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Reimagining Cancer Treatment

Syndax 2026 R&D Event

July 14, 2026

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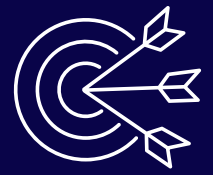
Syndax is delivering for patients and driving substantial long-term value

TRACK RECORD OF SUCCESS

Proven ability to translate scientific discoveries into novel therapies, with 3 FDA approvals between 2 drugs and thousands of patients treated

WORLD-CLASS R&D CAPABILITIES

Fully integrated biotech with deep expertise and strong partnerships with leading researchers



DEEP AND GROWING PIPELINE

Robust late- and early-stage pipeline with multiple near-term catalysts in 2H26 and blockbuster opportunities

SOLID FINANCIAL POSITION

Driving towards profitability with growing revenues; fully funded to advance late-stage trials and pipeline assets

Advancing the standard of care for R/R NPM1m AML and KMT2Ar acute leukemia and chronic GVHD with two first- and best-in-class medicines

First and only menin inhibitor with multiple indications

First and only CSF-1R-blocking antibody approved in R/R cGVHD

Revuforj® (revumenib) and Niktimvo™ (axatilimab-csfr) were both annualizing at ~$200M as of 1Q26, advancing the company towards profitability

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Syndax is driving innovation for patients




Expanding our pipeline to fuel the next phase of innovation and growth

Revuforj® (revumenib) tablets
25 mg • 110 mg • 160 mg

Ongoing trials across the acute leukemia treatment continuum

Positioned to be the 1st menin inhibitor approved in frontline AML

Niktimvo™ (axatilimab-csfr)
50 mg/mL for injection, for intravenous use

Ongoing trials in frontline cGVHD and IPF

Opportunities in several other inflammatory and fibrosing diseases

+

SNDX-4321

Mutant-selective allosteric EGFR inhibitor for NSCLC

Novel approach to addressing EGFRm NSCLC patient populations with high unmet need

Asset aligns with our proven in-license + develop strategy

Targeting IND submission in 4Q26

SNDX-62122

Next-generation menin inhibitor for MF

Novel, potentially disease-modifying mechanism in MF

1st candidate from our internally developed, wholly owned library of next-gen menin inhibitors

Targeting IND submission in 2027

PIPELINE TARGETS MULTIPLE BLOCKBUSTER OPPORTUNITIES

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R/R, relapsed or refractory; NSCLC, non-small cell lung cancer

Today's speakers

Syndax speakers

Michael A. Metzger
Chief Executive Officer and Director

Nick Botwood, MBBS
Head of R&D and Chief Medical Officer

Peter Ordentlich, PhD
Chief Scientific Officer and Founder

Thought leaders

John D. Crispino, PhD, MBA
Director, Division of Experimental Hematology, St. Jude Children's Research Hospital

Toby M. Maher, MD, PhD
Professor of Clinical Medicine and Director of Interstitial Lung Disease, Keck Medical School of University of Southern California

Michael J. Eck, MD, PhD
Professor, Department of Cancer Biology, Dana-Farber Cancer Institute; Professor, Department of Biological Chemistry & Molecular Pharmacology, Harvard Medical School

Today's agenda

Introduction	
Driving long-term growth through innovation	Michael A. Metzger, Syndax Pharmaceuticals
An R&D engine built to deliver breakthroughs	Nick Botwood, MBBS, Syndax Pharmaceuticals
Revuforj (revumenib) & Next-Gen Menin Inhibitors	
Advancing our leadership in menin inhibition	Nick Botwood, MBBS, Syndax Pharmaceuticals
Menin inhibition in myelofibrosis	John D. Crispino, PhD, MBA, St. Jude Children's Research Hospital
Q&A	Syndax leadership and Dr. Crispino
Niktimvo (axatilimab)	
Unlocking the potential of CSF-1R inhibition	Peter Ordentlich, PhD, Syndax Pharmaceuticals
Clinical perspective on IPF and CSF-1R inhibition	Toby M. Maher, MD, PhD, Keck Medical School of University of Southern California
Q&A	Syndax leadership and Dr. Maher
SNDX-4321	
A novel mutant-selective, allosteric EGFR inhibitor for NSCLC	Nick Botwood, MBBS, Syndax Pharmaceuticals Michael J. Eck, MD, PhD, Dana-Farber Cancer Institute and Harvard Medical School
Q&A	Syndax leadership and Dr. Eck
Closing remarks	Michael A. Metzger, Syndax Pharmaceuticals

An R&D engine built to deliver breakthroughs

Nick Botwood, MBBS
Head of Research & Development and Chief Medical Officer

Syndax is built to deliver innovative therapies in areas of high unmet need

WORLD-CLASS R&D ORGANIZATION

- Talented team with extensive experience developing novel medicines and building leading franchises
- Trailblazers in menin, CSF-1R, and EGFR inhibition

PARTNERSHIPS WITH LEADING RESEARCHERS

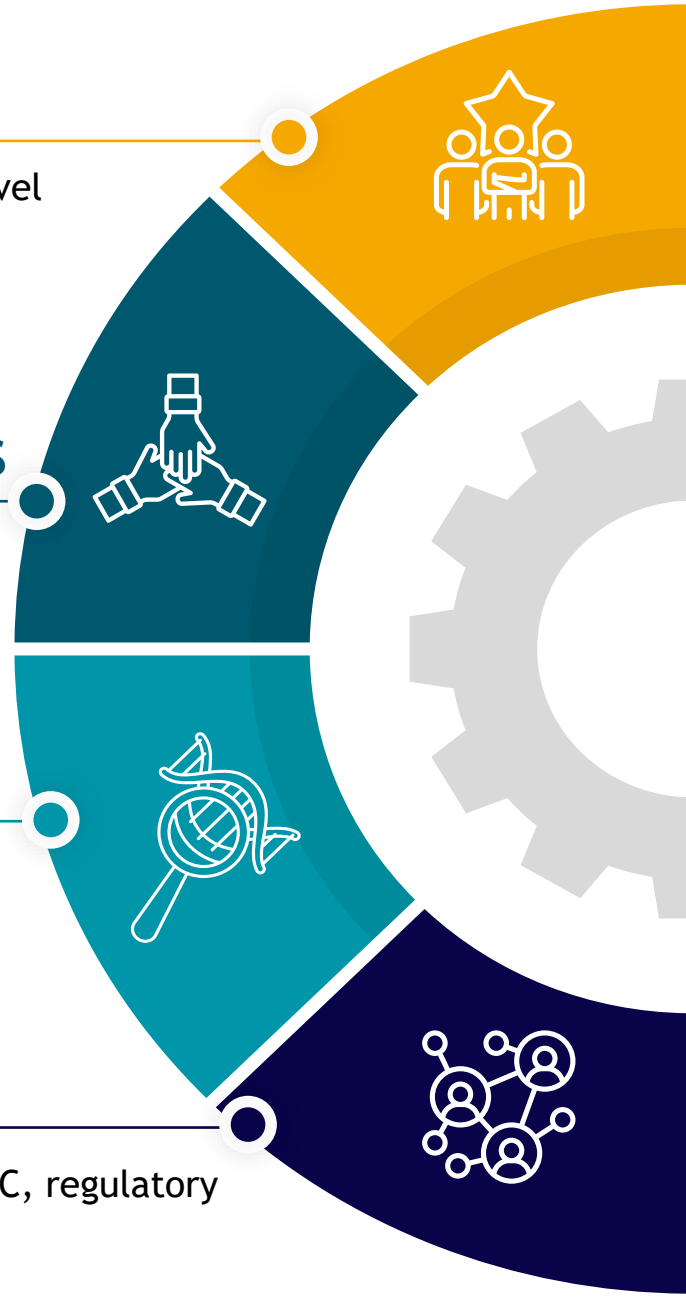
- New discoveries catalyzed by long-standing collaborations with leading researchers

DEEP MECHANISTIC UNDERSTANDINGS

- Proven ability to follow the science to deliver groundbreaking new treatments

FULLY INTEGRATED CAPABILITIES

- In-house expertise spanning discovery, development, CMC, regulatory approval, and commercialization
- Right-sized for innovation and rapid decision making



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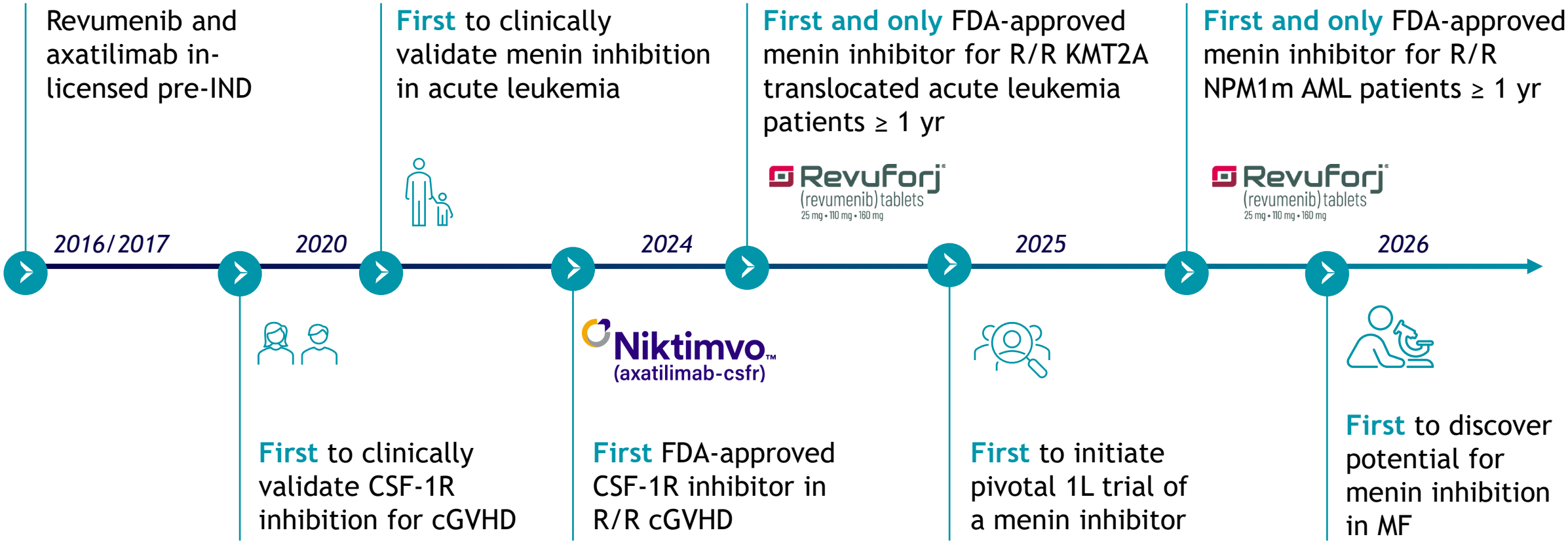
Proven track record of delivering breakthroughs



Achieved three FDA approvals between revumenib and axatilimab; both drugs advanced from IND to FDA approval in ~5 years

1L, frontline; R/R, relapsed or refractory; MF, myelofibrosis; FIH, first-in-human

PIONEERING MENIN & CSF-1R INHIBITION FOR PATIENTS

Multiple opportunities for expansion with revumenib and axatilimab

Asset	Setting	Pre-clinical	Ph 1	Ph 2	Ph 3	FDA approved
Revumenib	R/R acute leukemia					
	1L AML (with SOC drugs)					
	Post-HSCT maintenance					
	MRD relapse					
	Myelofibrosis (proof-of-principle)					
Axatilimab	R/R cGVHD					
	1L cGVHD (with steroids)*					
	1L cGVHD (with rux)*					
	IPF					

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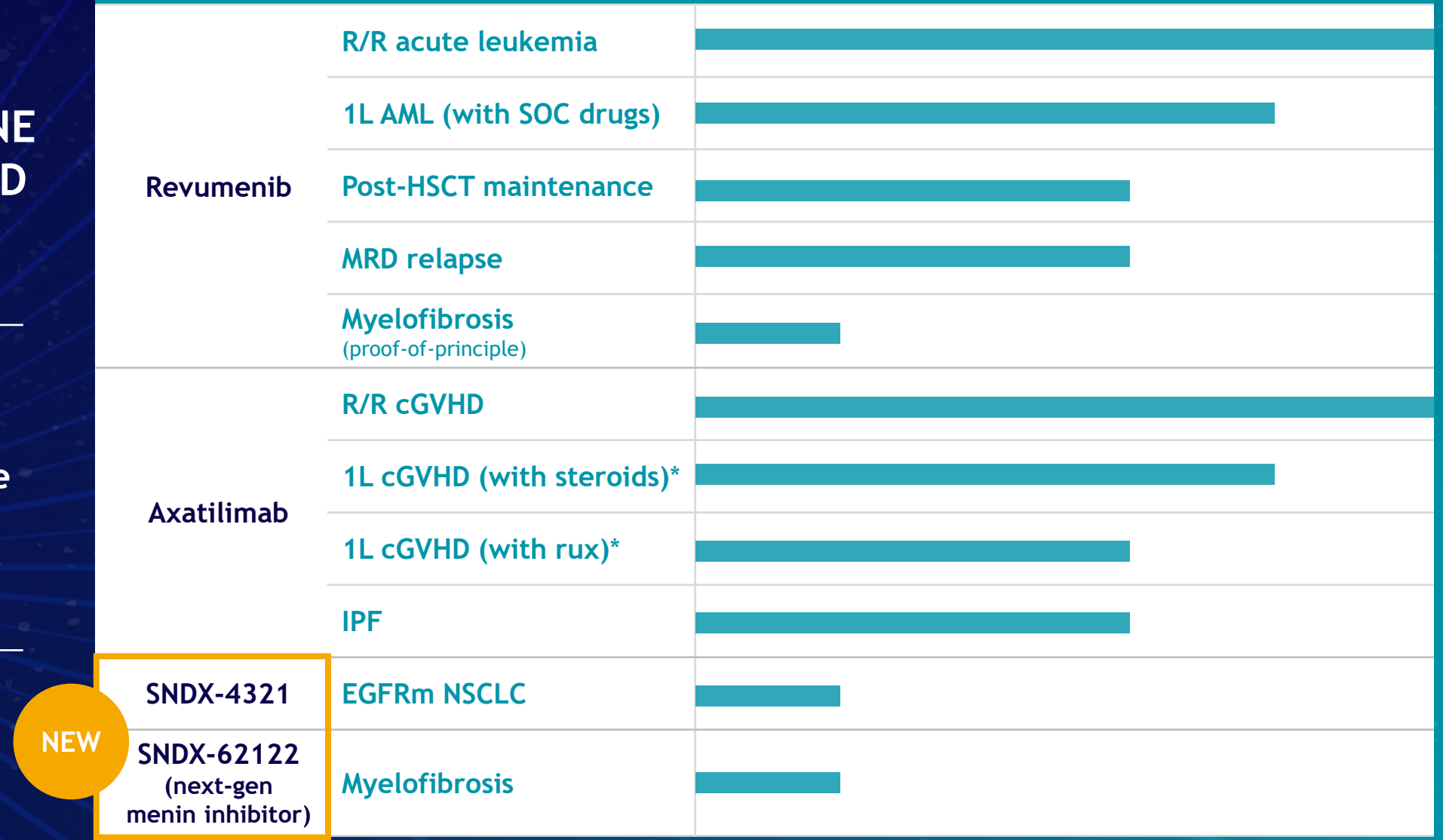
R/R, relapsed or refractory; 1L, frontline; AML, acute myeloid leukemia; SOC, standard of care; HSCT, hematopoietic; MRD, measurable residual disease; cGVHD, chronic graft-versus-host disease; rux, ruxolitinib; IPF, idiopathic pulmonary fibrosis; *Trials led by Incyte.

