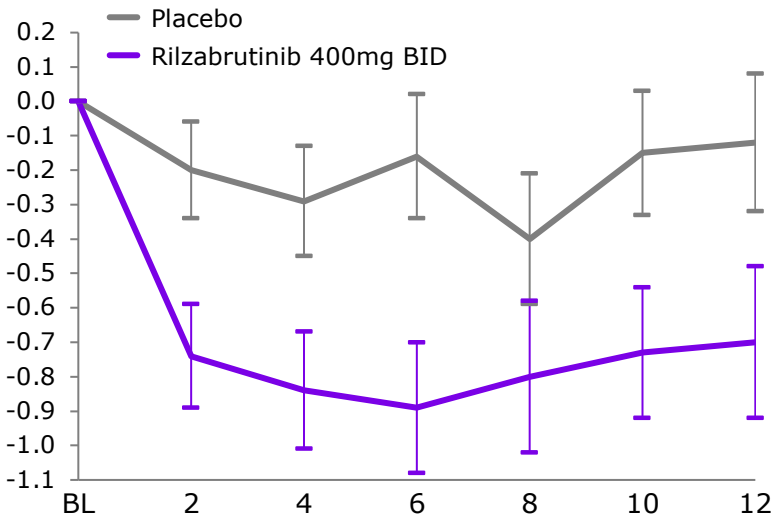
Rilzabrutinib shows marked symptomatic improvement in asthma patients with *trend toward reduction in LOAC*

Trend toward reduction in LOAC (loss of asthma control)[1]



Relative Risk Reduction 25%

Improvement in asthma symptoms (ACQ-5) at Week 12



LS mean difference -0.59; p-value=0.0184

- Low dose asthma cohort readout from Ph2 study
- Dramatic improvement in symptoms regardless of Type 2 status
- Higher dose cohort to readout **in H1 2024**

Potential for treating moderate asthma patients

A. Adjusted for baseline IgE stratum level, region, and number of exacerbation events within 2 years prior to screening. Rilzabrutinib is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Rilzabrutinib: Attractive *oral* treatment option investigated across a broad spectrum of patients

Indication	Status	Clinical evidence	Eligible population	Next milestone
Asthma	Phase 2	Improvement in asthma symptoms regardless of Type 2 status	**1.9M+**	Phase 2b data **in H1 2024**
PN	Phase 3	Itch improvement in AD and CSU	**0.2M**	Phase 3 starts **in 2024**
CSU	Phase 3	Improvement from baseline in UAS7	**0.7M**	Phase 3 starts **in 2024**
IgG4-RD	Phase 2	N/A	**45K**	Phase 2b data **in H2 2024**

More than 2.8M eligible patients

Potential RBD indications currently under development

Indication	Status	Clinical evidence	Eligible population	Next milestone
ITP	Phase 3	Rapid and durable increase in platelet count[1]	**50K**	Phase 3 data Submission **in H2 2024**
wAiHA[2]	Phase 2b	N/A	**20K**	Phase 2b **in H2 2024**

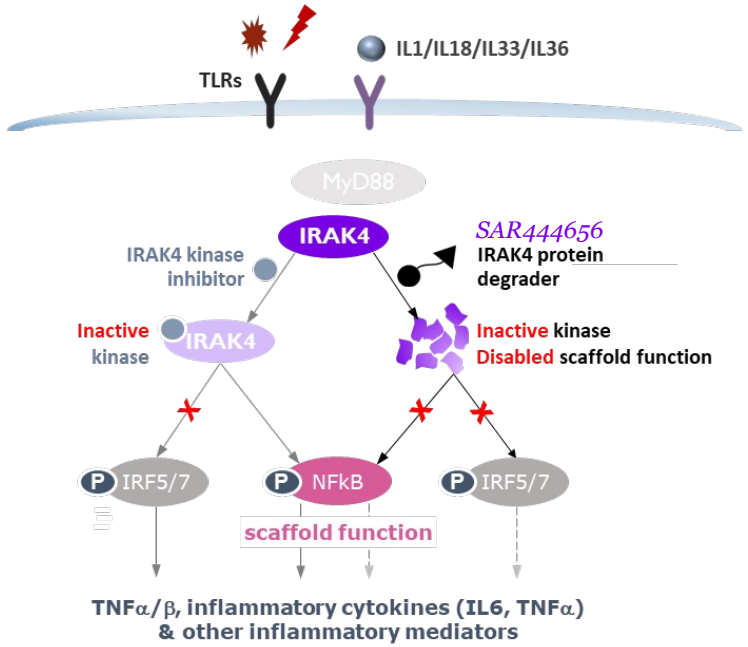
- ✓ Potential for first and/or best-in-class oral BTKi
- ✓ Fully owned
- ✓ Potential to work across dermatology and respiratory diseases

€2-5bn peak sales potential

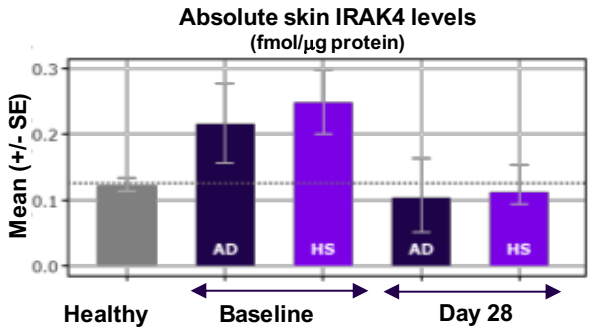
Advanced therapy eligible patients across U.S., EU5 (France, Germany, UK, Spain, Italy) and Japan. Additional details in Epidemiology Appendix. Rilzabrutinib is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

1. https://www.nejm.org/doi/full/10.1056/NEJMoa2110297. 2. Excludes Japan.

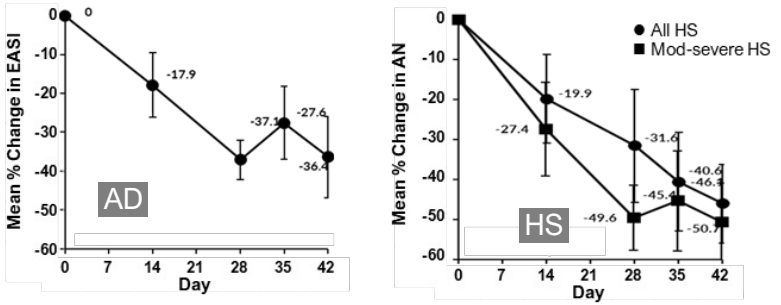
SAR444656: Potent *orally* bioavailable IRAK4 protein degrader



Robust IRAK4 degradation in skin



IRAK4 degradation improves AD and HS



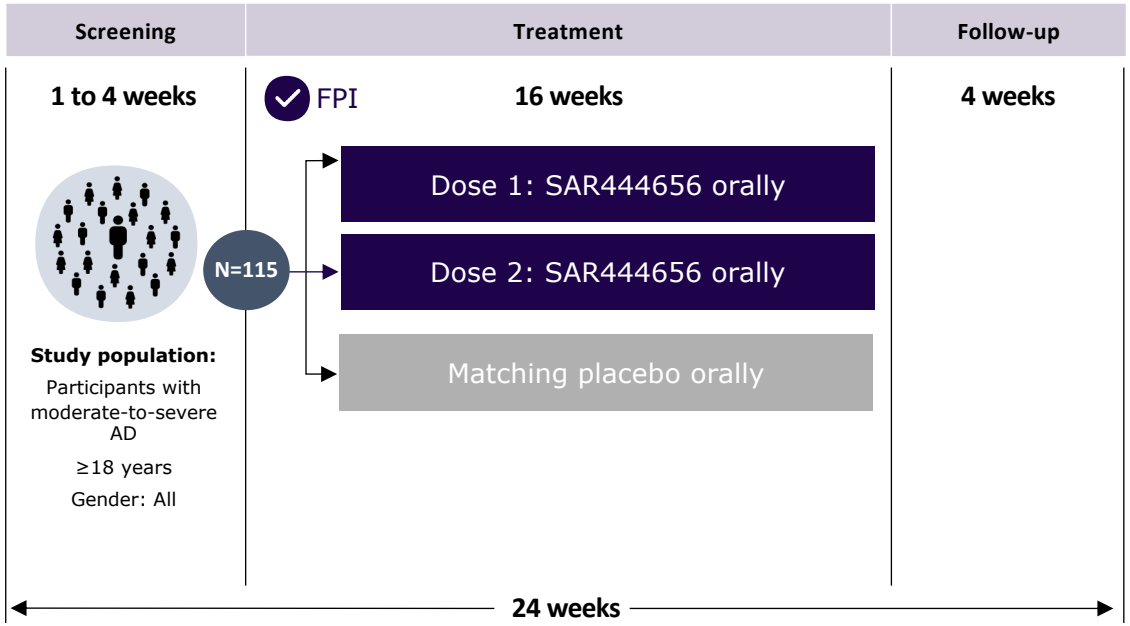
- Potential for *oral* immunology pathway drug across multiple indications
- *Promising* clinical activity in a small cohort of AD and HS patients[1]
- Impacted *multiple disease* outcomes, including skin lesions, inflammatory nodules, pruritus[1] and pain[1]
- Self-reported *clinical benefit* and improvement in skin lesions beyond dosing

1. Ackerman, L. et al. Nature Medicine, 2023. SAR444656 is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

SAR444656: Potential *first-in-class oral* IRAK4 degrader progressing into multiple inflammatory diseases

Atopic Dermatitis advanta

Phase 2, double-blind, placebo-controlled, parallel-group study

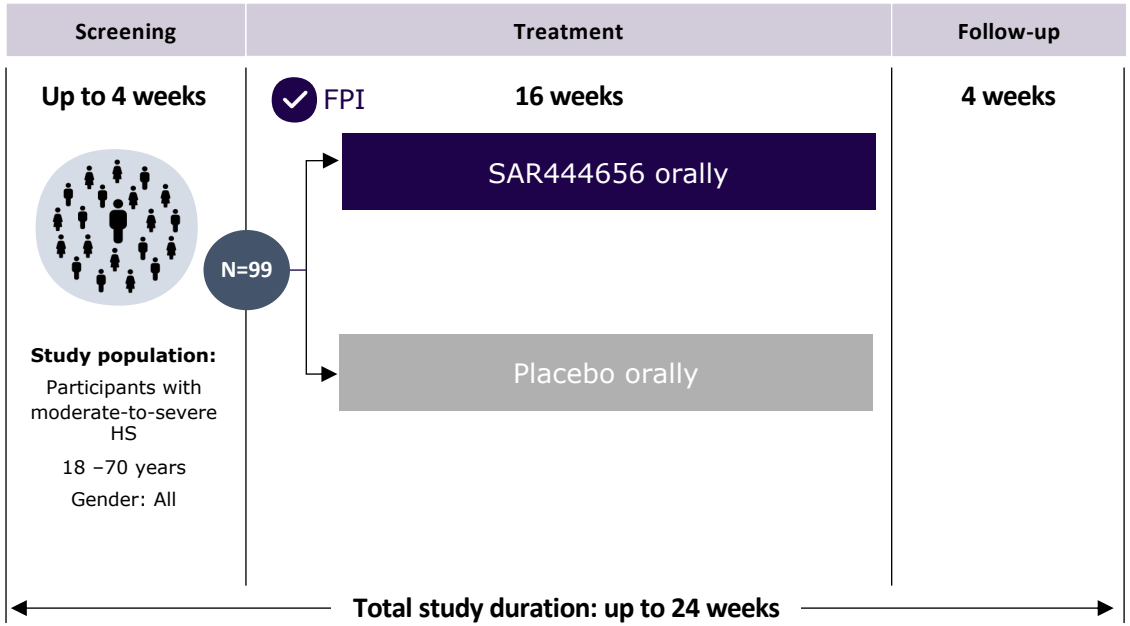


Primary outcome measure

Percentage change from baseline in EASI to Week 16

Hidradenitis Suppurativa zen

Phase 2, double-blind, parallel-group, placebo-controlled study



Primary outcome measure

Percentage change from baseline in total abscess and inflammatory nodules (AN) count to Week 16

advanta (NTC06058156). zen (NCT06028230). SAR444656 is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

SAR444656: *Robust* response drives additional indication opportunity of IRAK4 degrader

Indication	Status	Clinical evidence	Eligible population	Next milestone
AD[1]	Phase 2	Reduction of disease relevant inflammatory biomarkers in blood and skin of HS and AD patients	**3.0M**	Phase 2 data **in H1 2025**
HS[1]	Phase 2		**0.4M**	Phase 2 data **in H1 2025**

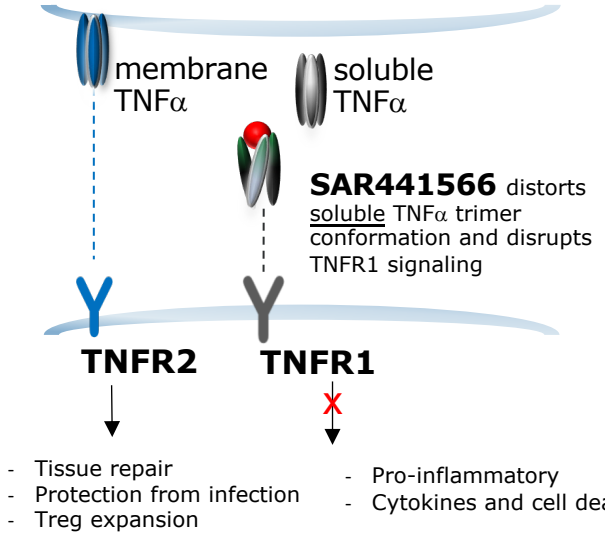
Around 3.4M eligible patients

- ✓ Potential first-in-class with oral convenience
- ✓ Risk sharing
- ✓ Progressing across immunology indications

€2-5bn peak sales potential

Advanced therapy eligible patients across U.S., EU5 (France, Germany, UK, Spain, Italy) and Japan. Additional details in Epidemiology Appendix. 1. Moderate to severe patients. SAR444656 is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

SAR441566: Differentiated *oral TNFR1* signaling inhibitor with potential for antibody-like efficacy



SAR441566 inhibits TNFR1 signal but allows membrane-bound TNFα (mTNFα) to bind to TNFR2 and executes its homeostatic functions[1,2]

Selective inhibitor of TNF R1 signaling offering potential for lower infection risk and improved efficacy

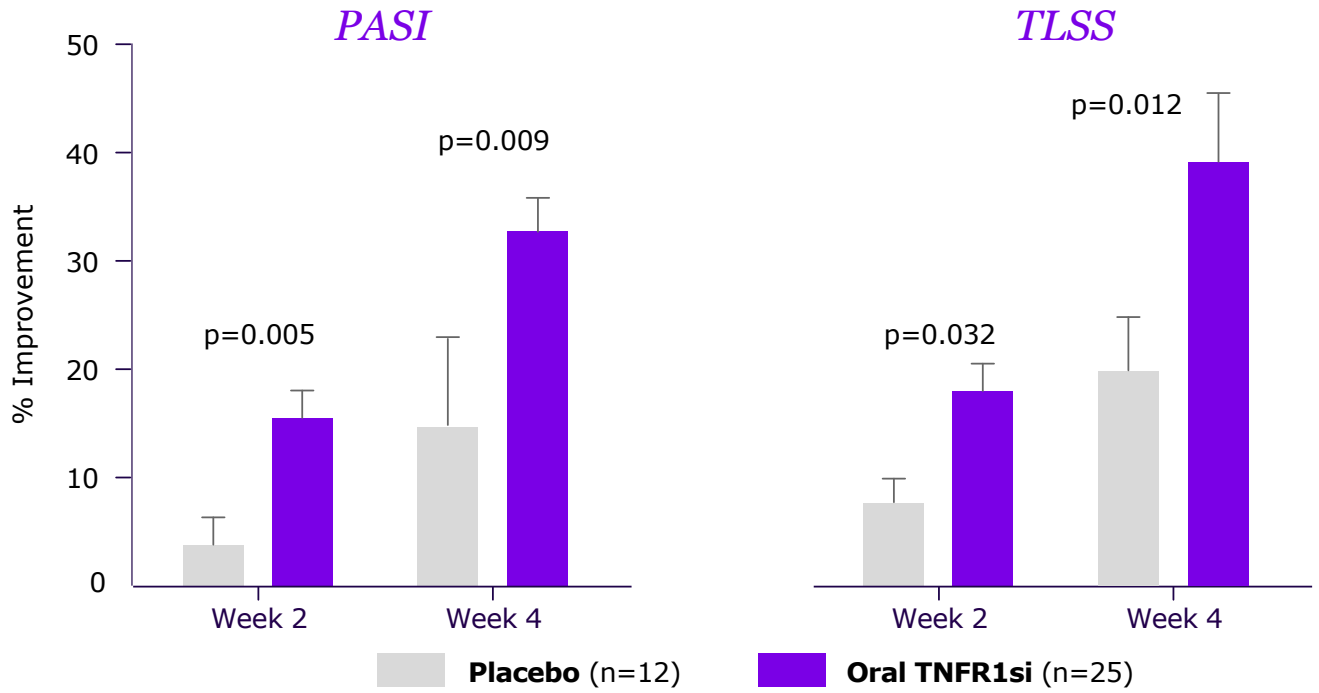
Could meet patient needs *across multiple large markets*, including RA, psoriasis and IBD

Phase 1b psoriasis data demonstrates efficacy and is well tolerated with *no serious adverse event*

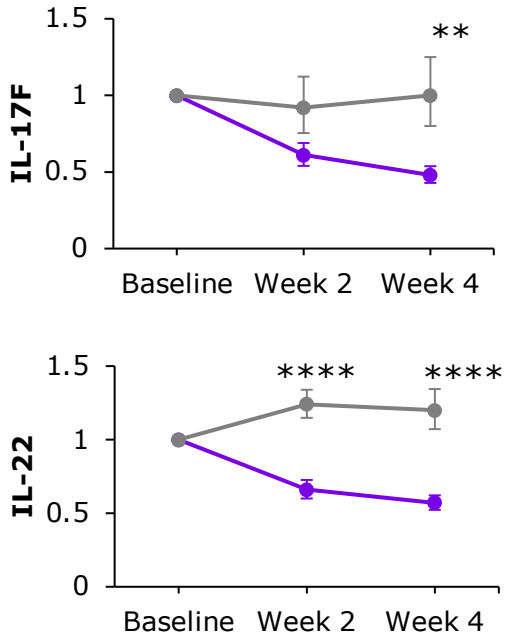
Compelling profile as a potential foundation of all-oral *combination* therapies

1. Vugler A, et al. Front Pharmacol. 2022;13:1037983. 2. McMillan D, et al. Nat Commun. 2021;12:582. SAR441566 is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Oral TNFR1si: Safe and well tolerated with efficacy in mild-to-moderate *psoriasis* in Phase 1b



PASI and TLSS improvement from baseline to Week 2 and 4[1,2]



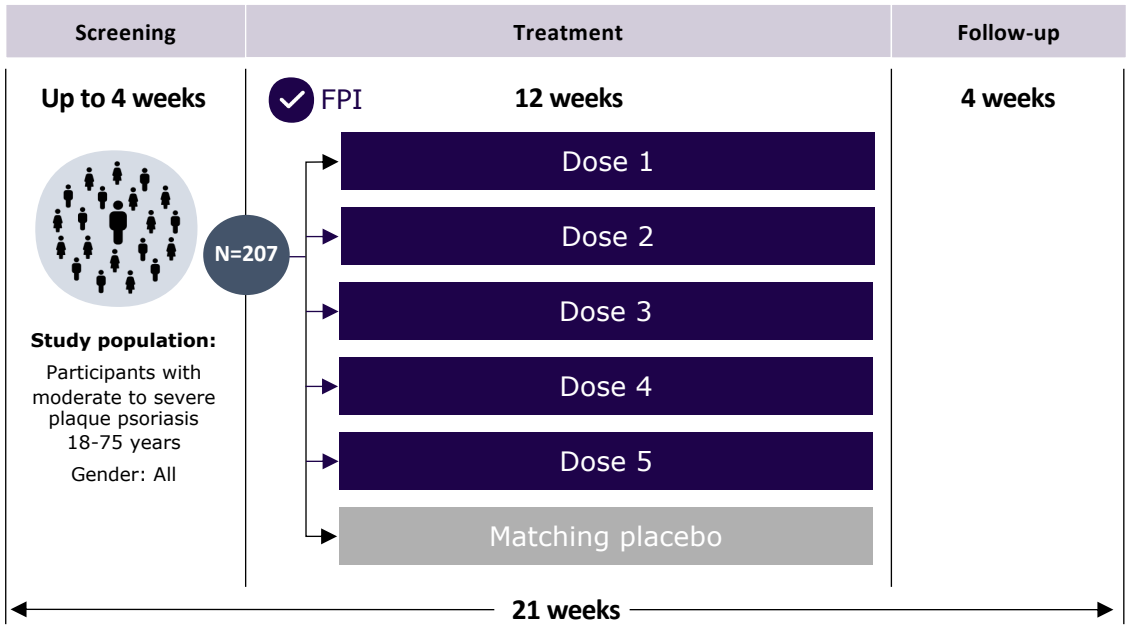
Decrease in biomarker[3] *levels consistent with clinical improvement in patients*

1. Efficacy and safety of a small molecule with innovative inhibition of TNFR1 signaling in plaque psoriasis: A double-blind, randomized, placebo-controlled study. T. Matos, M. Kohlmann. 2. p-values were provided for one sided test at 5% significant level comparing the adjusted means of the two groups from linear model (Mixed Model with Repeated measurements [MMRM]). 3. **p≤0.01; ****p≤0.0001. Data represent geometric mean ratio from baseline values (×/÷) geometric SEM. A two-sample t-test at significance alpha level of 5% was used for calculation of the p-values. SAR441566 is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Oral TNFR1si: Phase 2 program investigating *large market indications* with first-patient-in already achieved

Psoriasis SPECIFI-PSO

Phase 2b, double-blind, placebo-controlled, dose-ranging study

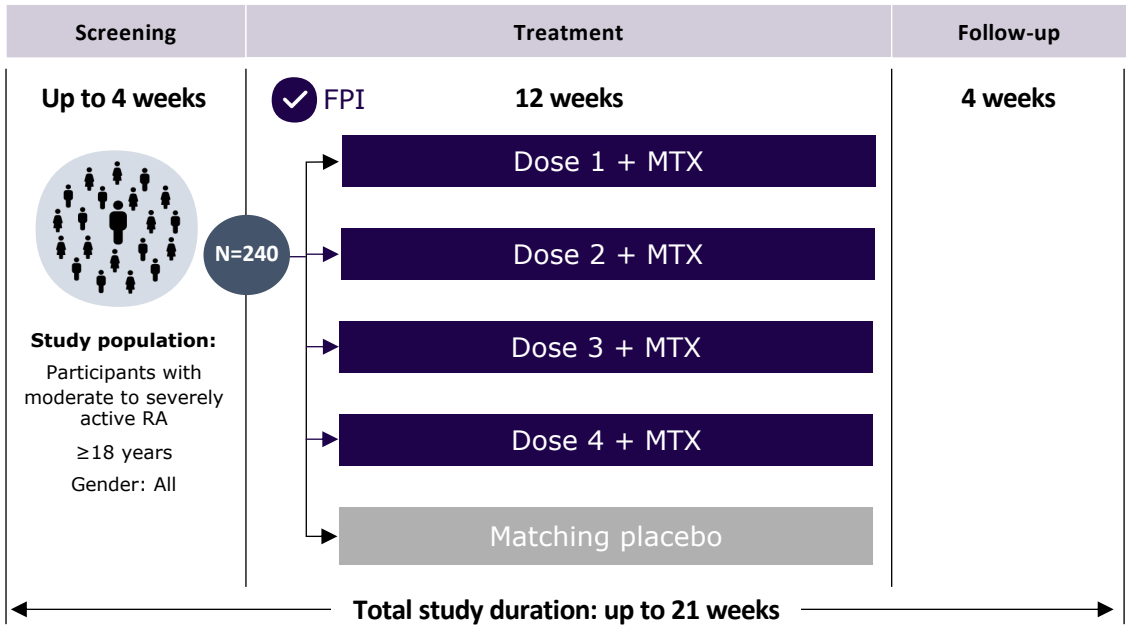


Primary outcome measure

Proportion of participants with a PASI75 score improvement from baseline at Week 12

Rheumatoid Arthritis SPECIFI-RA

Phase 2b, double-blind, placebo-controlled, dose-ranging study



Primary outcome measure

Proportion of participants achieving at least 20% improvement from baseline in ACR at Week 12

SPECIFI-PSO (NCT06073119). SPECIFI-RA (NCT06073093). SAR441566 is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Oral TNFR1si: Potential foundational oral regimen for large immune-mediated inflammatory diseases

Indication	Status	Clinical evidence	Population	Next milestone
Psoriasis	Phase 2b	Clinical efficacy sustained over treatment period Safe and well-tolerated	**2.4M**	Phase 2b data **in H1 2025**
Rheumatoid Arthritis	Phase 2b	Anti-TNF biologics indicated for this disease with proven efficacy	**2.4M**	Phase 2b data **in H2 2025**
IBD (Crohn's Disease, Ulcerative Colitis)			**2.3M**	Phase 2b to start **in 2024/2025**

More than 7.0M eligible patients

Adding potentially *another ~1.0M*

Indication	Eligible population	Next milestone
Psoriatic Arthritis	**1.0M**	Potential for straight to Phase 3 following positive outcomes of Pso/RA Phase 2b studies

- ✓ Oral with potential for antibody-like efficacy, further derisking in Phase 2b
- ✓ Fully owned
- ✓ Broad indication potential as monotherapy and combination

€5bn+ peak sales potential

Advanced therapy eligible patients across U.S. and EU5 (France, Germany, UK, Spain, Italy). Additional details in Epidemiology Appendix. SAR441566 is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

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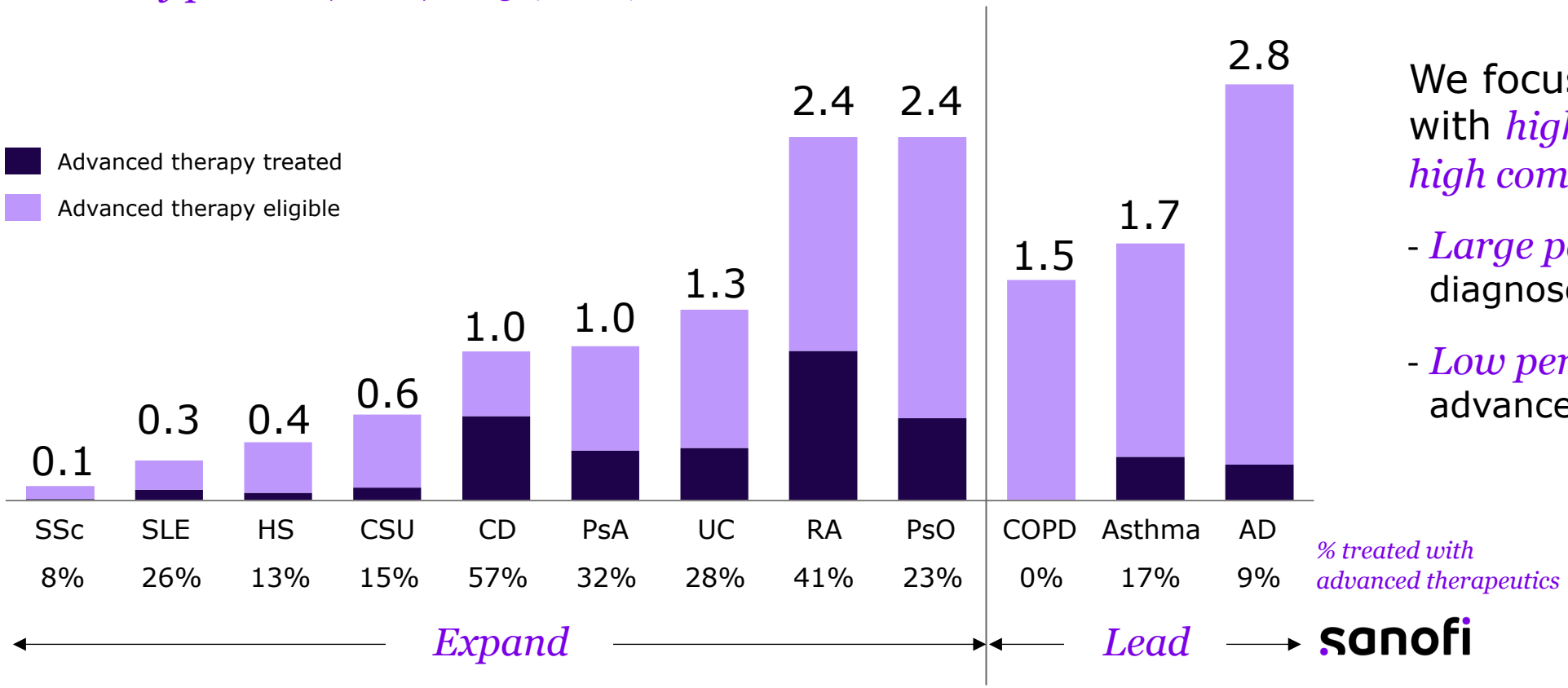
Multi-indication assets to drive future growth

Shaju Backer

Global Head of Immunology Franchise

Key immunology markets remain *underpenetrated*

Millions of patients, U.S., EU5 (2022)



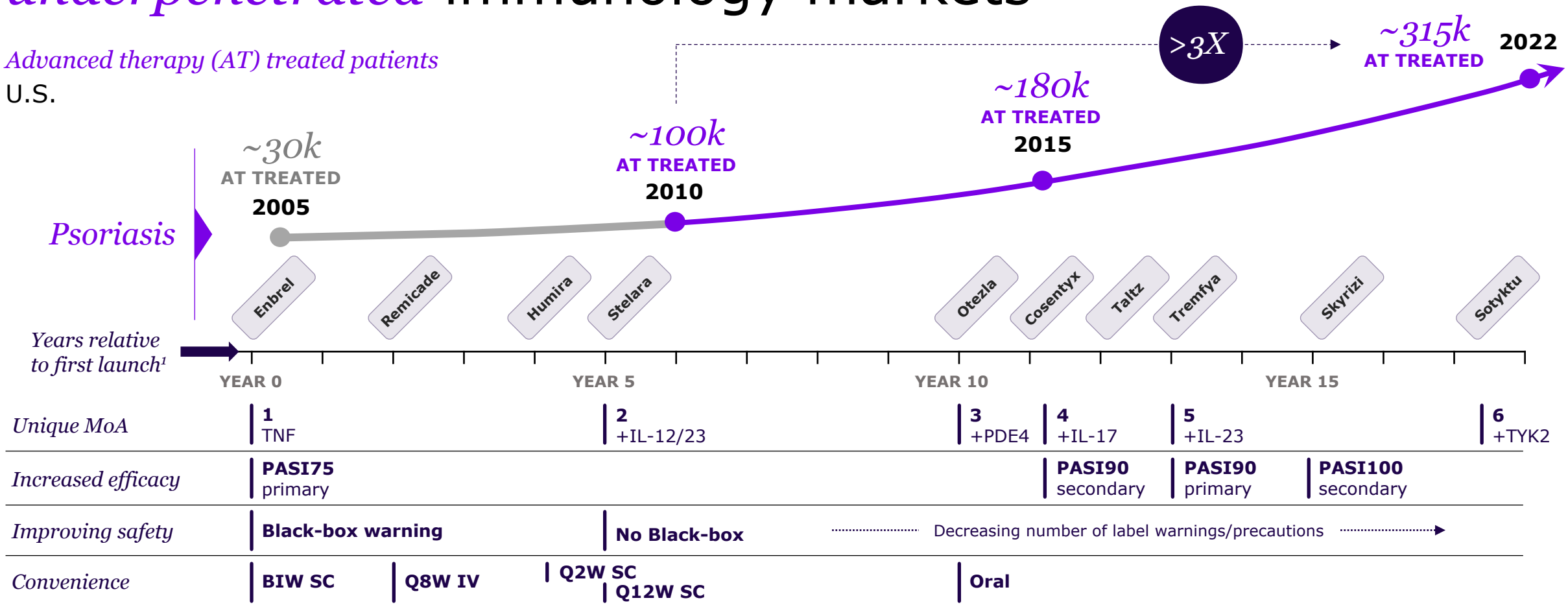
We focus on diseases with *high unmet need* and *high commercial potential*:

- *Large patient populations* / diagnosed prevalence
- *Low penetration* of advanced therapeutics

Note: Asthma includes epidemiology data for 12+y. population and COPD for 40+y population, all other diseases 18+. Source: Sanofi estimates. See Appendix for additional details on epidemiology.