A GROWING PIPELINE OF DIFFERENTIATED ASSETS

At least 4 innovative assets expected in the clinic in 2027

Asset	Setting	Pre-clinical	Ph 1	Ph 2	Ph 3	FDA approved
Revumenib	R/R acute leukemia					
	1L AML (with SOC drugs)					
	Post-HSCT maintenance					
	MRD relapse					
	Myelofibrosis (proof-of-principle)					
Axatilimab	R/R cGVHD					
	1L cGVHD (with steroids)*					
	1L cGVHD (with rux)*					
	IPF					
NEW SNDX-4321	EGFRm NSCLC					
NEW SNDX-62122 (next-gen menin inhibitor)	Myelofibrosis					



R/R, relapsed or refractory; 1L, frontline; AML, acute myeloid leukemia; SOC, standard of care; HSCT, hematopoietic; MRD, measurable residual disease; cGVHD, chronic graft-versus-host disease; rux, ruxolitinib; IPF, idiopathic pulmonary fibrosis; NSCLC, non-small cell lung cancer. *Trials led by Incyte.

Advancing our leadership in menin inhibition

Nick Botwood, MBBS
Head of Research & Development and Chief Medical Officer

Positioned to continue leading menin inhibition in acute leukemia and beyond

BROADEST INDICATION & CLINICAL ACTIVITY

- Only menin inhibitor approved for R/R **NPM1m** AML + **KMT2A** translocated acute leukemia in **adults and children**
- Only menin inhibitor with presented data showing clinical activity in **NUP98r**

INTEGRATED EVIDENCE GENERATION PLAN

- Rapidly growing body of **practice-informing**, potentially **guideline- and registration-enabling** data across multiple acute leukemia settings and genetic subtypes

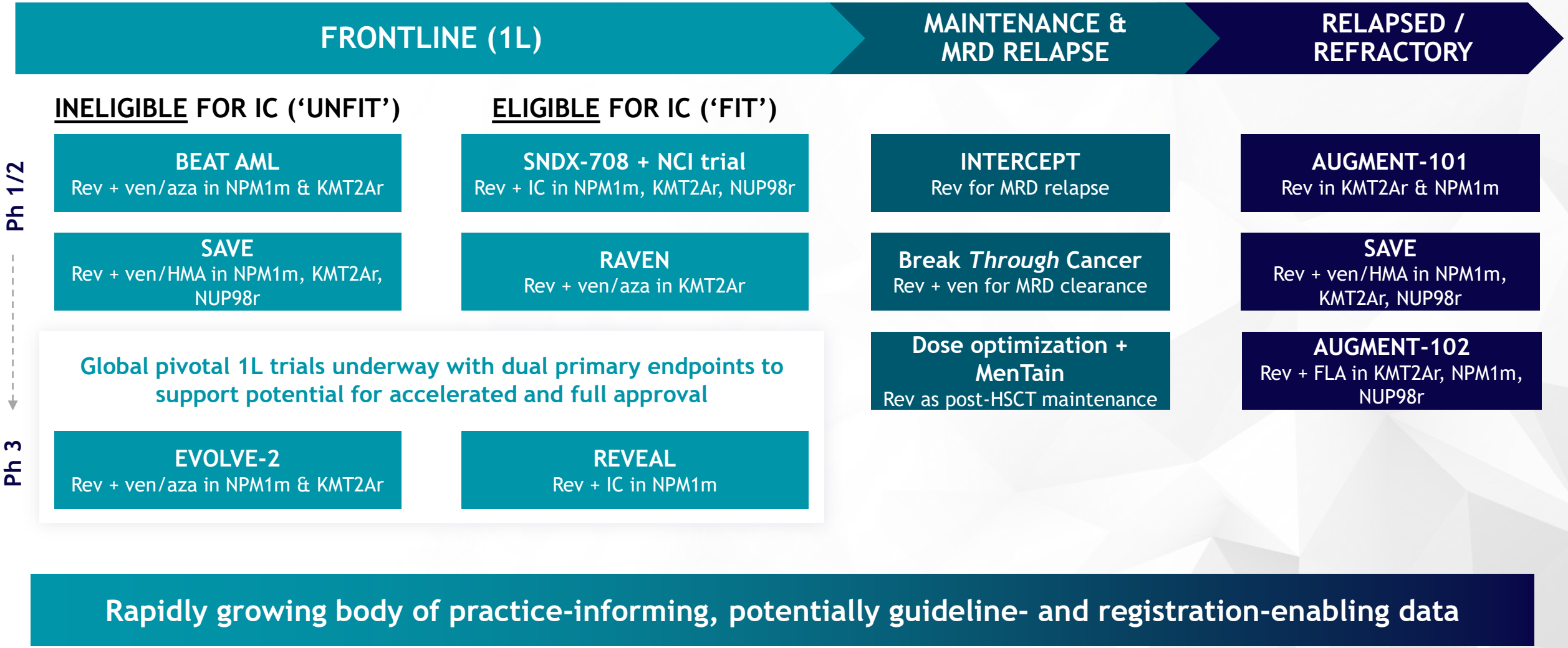
LIBRARY OF NEXT-GEN MENIN INHIBITORS

- **Internally developed library** coupled with the ability to leverage revumenib to inform and de-risk **development in promising new areas**

STRONG SCIENTIFIC PARTNERSHIPS

- **Collaborations with world-leading scientists and clinicians** catalyze translation of promising scientific discoveries into breakthroughs for patients

Syndax is pioneering menin inhibition across multiple acute leukemia settings and subtypes, including NPM1m, KMT2Ar, and NUP98r



Rapidly growing body of practice-informing, potentially guideline- and registration-enabling data

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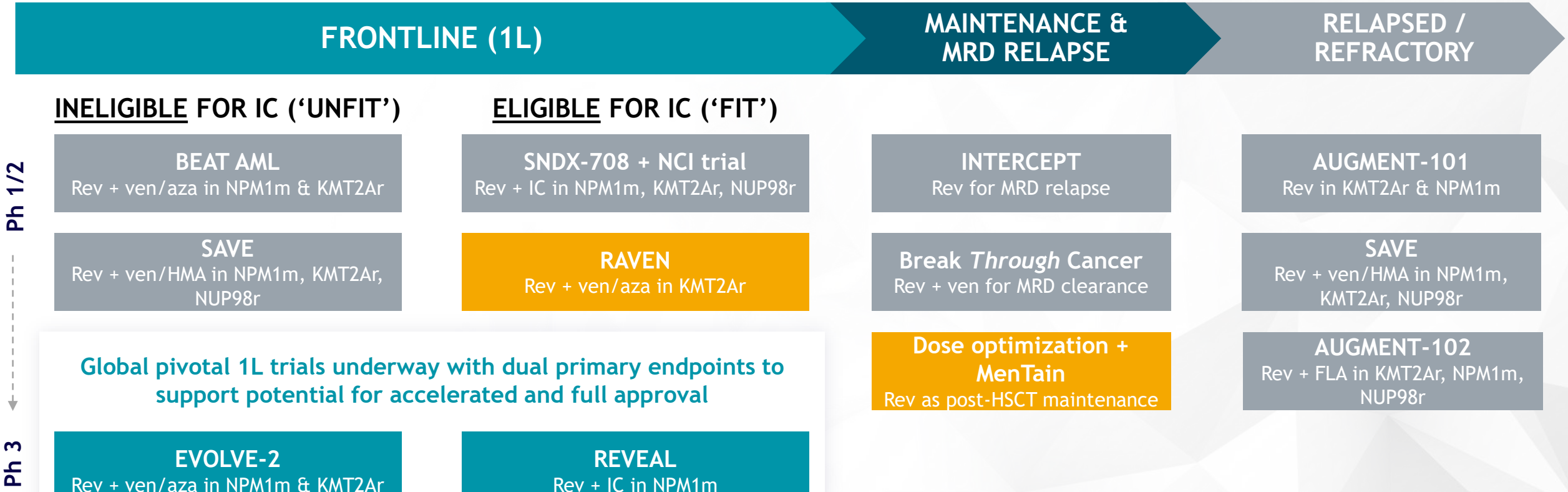
Rev, revumenib; IC, intensive chemotherapy; HSCT, hematopoietic stem cell transplant

Syndax is pioneering menin inhibition across multiple acute leukemia settings and subtypes, including NPM1m, KMT2Ar, and NUP98r



Pivotal 1L trials will be complemented by RAVEN (1st trial of a menin inhibitor + ven/aza in 1L fit KMT2Ar) + MenTain (1st placebo-controlled trial focused on revumenib as post-HSCT maintenance)

Syndax

IC, intensive chemotherapy; HSCT, hematopoietic stem cell transplant

Following the science to unlock the full potential of menin inhibition

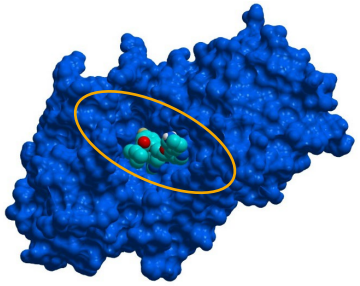
Growing body of evidence shows revumenib has robust activity across multiple acute leukemia subtypes and settings, including in combination with standard-of-care therapies

- Emerging data highlights the potential for revumenib in multiple diseases
- **Myelofibrosis (MF) selected as the next area for expansion based on:**
  - ✓ **High unmet need**
  - ✓ **Compelling preclinical data**
  - ✓ **Strategic fit**
  - ✓ **Potential for early clinical signal**

Leading menin inhibition into the future with a library of next-gen molecules plus the ability to leverage revumenib to de-risk development in new areas

Library of internally developed next-gen menin inhibitors

SNDX-62122 next-generation menin inhibitor



- Molecules will be deployed in new areas, starting with MF
- Rationally designed molecules informed by our deep molecular understanding of revumenib's interaction with menin
- Wholly owned assets with no financial encumbrances
- Multiple distinct scaffolds with composition of matter patents into late 2040s

- 1st molecule to emerge from our library
- IND submission in MF expected in 2027
- Profile:
  - ✓ Higher potency
  - ✓ Increased selectivity
  - ✓ Optimized PK
  - ✓ Active against common resistance mutations

Revumenib will be leveraged in preclinical and proof-of-principle clinical studies to generate data that informs development of next-gen molecules in new therapeutic areas

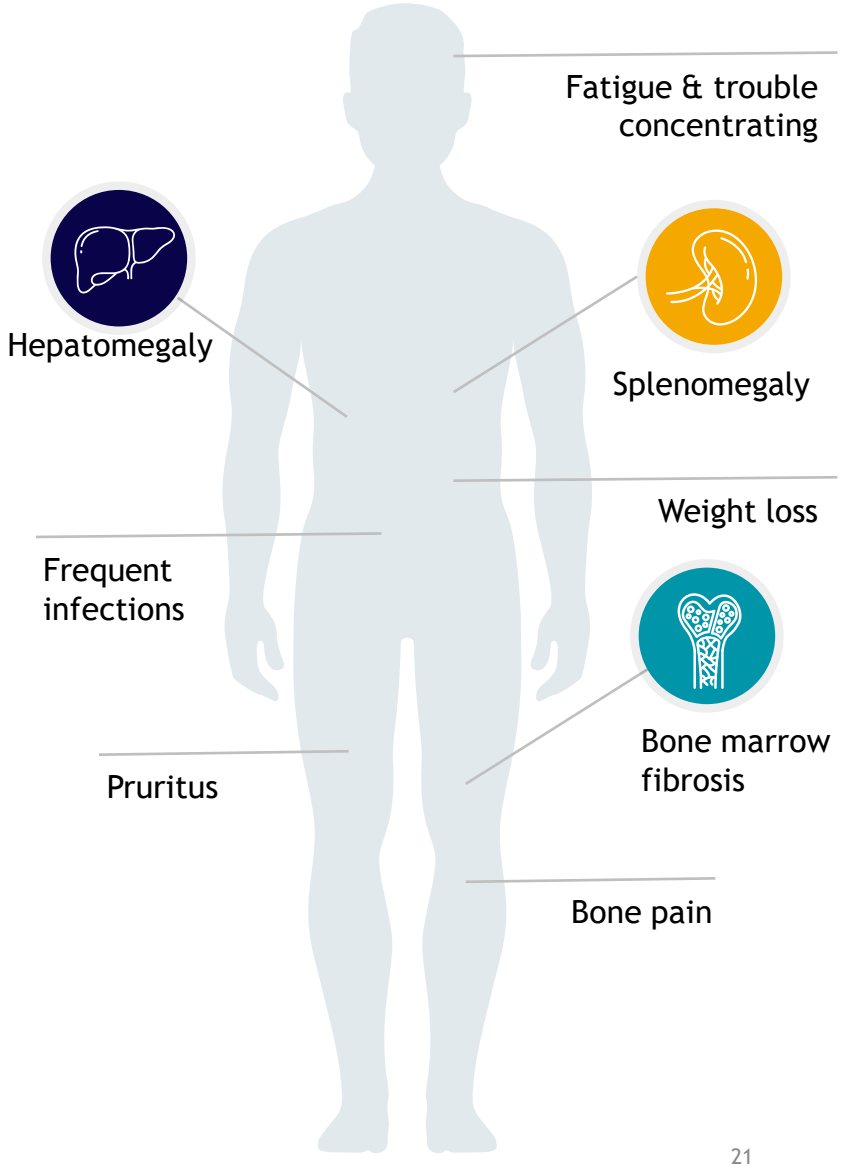
Menin inhibition in myelofibrosis

John D. Crispino, PhD, MBA
Director, Division of Experimental Hematology,
St. Jude Children's Research Hospital

New therapeutic strategies are needed in myelofibrosis (MF)

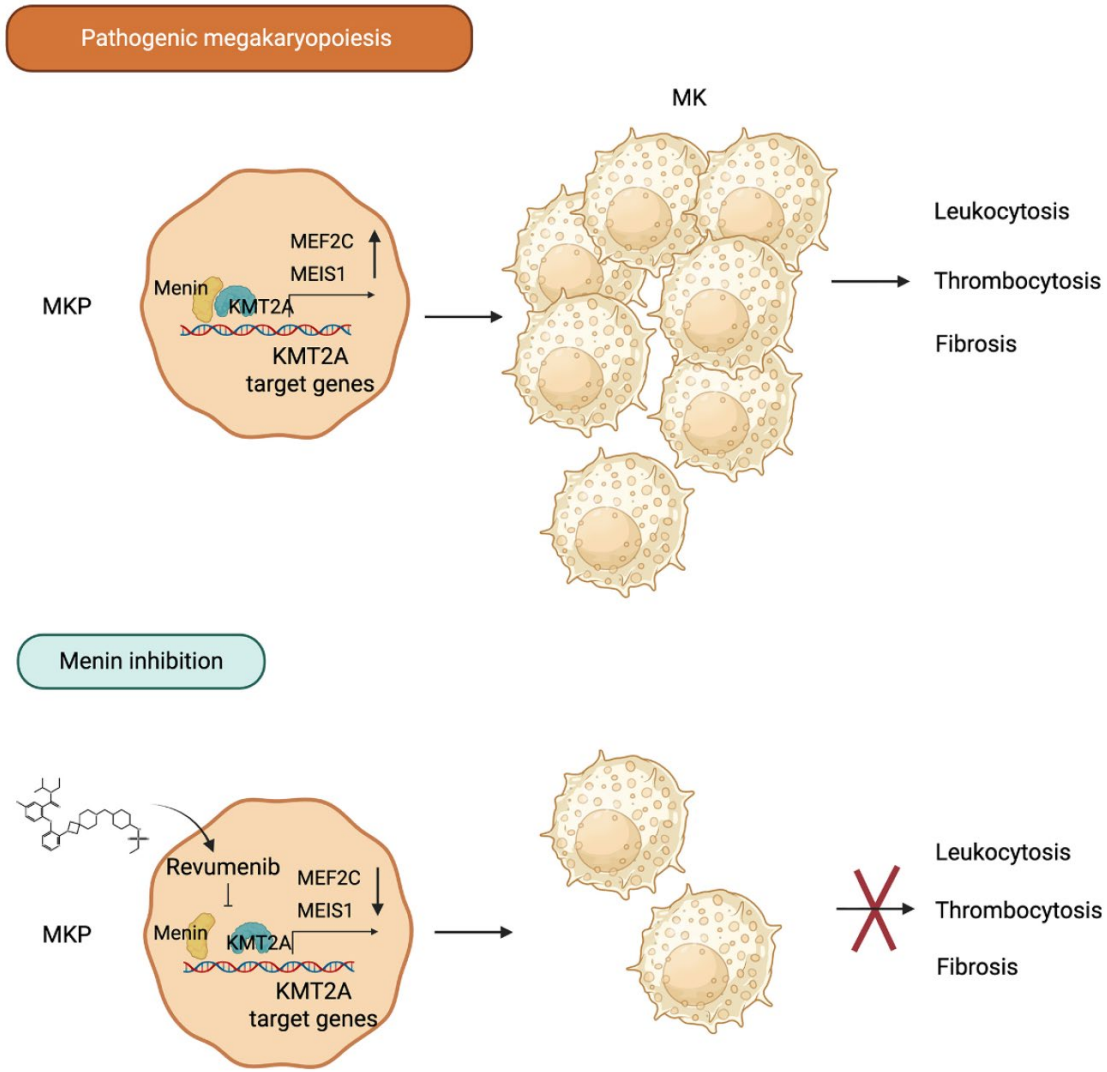
- **MF, a type of myeloproliferative neoplasm (MPN), affects ~20,000 people in the U.S.**
- MF is associated with:
  - Extramedullary hematopoiesis contributing to hepatosplenomegaly
  - Increased levels of inflammatory cytokines mediating debilitating symptom burden
  - Bone marrow fibrosis accompanying cytopenias
- Stem cell transplant is the only potentially curative option, but >90% of MF patients are not candidates for a transplant; JAK inhibitors (e.g., ruxolitinib) are the current SOC for the vast majority of patients

- While they reduce symptom burden and splenomegaly, **JAK inhibitors do not appreciably reduce fibrosis or the mutant allele burden**
- **Most patients stop responding to JAK inhibitors within 2-3 years with poor outcomes**



Menin inhibition is a promising new target in MF

- MF is characterized by an accumulation of atypical megakaryocytes (MKs), which contribute to fibrosis by secreting factors that increase collagen deposition
- **Emerging data reveal that menin is a novel dependency in proliferative MKs**
  - Menin inhibition suppresses megakaryopoiesis via downregulation of *MEF2C* and *MEIS1*
  - Menin inhibition selectively affects megakaryocyte progenitors (MKPs)
  - Revumenib showed striking anti-tumor activity in preclinical models of MPNs, supporting further investigation of menin inhibition for MF
  - Menin inhibition targets pathways independent of the JAK/STAT pathway



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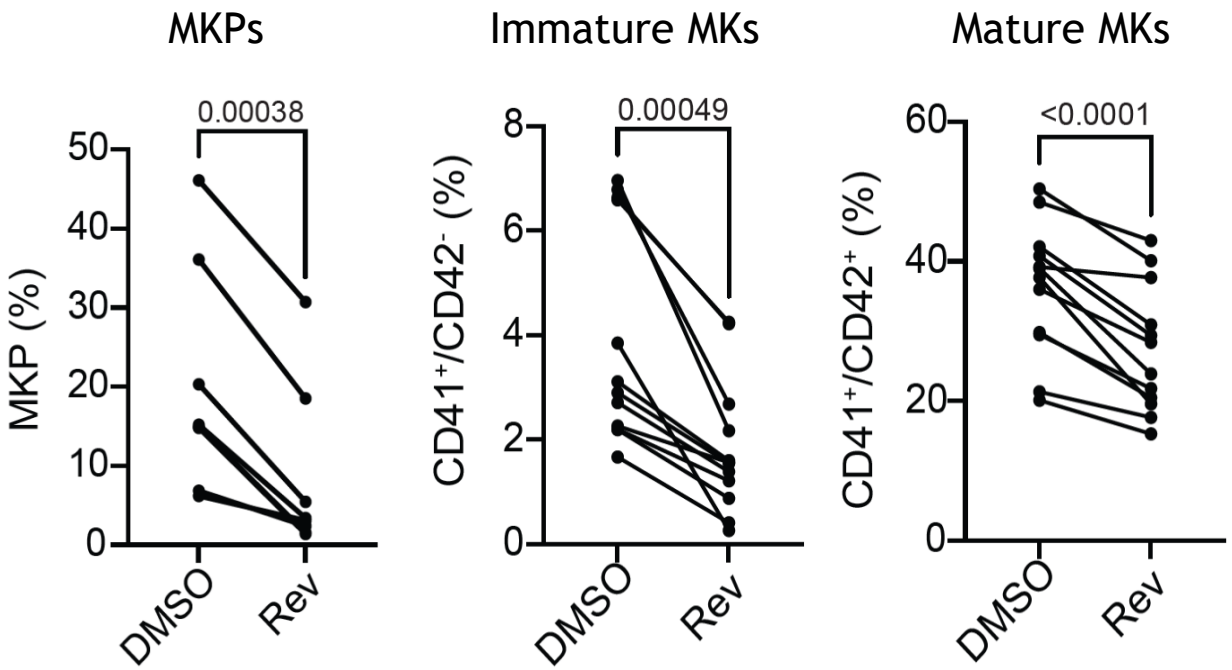
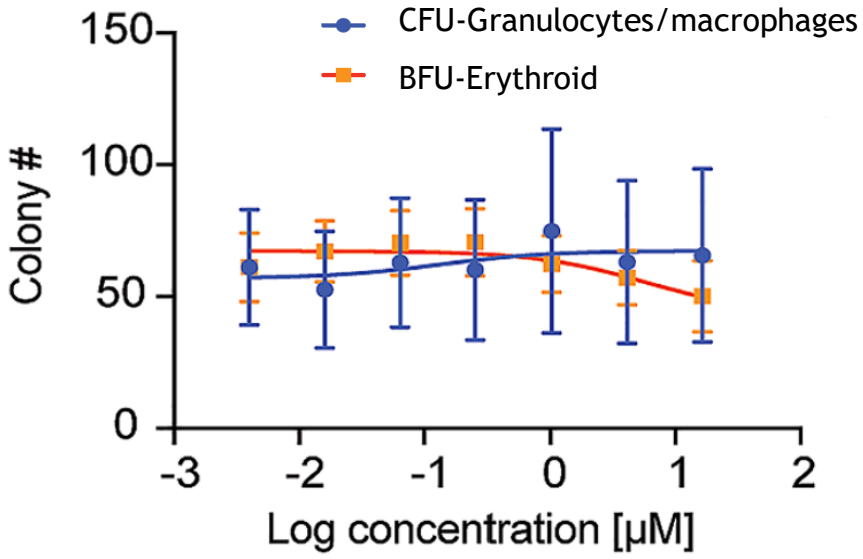
Wen et al. Cancer Cell 2026.

Our recently published preclinical data show revumenib selectively inhibits megakaryopoiesis

Revumenib reduced megakaryocyte progenitors (MKPs) and the formation of immature and mature megakaryocytes (MKs), without affecting myeloid or erythroid colonies



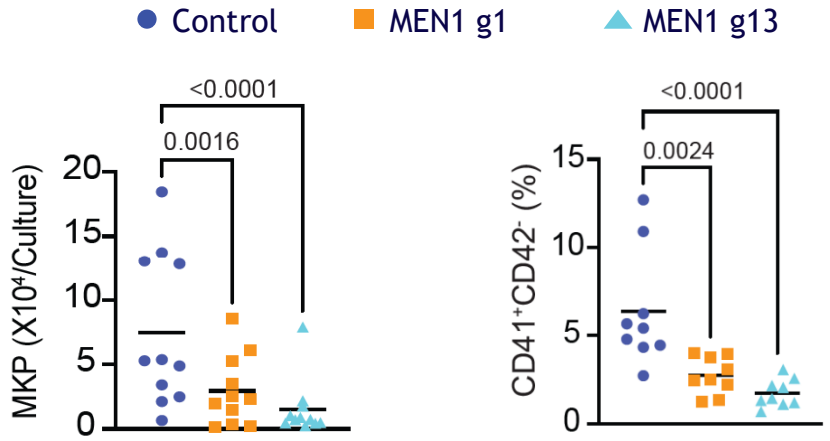


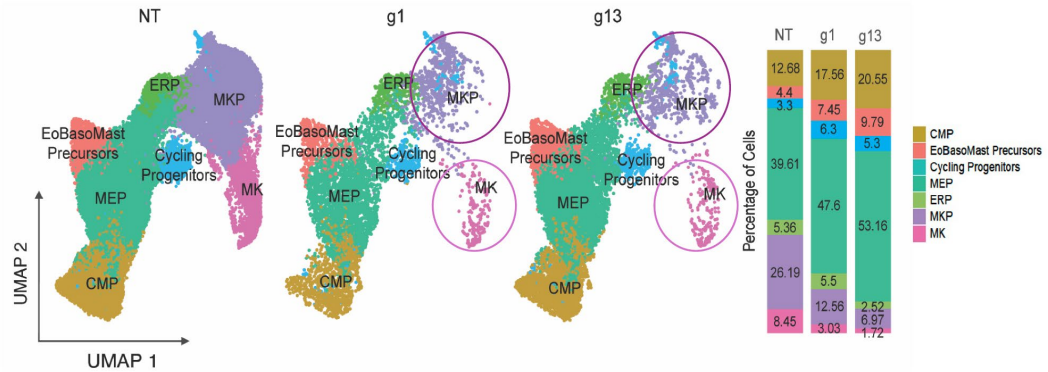
Wen et al. Cancer Cell 2026. CFU, colony-forming units; BFU, burst forming units

Loss of menin (MEN1) phenocopies revumenib, confirming on-target effect of the drug

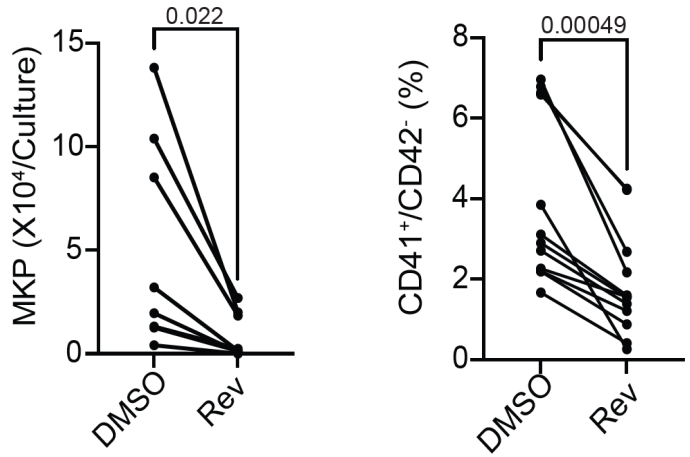
Both revumenib and MEN1 loss substantially decreased MKPs and immature MKs