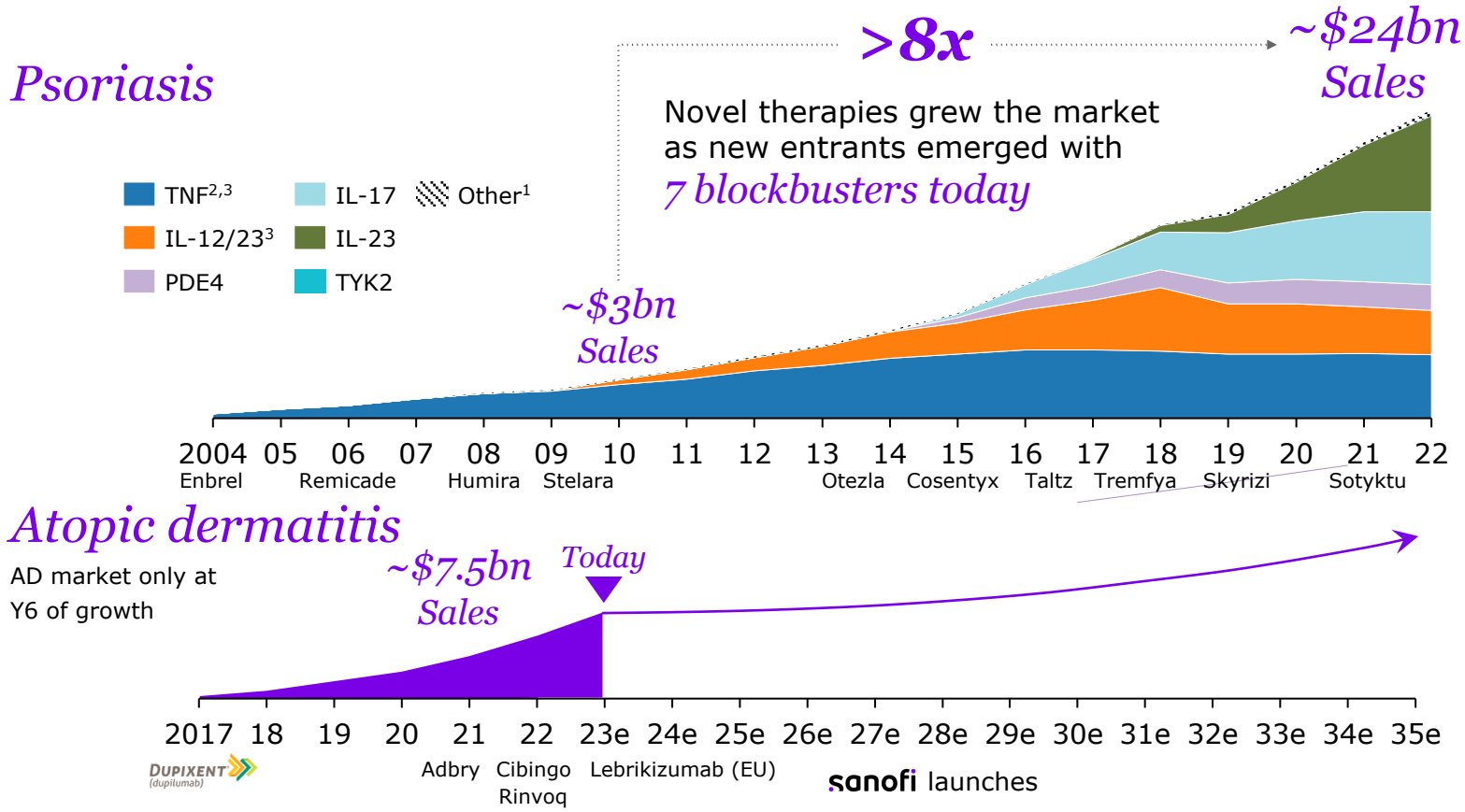
Psoriasis market evolution - Novel therapy entries grow *underpenetrated* immunology markets

Advanced therapy (AT) treated patients
U.S.



1. Enbrel, 2004 in psoriasis. Source: Evaluate analysis for Sanofi for epidemiology.

AD market is only starting its *growth journey* as psoriasis analogue shows



1. Includes AhR, GCR, Nrf2. 2. Revenues in 2010 extrapolated due to apparent EP artifact in Remicade revenues. 3. Includes biosimilar revenues where applicable.
Note: Enbrel, 2004 in psoriasis. Source: Evaluate Pharma October 2023.

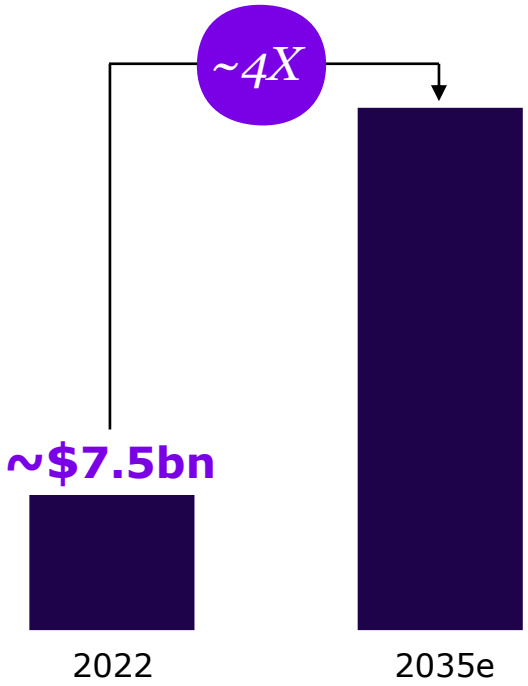
AD market expected to grow in a similar way to psoriasis

Atopic dermatitis is the *newest advanced therapy market* and is expected to grow with new MOAs

- 6 years since *1st AT launch*
- 5 products, 3 MOAs
- Only *1 blockbuster* to date

Sanofi to maintain *leadership in growing AD market*

Global AD Advanced Therapy Market



Potentially truly differentiated assets

amlitelimab
Anti-OX40L
Phase 3

- ✓ Pursuing BIC durable efficacy across heterogenous population
- ✓ Option for patients preferring less frequent dosing

SAR444656
IRAK4 degrader
Phase 2

- ✓ New pre-biologic option
- ✓ Increase advanced therapies penetration with a safe, high-efficacy oral

lunsekimig
Anti-IL13/TSLP
Phase 2 ready

- ✓ High efficacy option for cycling
- ✓ Retain long-term AD leadership

Sanofi poised to drive and benefit from *continued market expansion with differentiated therapies*

Source: Evaluate Pharma (Oct 2023) for 2022 number, Sanofi projection for 2035 (note Evaluate Pharma 2028 estimate ~€21bn).
These products are currently under clinical investigation and their safety and efficacy have not been evaluated by any regulatory authority.

Oral TNFR1 signaling inhibitor could meet patient needs across *multiple large markets*

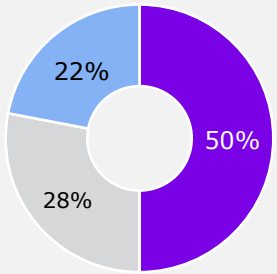
Aspiration for TNFR1si

Rheumatoid Arthritis

Orals today

- JAK

2022 TNF and oral market share



Orals TNFs Other

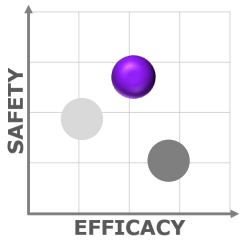
JAK: black box, limited to 2L per label in U.S.

Positioning strategy

- Pre-biologic
- Monotherapy (1L, 2L)
- Combination Therapy

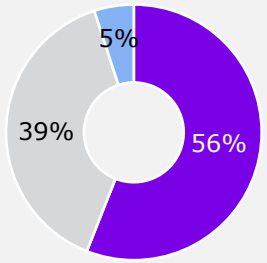
Potential to be the only safe oral option in RA

IBD (UC & CD)



Orals today

- JAK
- S1P



JAK: black box, limited to 2L per label in U.S.

S1P: Require baseline ECG and ocular exams

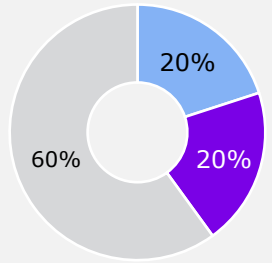
- Pre-biologic
- Monotherapy (1L, 2L)
- Combination Therapy

Strong strategic fit in portfolio as a safe 1L oral option

Psoriasis

Orals today

- TYK2
- PDE4



PDE4: Modest efficacy

TYK2: JAK class warnings in label

- Pre-biologic
- Monotherapy (1L, 2L)

Leveraging strong Immuno-dermatology commercial footprint

Sources: Sanofi analysis for positioning, Datamonitor 2023 (U.S.+EU5) for share estimates.

Leading in Immunology in the next decade and beyond

Significant unmet need
and opportunity remains

Aggressive *parallel development*
plans

Innovative science - breakthrough
differentiated therapies

World-class team experienced
in Development & Commercialization

Multiple Multi-indication assets
with blockbuster potential

Q&A session (Part 1)

Break

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Physician perspective on MS

Sharon Stoll, DO, MS
Director of Neurology
Stoll Medical Group

Priority for people with MS: minimize risk of long-term disability

A global survey assessing the impact of RMS and disability

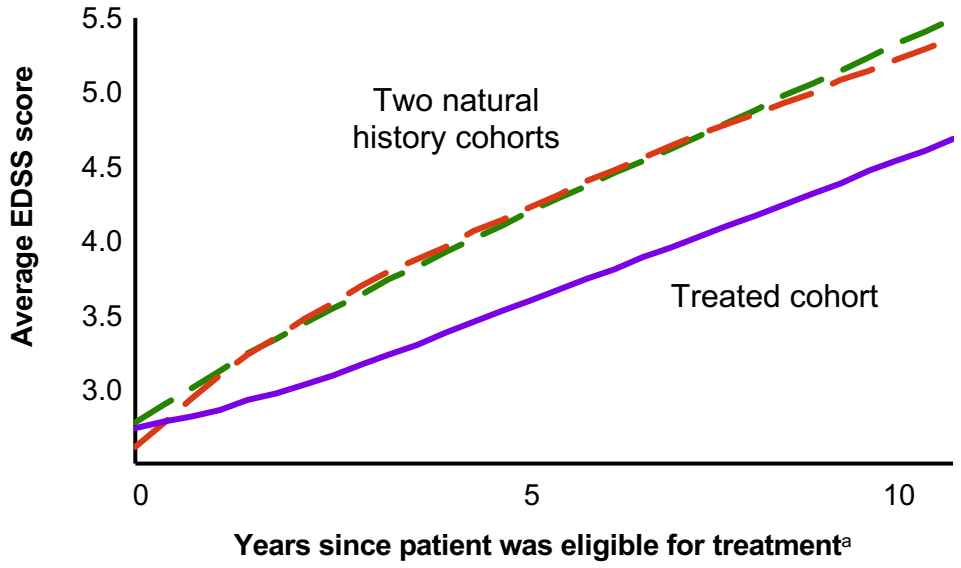
>70% of PwMS are concerned about **disease progression** and **future disability**[1]

>50% of PwMS reported **worsening physical functioning** since diagnosis[1]

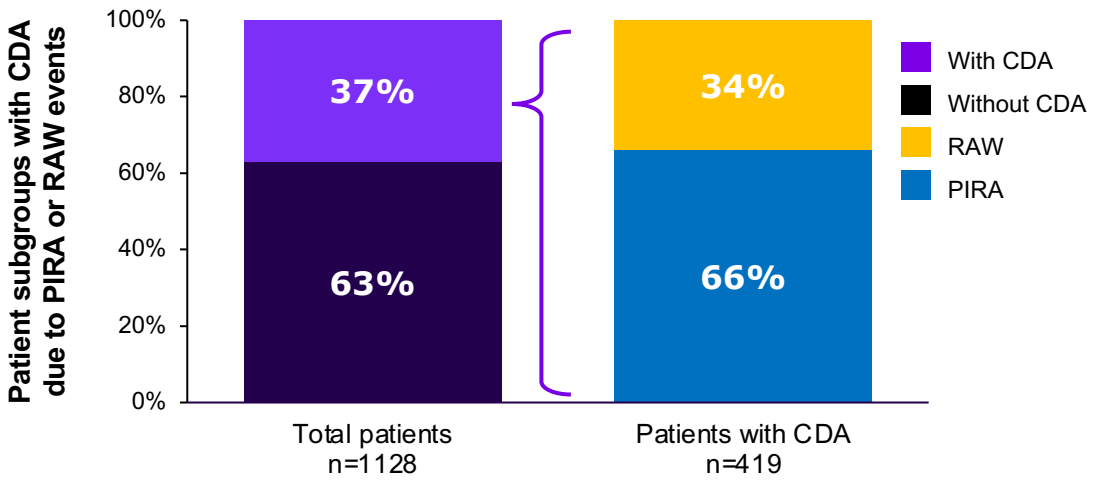
The vsMS survey was conducted during July and August 2015 and included 1075 people with RMS. 1. Bass A, et al. Int J MS Care 2020;22:158-164. 2. Bass A, et al. CMSC 2018, DX08. 3. Bass A, et al. CMSC 2017, LB01.

Many pwMS continue to experience disability accumulation with current therapies

*Continued **disability accumulation**[1]*



Retrospective single-cohort analysis:
***66%** of overall disability accumulation in treated pwMS was independent of relapse activity*[2,b]



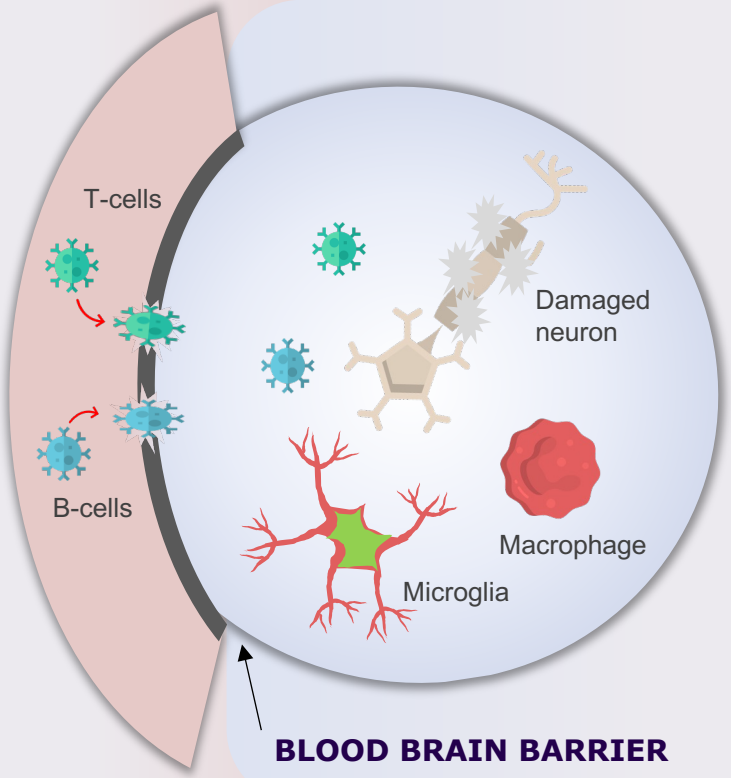
aCriteria for eligibility: age ≥18 years, EDSS score ≤6.5, occurrence of ≥2 relapses in the previous 2 years. bRetrospective analysis of data from patients prospectively included in the deeply phenotyped Barcelona cohort of patients with a first demyelinating attack from a single MS center. CDA=confirmed disability worsening; EDSS=Expanded Disability Status Scale; PIRA=progression independent of relapse activity; pwMS=people with MS; RAW=relapse-associated worsening; SPMS=secondary progressive MS.
1. Tilling K, et al. Health Technol Assess. 2016;20:1-483. 2. Tur C, et al. JAMA Neurol. 2023;80:151-60.

Our understanding of MS is evolving[1,2]

Acute neuroinflammation

Historical Focus[3-5]

- Acute neuroinflammation, acute lesions
- Mainly early in the disease course
- Progression happens later; relapse triggers progression



Smoldering neuroinflammation

Evolving Focus[6-9]

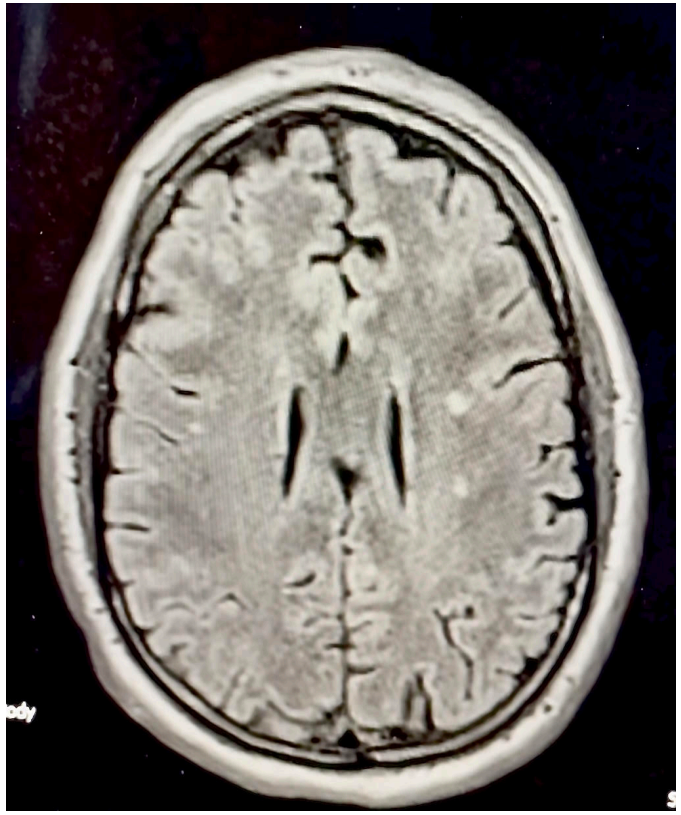
- Neurodegeneration, chronic active lesions, brain volume loss
- Smoldering neuroinflammation starts before clinical symptoms
- Progression happens in absence of relapse

PERIPHERY **CNS**

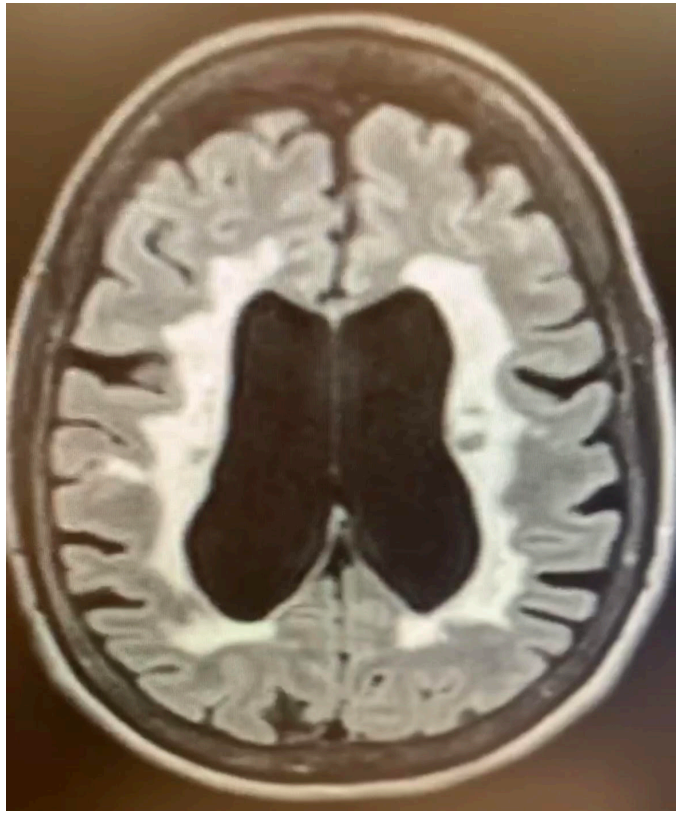
1. Li R et al. *Nat Immunol*. 2018;19:696-707. 2. Ahn JJ et al. *Cells*. 2021;10(7):1605. 3. Reich DS et al. *N Engl J Med*. 2018;378:169-80. 4. Häusser-Kinzel S, et al. *Front Immunol*. 2019;10:2015. 5. Gandhi R et al. *J Neuroimmunol*. 2010;221:7-14. 6. Guerrero BL, Sicotte NL. *Front Immunol*. 2020;11:374. 7. Elliott C, et al. *Brain* 2019;142:2787-99. 8. Maggi P, et al. *Ann Neurol*. 2020;88(5):1034-1042. 9. Dal-Bianco A, et al. *Brain* 2021;144:833-47.

MS is associated with loss of brain volume

Normal brain density
in a 20y with MS

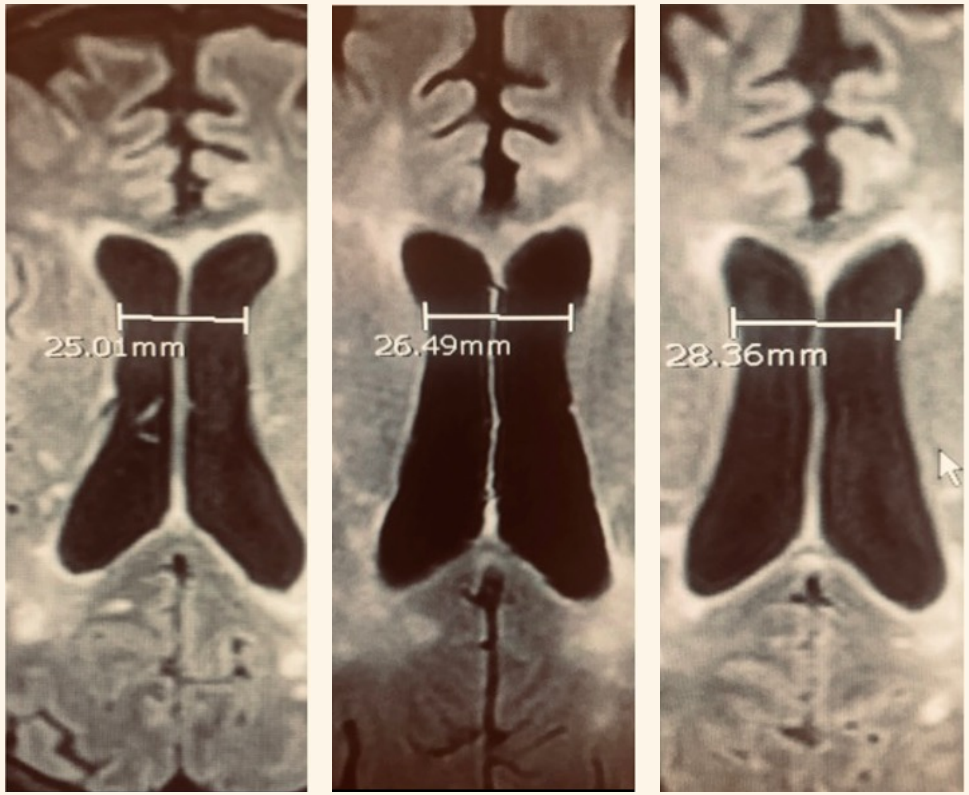


Severe atrophy
in a 55y with MS



Brain volume loss in MS can happen rapidly, even in “stable” patients

Atrophy over time



2016 2018 2020

Unmet need in Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

CIDP is the most common immune-mediated peripheral neuropathy

Characterised by demyelination of motor and sensory nerves[1]

Prevalence[2]
0.8–8.9
Cases per 100,000 persons

Incidence[2]
0.2–1.6
Cases per 100,000 persons per year

Symptoms:
motor/sensory deficits in >1 limb;
weakness in proximal and distal muscles[3]

The current treatment algorithm in CIDP has limitations[4–9]:

Efficacy rates	>30% of patients may be refractory to IVIg, steroids or PLEX[5–9]
Response to treatment	Of the ~ 70% of responders, the response is sometimes incomplete[4,5,7,9]
Route of administration	Treatments involves frequent infusions[4,9]
Sustained effects	there is often a "wearing off' effect'[9]
Disease progression	Axonal degeneration slowly continues despite therapies[5,7]

1. Querol LA, et al. Neurotherapeutics. 2022;19(3):864–873. 2. Bragazzi NL, et al. J Neuroinflammation. 2021;18(1):264. 3. Dalakas MC. Chapter 67 - Autoimmune Peripheral Neuropathies. In: Rich R, et al. Clinical Immunology (Fifth Edition). Elsevier; 2019. 903–915.e1. 4. Querol LA, et al. Neurotherapeutics. 2022;19(3):864–873. 5. Dalakas MC. Chapter 67 - Autoimmune Peripheral Neuropathies. In: Rich R, et al. Clinical Immunology (Fifth Edition). Elsevier; 2019. 903–915.e1. 6. Said G. Neuromuscul Disord. 2006;16(5):293–303. 7. Said G, Krarup C. Chapter 22 - Chronic inflammatory demyelinative polyneuropathy. In: Handbook of Clinical Neurology. 2013;115:403–413. 8. Dalakas MC. Neurology. 2002;59(12 Suppl. 6): S13–S21. 9. Dalakas MC. Nat Rev Neurol. 2011;7(9):507–517.

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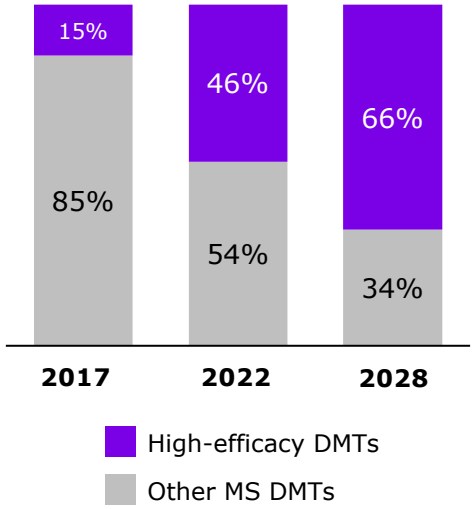
Addressing high unmet needs in neuro-inflammation through innovative mechanisms

Erik Wallstroem
Head of Development, Neurology

Despite current treatments, *more high-efficacy* options needed in MS

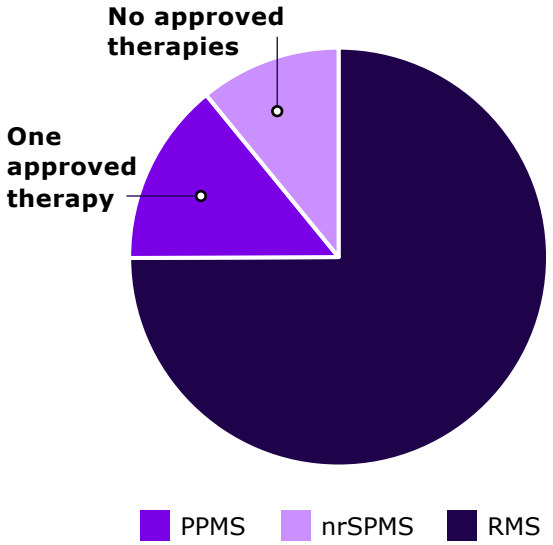
Only Anti-CD20s are driving the high efficacy segment, more MoAs needed

Treated RMS patients by DMT category (U.S.)