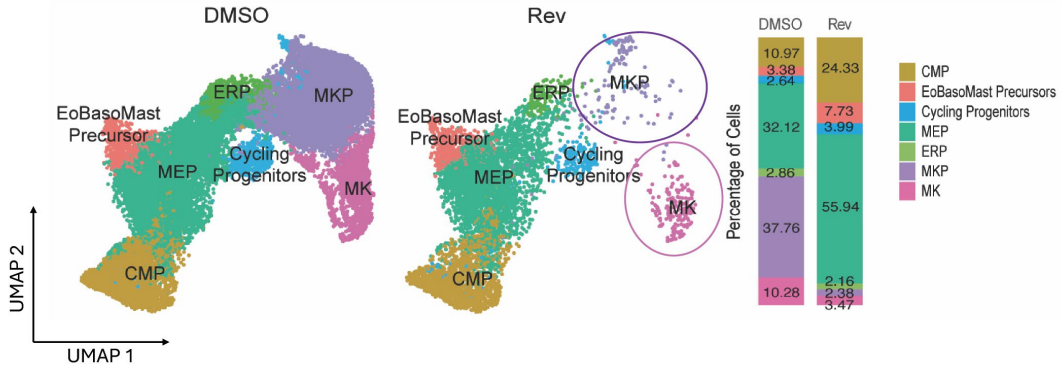
MEN1 knockouts





Revumenib





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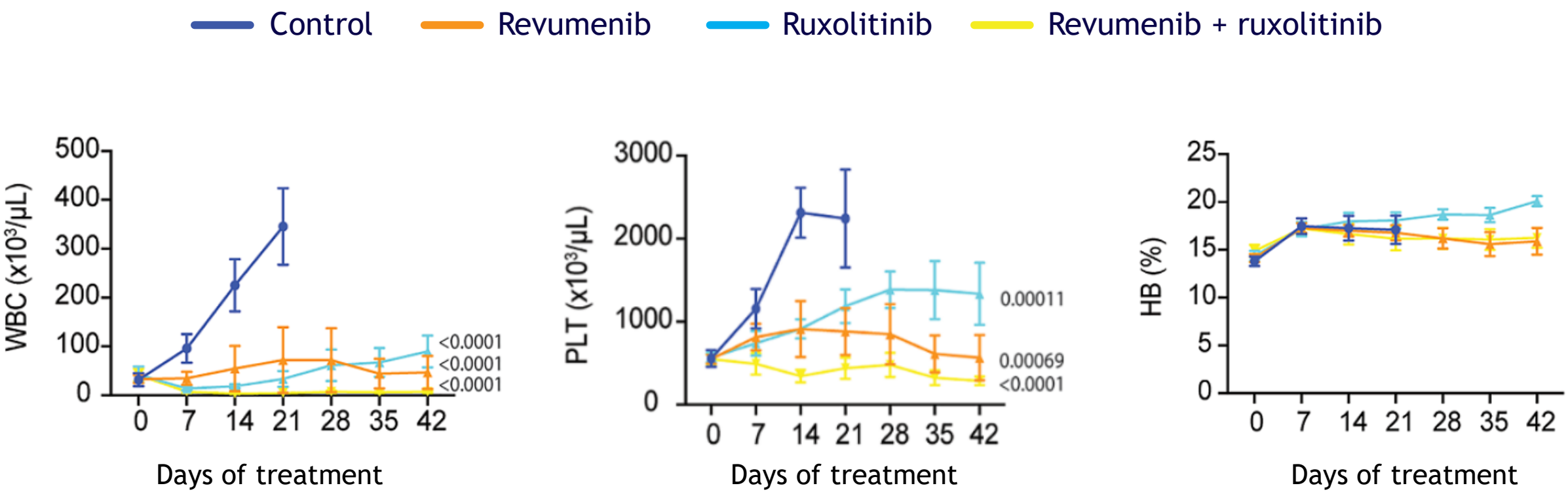
Wen et al. Cancer Cell 2026.

Revumenib alone and in combo with ruxolitinib improves peripheral blood counts in MPN animal models



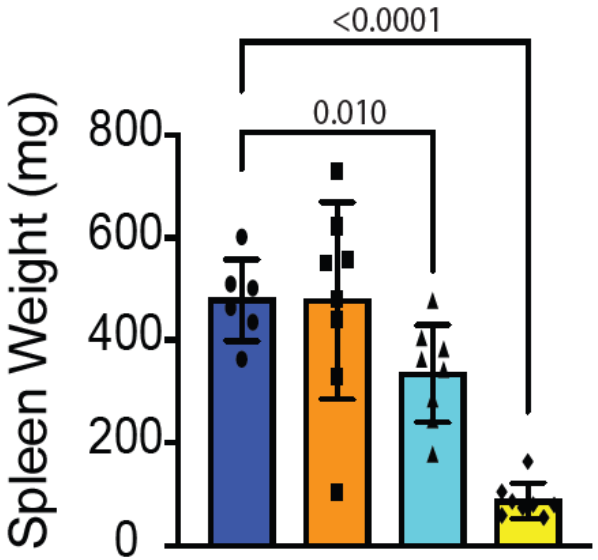
Wen et al. Cancer Cell 2026.

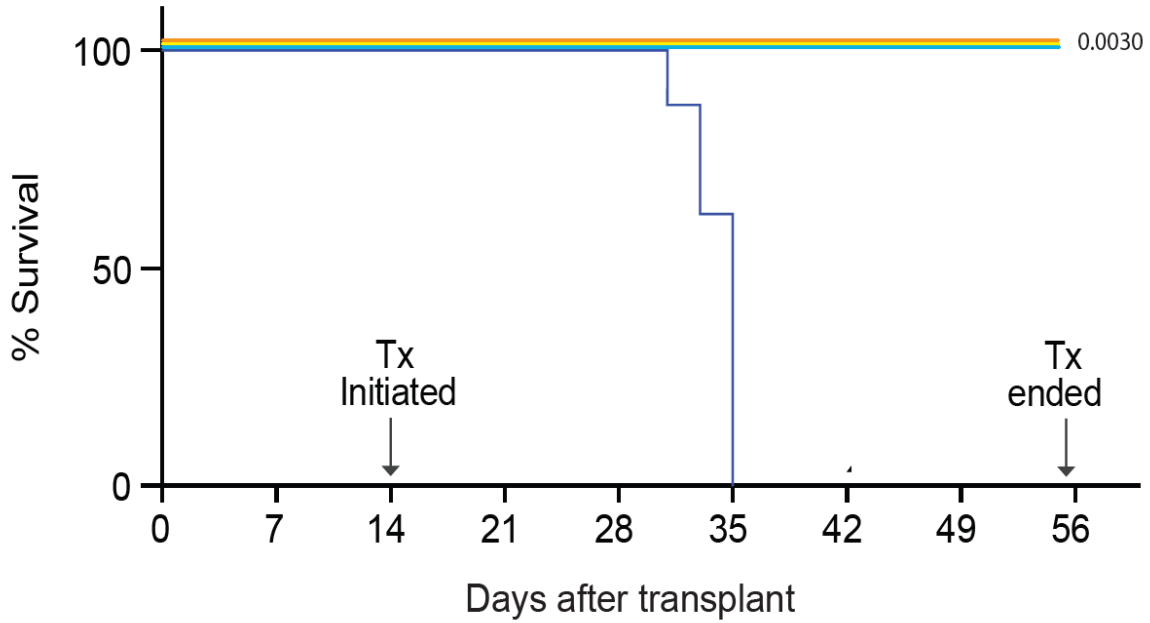
Revumenib increases survival and normalizes spleen weight in combination with ruxolitinib in MPN animal models

Rev + rux combo notably reduced spleen weight

Both single agent arms and the rev + rux combo showed extended survival compared to the control

Control Revumenib Ruxolitinib Revumenib + ruxolitinib





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Wen et al. Cancer Cell 2026.

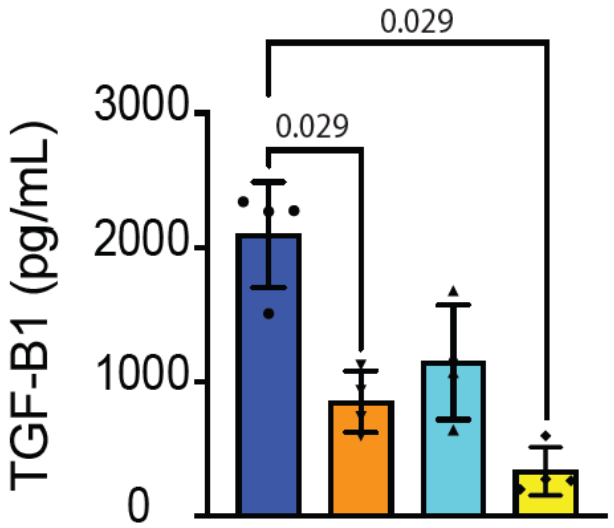
Revumenib alone and in combo with ruxolitinib suppressed levels of TGF-ß, megakaryocyte accumulation, and fibrosis more than ruxolitinib alone

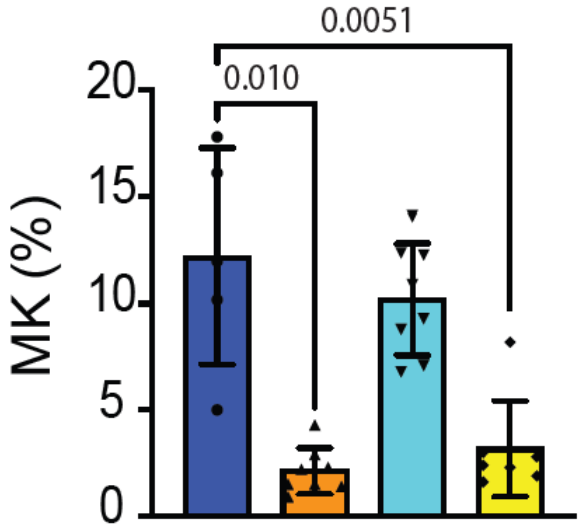
Both rev arms decreased TGF-ß, an inflammatory & profibrotic cytokine

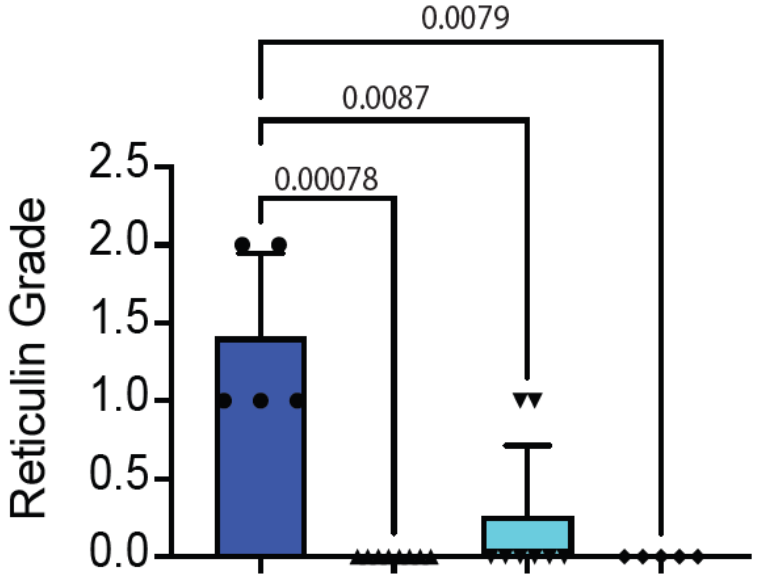
Both rev arms decreased MK numbers, while rux alone did not

Both rev arms reduced fibrosis more significantly than rux alone

Control Revumenib Ruxolitinib Revumenib + ruxolitinib







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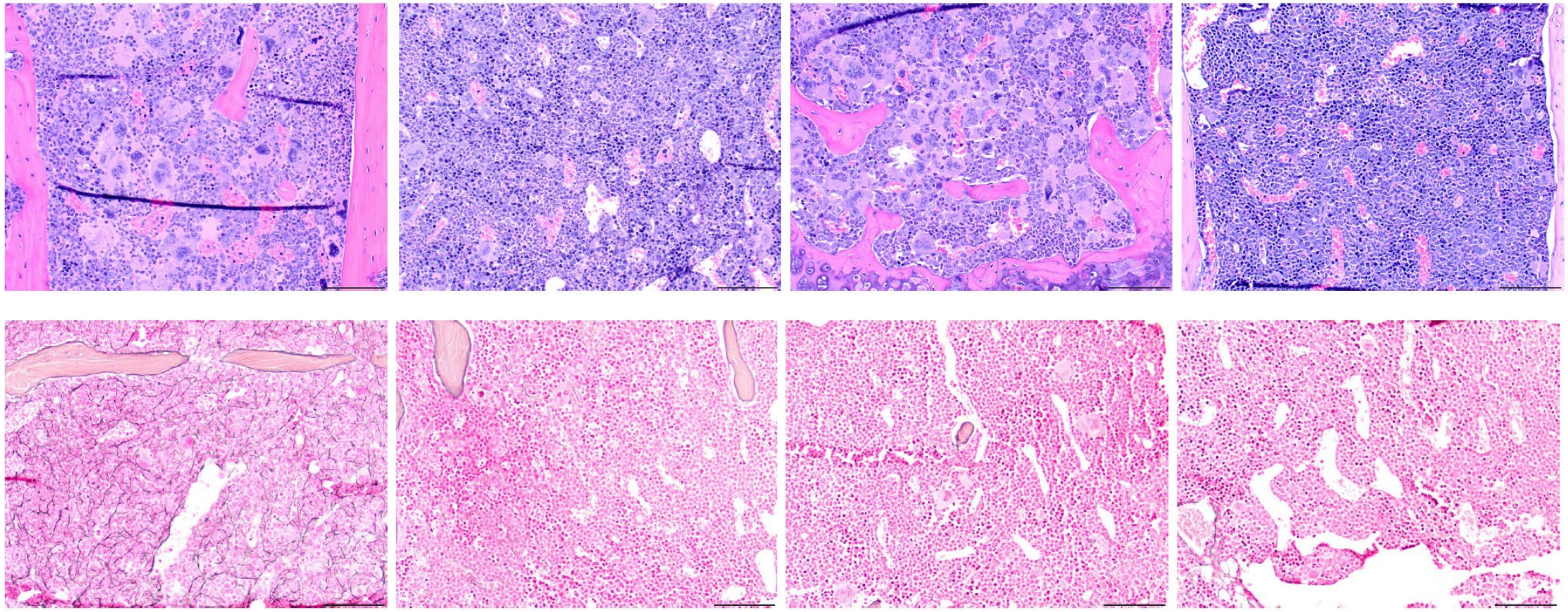
Wen et al. Cancer Cell 2026.