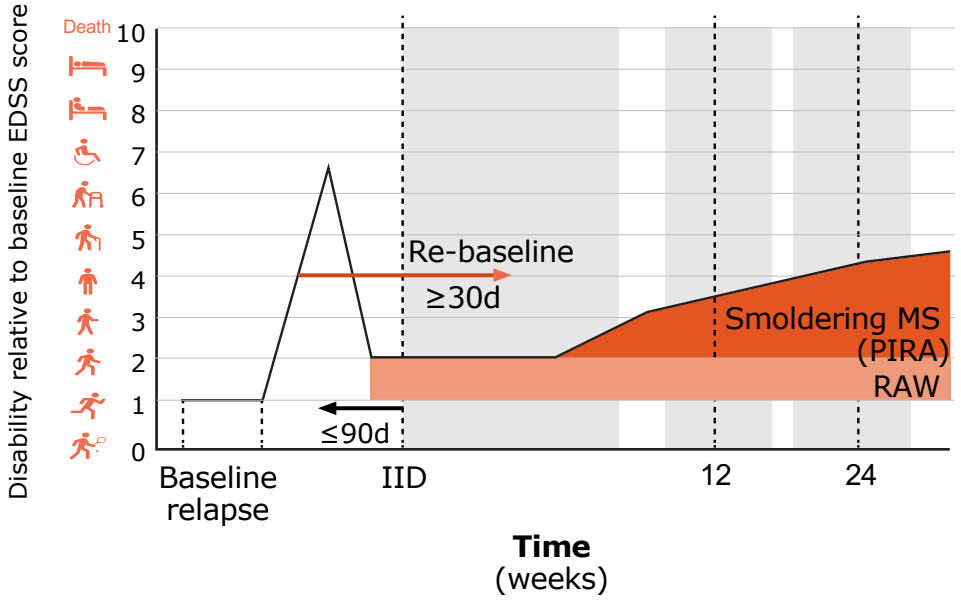
Few to no treatments for progressive MS

MS patients by subtype (U.S.)



Smoldering MS drives disability across the disease spectrum

Contributions of RAW and PIRA to disability in OPERA[1]

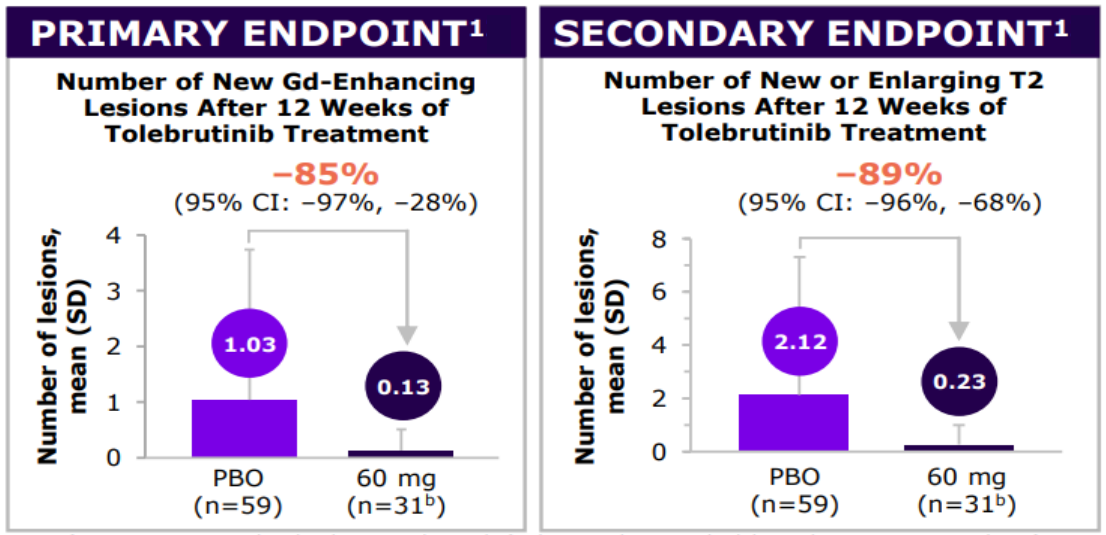


Source: Evaluate Pharma. Note: Platform injectables: IFN/GA, Orals: Aubagio, Fumarates, Gilenya, S1Ps, Other smaller HE: Lemtrada, Mavenclad; Briumvi PDUFA Dec 2022. 1. Adapted from Giovannoni G, et al. Ther Adv Neurol Disord 2022;15:1-18.

Tolebrutinib Ph2b results indicate *high-efficacy potential* and acting on smoldering neuroinflammation in the CNS

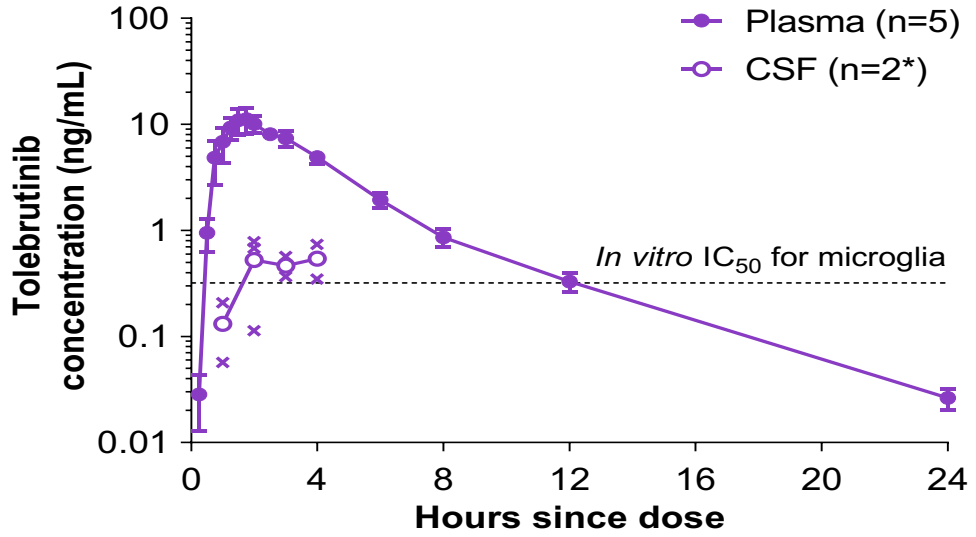
NEW

Significantly reduced disease activity associated with MS



[a]Data from participants in the placebo-treated period of cohort 2, who started tolebrutinib treatment at Week 4 after the placebo run-in. [b]1 patient withdrew in the 60 mg group due to contraception requirements and was not included in the efficacy analysis.

Brain penetration at pharmacologically active levels

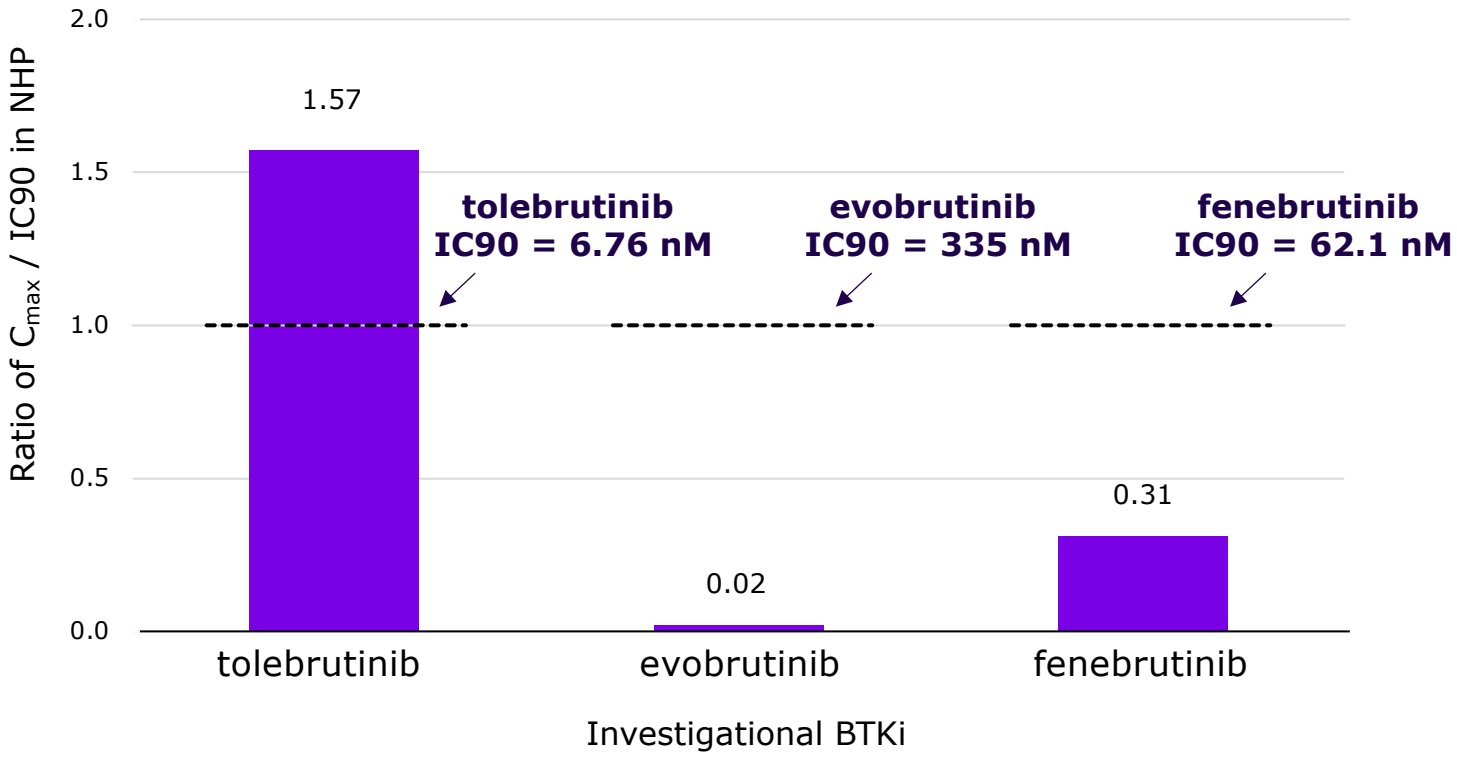


Tolebrutinib 60mg CNS In Vitro Cellular Potency in healthy humans[2]

For plasma, data are mean ± standard error. For CSF, data are mean, with crosses representing individual measurements. The sample size indicated for CSF represents the minimum number of participants sampled at each timepoint. *n=2 for all time points except t=2 hours which is n=3. 1. Reich, Lancet Neurology, 2021. 2. Nicolas O et al. ACTRIMS 2023, P151. All measured CSF concentrations exceed tolebrutinib's previously reported in vitro IC50 (0.32 ng/mL) for microglia, except for the concentration measured at the 1-hour timepoint for the 60 mg dose. Tolebrutinib is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Direct comparison supports *differentiation*

Only tolebrutinib exceeded the IC90 value in CSF



- Tolebrutinib was *more potent* in terms of BTK inhibition than evobrutinib (*50x*) or fenebrutinib (*9.3x*). Relative potency to inhibit B-cell activation was consistent with biochemical results.

- Tolebrutinib demonstrated *intrinsic CNS penetrance* in non-human primates, based on the unbound partition coefficient (*0.397*), approximately *3x* higher than evobrutinib (*0.131*), fenebrutinib (*0.147*).

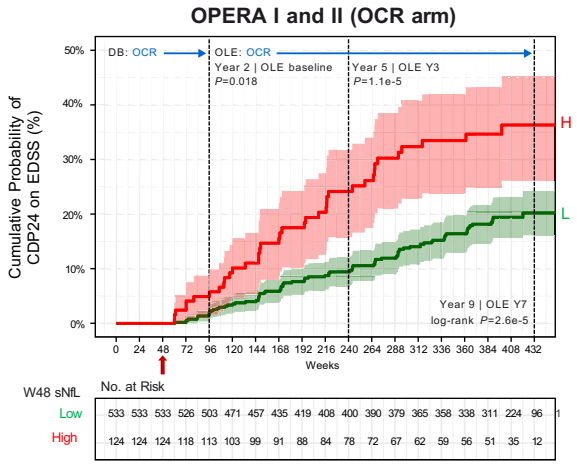
- The combination of high potency, reaction rates, and CNS exposure suggested that tolebrutinib inhibits BTK signaling in the CNS by *>90%*, consistent with *pharmacological activity in the brain and spinal cord*.

Tolebrutinib is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Biomarker data suggest tolebrutinib acts in CNS *addressing disability accumulation*

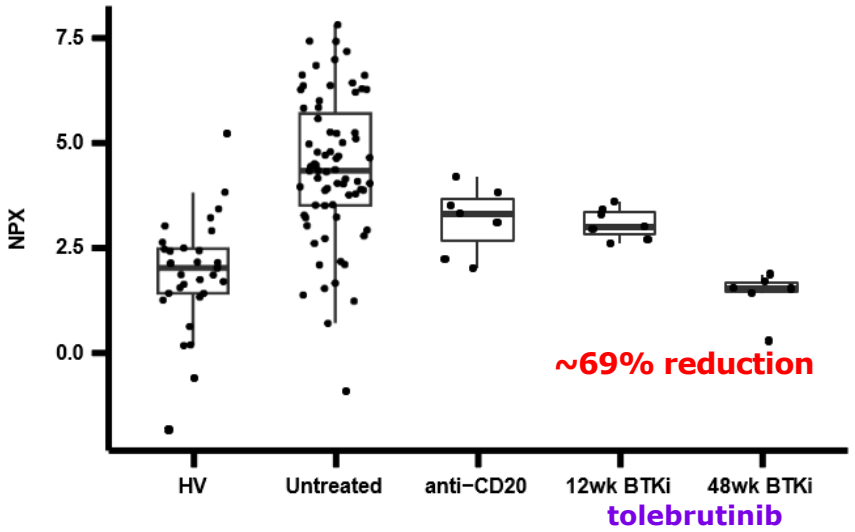
NEW

High NfL levels correlated with more disability accumulation after 9 years



NfL levels after 48 weeks of ocrelizumab treatment correlates with disability accumulation[1]

Tolebrutinib reduced NfL in CSF after switch from anti-CD20



Olink proteomic data expressed as "Normalized Protein eXpression" as units of 2-fold change

- Tolebrutinib *significantly reduced* NfL beyond levels achieved with anti-CD20 in MS patients switched to tolebrutinib treatment[2]
- Data supports that tolebrutinib has CNS *bioactivity*

1. Bar-Or A, Thanei GA, Harp C, et al. Blood neurofilament light levels predict non-relapsing progression following anti-CD20 therapy in relapsing and primary progressive multiple sclerosis: findings from the ocrelizumab randomised, double-blind phase 3 clinical trials. EBioMedicine. 2023;93:104662. 2. Blazier et al, P645, ECTRIMS 2023). Tolebrutinib is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Continued confidence in tolebrutinib as a potentially *transformative oral* treatment option for people with MS

FDA **positive feedback** to address the partial clinical hold

- Multiple workstreams to *mitigate* DILI risks
- Monitoring, and point-of-care ALT test, AI-enabled patient stratification options

FDA **to modify** the partial clinical hold for nrSPMS (HERCULES) and PPMS (PERSEUS)

- Sanofi will *resume enrollment of PPMS* participants from the U.S. to support WW enrollment
- Sanofi will provide *open-label* tolebrutinib to participants from the U.S. who are in the PERSEUS and HERCULES trials who reach the 6-month confirmed disability progression endpoint
- Participants from the U.S. who are in HERCULES and PERSEUS and who complete the double-blind treatment period will have the option to receive tolebrutinib treatment in the *open-label LTS* trial beginning in 2024

Continued dialogue with the FDA to *resolve the partial clinical hold on RMS* participants which currently remains in place (RMS trials GEMINI I & II fully recruited)

Tolebrutinib is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Broadest BTKi Phase 3 development program underway with tolebrutinib across all forms of MS

Relapsing-remitting multiple sclerosis

	Screening Period Recruitment Status	Treatment Period: approximately 18 to 36 months (event driven trials)	Expected readout
GEMINI 1 RMS **N=974**		1 tablet daily tolebrutinib 1 tablet daily teriflunomide	**Mid 2024**
GEMINI 2 RMS **N=899**		1 tablet daily tolebrutinib 1 tablet daily teriflunomide	**Mid 2024**

Progressive forms of multiple sclerosis

	Screening Period Recruitment Status	Treatment Period: 24 to 48 months (event driven trials)	Expected readout
HERCULES nrSPMS **N=1131**		1 tablet daily tolebrutinib 1 tablet daily placebo	**Mid 2024**
PERSEUS PPMS **N=~700**		1 tablet daily tolebrutinib 1 tablet daily placebo	**2025**

- Three out of the four trials are *fully recruited*
- Enrollment of PPMS participants *to resume* in the U.S.
- Weekly liver *monitoring* during months 2 and 3 to ensure safe treatment initiation

GEMINI 1 (NCT04410978). GEMINI 2 (NCT04410991). HERCULES (NCT04411641). PERSEUS (NCT04458051). Tolebrutinib is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Tolebrutinib Phase 3 trials address the *full spectrum of MS*

Indication	Status	Clinical evidence	Eligible population	Next milestone
RMS	Phase 3	85% reduction in new Gd+ lesions (Ph2b)	**910k**	Phase 3 data **mid 2024** Submission **in 2024**
nrSPMS	Phase 3	Brain penetrance and bioactivity suggesting direct effect on disease-associated microglia	**170k**	Phase 3 data **mid 2024** Submission **in 2024**
PPMS	Phase 3	Brain penetrance and bioactivity suggesting direct effect on disease-associated microglia	**120k**	Phase 3 data **in 2025**

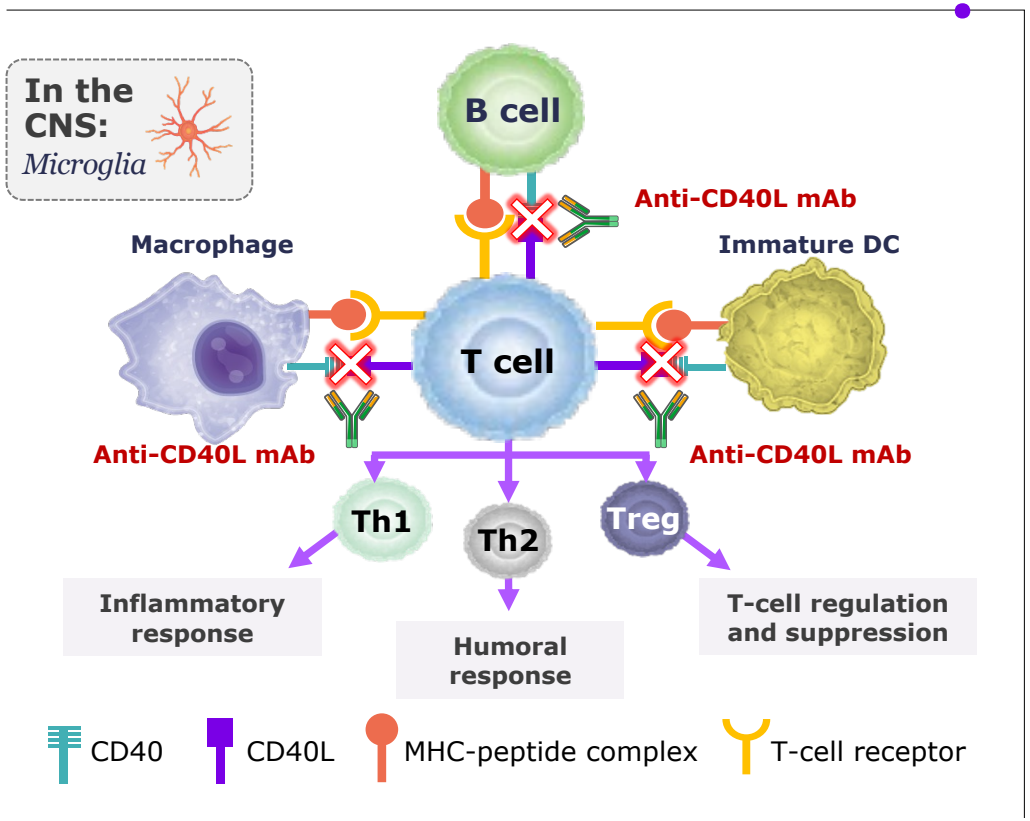
More than 1.2M eligible patients

- ✓ Strong science with potential for best-in-class efficacy
- ✓ Fully owned
- ✓ Broadest BTKi Phase 3 development program including nrSPMS where no approved therapies exist

€2-5bn peak sales potential

Diagnosed patients across U.S. and EU5 (France, Germany, UK, Spain, Italy). Additional details in Epidemiology Appendix. Tolebrutinib is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Frexalimab *pleiotropic approach to MS therapy* targeting adaptive and innate immune mechanisms



Novel MoA with adaptive and innate immune effects

Clinical and pathological evidence suggest a key role of CD40/CD40L in the development and progression of MS, with possible links to *peripheral tolerance*

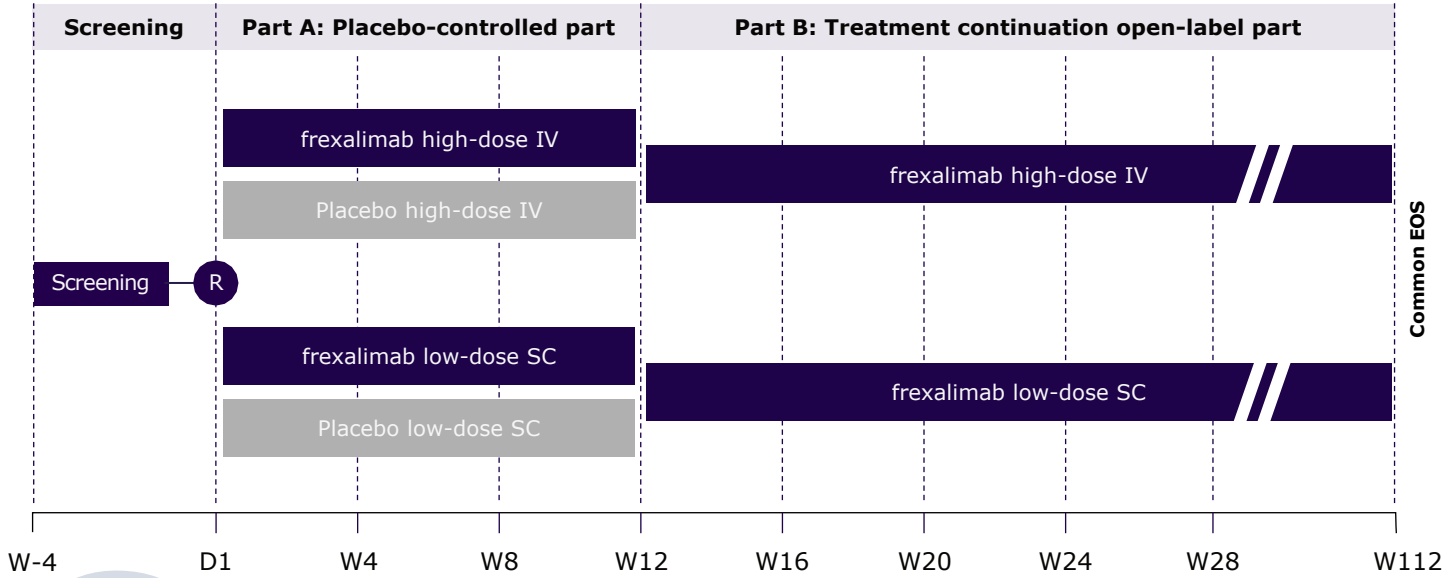
Potential as *high-efficacy, non-lymphocyte depleting* MS therapy

Key pathway in immune diseases, with potential for *pipeline-in-a-product*

Frexalimab is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Phase 2 trial design *explored high-dose IV and low-dose SC*

Phase 2, double-blind, randomized, placebo-controlled study RMS



N=129

Patient Eligibility Criteria

- Adult participants aged ≥18 to ≤55 years
- Diagnosis of RMS
- ≥1 documented relapse in previous year, or ≥2 documented relapses in prior 2 years, or ≥1 active Gd+ lesion within 6 months

Primary objective

Number of new gadolinium-enhancing (Gd+) T1-hyperintense lesions at Week 12

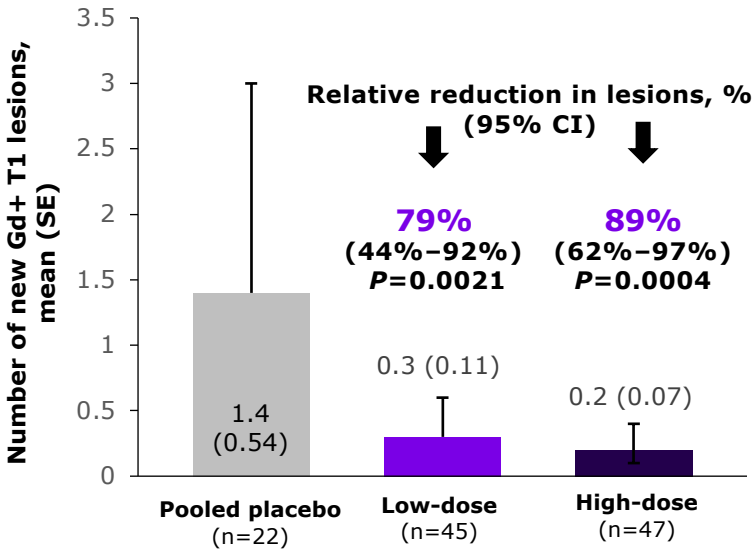
Secondary objectives

- Number of new or enlarging T2 lesions at Week 12
- Total number of Gd+ T1 lesions at Week 12
- Number of patients with antidrug antibodies
- Safety and tolerability
- PK: C_{max}, T_{max}, $AUC_{0-\tau}$, $t_{1/2z}$, until Week 112

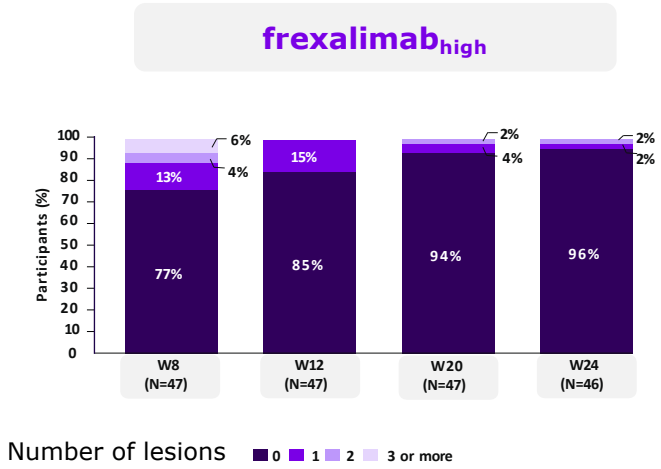
NCT04879628. Frexalimab is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Strength of Phase 2 data demonstrates *high-efficacy potential* for frexalimab in MS

Significant reductions in new Gd+ lesions at Week 12



96% of participants free of new Gd+ lesions at Week 24



96% of participants showed sustained reduction of disease activity over Week 24 in the high-dose group and *80%* in the low-dose group being free of new Gd+ T1 lesions at Week 24

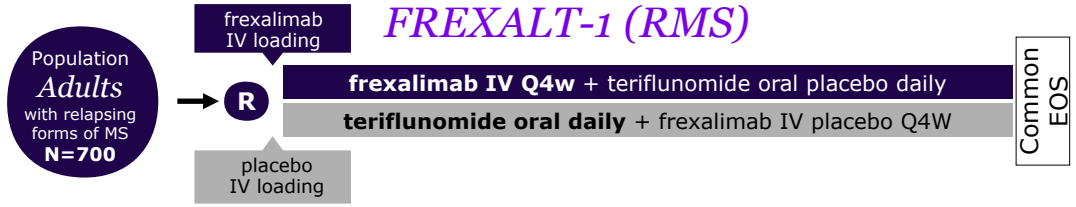
Rapid and marked *reduction* at Week 24 in the number of lesions in the placebo group upon switching to high group at Week 12

Safe and generally *well-tolerated* over Week 24, no serious of severe TEAEs were reported
Continued monitoring in the open-label Part B

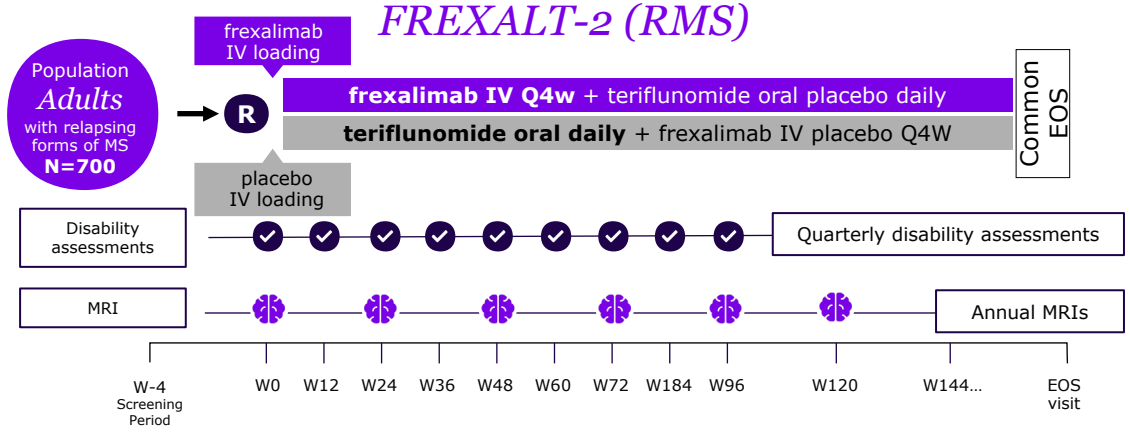
Source: Vermersch P, et al. Frexalimab, a CD40L Inhibitor, in Relapsing Multiple Sclerosis: Results from a Randomized Controlled Phase 2 Trial. LB02 presented at Consortium of Multiple Sclerosis Centers (CMSC), Colorado, May 31–June 3, 2023.
Frexalimab is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Phase 3 program initiated to confirm frexalimab as high-efficacy, *non-lymphocyte depleting* MS therapy

FREXALT-1 (RMS)



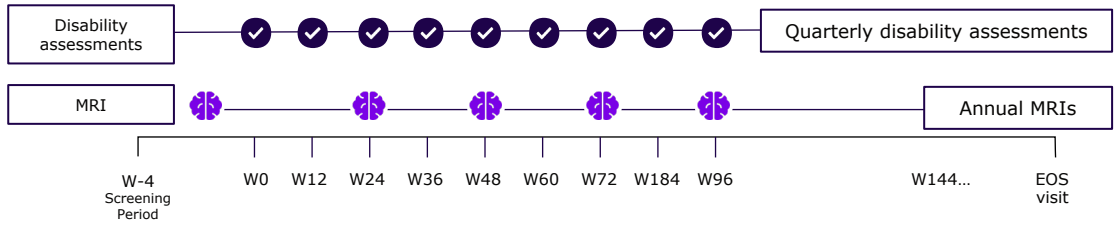
FREXALT-2 (RMS)



Primary endpoint

Adjudicated annualized relapse rate (ARR) during the study period assessed by confirmed protocol-defined adjudicated

FREVIVA (nrSPMS)



Primary endpoint

Time to onset of 6m-cCDP as assessed by the composite of:

- Increase of ≥1.0 point from the baseline EDSS score when the baseline score is <5.5, OR increase of ≥0.5 points when the baseline EDSS score is ≥5.5
- Or ≥20% increase from baseline score in the 9-HPT test or T25-FW test

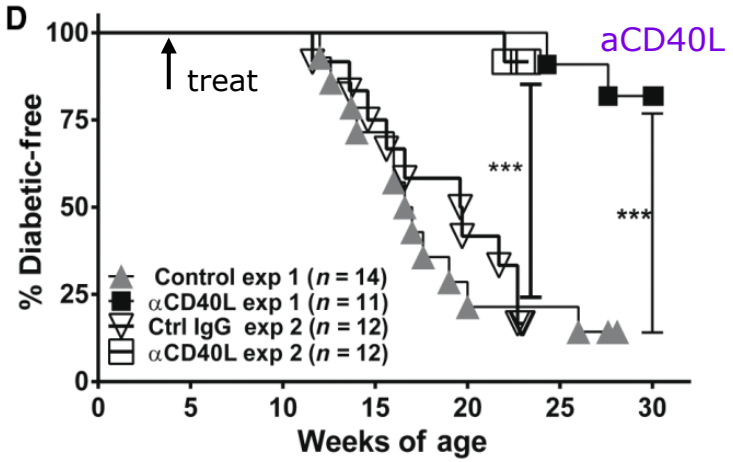
Disability assessments refer to EDSS, T25FW, 9HPT and SDMT, at screening only EDSS will be assessed. Continued development of SubQ dosing in parallel. FREXALT (NCT06141473). FREVIVA (NCT06141486).
Frexalimab is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Frexalimab: Potential *disease modification* of type 1 diabetes through protection of pancreatic β-cells

- Type 1 diabetes is an autoimmune disorder in which cytotoxic CD8 T cells kill the pancreatic β-cells leading to a life-long dependency on insulin treatment
- Frexalimab acts by blocking a key amplification step between T- and B-cells minimizing T-cell activation and protecting further loss of β-cells

Mouse model data

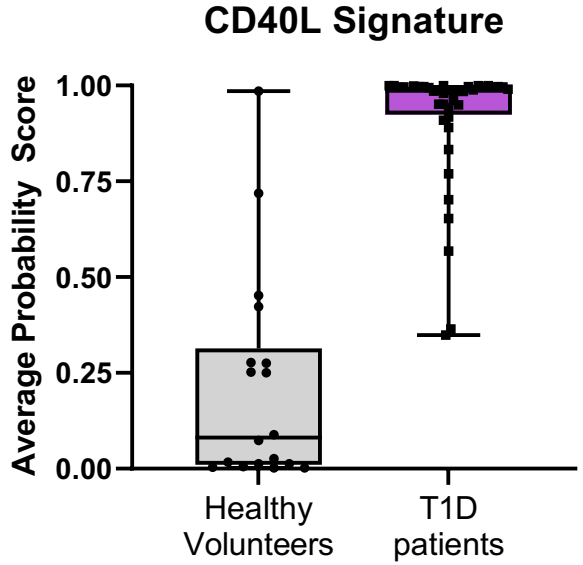
Female NOD/LtDvs mice treated with a single dose of anti-CD40L mAb at 4 weeks-of-age show significantly reduced progression to Type 1 diabetes



Non-obese diabetic (NOD) mice are an autoimmune strain of mice that develop spontaneous T1D as well as autoantibodies such as anti-insulin autoantibodies

Human gene expression data

Sanofi integrative analysis of CD40L pathway gene expression shows a highly significant enrichment in gene score in the blood of T1D patients (p<0.0001)



1. Mahmoud T.I. et al, Autoimmune manifestations in aged mice arise from early-life immune dysregulation, Sci Trans Med, 2016 Oct 19;8(361) 2016. 2. https://www.finngen.fi/en. 3. https://innodia.cpr.ku.dk/.
Frexalimab is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Frexalimab: *Pipeline-in-a-product* with significant indications under development

Indication	Status	Clinical evidence	Eligible population	Next milestone
MS	Phase 3	Significant reduction in new lesions at Week 12	**1.1M**[1]	Phase 3 data RMS Submission **in H2 2027**
T1D	Phase 2b	Circulating CD40L pathway gene expression significantly upregulated in T1D patients[3]	**2.8M**[2]	Phase 2b data **in 2027**

More than 3.9M eligible patients

Additional indications being explored adding potentially *another ~0.5M*

Indication	Status	Preliminary clinical evidence	Eligible population	Next milestone
Sjogren's syndrome[4]	Phase 2a	Potent pharmacological activity on a disease related biomarker (CXCL13)[5]	**0.2M**	Phase 2a data **in H1 2024**
SLE[6]	Phase 2a	Supportive data from other CD40L program[7]	**0.3M**	Phase 2a data **in H2 2025**

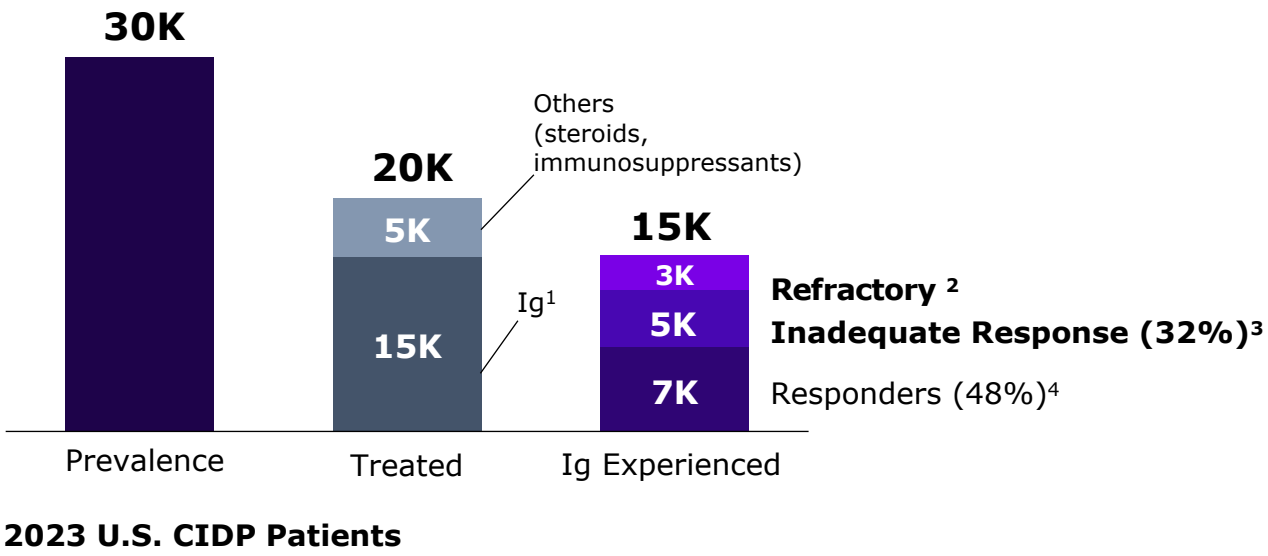
- ✓ Potential first-in-class
- ✓ Potential pipeline-in-a-product

€5bn+ peak sales potential

Advanced therapy eligible patients across U.S. and EU5 (France, Germany, UK, Spain, Italy). Additional details in Epidemiology Appendix. 1. MS includes RMS and nrSPMS diagnosed patients. 2. Prevalence all ages; Prevalence <20y 0.3M (U.S. 0.168M + EU5 0.136M), Incidence <20y 30k (U.S. 19k + EU5 14k). 3. Sanofi internal analysis. 4. Moderate to severe patients. 5. Based on internal interim analysis. 6. Excludes Lupus Nephritis, treated patients. 7. https://pubmed.ncbi.nlm.nih.gov/33956056/
Frexalimab is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Significant *unmet need* in Chronic Inflammatory Demyelinating Polyneuropathy

Highest unmet need remains in CIDP for patients with partial or no response to SOC



2023 U.S. CIDP Patients

Most common peripheral autoimmune demyelinating condition, ~30% of patients becoming *wheelchair bound*

30 to 40% of patients do not respond or respond inadequately to SOC IVIg

More effective and convenient treatments *needed*

1. Includes IVIg: Intravenous Immunoglobulin, SCIg: Subcutaneous Ig, patients treated with Ig + steroids in combination. 2. Ig-refractory: patient who is no longer undergoing Ig treatment due to failure or inadequate response (INCAT 2-9), or unable to take IG due to side effects. 3. Ig Treated with remaining disability (i.e., INCAT 2): patient on Ig treatment with remaining disability (with an INCAT higher or equal to 2). 4. Fully responding to Ig without remaining disability (i.e. INCAT 0-1): patient fully responding to Ig treatment and stable without remaining disability (with an INCAT score of 0-1). Details in Epidemiology Appendix.

Phase 2 in CIDP *met primary* and secondary endpoints at planned interim analysis

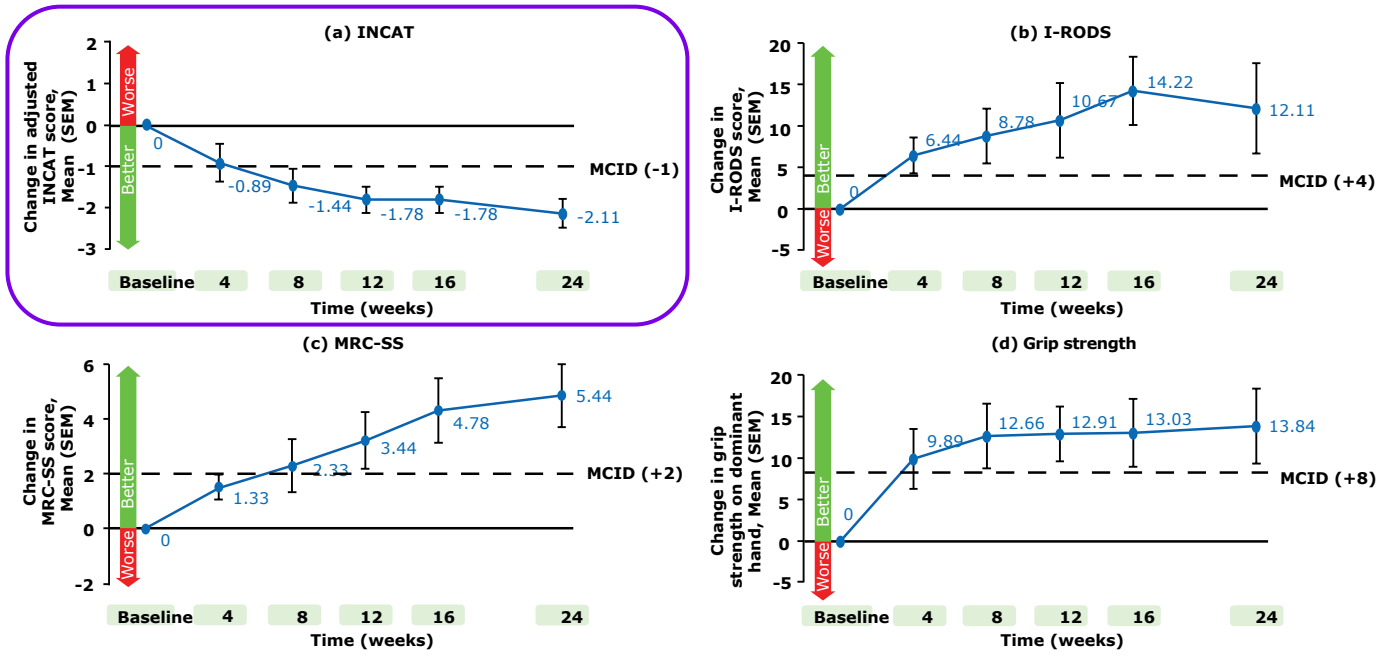
- *riliprubart* is a subcutaneously administered humanized monoclonal Ab that targets active C1s in the classical complement pathway

- Potential to *block* key inflammatory mechanisms causing demyelination and axonal damage in CIDP

- Positive endpoints were *met* in both refractory and SOC treated patients

NEW

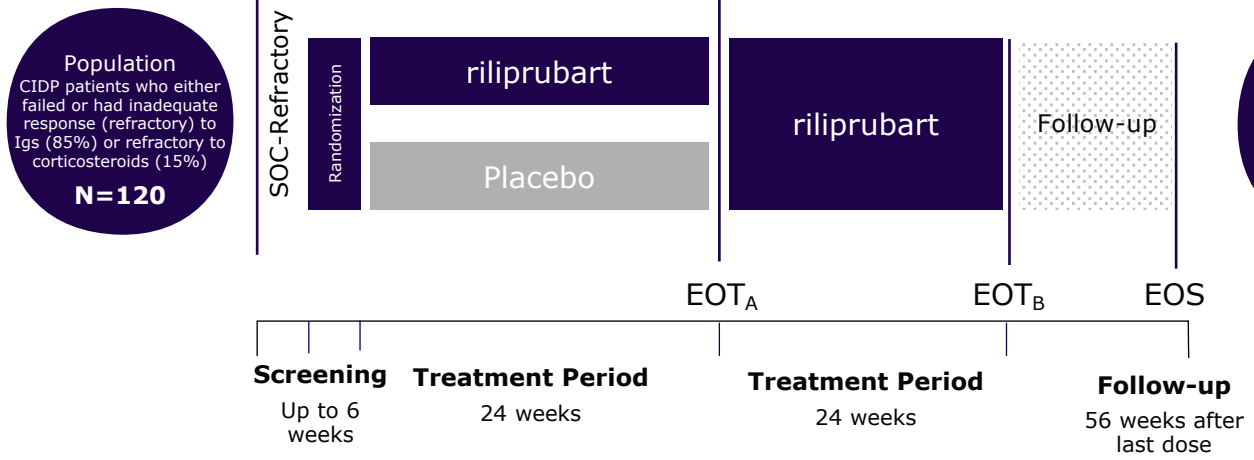
*50% of participants[1] experienced a meaningful improvement in function and muscle strength observed (≥1 point decrease in INCAT) in **SOC-Refractory group** N=18*



1. Out of 18 participants, 14 completed 24 weeks, while 4 discontinued (due to Pneumonia klebsiella, muscular weakness, death, visit schedule burden).
Riliprubart is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Riliprubart Phase 3 *program* in CIDP

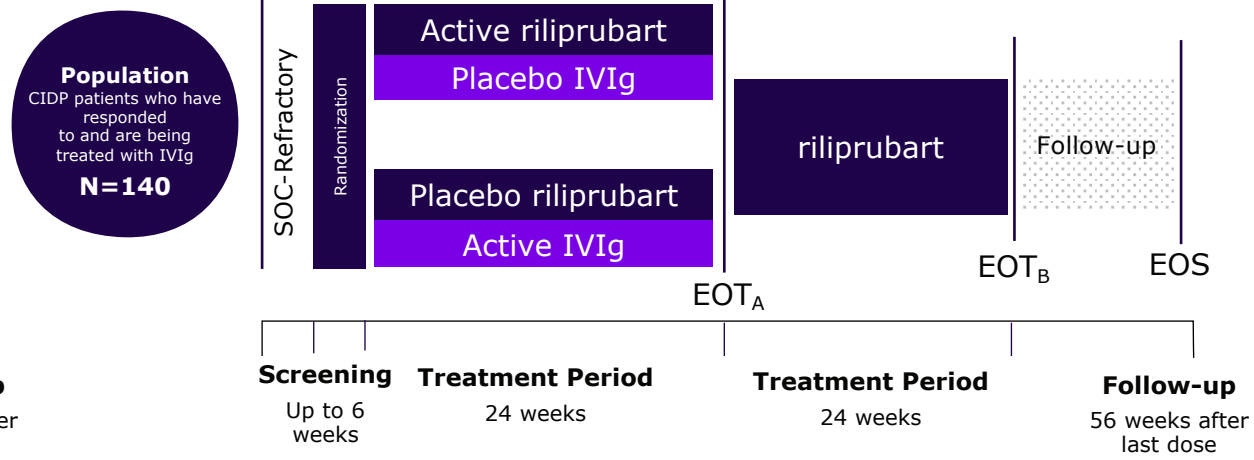
Mobilize (SOC-Refractory CIDP)



Primary Endpoint
- Percentage of participants achieving 1-point decrease in adjusted INCAT disability score at Week 24, compared to baseline

Secondary Endpoint
- Improvement in functional disability monitored (I-RODS, INCAT), muscle strength measured by MRC-SS, quality of life (EQ-5D-5L), and fatigue (R-FSS)
- Safety and Immunogenicity

Vitalize (IVIg-Treated CIDP)



Primary Endpoint
- Percentage of participants achieving 1-point decrease in adjusted INCAT disability score at Week 24, compared to baseline

Secondary Endpoint
- Improvement in functional disability monitored (I-RODS, INCAT), muscle strength measured by MRC-SS, quality of life (EQ-5D-5L), and fatigue (R-FSS)
- Safety and Immunogenicity

Riliprubart is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Maximizing the value of multiple late-stage assets in neuroinflammation

Neuroinflammation

Compound	Description	Target indication	Phase	Planned submission
tolebrutinib	BTK inhibitor	RMS	3	H2 2024
tolebrutinib	BTK inhibitor	nrSPMS	3	H2 2024
tolebrutinib	BTK inhibitor	PPMS	3	2025
frexalimab	Anti-CD40L mAb	RMS, nrSPMS	3	2027 (RMS)
riliprubart	Complement C1s inhibitor	CIDP	3	2026
SAR443820	RIPK1 inhibitor	MS	2	

Neurodegeneration

Compound	Description	Target indication	Phase
SAR443820	RIPK1 inhibitor	ALS	2
SAR443820	RIPK1 inhibitor	Alzheimer's Disease	1 (opt-in)
SAR446159[1]	Anti-alpha-synuclein and IGF1R bispecific Ab	Parkinson's Disease	1

1. Also known as ABL301, developed in collaboration with ABL Bio. These products are currently under clinical investigation and their safety and efficacy have not been evaluated by any regulatory authority.

sanofi

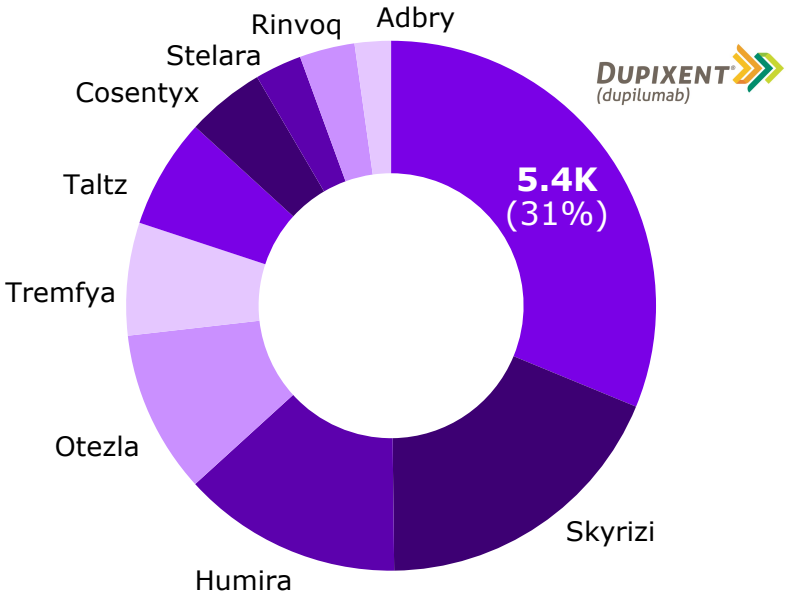
Expanding leadership in respiratory

Manuela Buxo

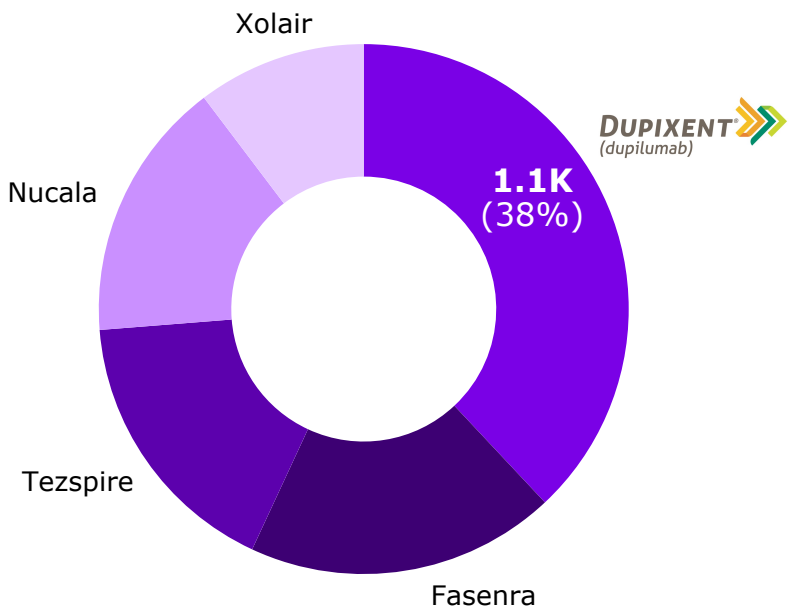
Global Head of Dupixent Franchise

DUPIXENT® (dupilumab) Building a *superbrand*

Leading with *Dermatologist* Weekly NBRx[1]



Leading with *Pulmonologist* Weekly NBRx[1]



9 Approved indications[2]

- Adults
- Adolescents
- Pediatric to 6mo+

>750k Patients treated[3]

#1 U.S. NBRx share across all indications[4]

>7 m Biologics eligible patients in major markets[5]

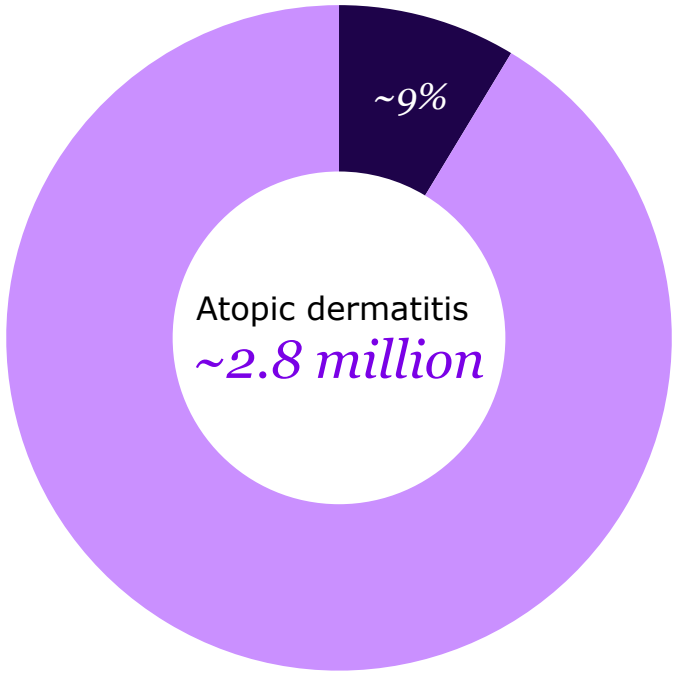
1. IQVIA SMART – Patient Insights Edition (Nov 2023 Extract). 2. AD (4), Asthma (2), CRSwNP, PN, EoE. 3. Across >50 geographies where currently approved in at least one indication.
4. IQVIA NSOB, Nov 2023. 5. Japan, Germany, France, Italy, Spain, and UK.

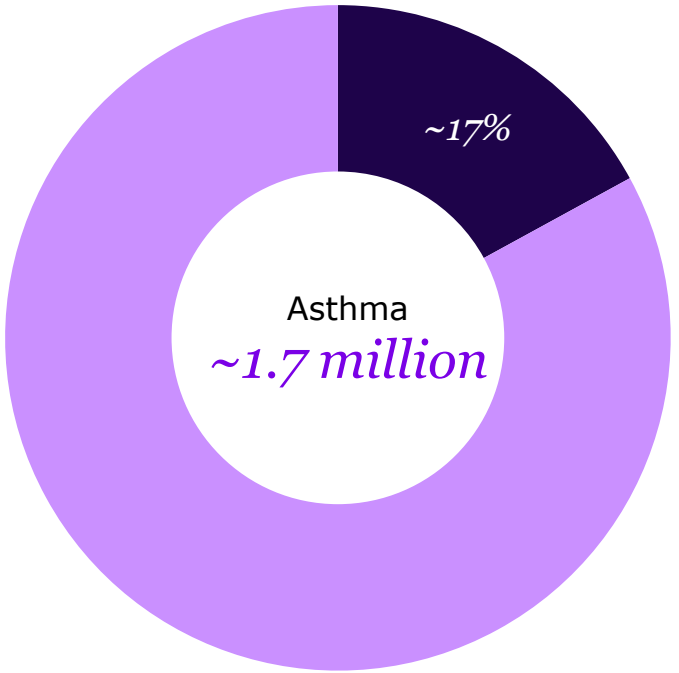
Dupixent: addressing *large patient populations* in markets with low penetration of advanced therapies

Estimated patients (18+) in U.S., EU5 (2022)

Advanced therapy treated

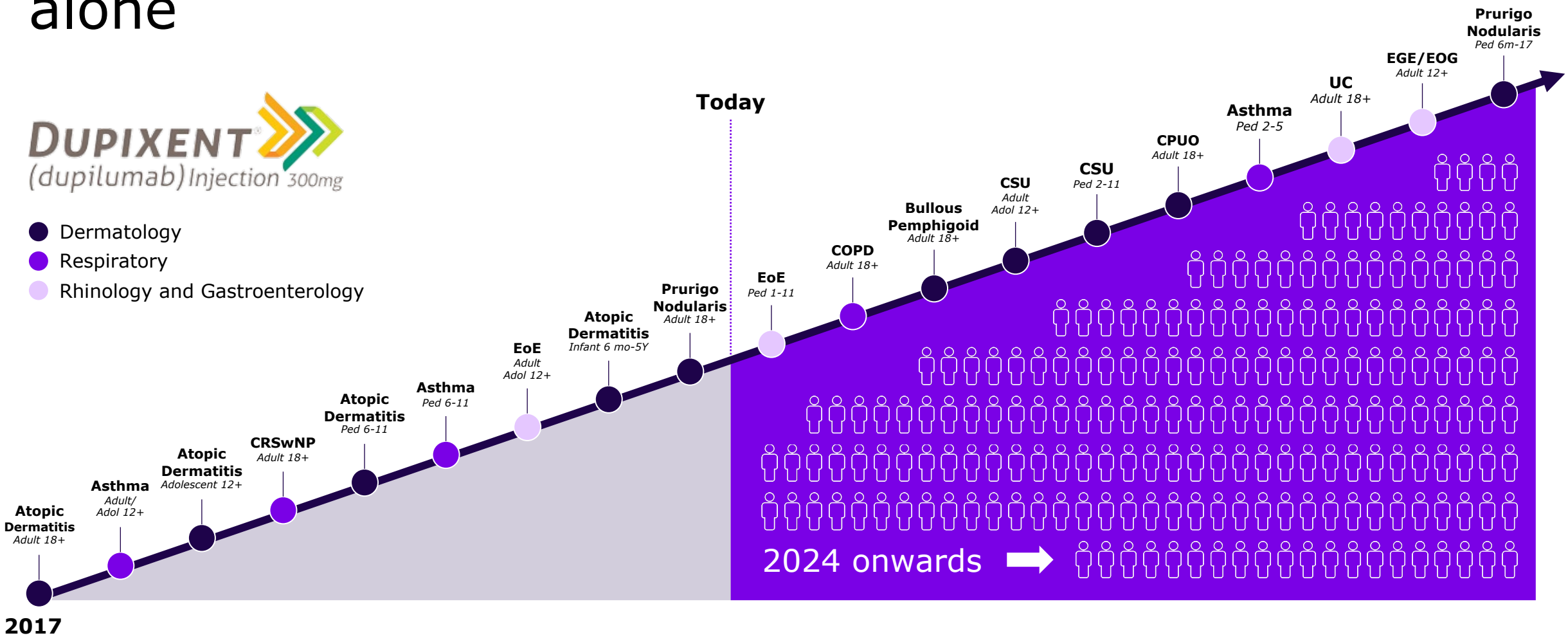
Advanced therapy eligible





Advanced therapy eligible patients across U.S. and EU5 (France, Germany, UK, Spain, Italy). Additional details in Epidemiology Appendix.