Revumenib as a single agent and in combo with ruxolitinib normalizes bone marrow cellularity and abrogates fibrosis in MPN animal models

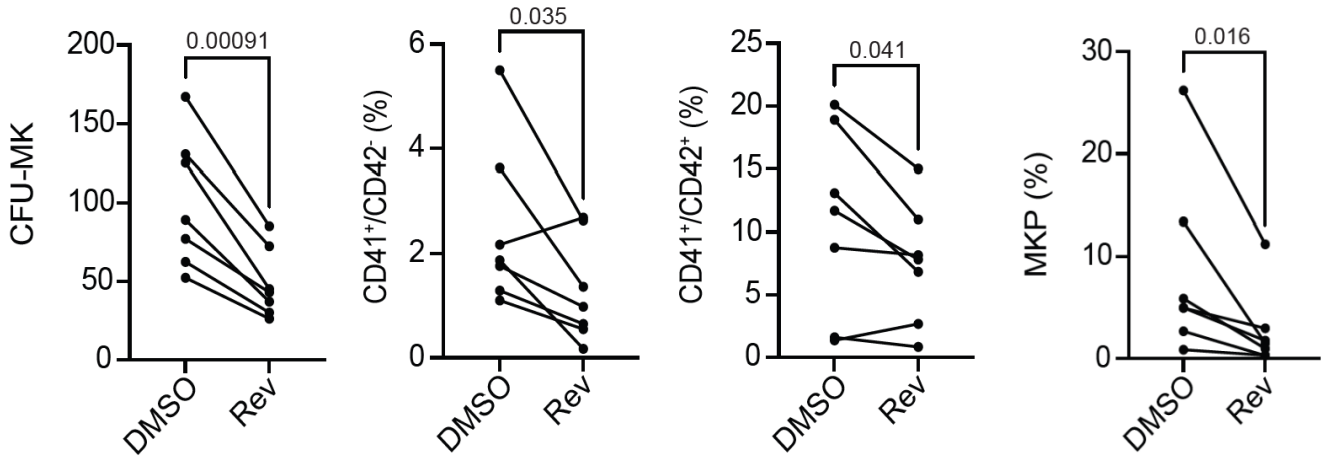


Control | Revumenib | Ruxolitinib | Revumenib + ruxolitinib

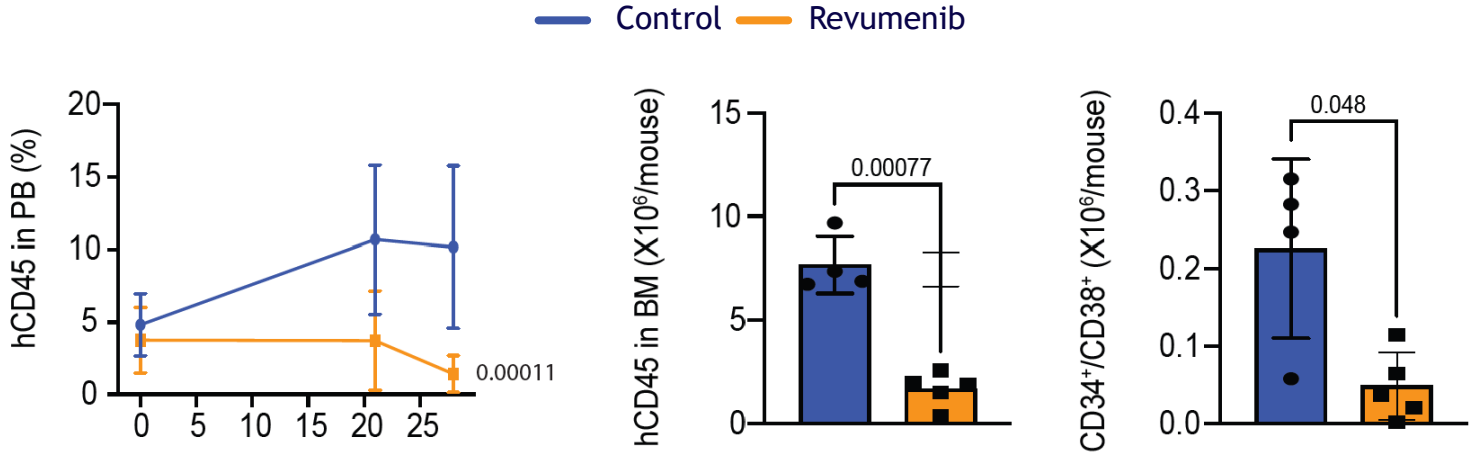
Wen et al. Cancer Cell 2026.

Revumenib targets malignant megakaryocyte progenitors (MKPs) in MF patient samples

***In vitro*, revumenib reduced MKs and MKPs derived from human MF samples**



***In vivo*, revumenib reduced the proportion of human cells in the peripheral blood (PB) and bone marrow (BM) and the number of $CD34^{+}CD38^{-}$ HSPCs in the BM**

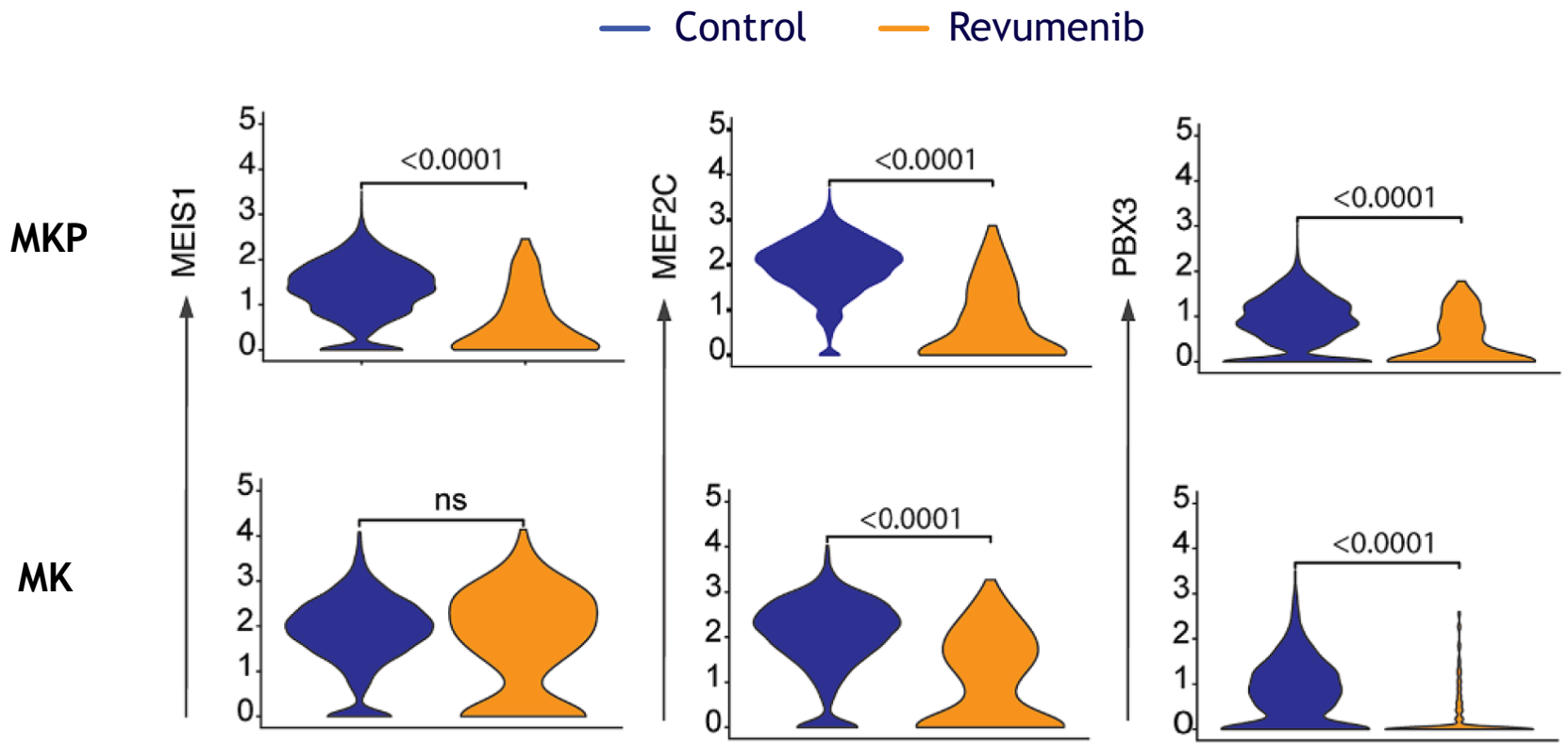


Wen et al. Cancer Cell 2026. Samples include CALR and JAK2 mutant cases. HSPCs, hematopoietic stem and progenitor cells; DMSO = vehicle

Revumenib could provide a unique and complementary mechanism of action in myelofibrosis

Revumenib's effects are mediated by downregulation of key MKP genes, such *MEF2C* and *MEIS1*

Revumenib reduced expression of key menin-KMT2A target genes in MKPs and MKs



Wen et al. Cancer Cell 2026.

Summary

- **Menin inhibition suppresses megakaryopoiesis in times of stress or disease** when progenitors are highly proliferative; on-target effect in MF is driven in part by downregulation of *MEF2C* and *MEIS1*
- **Revumenib has anti-tumor effects in multiple MPN mouse models** as a single agent and in combination with ruxolitinib
- **Revumenib and ruxolitinib appear to synergistically suppress MF cell growth** by targeting regulation of key MKP genes and JAK/STAT signaling, respectively
- **Menin inhibition may be complimentary to other emerging targeted therapies for MF** (e.g., mutCALR-targeted, JAK2 selective) which target activated JAK/STAT pathway
- Our study provides rationale for **further clinical investigation of menin inhibition in MPNs**

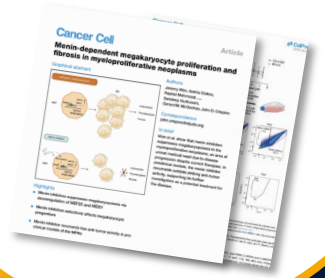
Menin inhibition in MF - Next steps

Nick Botwood, MBBS
Head of Research & Development and Chief Medical Officer

Leveraging revumenib to inform and de-risk development of SNDX-62122 in MF

Anticipated path forward

✓ Publish preclinical MF data



Initiate revumenib proof-of-principle MF trial in 4Q26

Submit IND for SNDX-62122 (next-gen menin inhibitor) in 2027

Initiate Ph 1 of SNDX-62122 in MF in 2027, leveraging learnings with revumenib

Proof-of-principle trial with revumenib expected to generate data that will inform the trial design and dosing of SNDX-62122 in MF

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IND, investigational new drug

Phase 1/2 proof-of-principle trial of menin inhibition in MF expected to initiate in 4Q26 in partnership with the MPN-RC consortium

The Myeloproliferative Neoplasm Research Consortium (MPN-RC) is a group of leading researchers from 15 institutions

Key inclusion criteria:

- Myelofibrosis (MF) diagnosis
- Post-ET MF
- Post-PV MF
- DIPSS Int-1 or higher
- Platelet count ≥ 75 x 10^9/L

(N ≈ 30)

R/R MF with prior treatment with JAKi

Revumenib monotherapy

Objectives

- **Primary: Safety** (DLT)
- Secondary: ORR, CR, PR, CI after 6 cycles, symptom burden, and spleen size

Newly diagnosed MF, treated with JAKi >12wks

Revumenib + ruxolitinib

Objectives

- **Primary: Efficacy** (ORR, CR, PR, CI after 6 cycles)
- Secondary: Safety/DLT, symptom burden, and spleen size

Correlatives to be assessed:

- Platelets, WBC
- MK cells, bone marrow fibrosis
- Cytokines (TNF-α, TGF-β, IL-6)
- VAF

Validation of revumenib clinical activity in MF anticipated in 2H27

Syndax

Post-ET MF, post-essential thrombocythemia myelofibrosis; Post-PV MF post-polycythemia vera myelofibrosis; DIPSS: Dynamic International Prognostic Scoring System; ORR, overall response rate; CR, complete remission; PR, partial remission, CI, clinical improvement; WBC, white blood cells; MK, megakaryocyte; VAF, variant allele frequency; JAKi, JAK inhibitor; DLT, dose limiting toxicity

Q&A - Revumenib and Next-Gen Menin Inhibitors

Michael A. Metzger
Chief Executive Officer and Director

Nick Botwood, MBBS
Head of R&D and Chief Medical Officer

Peter Ordentlich, PhD
Chief Scientific Officer and Founder

John D. Crispino, PhD, MBA
Director, Division of Experimental Hematology,
St. Jude Children's Research Hospital

Unlocking the potential of CSF-1R inhibition

Peter Ordentlich, PhD
Chief Scientific Officer and Founder

Axatilimab development driven by deep mechanistic understandings of the CSF-1R pathway

- Colony stimulating factor 1 receptor (CSF-1R) signaling is essential for the activation, proliferation, and differentiation of monocytes and monocyte-derived macrophages