Opportunity to add *1 million* eligible patients in the U.S. alone

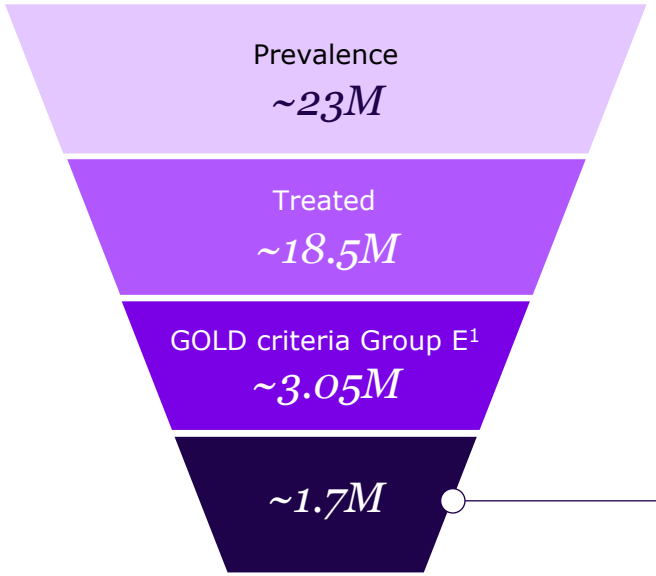


Sanofi develops first advanced therapy addressing *unmet need in COPD* with huge burden for society

No new treatment options were approved in more than 10 years

- 3rd leading cause of death worldwide, ~150K annual deaths in U.S.
- Significant impact on quality of life
- Leading to 1.5m hospitalizations in the U.S. per year
- Major driver of healthcare costs, ~$50bn of economic cost annually in U.S.
- **No biologics treatment approved**

COPD patients in U.S., EU5, Japan



Highest unmet need in *patients uncontrolled* on triple therapy or double therapy (LAMA/LABA)

Sanofi is deploying a phenotype-driven approach with Dupixent and itepekimab to tackle the burden of uncontrolled COPD

Advanced therapy eligible patients across U.S., EU5 (France, Germany, UK, Spain, Italy) and Japan, 2023 estimate. Additional details in Epidemiology Appendix. 1. GOLD criteria: Global Initiative for Chronic Obstructive Lung Disease - Group E defined as high risk (≥2 exacerbations / year, or one+ requiring hospitalization). Sources: WHO, cfah, American Lung Association, ATS, GOLD

Dupixent – 2nd Phase 3 trial *confirms* results of landmark BOREAS pivotal trial in uncontrolled COPD

Dupixent COPD Phase 3 program

- NOTUS and BOREAS are replicate Phase 3 trials enrolling a total of 1,874 patients
- All patients had uncontrolled COPD and *evidence of type 2 inflammation* (blood eosinophils ≥300 cells/µL)
- Dupixent was added to maximal standard-of-care inhaled therapy[1]
- The primary endpoint for NOTUS and BOREAS evaluated the annualized rate of acute moderate or severe COPD exacerbations

Key findings in phase 3 NOTUS trial

Significant, clinically meaningful, 34% reduction in moderate or severe exacerbations compared with placebo

Significant improvements in lung function relative to the placebo at 12 weeks

Safety findings consistent with known safety profile of Dupixent

Next steps:

Full data to be presented at an upcoming scientific meeting

Data to be submitted, along with positive results from the Phase 3 BOREAS trial, to the FDA *by the end of the year*

Under review by EMA, based on results from the BOREAS trial; discussions with other regulatory authorities around the world ongoing

Dupixent is under investigation in COPD and not yet approved by any regulatory agency to treat this indication. 1. Including corticosteroids, long-acting beta agonists, and long-acting muscarinic antagonists.

itepekimab (anti-IL 33)

Potent IL-33 blocker with *best-in-class* and *first-in-class* potential

Phase 2a results in uncontrolled COPD patients fully published

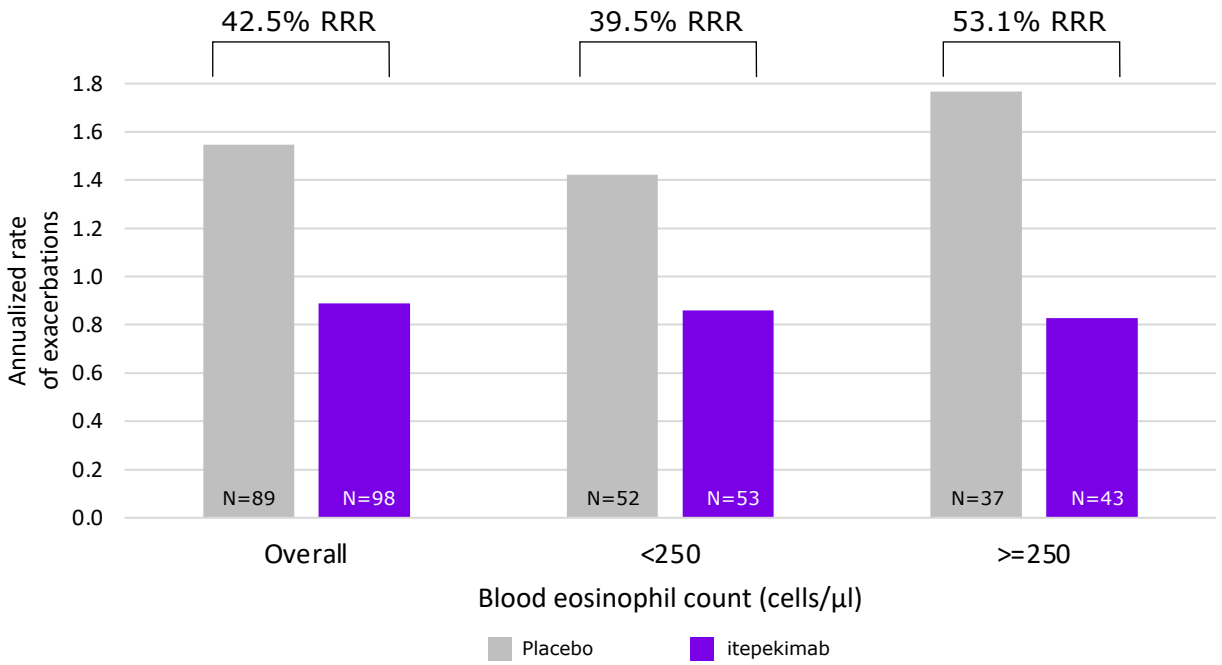
- Numerically lower rate of exacerbations in all patients (not statistically significant)
- >40% reduction in exacerbations in COPD *in former smoker population*
- Generally well tolerated, with an acceptable safety profile

THE LANCET
Respiratory Medicine

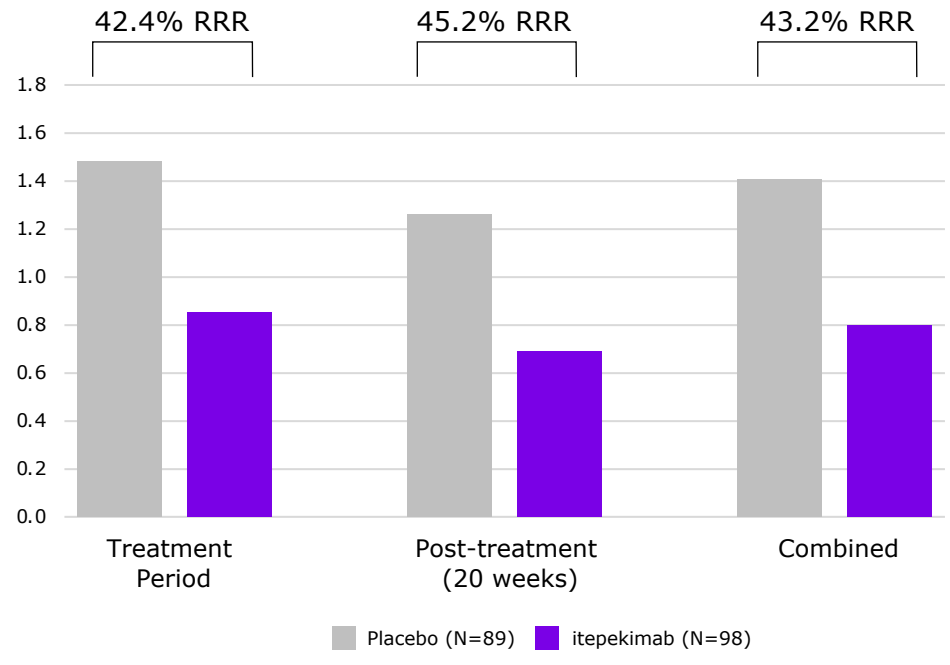
Itepekimab is under investigation and not yet approved by any regulatory agency; Itepekimab is being developed in collaboration with Regeneron. Source: Rabe et al. Lancet Respir Med. 2021

Itepekimab: unprecedented impact in COPD *former smokers* (Phase 2a)

Effect present in *both high and low eosinophil* population



Sustained efficacy 20 weeks post treatment



tepekimab Significantly Reduced Hospitalizations and Emergency Department Visits in Former Smokers With Moderate-to-Severe Chronic Obstructive Pulmonary Disease, Klaus F. Rabe. Rabe et al. Lancet Respir Med. 2021 (Post-hoc analysis). Itepekimab is under investigation and not yet approved by any regulatory agency. Itepekimab was generally well tolerated. Treatment emergent adverse events occurred in 78% of itepekimab patients and 80% of placebo patients. Left graph is showing adjusted values, right graph is showing unadjusted values.

Itepekimab: Phase 3 data expected *in 2025*

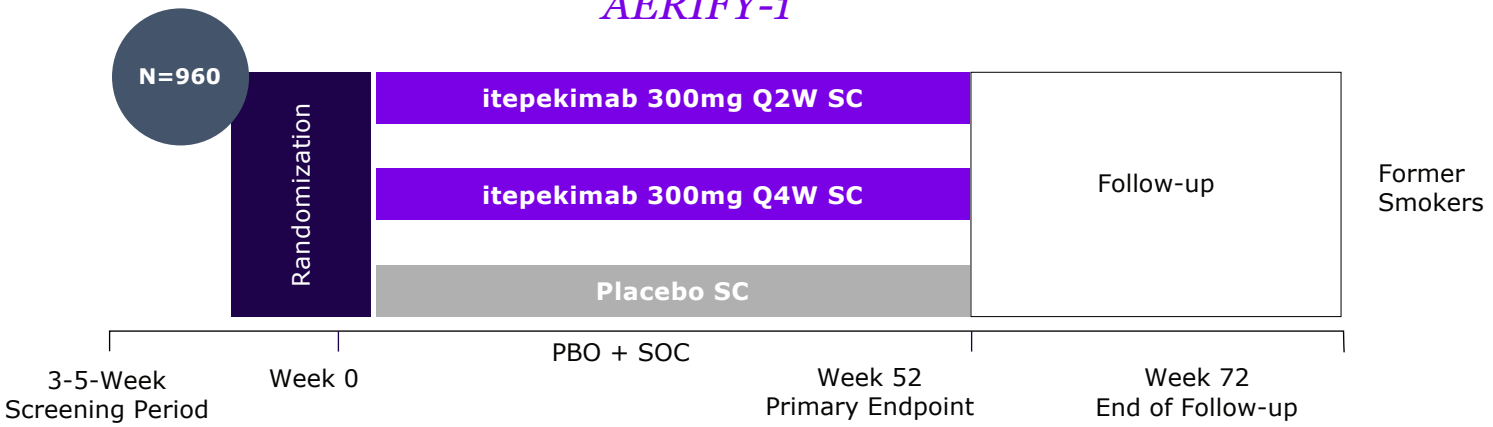
Study population:

Mod-to-severe COPD w/smoking history of ≥10 pack-years

≥40-85 yrs

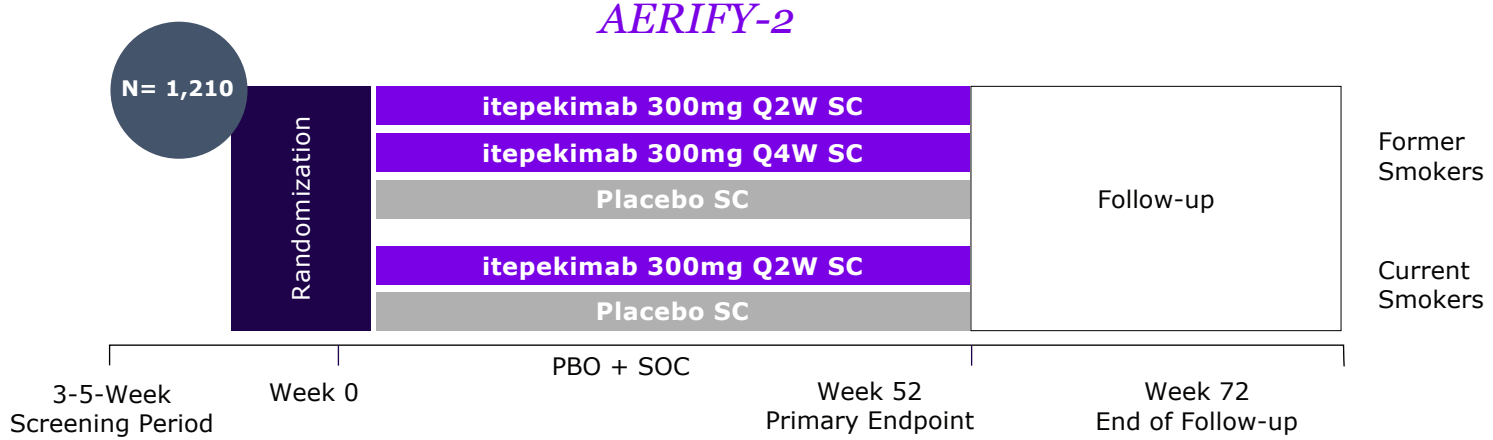
Gender: All

AERIFY-1



FDA Fast Track Designation[1]

AERIFY-2



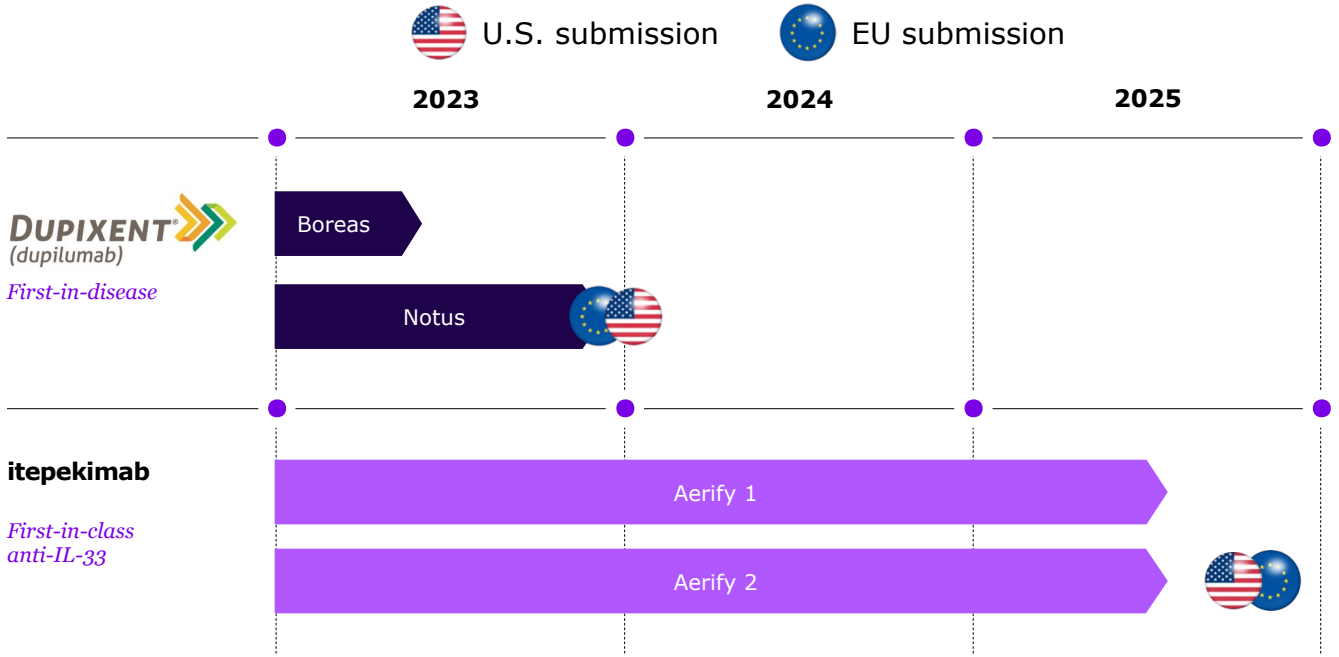
Passed futility analysis

Itepekimab is under investigation and not yet approved by any regulatory agency. 1. For COPD in former smokers.

Peak sales potential for Dupixent and itepekimab in COPD of *>€5bn combined*

Patient population G7[1] – 2035e

	Non-Type 2	Type 2
Former smokers (70%)	**itepekimab[2]** ~1,139K patients	**Dupixent®[3] and itepekimab[2]** ~640K patients
Current smokers (30%)		**Dupixent®[3] only** ~270K patients



Dupixent and itepekimab have both the potential to address different COPD populations with limited overlap

1. G7 countries: U.S., France, Germany, Italy, Japan, UK, Canada; GOLD criteria Group E and uncontrolled with triple therapy or LAMA/LABA contraindicated to ICS. 2. Itepekimab not yet approved by any regulatory agency. 3. Dupixent is under investigation and not yet approved for COPD and is being studied in patients with uncontrolled COPD treated with current SoC triple therapy among GOLD E. Patient populations exclude never smokers.

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Physician perspective on COPD

Brian Foard
Global Head of Specialty Care ad interim

Elizabeth Laws
Global Program Head, Dupixent

MeiLan Han
Chief, Division of Pulmonary & Critical Care
at the University of Michigan

Q&A session (Part 2)

Break

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Leading in Immunology Research

Frank Nestle
Global Head of Research, Chief Scientific Officer

Building a *leading* Research organization

Generation of differentiated FIC/BIC molecules to sustainably fuel our R&D pipeline

Establish strategic innovation engines

- Immunology & Inflammation
- Precision Medicine
- Genomic Medicine Unit
- Portfolio Excellence

Build enablers and capabilities

- Next generation biologics
- AI Research Factory
- Scientific talent & leadership

Capitalize on the breadth of external innovation

- Open innovation
- Focus on external partnerships

Value delivery

Industry-leading I&I pipeline[1]

- ✓ 12 I&I FIH in 3 years[2]
- ✓ Disciplined prioritization; "fast-track" project proof points (idea to FIH in 3-4 years)

External partnerships to capture innovation

- ✓ ~25% of projects leverage external capabilities

Innovative technologies

- ✓ Flywheel Platform technologies
- ✓ Automation, digital enablement, and AI
- ✓ AI supported target and indication ID engine

Doubling research productivity & FIH entries / year[3,4]

1. According to KMR benchmarking report, 33% of Sanofi development pipeline are I&I NMEs vs 15% industry median. 2. # FIH 2021-2023. 3. # clinical candidates/investment (triennial average, 2015-2023e).
4. FIH entries (triennial average, 2015-2023e).

Strategic pillars for leadership in Immunology Research

Ambition: break efficacy ceilings, achieve a durable response, expand into new indications

Focus on…

Multiple Cytokines, Co-stimulators, Transcription Factors

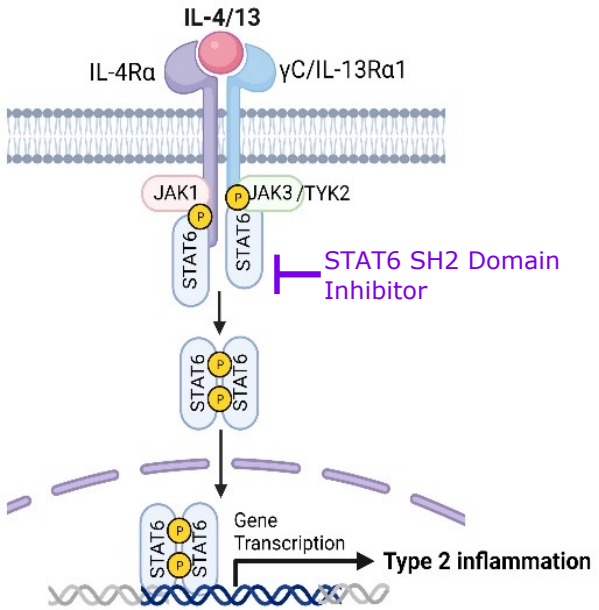
Breaking new frontiers…

Next Gen. Biologics, AI-driven Drug Discovery, RNA-Targeting, Protein Degraders

Leverage…

Target Discovery Engines, Single Cell Genomics, Virtual Patient Engines

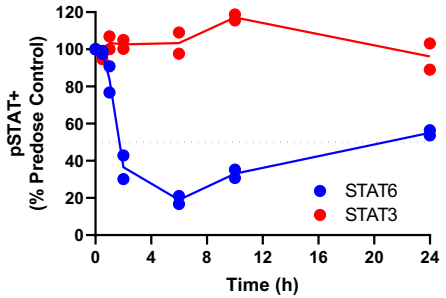
STAT6 pathway inhibitor: an *oral* small molecule that blocks type 2 IL-4 and IL-13 pathways



STAT6 SH2 domain inhibitors selectively target type 2 cellular responses and differentiate from JAK inhibitors

	STAT6 inhibitor	IL-4/13 antagonist[1]	JAK inhibitor[1]
T Cell Function (IC50)			
Th2	26nM	26nM	4nM
Th17	>100X	>35X (highest tested)	2X
Th1	>100X	>35X	9X
Hematological homeostasis			
EPO-STAT5	>300X	>35X	17X
TPO-STAT5	>300X	>35X	5X

Durable and selective pSTAT6 inhibition following single oral dose of STAT6 SH2 domain inhibitor in preclinical model



STAT6 inhibitor offers potential for *antibody-like efficacy* with oral convenience in type 2 diseases

Strong human *genetic evidence* for critical role of STAT6 with associated GWAS and gain of function mutations driving allergic disease[2,3,4,5]

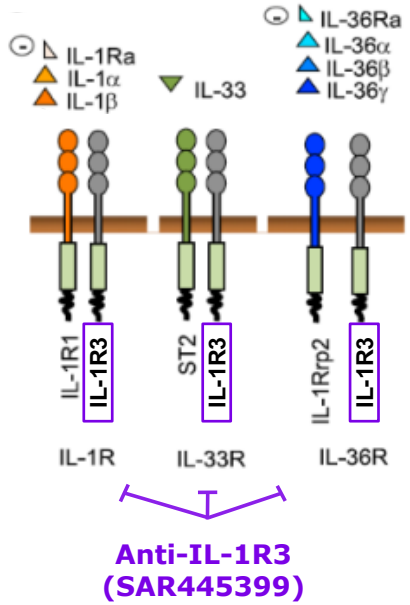
Entered strategic collaboration with Recludix Pharma to advance novel oral STAT6 SH2 domain inhibitors with *IND projected in 2025*

1. Corporate presentation, Recludix Pharma, JPM HealthCare Conference, Jan 2023. 2. Baris et al., JACI 152, 2023. 3. Sharma et al., J Exp Med 220, 2023. 4. Takeuchi et al., JACI 151, 2023. 5. Suratannon et al., JACI 151, 2023.

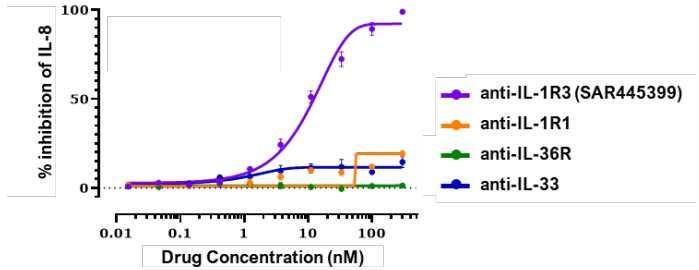
Anti-IL-1R3 (SAR445399): a *multi-pathway* targeting Ab

Targeting 3 cytokine pathways with one molecule for potent IL-1, IL-33 and IL-36 family inhibition

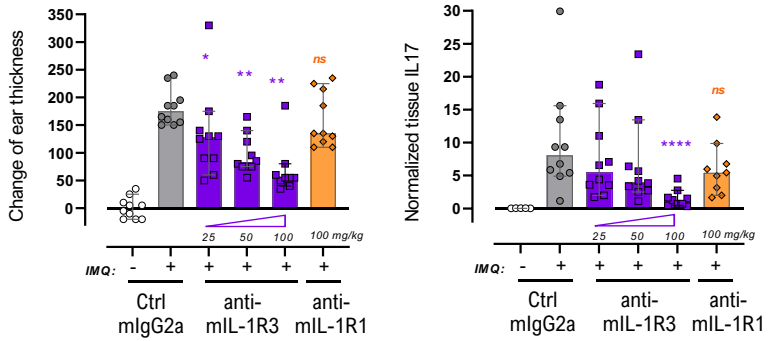
IL-1R3 shared co-receptor for IL-1, 33, 36



SAR445399 blocks IL-1, IL-33 and IL-36 cytokine activity
IL-1β + IL-36γ + IL-33 triple stimulation



Anti-IL-1R3 blocks imiquimod-induced skin inflammation



Co-inhibition of 3 validated cytokine pathways to boost anti-inflammatory efficacy

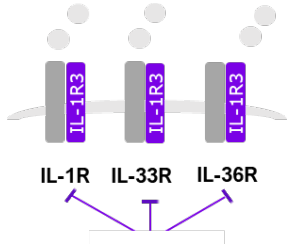
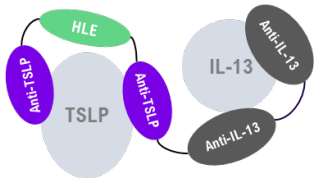
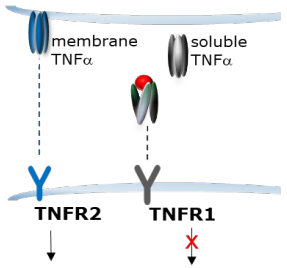
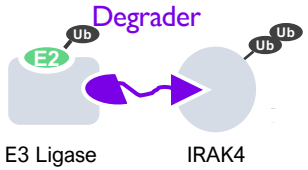
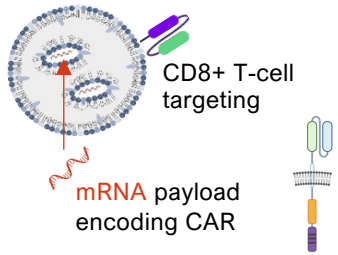
Target *innate cytokines* driving and perpetuating inflammation of barrier tissues (e.g. skin, lung, gut)

Pipeline-in-a-drug potential across multiple inflammatory indications

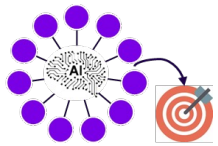
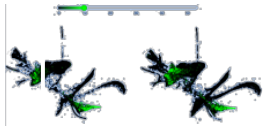
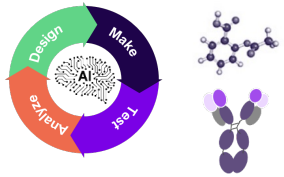
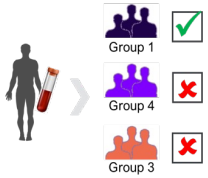
Phase 1 SAD/MAD study ongoing, expecting readout in 2024; multiple inflammatory indications

Asset is under clinical investigation and has not been approved by any regulatory authority

Technology innovation driving Immunology pipeline

Next Generation Antibody	Multi-specific Nanobody® VHH	Next Generation Small Molecule	Targeted Protein Degrader	*In Vivo* Cell Reprograming
Program highlights				
				
Anti-IL-1R3	*Anti-IL-13/TSLP*	*TNFR1 signaling inhibitor*	*IRAK4 degrader*	*in vivo CAR-T*
Pipeline programs				
Phase 3 - amlitelimab (AD) **Phase 2** - frexalimab (SjS, T1D, MS, SLE) - amlitelimab (Asthma, HS) - Anti-TL1A (UC, CD) **Phase 1** - Anti-IL-1R3 **Discovery** - 11 Programs	**Phase 2** - Anti-TNFα/OX40L Nanobody® VHH (HS) - Anti-IL-13/TSLP Nanobody® VHH (Asthma) **Phase 1** - Anti-CX3CR1 Nanobody® VHH **Discovery** - 13 programs	**Phase 3** - rilzabrutinib (ITP) **Phase 2** - rilzabrutinib (CSU, Asthma, IgG4-RD) - Oral TNFR1si (Pso, RA) - RIPK1i (UC) **Discovery** - STAT6i - 17 programs	**Phase 2** - IRAK4 degrader (AD, HS) **Discovery** - 4 programs	**Discovery** - *in vivo* CAR-T (Oncology) - 3 programs

AI Research Factory: Artificial Intelligence *empowered* drug discovery and development

Disease Biology		Drug *Invention*		Clinical *Translation*
Target Identification Engine	*Single Cell Genomic Disease Maps*	*Accelerated Drug Molecule Design & Optimization*	*Virtual Patient Engines*	*Disease Endotyping & Patient Stratification*
				
Discovered *> 90 novel targets* Advanced *7 targets* to research pipeline in *<12 months*	Clinical insights into MoA *90% of targets* credentialed using single cell genomics	*75% of small molecule* projects enabled by AI/ML compound design Established biologics AI foundations	Virtual patients for *12 therapeutic indications* to drive in-silico clinical trials	Genomics-based precision medicine *empowering clinical trials* (e.g. Anti-CD40L, SLE)

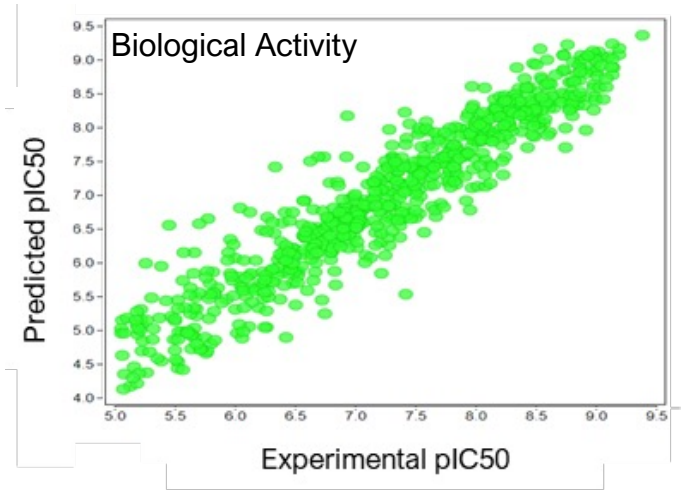
Partnerships

AQEMIA · Atomwise · BioMap · CytoReason · Exscientia · Insilico Medicine · OWKIN

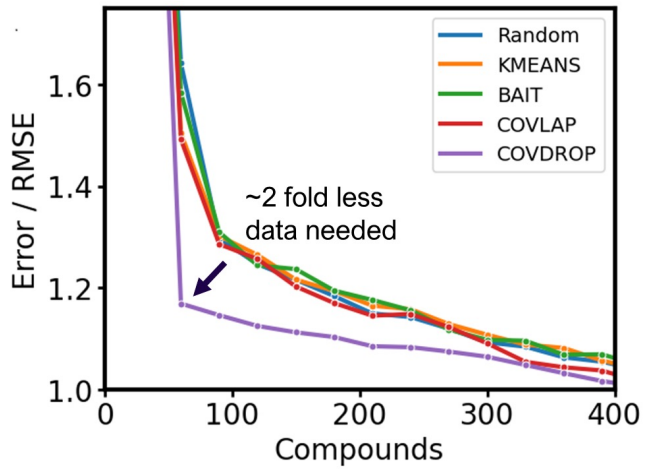
Leveraging GenAI to improve *quality and speed* of Small Molecule Drug Discovery

Key AI models achieve >80% predictivity while active learning improves AI model training

Predictivity of AI models vs. cell-based assay[1]

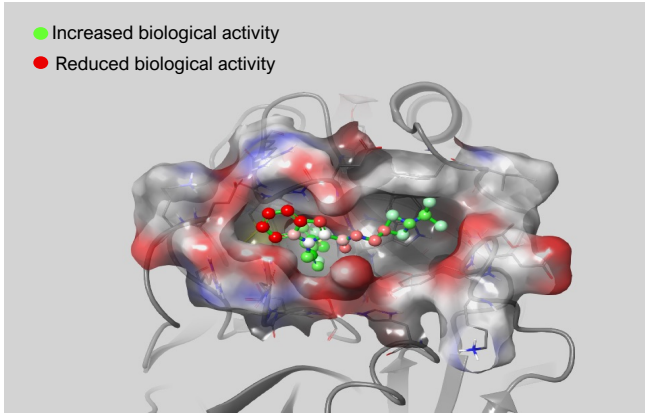


Amount of data required to reduce AI model errors[2]



Explainable AI and Virtual Reality to apply AI learnings

Highlighting key structural elements to guide design cycles[3]



75% of small molecule projects enabled by AI/ML compound design

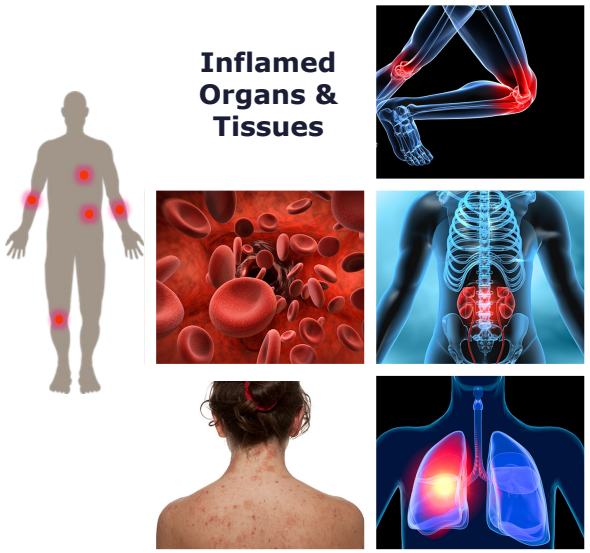
1. Example molecule data. 2.Michael, B. et al, 2023, eLife. 3. Harren, T. et al. J. Chem. Inf. Model. 2022.

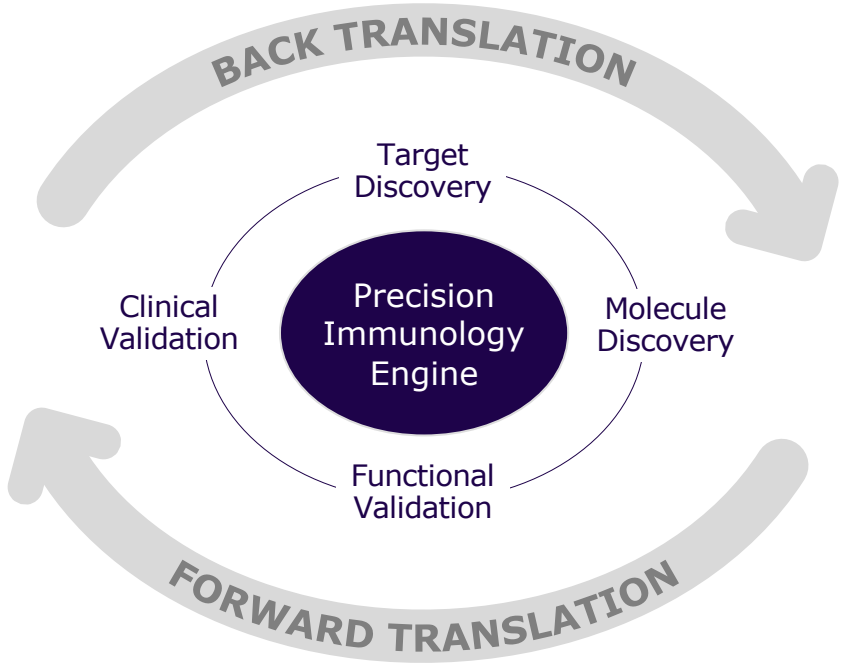
Patients at the *center* of Immunology Research

Matching disease mechanisms with novel modalities

Precision Immunology

Focus on patients and human immune biology





Precision Immune Therapies

Utilize novel technology platforms

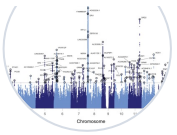
- Next Gen. Antibody
- Multi-specific Nanobody® VHH
- Next Gen. Small Molecule
- Protein Degrader
- *in vivo* Cell Reprogramming

AI and disease data empowered target ID & *prioritization*

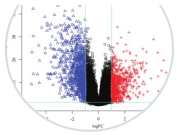
Example use case: Target Immune Engines (TIE) in Ulcerative Colitis

Input: Sanofi multi-modal data

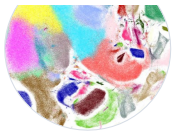
GWAS & causality inference



Bulk transcriptomics



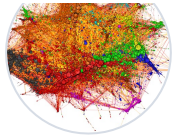
Single-cell genomics



Network/ pathways

External benchmarking

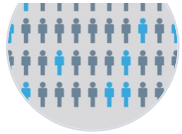
Predictive knowledge graph



Safety

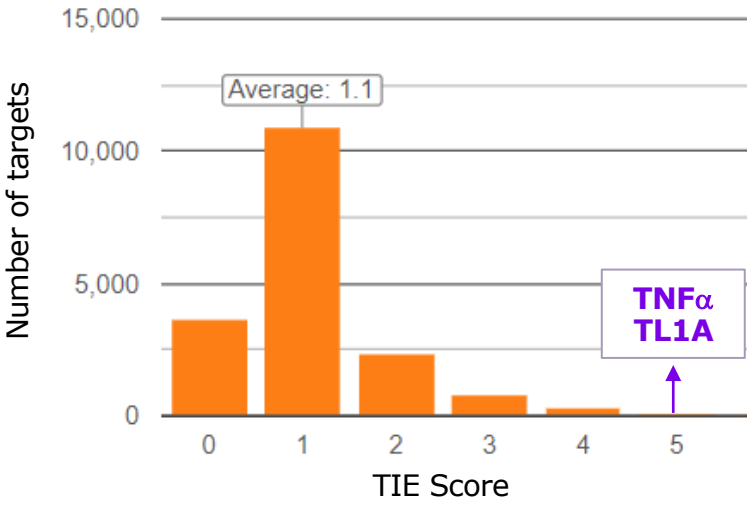
Competition

Disease endotypes



AI-driven prioritization

Output: Target Assessment Score



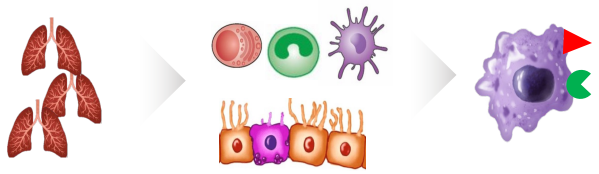
Top score (5) for clinically validated UC targets demonstrates high predictive performance of TIE

More than 50 target hypotheses generated in <12 months | 7 novel targets advanced to the research pipeline in 2023

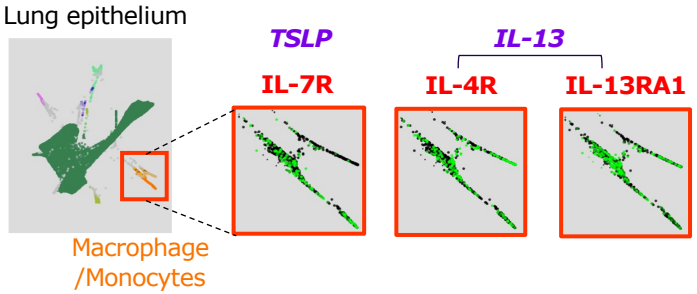
Pioneering *single cell genomic analysis* to understand MoA of lunsekimig

Asthma patient samples

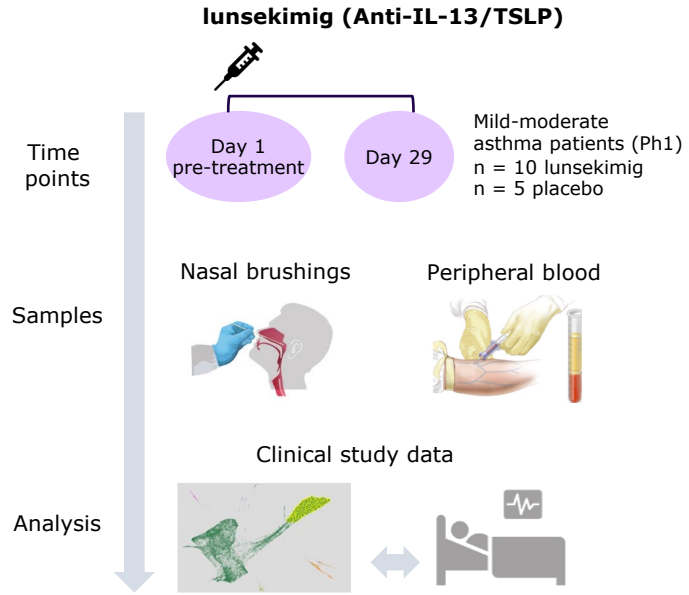
Disease-relevant tissue | Disease-relevant cell types | Receptor co-expression



Deconvoluting Anti-IL-13/TSLP MoA in single cells



Pre- and post lunsekimig treatment



Mechanism of Action

Decrease of *nonclassical monocytes* in nasal brushings

Decrease of *CCL26/Eotaxin-3* in nasal epithelial subsets

Decrease of *neutrophil IL-4-, IFNγ-, and IFNα-pathway activity* in peripheral blood

NK cell reduction correlates with positive lunsekimig clinical response

Back translation of single cell genomic data provides novel insights into lunsekimig indication expansion and novel target hypotheses

Expected advances in *early clinical* Immunology Pipeline

Phase 1 readouts

2024

- Anti-CX3CR1 Nanobody® VHH
- Anti-IL-1R3
- Non-beta IL-2 SYNTHORIN™

2025

- Anti-CD28/OX40

Phase 1b (PoM) readouts[1]

2024

- Anti-CX3CR1 Nanobody® VHH
- Anti-IL-1R3
- Non-beta IL-2 SYNTHORIN™

2025

- Anti-CD28/OX40

Phase 2 readouts

2024

- amlitelimab (anti-OX40L): Asthma
- rilzabrutinib (BTKi): Asthma, IgG4-RD, wAiHA
- frexalimab (anti-CD40L): SJS
- Anti-TL1A: IA IBD

2025

- frexalimab (anti-CD40L): SLE
- amlitelimab (anti-OX40L): HS
- Oral TNFR1si: RA, Pso
- IRAK4 degrader: AD, HS
- eclitasertib (RIPK1i): UC
- Anti-TNFα/OX40L Nanobody® VHH: HS

These products are currently under clinical investigation and their safety and efficacy have not been evaluated by any regulatory authority. 1. Challenge studies on healthy subjects.

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Advancing a productive and maturing development pipeline

Dietmar Berger
Global Head of Development, Chief Medical Officer

We have drastically stepped-up *R&D productivity* to improve patient lives

Major progress in our R&D productivity in recent years

Number of NMEs[1]	*26* Ph1 to Ph3 in 2019	Shift to clinical stage portfolio →	*34* Ph1 to Ph3 in 2022
Number of FIH NMEs/year[1]	*~3* '16-'18	Increase in research output →	*~7* '20-'22
Pipeline value[2]	*1x* 2019	Expansion of pipeline value →	*~4x* 2023

3 key levers of our progress

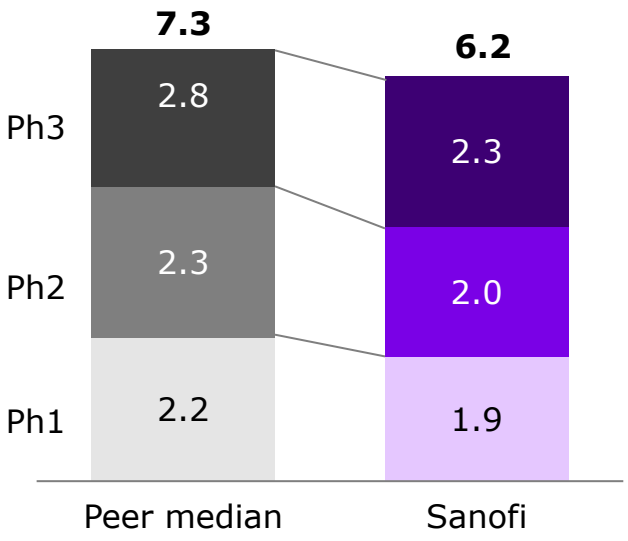
- *Lean & fast Development engine*
- *Leading-edge digital / AI capabilities*
- *Decisive portfolio management*

1. KMR Benchmark, excludes Vaccines. 2. Evaluate Pharma August 2019 vs. November 2023.

We have an industry-leading *lean and fast* development engine

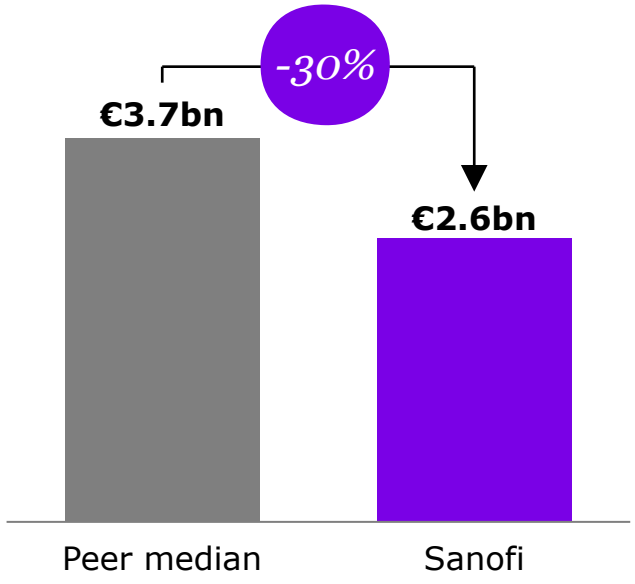
Shorter trial duration

Average trial duration '18-'22 (in years)



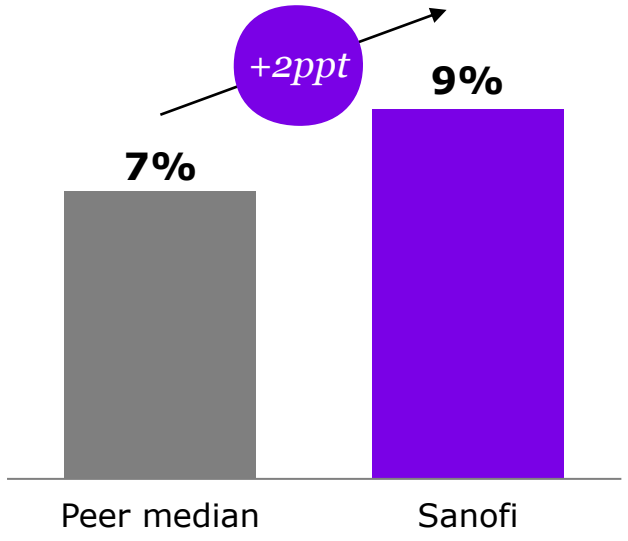
Increased efficiency

Development spending per NME approval '20-'22[1]



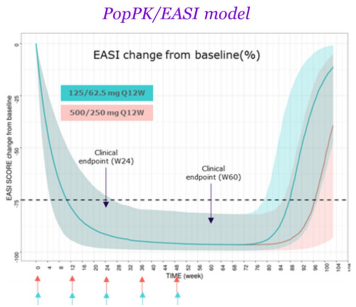
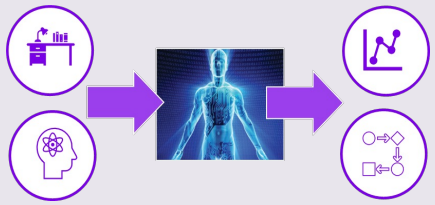
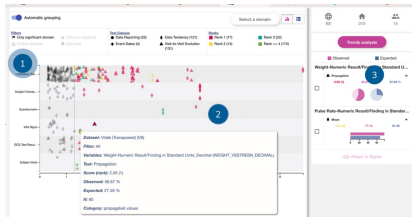
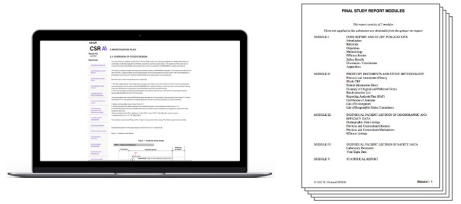
Higher PoS

Overall NME success rate '18-'22[1]



Source: KMR benchmarking report, October 2023. 1. From preclinical to Registration.

Leading digital/AI capabilities to *enhance* R&D productivity

Research	Translational Medicine	Clinical Trials	Regulatory	Patient Safety
Dose optimization	*Generation of virtual patients using QSP*	*Study design & data analysis*	*GenAI document writing*	*Signal detection & risk evaluation*
				
amlitelimab exposure-response analyses to optimize dosage	Prediction of *lunsekimig* best in disease potential through virtual asthma patients	*tolebrutinib* liver toxicity risk mitigation via AI-driven patient segmentation	*Regulatory Report* generation and predictive approval date	Automated *Adverse Event* case processing

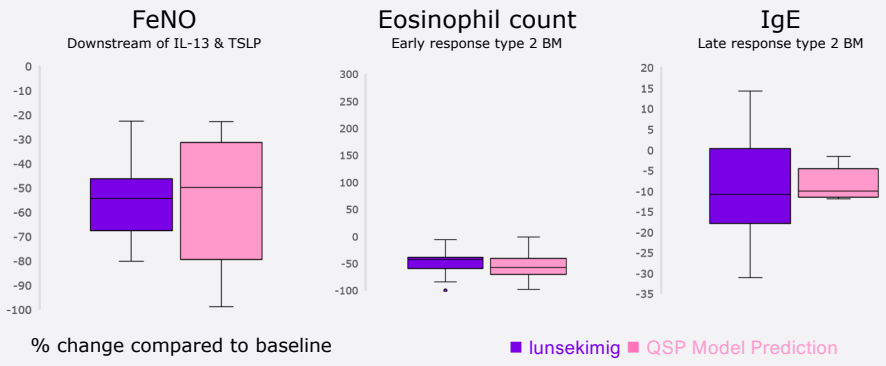
Lunsekimig Phase 2b acceleration leveraging QSP to predict *best-in-class* potential

Generation of virtual asthma patients powered by *Quantitative Systems Pharmacology (QSP)*

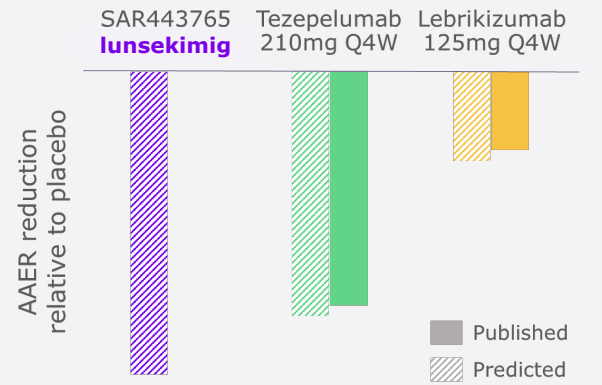
- Integrating available data on physiology, pathophysiology, and pharmacology
- Capturing current knowledge

Correct prediction of lunsekimig BIC potential through virtual asthma patients

Expected biomarker changes at Week 4



Outcome of head-2-head in-silico clinical trial



Successful blind prediction of biomarker responses in PoM study, with observed changes accurately predicted by the QSP model

lunsekimig *best-in-disease potential*, showing highest reduction of AAER observed for Nanobody in virtual asthma patients[1]

1. Not head-to-head comparisons; patient populations and baseline characteristics may differ between studies. Estimates of FeNO change from baseline versus placebo derived from published data. Difference vs placebo estimate from a mixed-effects model over time taking into account baseline FeNO and sex as co-variates.

Therapies driven by *insights from the health community*

Patient-Informed R&D

- *100%* of our trials are informed by patient insights
- Our patient charter, co-created with 80+ patient advocacy groups, *has set the industry standard*
- We are committed to transparency, with *robust annual metrics* holding us accountable

Diversity in Clinical Trials

- Designing for inclusivity, so our trials *are representative of the populations* most likely to benefit
- Assigning *diversity targets to 100% of our trials*
- Reshaping clinical research programs around technology by decentralizing clinical trials to *extend life-changing opportunities to patients around the world*

Near-term milestones of our *development pipeline*

H1 2024

rilzabrutinib ITP	Ph3
venglustat GM2 Gangliosidosis	Ph3
frexalimab SjS	Ph2
SAR443820 (RIPK1i) ALS IA	Ph2
rilzabrutinib Asthma	Ph2

H2 2024

Dupixent CSU	Ph3
Dupixent BP	Ph3
Dupixent CPUO	Ph3
Sarclisa Subcutaneous	Ph3
tolebrutinib RMS	Ph3
tolebrutinib SPMS	Ph3
amlitelimab Asthma	Ph2
Anti-TL1A IBD IA	Ph2
rilzabrutinib IgG4-RD	Ph2
rilzabrutinib wAIHA	Ph2

2025

itepekimab COPD	Ph3
tolebrutinib PPMS	Ph3
amlitelimab HS	Ph2
eclitasertib UC	Ph2
frexalimab SLE	Ph2
IRAK4 degrader AD	Ph2
IRAK4 degrader HS	Ph2
Oral TNFR1si RA	Ph2
Oral TNFR1si PSo	Ph2
TNFa/OX40L HS	Ph2

Expected *submission* timelines

2024	
Dupixent COPD	**venglustat** GM2 gangliosidosis
Sarclisa 1L Newly Diag. MM Ti (IMROZ)	**rilzabrutinib** ITP
tolebrutinib RMS	**fitusiran** Hemophilia A/B
tolebrutinib SPMS	**MenQuadfi** 6w+

2025	
Dupixent Bullous pemphigoid	**Nexviazyme** Pompe Disease - Infantile Onset
itepekimab COPD	**venglustat** Fabry Disease
Sarclisa SubQ 3L RR MM (IRAKLIA)	**VRVg** Purified vero rabies vaccine
Sarclisa 1L Newly Diag. MM Te (GMMG)	**SP0218** Yellow fever
tolebrutinib PPMS	

2026 and beyond[1]	
Dupixent CPUO	**venglustat** Gaucher Type 3
amlitelimab Atopic Dermatitis	**ExPEC Vaccine** E. Coli Vaccine
frexalimab RMS	**SP0125** RSV toddler
riliprubart CIDP	**SP0202** Pneumococcal

- Immuno-inflammation
- Oncology
- Neurology
- Rare Diseases
- Rare Blood Disorders
- Vaccines

As of December 7, 2023. Excluding Phase 1 and 2 (without Proof of Commercial Concept). Projects within a specified year are not arranged by submission timing. 1. Selected submissions.

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Employing AI to increase R&D productivity

Helen Merianos
Global Head of R&D Portfolio Strategy

Unlocking R&D productivity through Portfolio management

Portfolio Management Focus

- R&D ROI & resource allocation
- Execution speed & time to market
- Patient focused

Transformation principles

- Quantitative & data driven
- Radical transparency
- Increased external focus
- Link strategic choices with operational decisions
- Smarter & faster decisions enhanced by AI

~ 4x

Pipeline value since 2019[1]

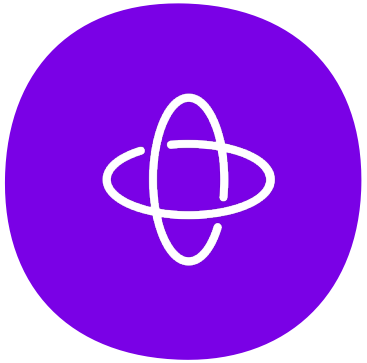
Where do we stand in our transformation: 25% 50% 75% 100%

1. Evaluate Pharma August 2019 vs. November 2023.

Smarter and faster decisions enhanced by AI - PLai

Recommendations
from strategy to ops

Predictions
near real-time



360° view across
Sanofi & competition

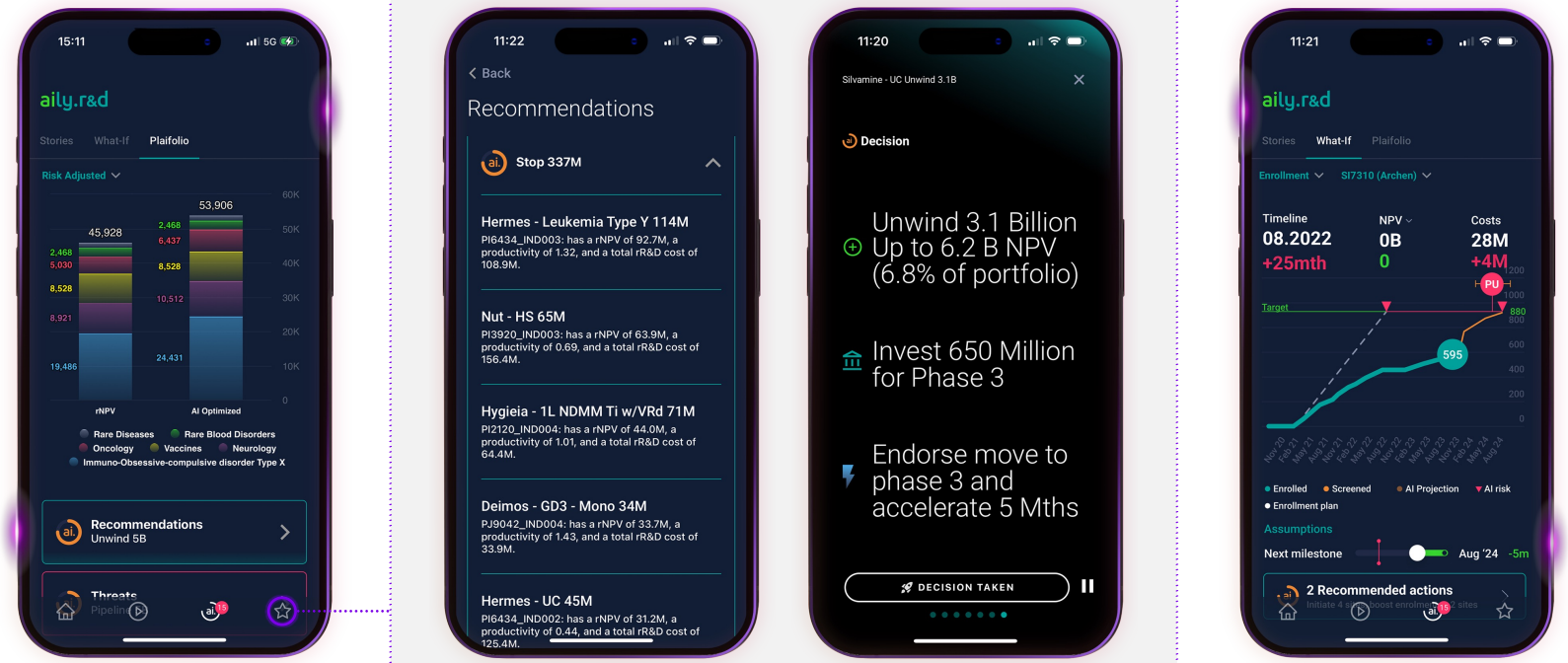
Portfolio
simulations

+1bn data points correlated into PLai

AI-powered transformation towards an agile decision-making culture

From strategy...