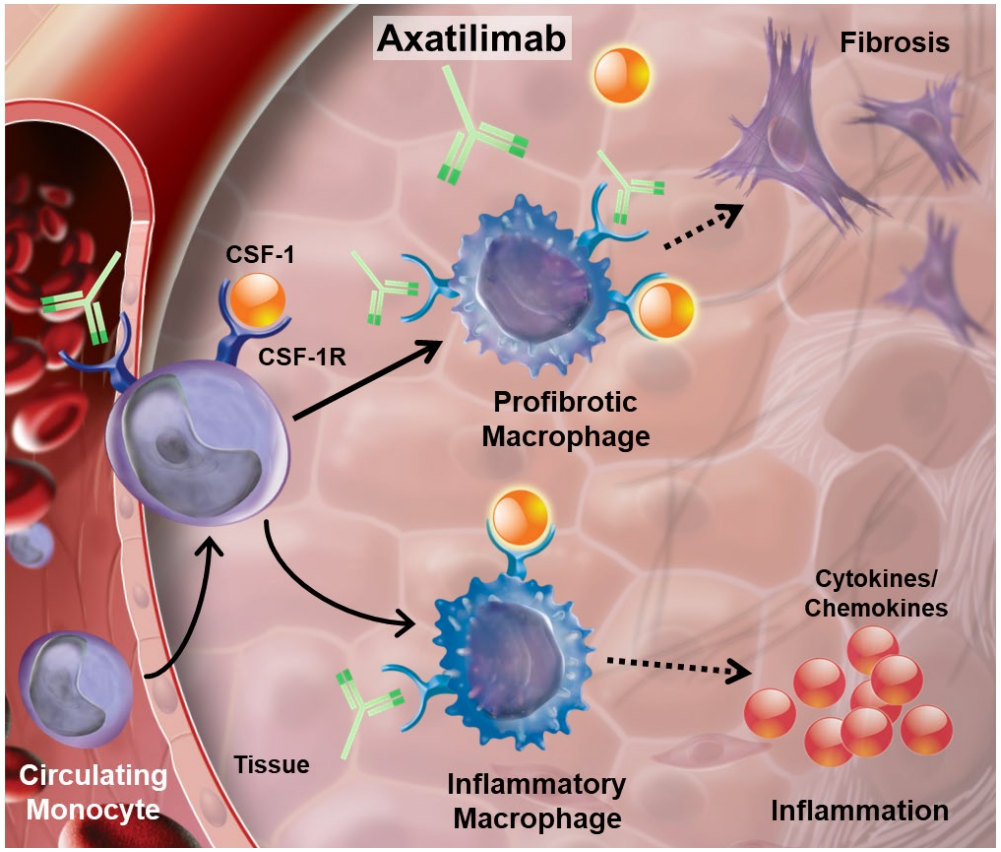
- Axatilimab is a monoclonal antibody that blocks the activation of CSF-1R by its two ligands, CSF-1 and IL-34, which:

1 Inhibits the inflammatory process by:

- Suppressing the activity of monocytes and macrophages, reducing proinflammatory cytokine secretion

2 Inhibits the fibrotic process by:

- Reducing monocyte levels, suppressing their differentiation into profibrotic macrophages
- Inhibiting macrophages, disrupting the TGF-ß-mediated development of fibrosis



CSF-1R inhibition has the potential to impact an array of inflammatory and fibrosing diseases

Following the science to unlock the full potential of CSF-1R inhibition

R/R cGVHD

Pivotal trial showed robust responses across all organs studied, including in the lung and skin

FDA approved in 2024 for cGVHD patients with ≥2 prior lines of therapy

1L cGVHD

Ongoing trials could advance axa into 1L cGVHD, with the potential for a steroid-sparing approach

Ph 2 axa + rux data expected 4Q26

Ph 3 axa + steroid data expected early 2028

IPF

Topline Ph 2 MAXPIRe data expected 4Q26

Ph 3 trial planned with current formulation

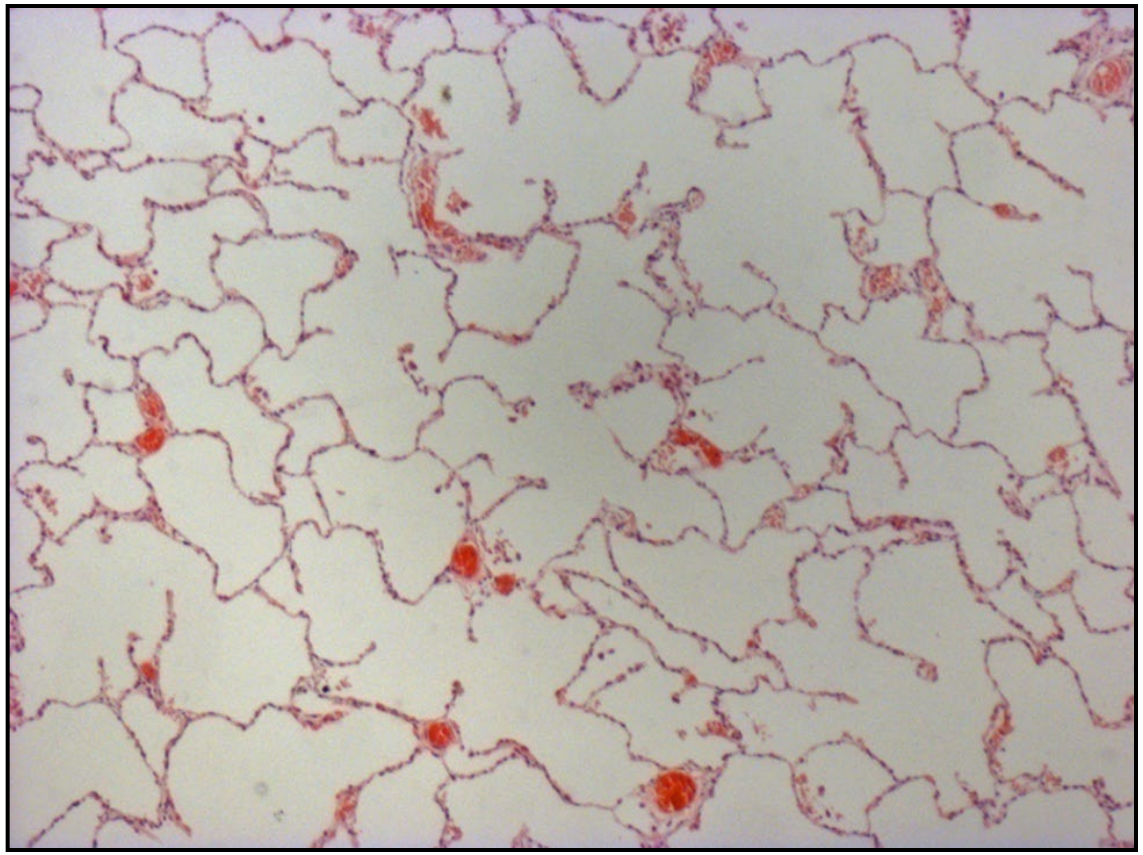
Sub-q formulation in development

BEYOND

Mechanism holds promise across an array of diseases with inflammatory and fibrosing components, e.g., other interstitial lung diseases or scleroderma

Clinical perspective on IPF and CSF-1R inhibition

Toby M. Maher, MD, PhD
Professor of Clinical Medicine and Director of Interstitial Lung Disease,
Keck Medical School of University of Southern California



OROPHARYNGEAL REGION

(mouth and nose)