Dynamic portfolio with recommendations



...to operations

What-if scenarios for enrollment/ operations, including competitors view

Data for presentation purposes only.

Selected examples of using our enhanced portfolio capabilities

	Objective	*Outcomes*
Holistic portfolio decisions	Embed longer-term strategic planning at portfolio level by *modelling pre-phase 2 assets*	- Pursued *more aggressive asset strategy at first sign of clinical efficacy* based on portfolio shape from modeling - Included *Anti-IL13/TSLP Nanobody® VHH and Oral TNFR1si*
Portfolio trade-offs	Decide between: - Incremental investment in phase 3 for *enhanced differentiation for amlitelimab* - Similar investment to pursue *geographic expansion for a marketed product*	- *Funded amlitelimab* to fortify differentiation - Product team identified *RWE approach for geographic expansion* at minimal additional cost

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Concluding remarks

Houman Ashrafian

Head of Research and Development

Turning point for Sanofi's R&D

1. Leading in *Immunology* with our *key pipeline assets*

2. Going at speed to fully *fund Development opportunities*

3. Stepping-up *R&D productivity*

4. Becoming first *AI-powered R&D* in Biopharma

>€10bn

Sales contribution from Pharma launches by 2030

12 *NMEs*

in development with €2-5bn or €5bn+ peak sales potential[1]

1. Includes Pharma and Vaccines.

Q&A session (Part 3)

Scientific deep-dives

Overview of scientific deep-dive sessions

14:00 – 16:00

Session	*Speaker*
tolebrutinib	Tim Turner
frexalimab	Frederic Marrache
itepekimab	Helene Goulaouic
amlitelimab	Karl Yen
rilzabrutinib	Leda Mannent
lunsekimig	Heribert Staudinger
Oral TNFR1si	Maria Wiekowski

Appendix

Leading in *Immunology* with key pipeline assets

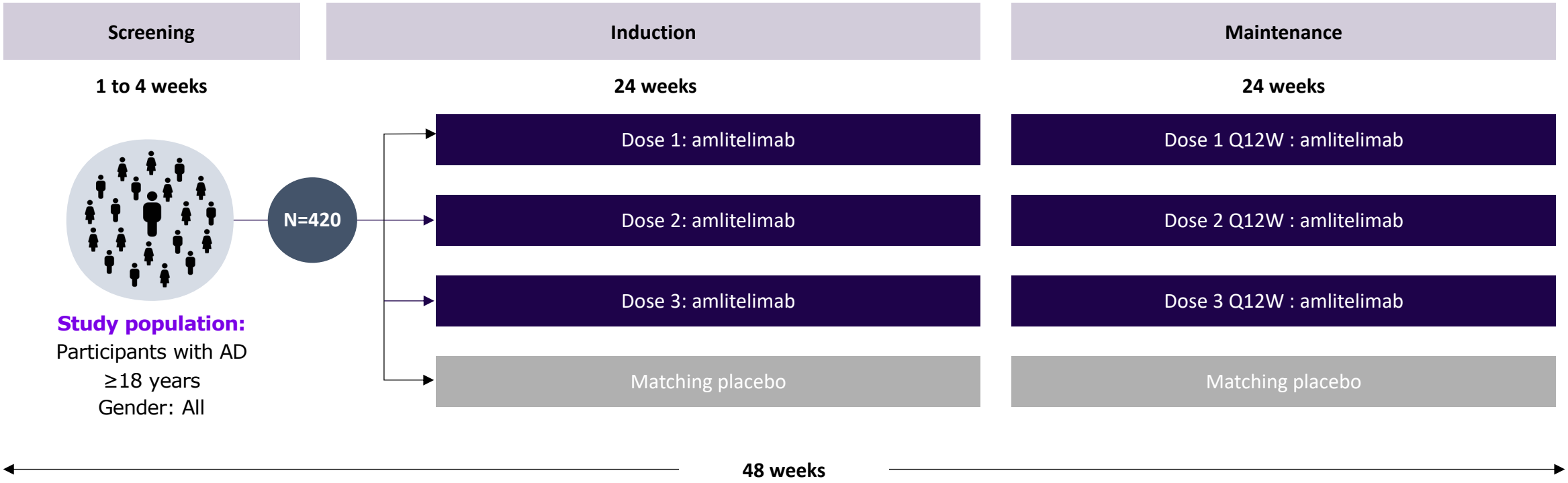
	Ambition	*Potential peak sales*[1]
tolebrutinib (BTKi)	Potential *transformative oral therapy* for full spectrum of MS	*€2-5bn*
rilzabrutinib (BTKi)	Potential *1st safe oral advanced therapy* for moderate Asthma and other Immunology conditions	*€2-5bn*
itepekimab (Anti-IL-33)	Pursuing potent *first-in-class IL-33* in COPD for former smokers	*€2-5bn*
amlitelimab (Anti-OX40L)	Targeting best-in-disease *durability* (4 shots/year in AD), with unique ligand MoA	*€5bn+*
frexalimab (Anti-CD-40L)	Aiming 1st *high efficacy, non-lymphocyte depleting* therapy for AI diseases	*€5bn+*
lunsekimig (Anti-IL-13/TSLP)	*Breaking efficacy ceilings* in Type 2 and beyond through synergistic effect of IL-13 and TSLP	*€2-5bn*
SAR441566 (Oral TNFR1si)	Target profile as foundational *oral* regimen for Immunology diseases	*€5bn+*
SAR444656 (IRAK4 degrader)	*First-in-class oral* IRAK4 protein degrader for multiple inflammatory diseases	*€2-5bn*
TEV'574 (Anti-TL1A)	Potential *best-in-class Anti-TL1A* for Gastro-intestinal diseases	*€2-5bn*

1.Non-risk-adjusted; 2. For ITP.

Amlitelimab: Phase 2b asthma Program

LPI Achieved

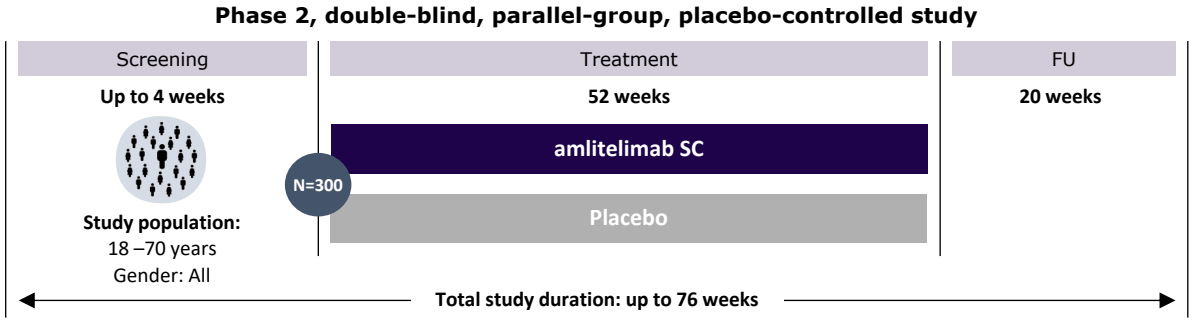
Phase 2b, double-blind, placebo-controlled, parallel-group, 5-arm study



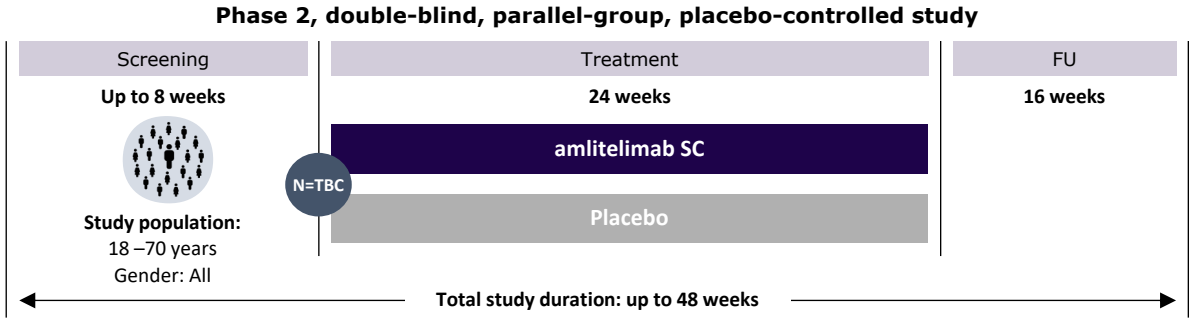
NCT05421598.

Amlitelimab: Four New indications to start in 2023/2024

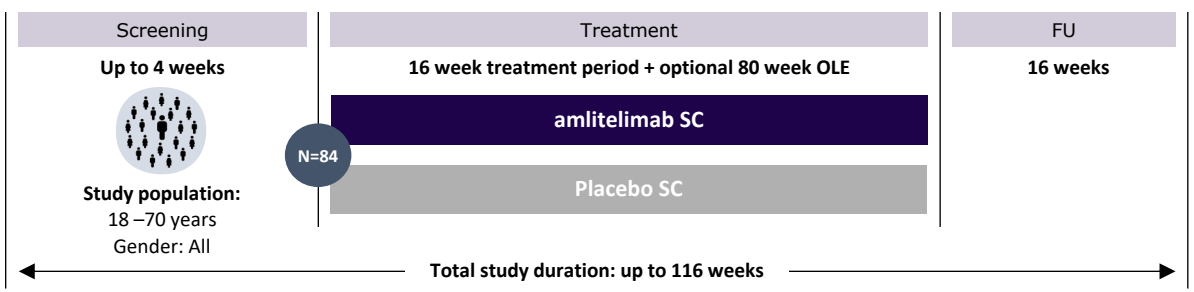
Systemic Sclerosis



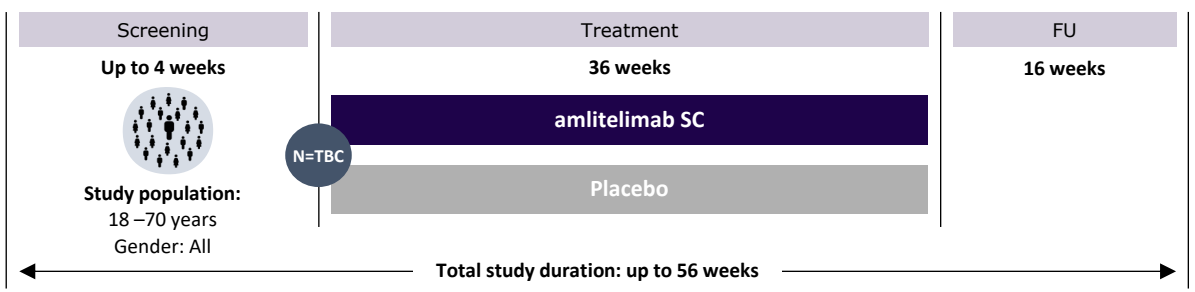
Celiac Disease



Hidradenitis Suppurativa



Alopecia Areata

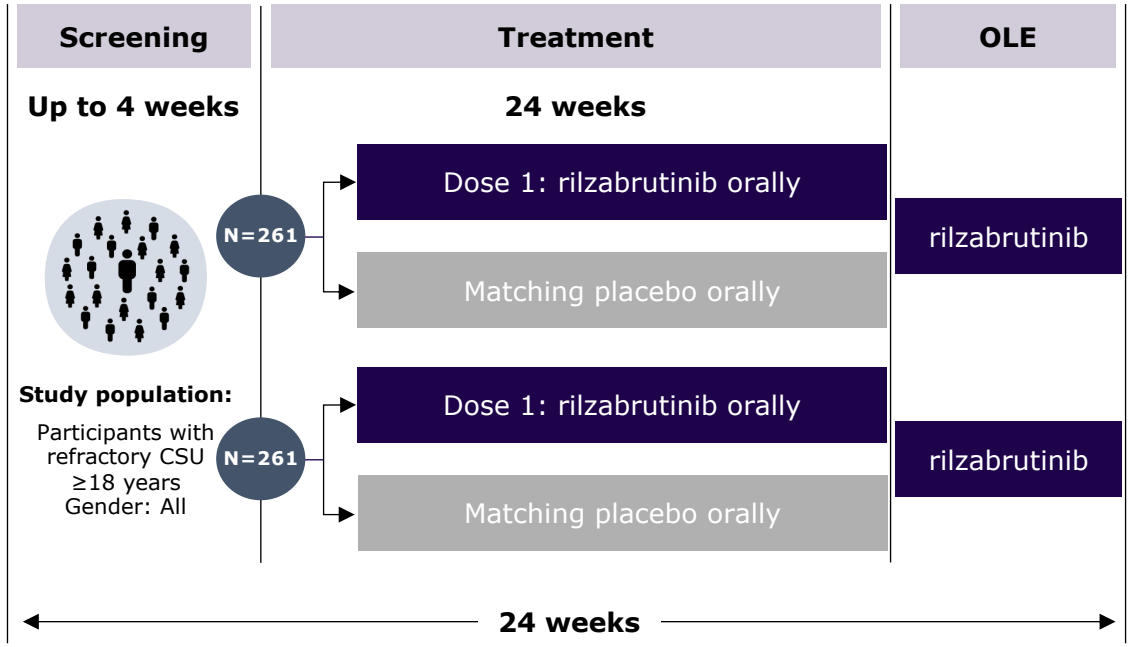


HS (NCT06118099).

Rilzabrutinib Ph3 Program in CSU and PN

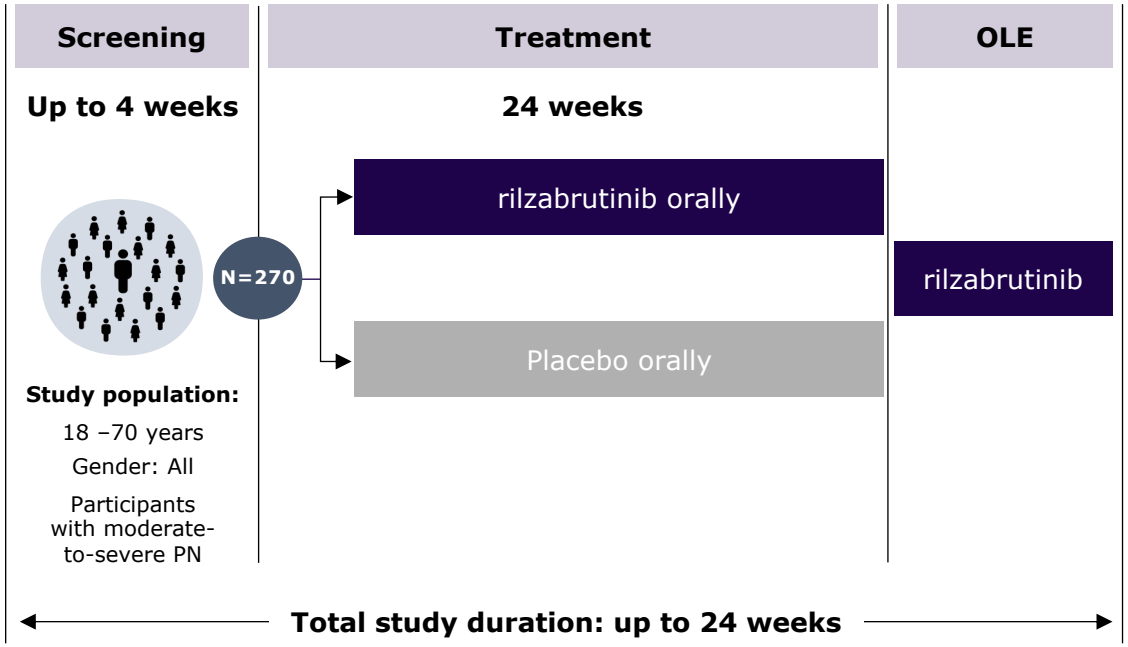
CSU

Phase 3 Program



Purigo Nodularis

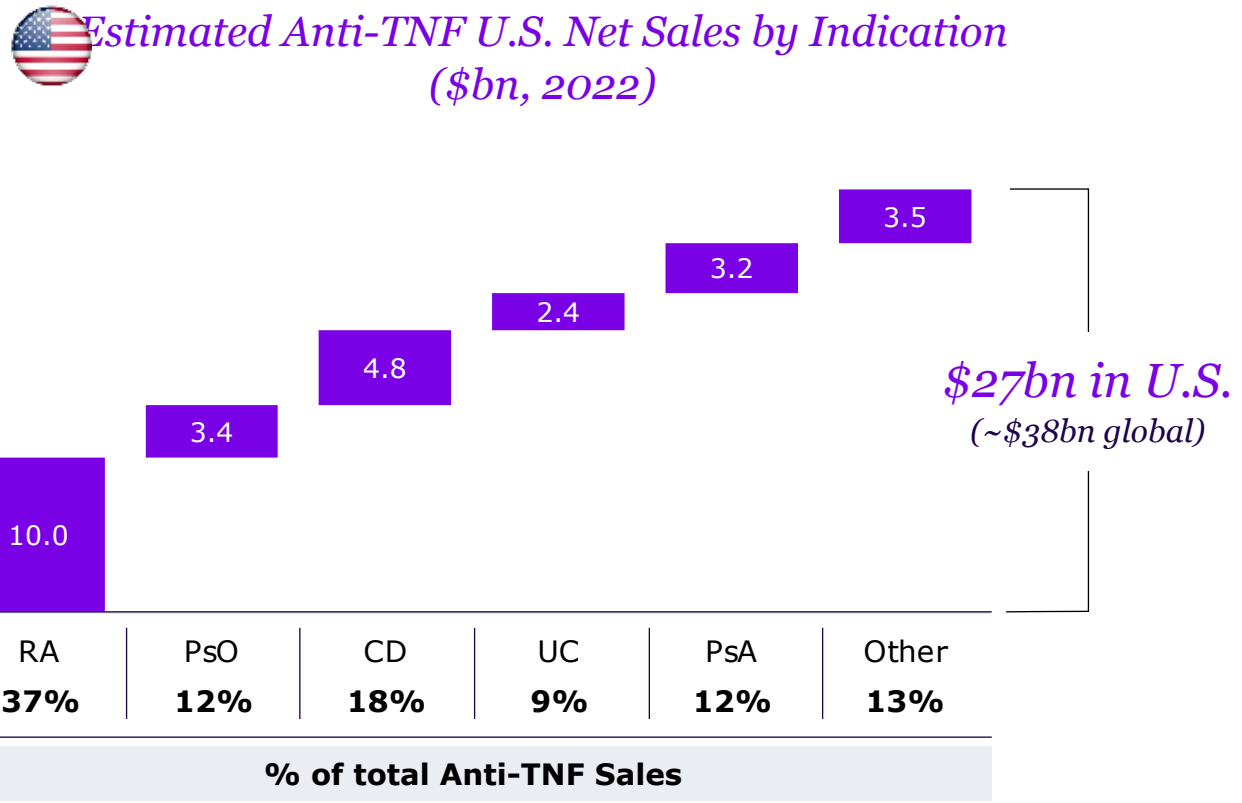
Phase 3, double-blind, parallel-group, placebo-controlled study[a]



New Phase 3 Program Starts in CSU and PN, additional studies in dermatology and respiratory indications

RILECSU (NCT05107115).

Biologic Anti-TNFs were a *$38bn global market* in 2022, with ~90% of sales across 5 key indications

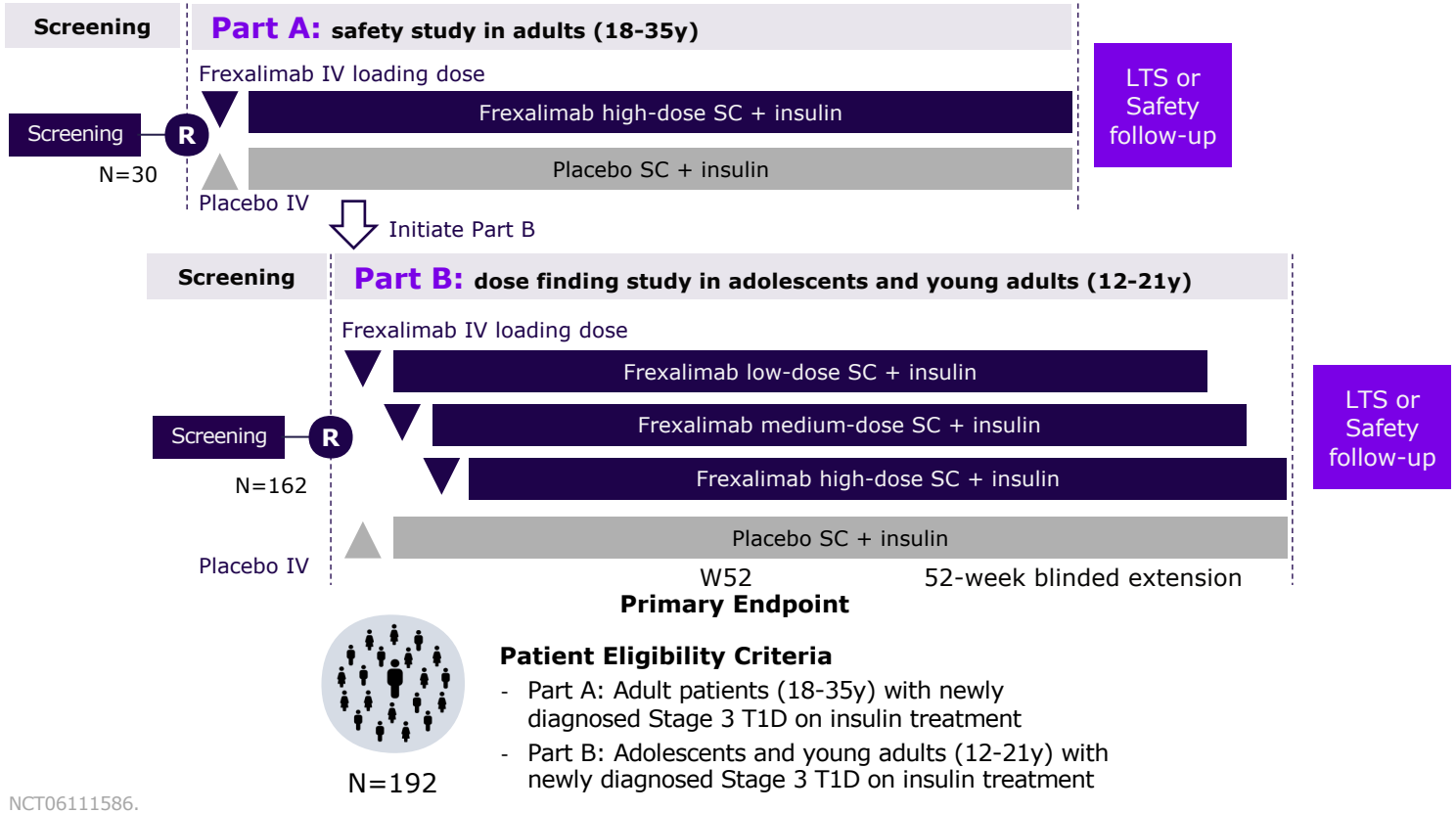


- *Largest I&I class* despite worldwide biosimilar entrants
- Indicative of *front-line opportunity in key indications*, with opportunity to position as pre-biologic
- Opportunity to *address all indications* across multiple TAs with Oral TNFR1si

Sources: IQVIA FIA, NMTA & NPA & NSP databases, DataMonitor 2021/2022 reports (including biosimilars), corporate presentations.

Phase 2b trial design in *newly diagnosed Stage 3 T1D*

Phase 2b, double-blind, randomized, placebo-controlled study



NCT06111586.

Primary endpoint

Change from baseline to W52 in mean 2h mixed meal tolerance test (MMTT) stimulated C-peptide concentration, calculated from AUC

Secondary endpoints

- Time-In-Range,
- Change in insulin dose,
- HbA1c level and its change,
- Safety and tolerability
- Pharmacokinetics
- Potential for immunogenicity
- Caregiver and/or patient reported clinical outcome measurements

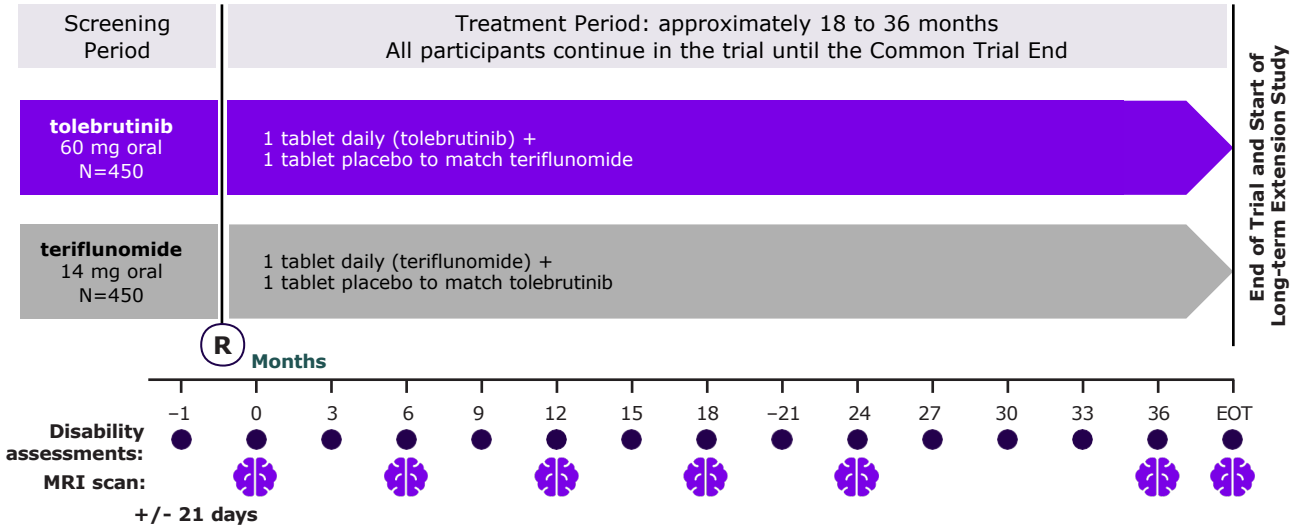
Tolebrutinib Phase 3 Trial Design in Relapsing MS: GEMINI I&II

Study Objectives
Evaluate efficacy and safety of tolebrutinib versus teriflunomide in participants with RMS

Patient Eligibility Criteria
Completed enrollment (estimated N=900 for each GEMINI 1 and 2)

- Adult participants aged ≤55 years
- Diagnosis of RMS in accordance with the 2017 revised McDonald criteria[16]
- EDSS score ≤5.5 at the first screening visit
- ≥1 of the following prior to screening:
  ≥1 documented relapse within the previous year, ≥2 documented relapses within the previous 2 years, or ≥1 documented Gd+ brain lesion on MRI within the previous year

Phase 3, randomized, double-blind, double-dummy, parallel-group, event-driven (6-month CDW) trial



GEMINI 1 (NCT04410978). GEMINI 2 (NCT04410991).

Primary endpoint

- ARR during the trial period assessed by confirmed protocol defined relapses

Secondary endpoints

- Time to onset of 3- and 6-month CDW
- Total number of new and/or enlarging T2-hyperintense lesions and new Gd+ T1-hyperintense lesions
- Time to confirmed disability improvement (CDI)
- Change in brain volume over time versus teriflunomide
- Change in cognition across several dimensions as measured by the Symbol Digit Modalities Test (SDMT) and California Verbal Learning Test-II (CVLT-II) methods, where available
- Change in Multiple Sclerosis Quality of Life-54 (MSQoL-54) questionnaire score
- AEs, SAEs, AEs leading to permanent trial intervention discontinuation, AEs of special interest, and potentially clinically significant safety signals
- Plasma concentration of tolebrutinib (population PK assessment) at Months 6,9, and 12
- Change in plasma neurofilament light chain (NfL), lymphocyte phenotype subsets in whole blood, serum immunoglobulin, and chitinase 3–like 1 (Chi3L1) levels

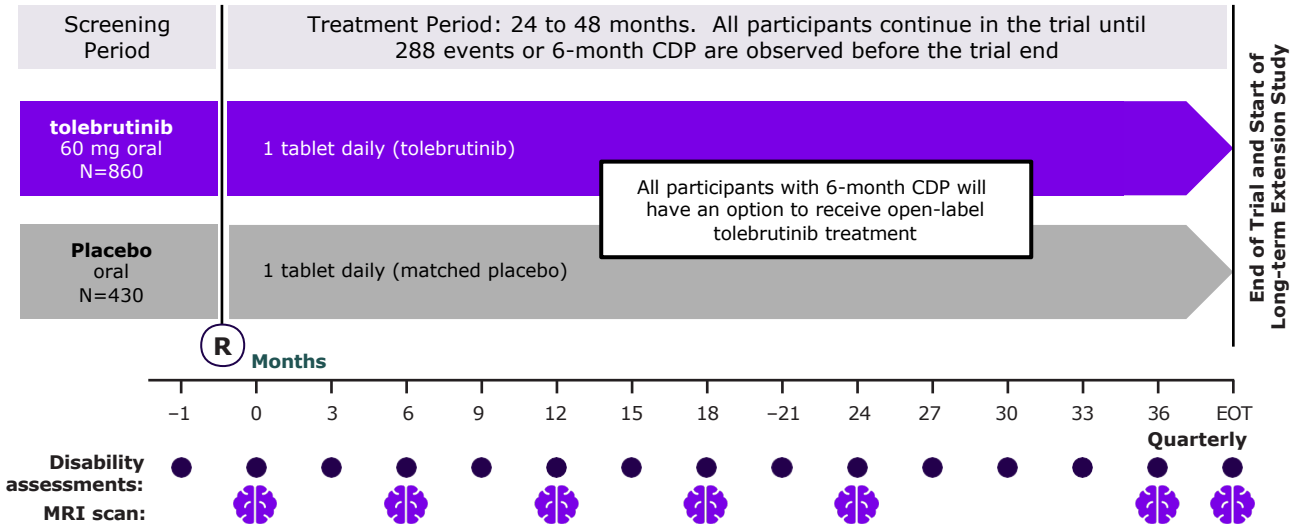
Tolebrutinib Phase 3 Trial Design in nrSPMS: HERCULES

Study Objectives
Evaluate efficacy and safety of tolebrutinib versus placebo in participants with nrSPMS

Patient Eligibility Criteria
Completed enrollment (estimated N=1290)

- Adult participants aged ≤60 years
- Previous diagnosis of RRMS in accordance with the 2017 revised McDonald criteria[16] and a current diagnosis of SPMS
- Documented evidence of disability progression observed during the 12 months before screening
- Absence of clinical relapses for ≥24 months
- EDSS score ≥3 and ≤6.5 at the first screening visit

Phase 3, randomized, double-blind, placebo-controlled, parallel-group, event-driven (6-month CDP)[a] trial



HERCULES (NCT04411641).

Primary endpoint

- Time to onset of 6-month CDP

Secondary endpoints

- Time to onset of sustained 20% increase in the 9-HPT for at least 3 months
- Time to onset of sustained 20% increase in the T25-FW for at least 3 months
- Time to onset of 3-month CDP as assessed by the EDSS score
- Total number of new and/or enlarging T2-hyperintense lesions
- Time to onset of CDI
- Change in brain volume over time versus placebo
- Change in cognitive function as assessed by the SDMT and CVLT-II methods, where available
- Change in MSQoL-54 questionnaire score
- AEs, SAEs, AEs leading to permanent trial intervention discontinuation, AEs of special interest, and potentially clinically significant safety signals
- Plasma concentration of tolebrutinib (population PK assessment) at Months 6, 9, and 12
- Change in plasma NfL, lymphocyte phenotype subsets in whole blood, serum immunoglobulin, and Chi3L1 levels

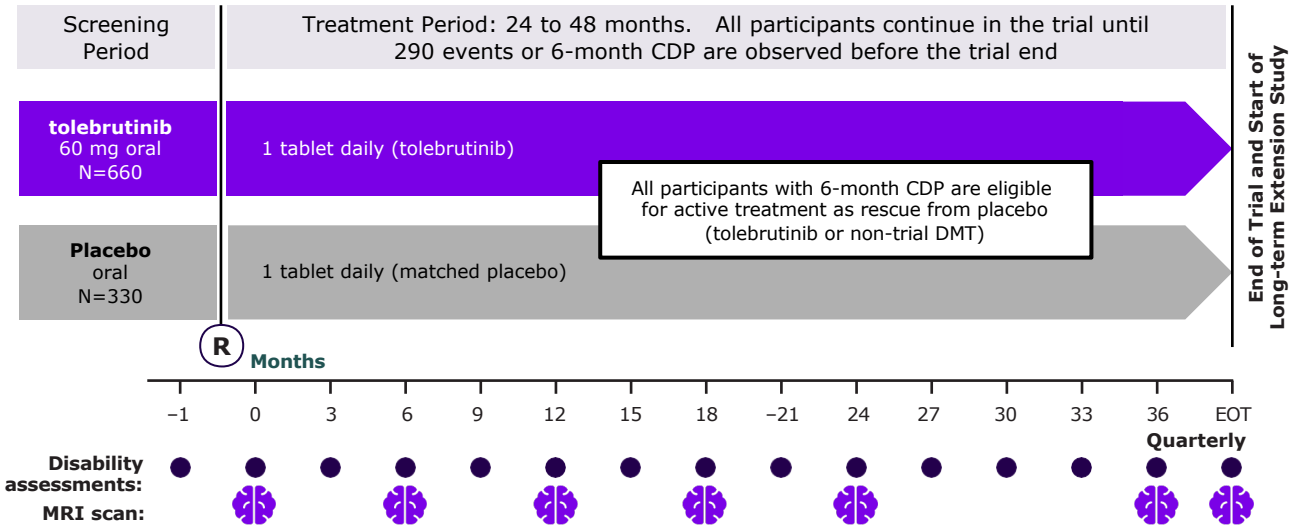
Tolebrutinib Phase 3 Trial Design in Progressive MS: PERSEUS

Study Objectives
Evaluate efficacy and safety of tolebrutinib versus placebo in participants with PPMS

Patient Eligibility Criteria
(estimated N=990)

- Adult participants aged ≤55 years
- Diagnosis of PPMS in accordance with the 2017 revised McDonald criteria[16]
- EDSS score ≥2 and ≤6.5 at the first screening visit
- Disease duration <15 years in participants with EDSS scores >5.0 at screening or <10 years in participants with EDSS scores ≤5.0 at screening and positive cerebrospinal fluid (isoelectric-focusing evidence of oligoclonal bands and/or elevated IgG index) either during screening or previous historical assessment

Phase 3, randomized, double-blind, placebo-controlled, parallel-group, event-driven (6-month CDP)[a] trial



PERSEUS (NCT04458051).

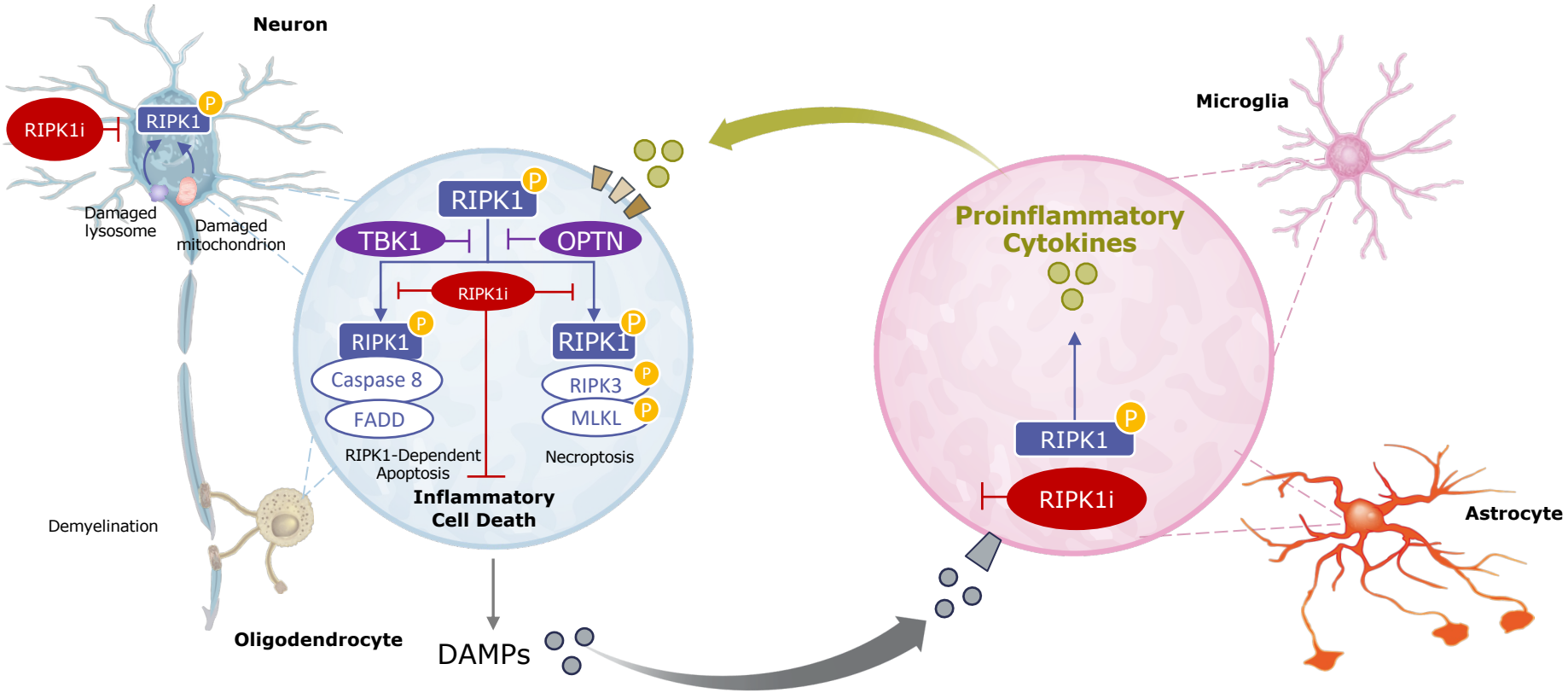
Primary endpoint

- Time to onset of 6-month CDP

Secondary endpoints

- Time to onset of sustained 20% increase in the 9-HPT for at least 3 months
- Time to onset of sustained 20% increase in the T25-FW for at least 3 months
- Time to onset of 3-month CDP as assessed by the EDSS score
- Total number of new and/or enlarging T2-hyperintense lesions
- Time to onset of CDI
- Change in brain volume over time versus placebo
- Change in cognitive function as assessed by the SDMT and CVLT-II methods, where available
- Change in MSQoL-54 questionnaire score
- AEs, SAEs, AEs leading to permanent trial intervention discontinuation, AEs of special interest, and potentially clinically significant safety signals
- Plasma concentration of tolebrutinib (population PK assessment) at Months 6, 9, and 12
- Change in plasma NfL, lymphocyte phenotype subsets in whole blood, serum immunoglobulin, and Chi3L1 levels

SAR443820 (RIPK1 inhibitor)



Proposed impact on inflammation and degeneration

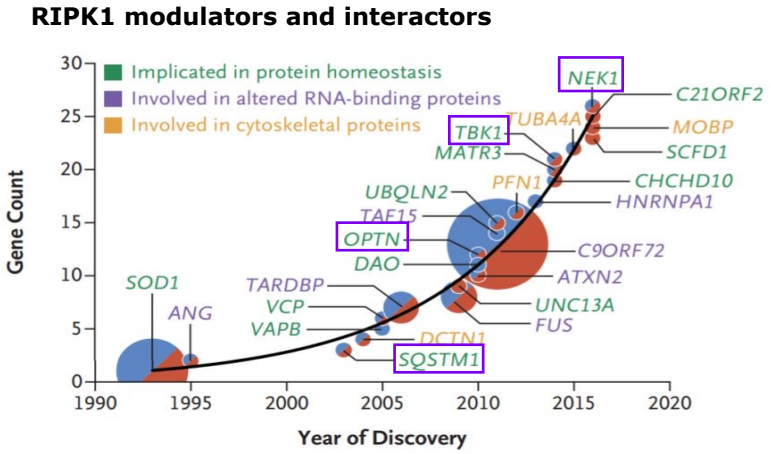
Left: RIPK1 inhibition abrogates inflammatory cell death and promotes survival of *neurons* and *oligodendrocytes*[1]

Right: RIPK1 inhibition reduces *microglial activation* and *proinflammatory cytokine* production by glial cells[2,3,4]

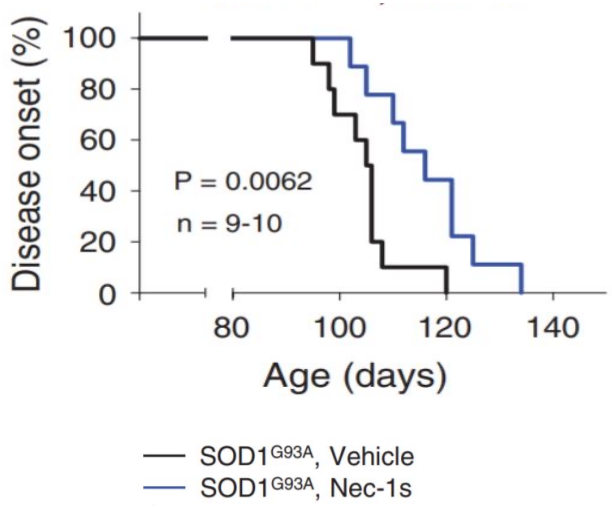
1. Yuan et al, Nat Rev Neurosci. 2019;20:19–33. 2. Zelic et al., Cell Reports. 2021;35:109-12. 3. Mifflin et al., Nat Rev Drug Discov.2020;19:553-71. 4. Ito et al., Science. 2016;353:603-8.

Genetic, model and human tissue rationale for *RIPK1 inhibition* in ALS

Genetics of ALS are enriched in RIPK1 interactors[1]

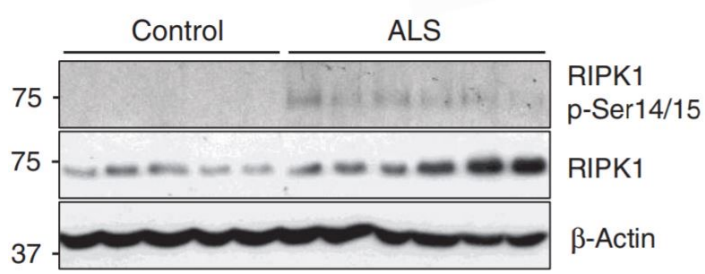


RIPK1 inhibition in a mouse model of ALS (SOD1G93A model)[2]



RIPK1 activation is prominent in ALS patient derived tissue[2]

Western blot analysis of human post-mortem spinal cord samples

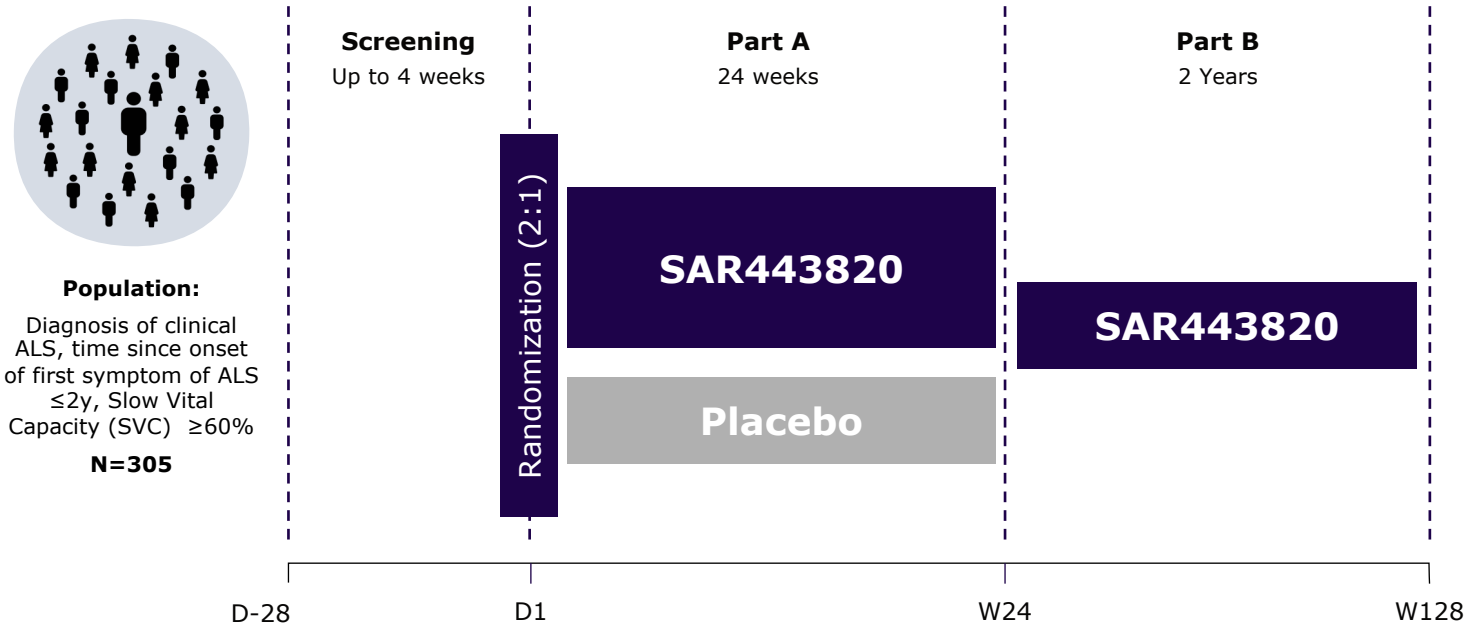


Increased RIPK1 activation (pS166 RIPK1) and expression was also detected by MSD assay in post-mortem spinal cord samples[2]

1. Brown and Al-Chalabi, N Engl J Med. 2017;377:162-72; 2. Ito et al., Science. 2016;353:603-8. Additional endpoints improved (function, weight).
MSD: Meso Scale Discovery; Nec-1s: Necrostatin-1s; NEK1: Never-in-mitosis A related protein Kinase 1; OPTN: Optineurin; SOD1: Superoxide Dismutase; SQSTM1: Sequestosome-1; TBK1: Tank-Binding Kinase 1.

Phase 2 HIMALAYA trial design

Phase 2, multi-center, randomized, double-blind, placebo-controlled study



Population:

Diagnosis of clinical ALS, time since onset of first symptom of ALS ≤2y, Slow Vital Capacity (SVC) ≥60%

N=305

Primary endpoint

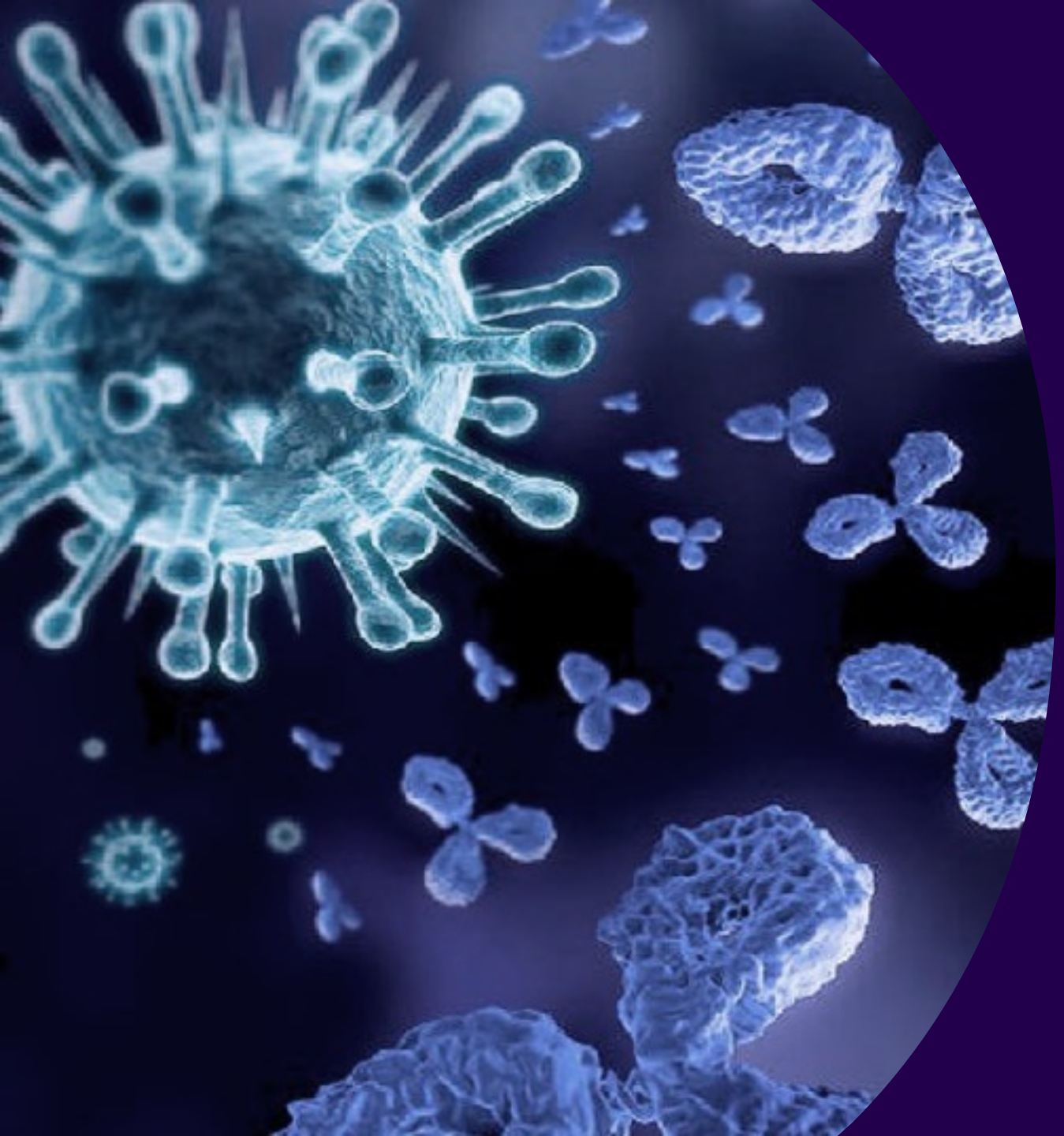
- Change from baseline in ALSFRS-R score

Secondary endpoints include

- Combined Assessment of Function and Survival (CAFS score)
- Respiratory function (SVC)
- Muscle strength (HHD)
- Quality of Life (ALSAQ-5)
- Plasma Neurofilament Light chain (NfL)
- Safety and tolerability
- Pharmacokinetics

Topline results **in H1 2024**

ALSAQ-5: ALS Assessment Questionnaire. ALSFRS-R: ALS Functional Rating Scale-Revised. HHD: Handheld Dynamometry. SVC: Slow Vital Capacity.



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Expand leadership in vaccines

Thomas Triomphe
Head of Vaccines GBU

Jean-François Toussaint
Head of Vaccines R&D

Sanofi drives *innovation* with BiC/FiC vaccines pipeline

3	New products approved since Vaccines Investor Event in December 2021
mRNA	Leading-edge mRNA platform to lift our influenza standard of care and deliver innovation to address unmet needs
6	New vaccine candidates expected in phase 1/2 trial in 2022/23
At least 5	First-in-Class / Best-in-Class vaccine candidates expected in phase 3 by 2025 across diverse preventative and therapeutic areas

New data from 12 assets featured today

Deepen our leadership in existing franchises

New growth areas

Influenza	*Meningitis Travel & Endemic*	*RSV*	*Pneumo*	*New frontiers*
Fluzone HD	**MenQuadfi**	**Beyfortus**	**PCV21**	**Chlamydia**
Influenza QIV mRNA	**MenB**	**RSV toddler**		**Acne**
Next-gen mRNA Flu vaccine	**MenPenta**	**RSV older adult (OA)**		
Fluzone HD pediatric	Next-gen Yellow fever	RSV OA respiratory combo		
Pandemic Influenza	Next-gen rabies			

Data to be shared today

On a clear path to generate *>€10bn sales by 2030*

- Launch Beyfortus blockbuster and build BiC *RSV franchise*
- Continue to win in *Influenza*
- Enter *Pneumococcal market* with PCV blockbuster candidate
- Sustain growth of *established business*
- Introduce our *new mRNA vaccines* to market

Sanofi Vaccines sales
>€10bn
by 2030[1]

1. At 2023 rate

Abbreviations

Ab	Antibody
ACQ-5	5-item Asthma Control Questionnaire
ACR	American College of Rheumatology
AD	Atopic Dermatitis
ADPKD	Autosomal Dominant Polycystic Kidney Disease
AE	Adverse Event
AI/ML	Artificial Intelligence/Machine Learning
ALS	Amyotrophic Lateral Sclerosis
ALT	Alanine aminotransferase
APC	Antigen Presenting Cell
ARR	Annualized Relapse Rate
BIC	Best-in-class
BID	Bis In Die
BTK	Bruton's Tyrosine Kinase
C1s	Complement 1s
CD	Cluster of Differentiation
CD	Crohn's Disease
CDI	Confirmed Disability Improvement
CDP	Confirmed Disability Progression
CDW	Confirmed Disability Worsening
Chi3L1	Chitinase 3–Like 1
CI	Confidence Interval
CIDP	Chronic inflammatory Demyelinating Polyneuropathy
CNS	Central Nervous System
COPD	Chronic Obstructive Pulmonary Disease
CPUO	Chronic Pruritis of Unknown Origin
CRSwNP	Chronic Rhinosinusitis with Nasal Polyps
CSF	Cerebrospinal Fluid
CSU	Chronic Spontaneous Urticaria
CVLT-II	California Verbal Learning Test-II
DAMPs	Damage-Associated Molecular Patterns
DILI	Drug-Induced Liver Injury
DMT	Disease Modifying Therapies
DSS	Expanded Disability Status Scale
EASI	Eczema Area and Severity Index
EDSS	Expanded Disability Status Scale
EGE	Eosinophilic gastroenteritis
EOD	Eosinophilic Duodenitis
EoE	Eosinophilic Esophagitis
EOS	End Of Study
EOT	End Of Treatment
EOT	End Of trial
EQ-5D-5L	EuroQol 5-Dimension, 5-Level Health Scale
ExPEC	Extra-intestinal Pathogenic Escherichia Coli
FADD	Fas-Associated protein with Death Domain
FeNO	Fractioned exhaled Nitric Oxide
FEV1	Forced Expiratory Volume
FIC	First-in-class
HD	High Dose
HS	Hidradenitis Suppurativa
I-RODS	Inflammatory Rasch-built Overall Disability Scale
IA	Interim Analysis
IBD	Inflammatory Bowel Disease
ICS	Inhaled Corticosteroids
Ig	Immunoglobulin
IGA	Investigator Global Assessment
IID	Initially Assessed Increase Of Disability
INCAT	Inflammatory Neuropathy Cause And Treatment
IND	Investigational New Drug Application
IRAK4	Interleukin-1 Receptor-Associated Kinase 4
ISS7	Ich Severity Score over 7 days
ITP	Immune Thrombocytopenia
JAK	Janus Kinase
LABA	Long-Acting Beta-Agonist
LAMA	Long-Acting Muscarinic Antagonists
LD	Loading Dose
LOAC	Loss Of Asthma Control
LoE	Loss of Exclusivity
LS	Least Square
LTS	Long-Term Study
mAb	monoclonal Antibody
MAD	Multiple Ascending Dose study
MLKL	Mixed Lineage Kinase domain-Like protein
MM	Multiple Myeloma

Abbreviations

I-RODS	Inflammatory Rasch-built Overall Disability Scale
MoA	Mechanism of Action
MRC-SS	Medical Research Council Sum Score
MRI	Magnetic Resonance Imaging
MSQoL-54	Multiple Sclerosis Quality of Life-54
NBRx	New-to-Brand Prescription
NfL	Neurofilament Light chain
NME	New Molecular Entity
nrSPMS	non-relapsing Secondary Progressive Multiple Sclerosis
OPTN	Optineurin
PASI	Psoriasis Area Severity Index
PCV	Pneumococcal Conjugate Vaccines
PIRA	Progression Independent of Relapse Activity
PK	Pharmacokinetics
PLEX	Plasmapheresis
PN	Prurigo Nodularis
PoM	Proof of Mechanism
PP-NRS	Peak Pruritus Numerical Rating Scale
PPMS	Primary Progressive Multiple Sclerosis
PsA	Psoriatic Arthritis
QPM	Quaque Die Post Meridiem
R-FSS	Modified Rasch-built Fatigue Severity Scale
RA	Rheumatoid Arthritis
RAW	Relapse-Associated Worsening
RD	Related Disease
MoA	Mechanism of Action

MRC-SS	Medical Research Council Sum Score
RI	Responder Index
RIPK1	Receptor Interacting Serine/Threonine Kinase 1
RMS	Relapsing Multiple Sclerosis
RR	Risk Reduction
RRR	Relative Risk Reduction
RSV	Respiratory Syncytial Virus
Rx	Prescription
SAD	Single Ascending Dose study
SAE	Serious Adverse Event
SC	Subcutaneous
SDMT	Symbol Digit Modalities Test
SE	Standard Error
SERD	Selective Estrogen Receptor Degrader
SjS	Sjogren's Syndrome
SLE	Systemic Lupus Erythematosus
SOC	Standard Of Care
SSc	Systemic Sclerosis
TBK1	Tank-binding Kinase 1
Te	Transplant eligible
TEAE	Treatment Emergent Adverse Event
Ti	Transplant ineligible
TID	Ter In Die
TLSS	Total Lesion Severity Score
TNFR	Tumor Necrosis Factor Receptor
TSLP	Thymic Stromal Lymphopoietin
UAS7	Urticaria Activity Score over 7 days

Collaborations

Name	Developed in collaboration with…
Dupixent itepekimab	Regeneron
frexalimab	ImmuNext
TEV'574	Teva Pharmaceuticals
eclitasertib SAR443820	Denali
SAR444656	Kymera
SAR446159	ABL Bio
STAT6 inhibitor	Recludix
ExPEC Vaccine	Janssen Pharmaceuticals, Inc., a Johnson & Johnson company
SP0202	SK