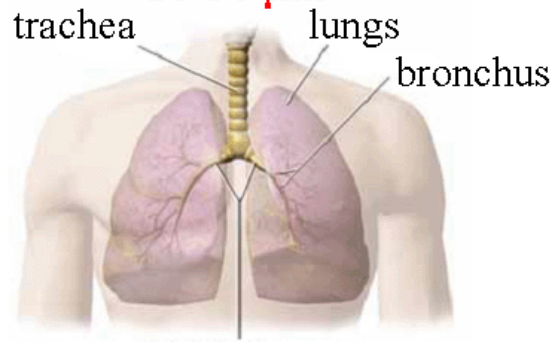
10-30 µm

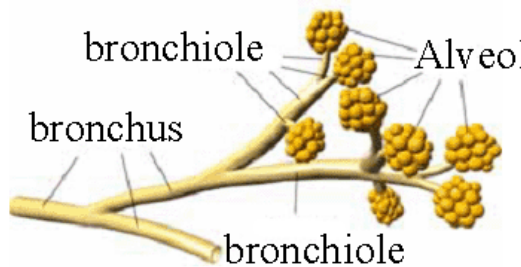
TRACHEA

BRONCHIAL

BRONCHIOLAR REGION

2-10 µm

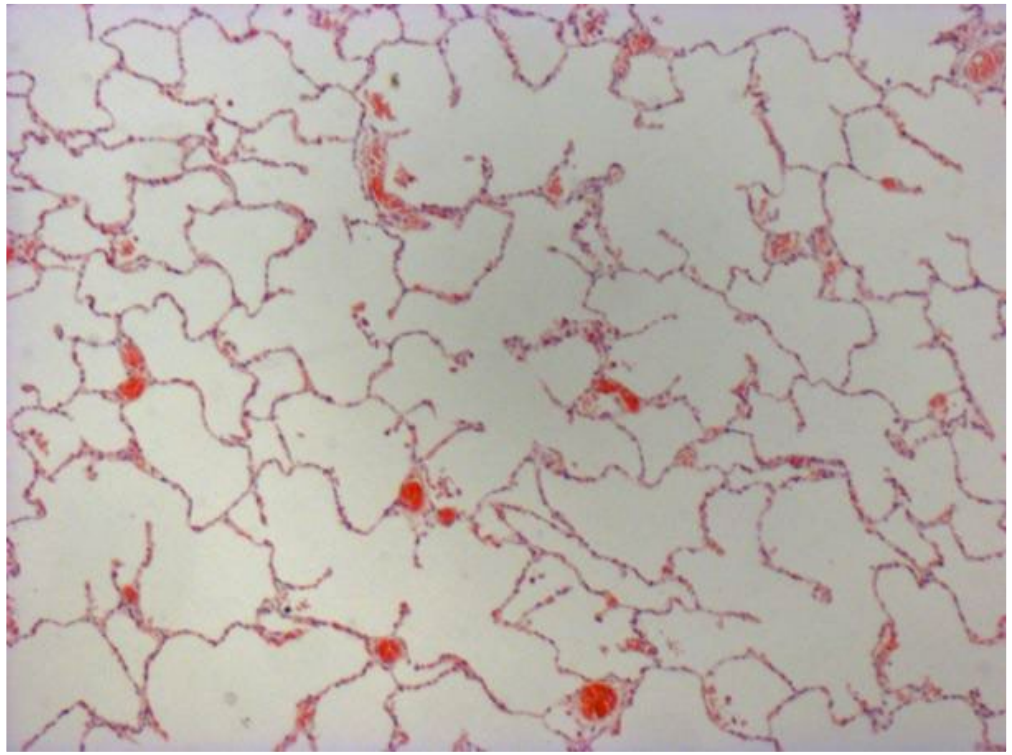


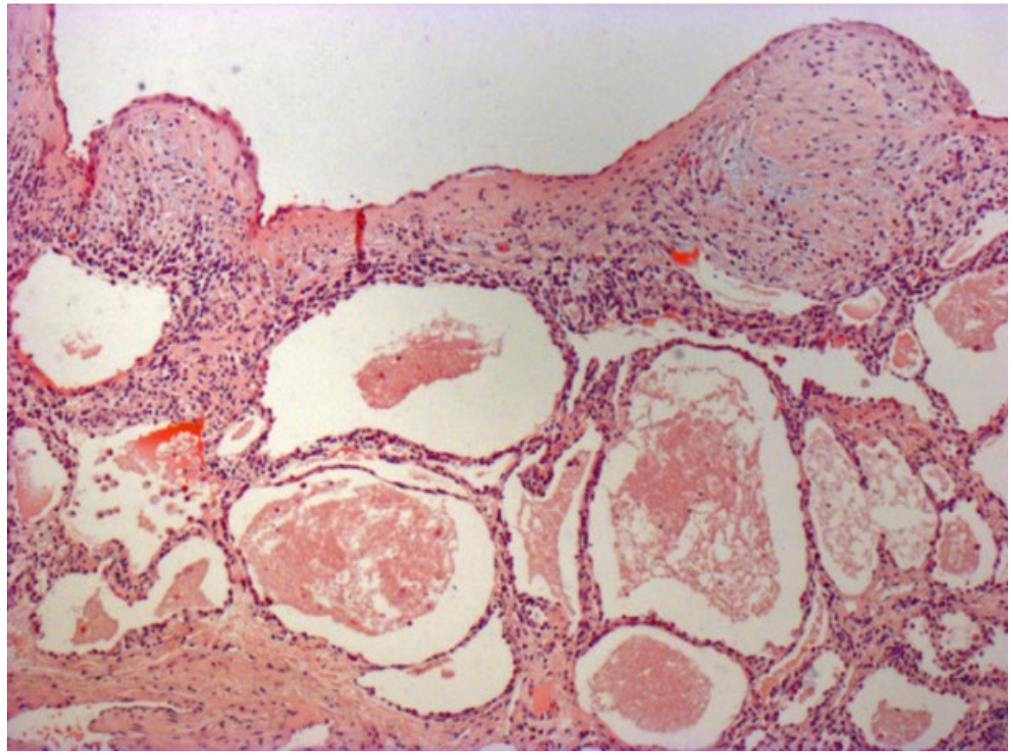


ALVEOLAR REGION

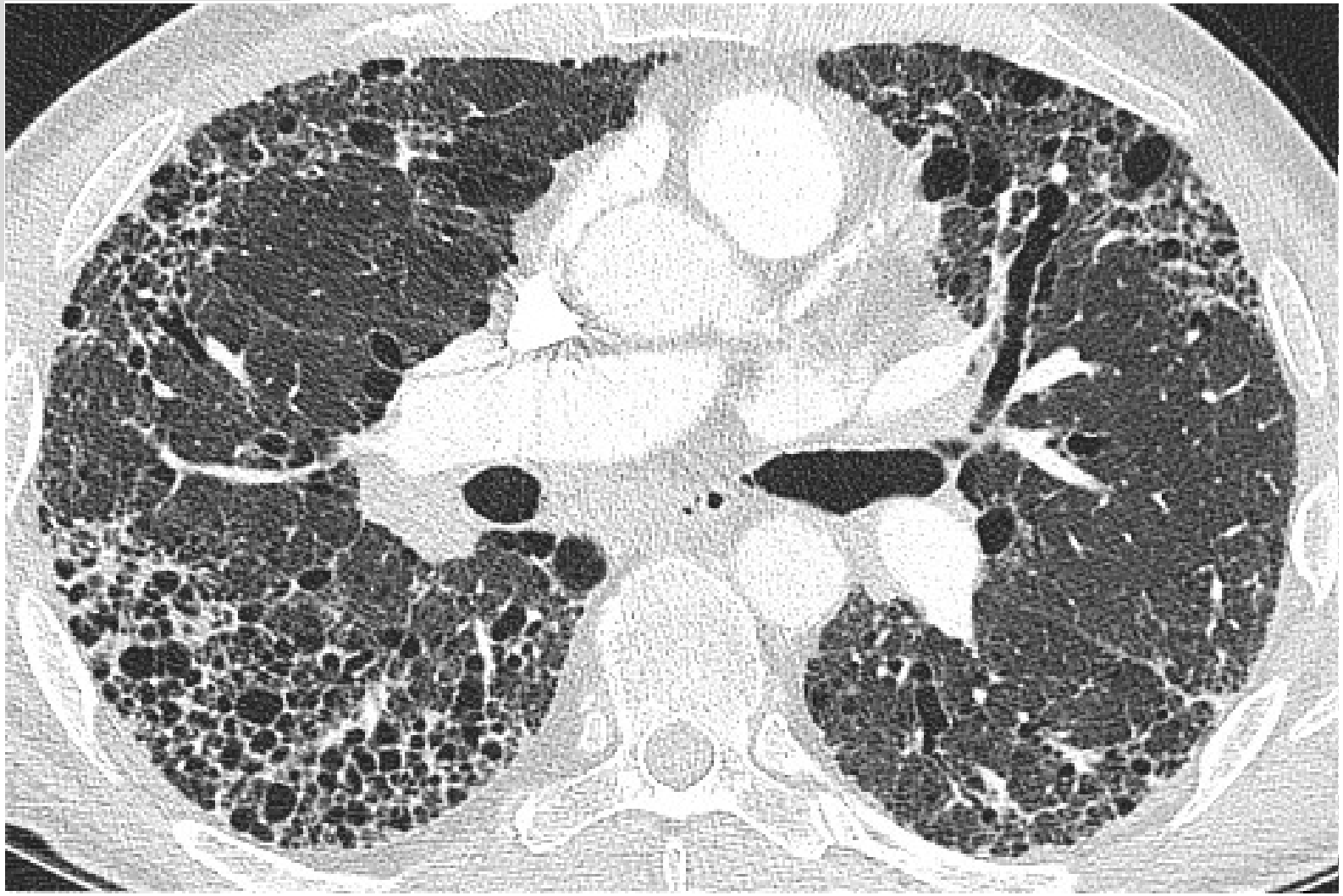
< 2 µm

IPF - Histology



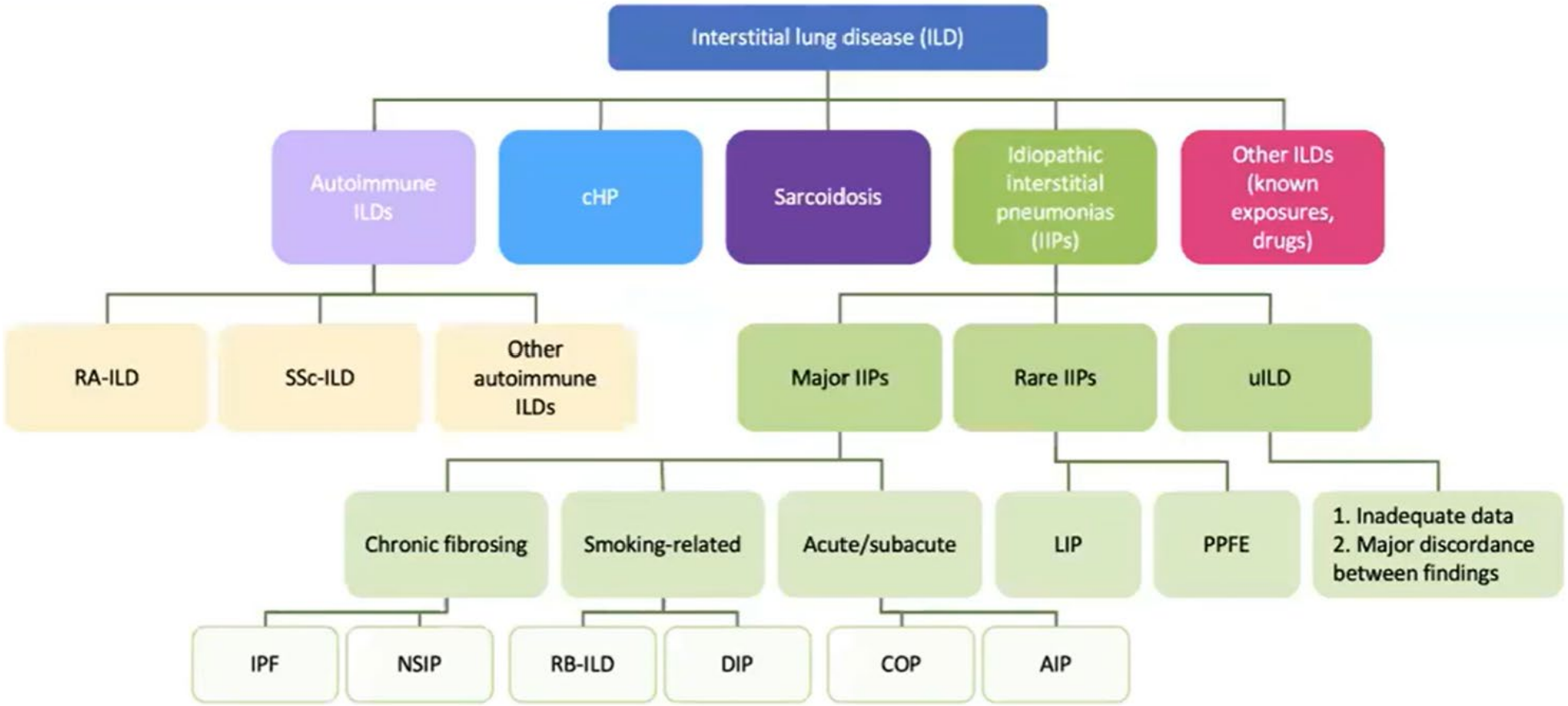


Idiopathic pulmonary fibrosis



Maher TM JAMA 2024

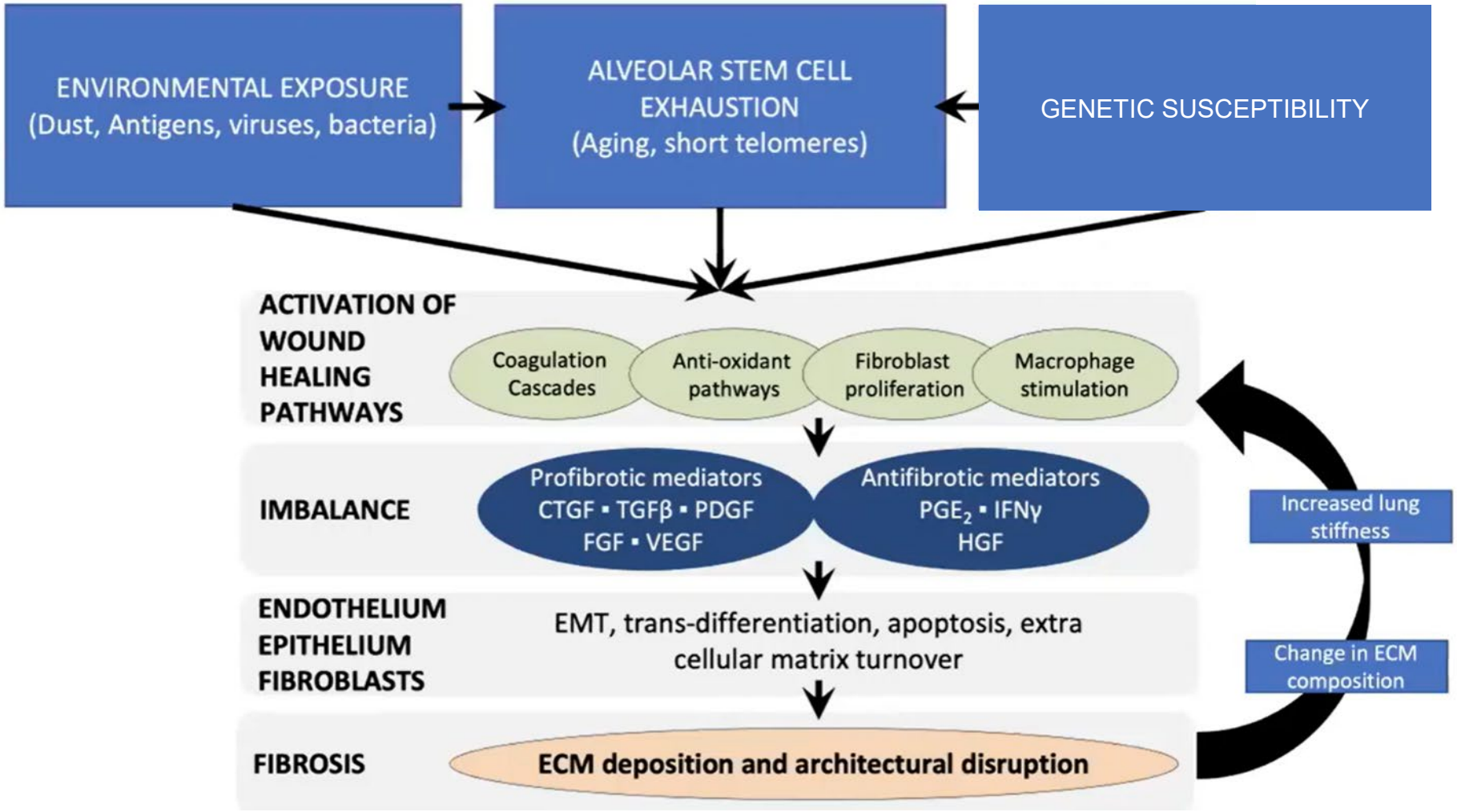
IPF is one of several interstitial lung diseases with shared pathophysiology



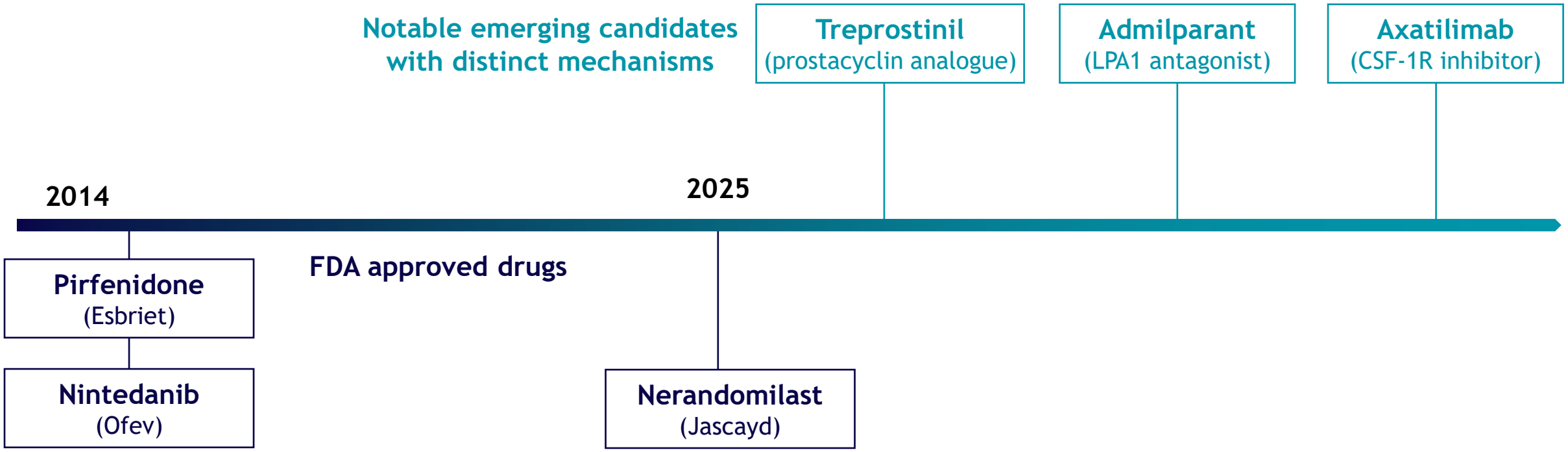
AIP, acute interstitial pneumonia; ATS, American Thoracic Society; COP, cryptogenic organising pneumonia; ERS, European Respiratory Society; IPF, idiopathic pulmonary fibrosis; LAM, lymphangioleiomyomatosis; LCH, Langerhans cell histiocytosis; LIP, lymphocytic interstitial pneumonia; PPFE, pleuroparenchymal fibroelastosis

Adapted from: ATS/ERS. *Am J Respir Crit Care Med.* 2002;165:277–304; Ryerson CJ, Collard HR. *Curr Opin Pulm Med.* 2013;19:453–459; Travis WD, et al. *Am J Respir Crit Care Med.* 2013;188:733–748; Cottin V, et al. *Eur Respir Rev.* 2018;27:pii180076

IPF is a complex, multi-factorial disease



Evolving Tx landscape and multiple emerging modalities could advance patient outcomes in IPF

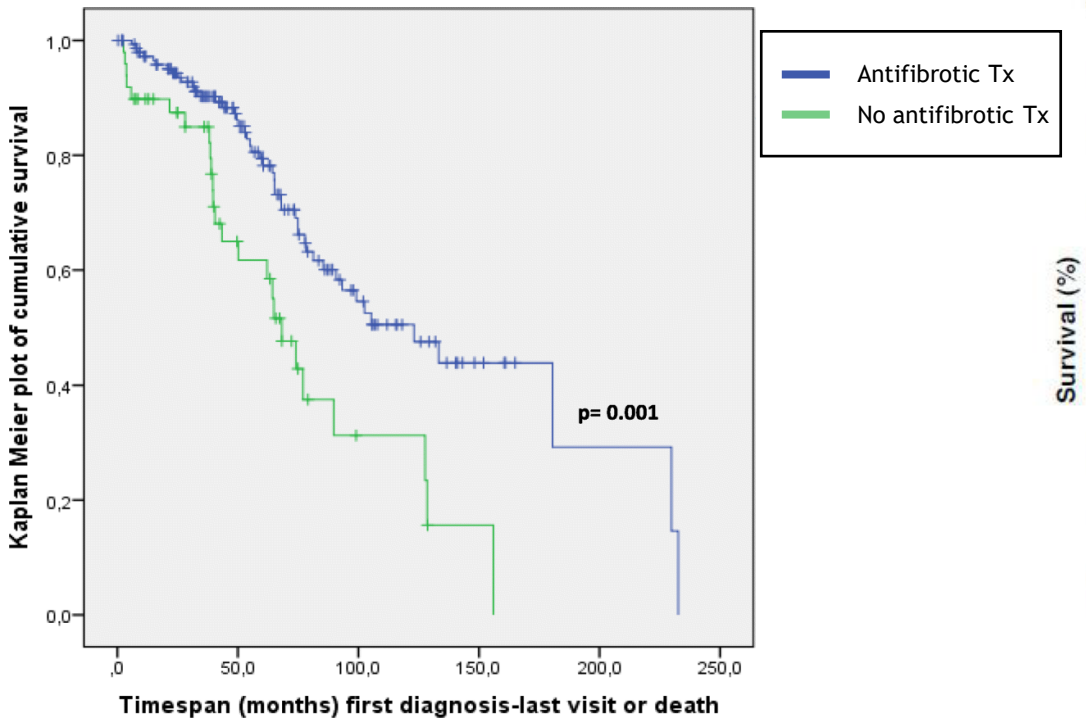


Combination approaches targeting multiple pathways will likely be needed to meaningfully impact survival in IPF

Real-world outcomes with first generation antifibrotics underscore need for new therapeutic approaches in IPF

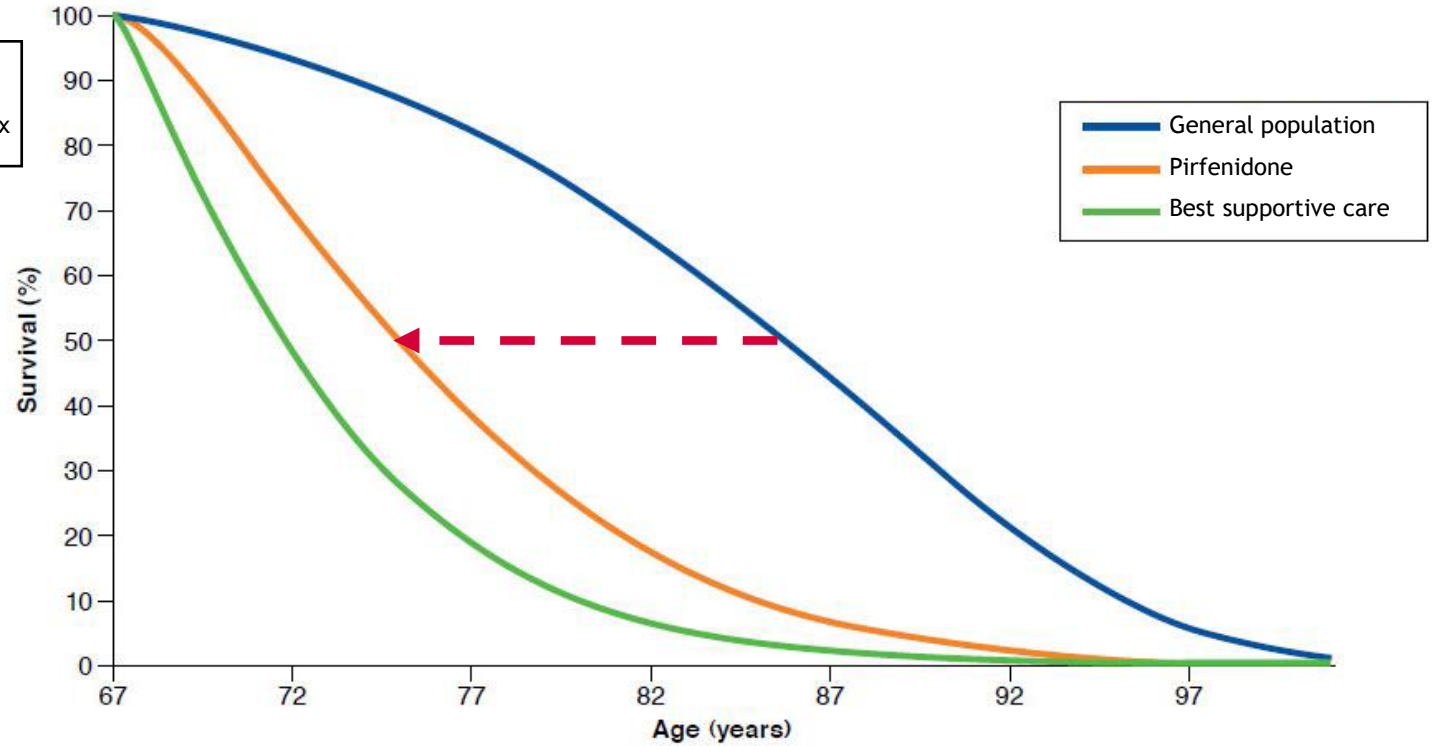
The European IPF registry (eurIPFreg): baseline characteristics and survival of patients with idiopathic pulmonary fibrosis

Andreas Guenther[1,2,3,4,16*], Ekaterina Krauss[1,2], Silke Tello[1,2], Jasmin Wagner[1,2], Bettina Paul[1,2], Stefan Kuhn[1,2], Olga Maurer[1,4], Sabine Heinemann[1,2], Ulrich Costabel[1,8], María Asunción Nieto Barbero[1,9], Veronika Müller[1,10], Philippe Bonniaud[1,5], Carlo Vancheri[1,6], Athol Wells[1,7], Martina Vasakova[1,11], Alberto Pesci[1,12], Matteo Sofia[1,13], Walter Klepetko[1,14], Werner Seeger[1,2,3], Fotios Drakopanagiotakis[1,2] and Bruno Crestani[1,15]



Predicting Life Expectancy for Pirfenidone in Idiopathic Pulmonary Fibrosis

Mark Fisher, MSc; Steven D. Nathan, MD; Christian Hill, BSc; Jade Marshall, MSc; Fred Dejonckheere, MD; Per-Olof Thuresson, MSc; and Toby M. Maher, MD

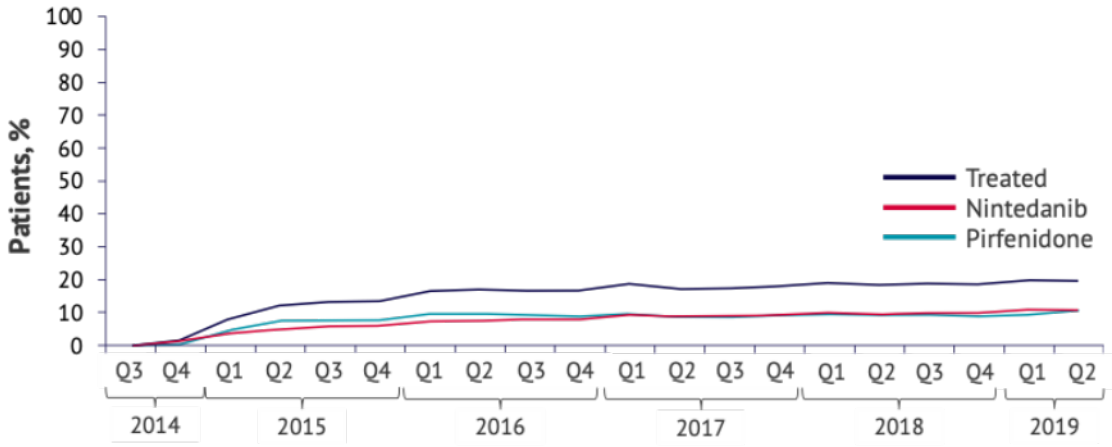


Syndax

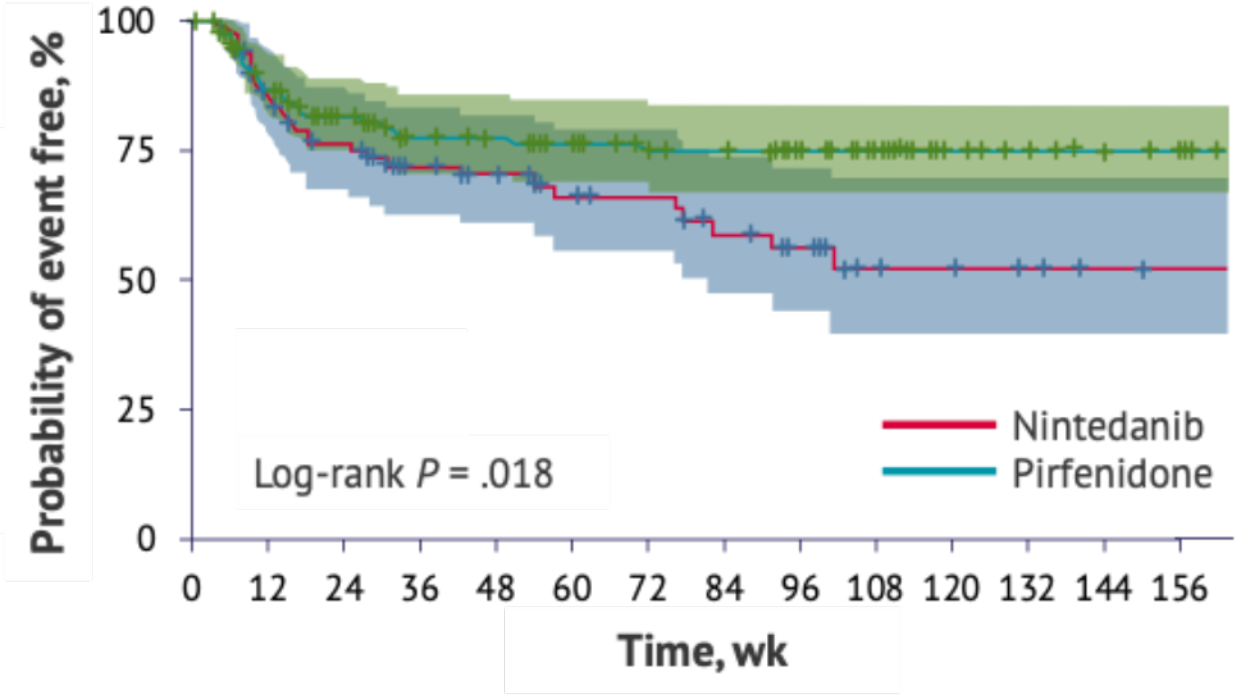
Guenther et al. Respir Res. 2018; Fisher et al. J Manag Care Spec Pharm 2017.

Pirfenidone and nintedanib use and persistence in the US

Anti-fibrotic use in US



Anti-fibrotic persistence in US



Dempsey T et al Annals ATS 2021
Ortiz et al BMJ Respir Open 2024

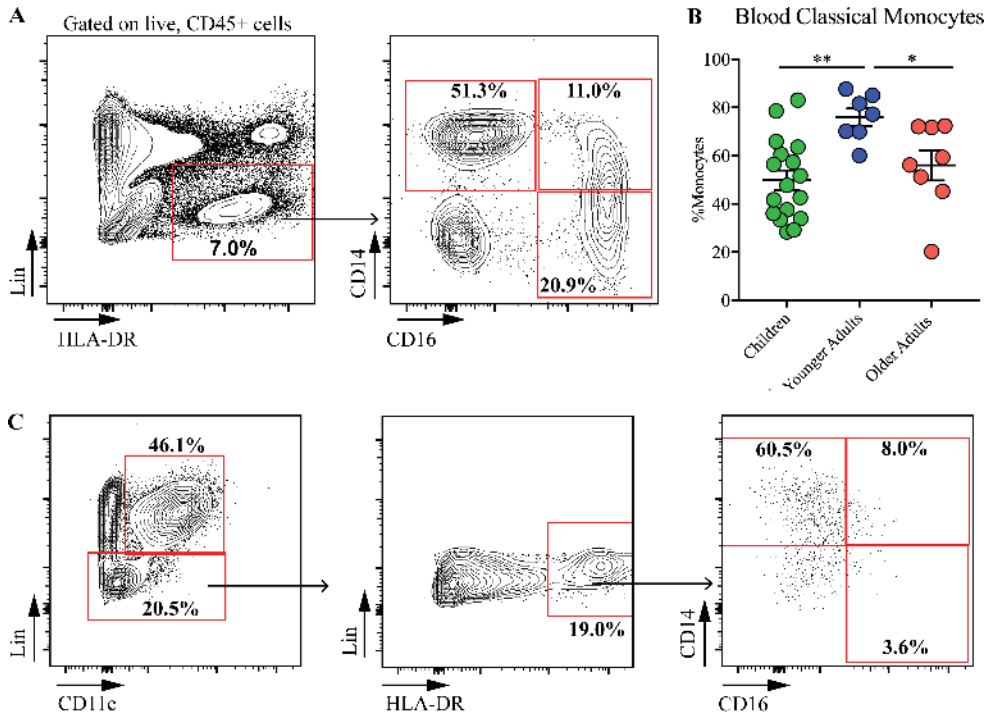
The monocyte-derived alveolar macrophages is a promising target in IPF

JEM Journal of Experimental Medicine

BRIEF DEFINITIVE REPORT

Dynamics of human monocytes and airway macrophages during healthy aging and after transplant

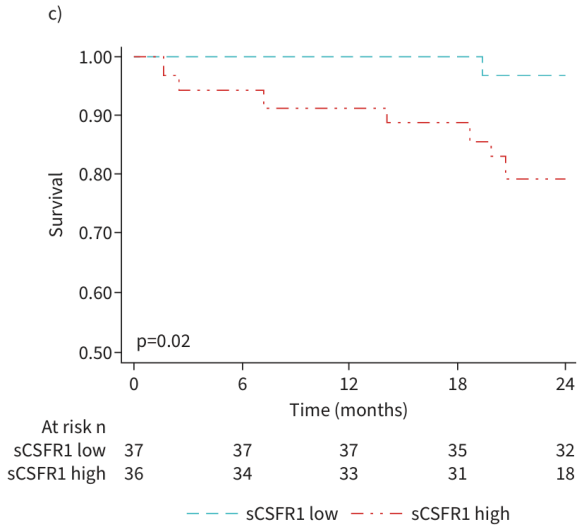
Adam J. Byrne[1,7], Joseph E. Powell[3,4], Brendan J. O'Sullivan[5,6], Patricia P. Ogger[1], Ashley Hoffland[1,7], James Cook[1,7], Katie L. Bonner[1,7], Richard J. Hewitt[1,7], Simone Wolf[1], Poonam Ghai[1], Simone A. Walker[1], Samuel W. Lukowski[8], Philip L. Molyneaux[1,7], Sejal Saglani[1,2,7], Daniel C. Chambers[5,6], Toby M. Maher[1,7*], and Clare M. Lloyd[1,2*]

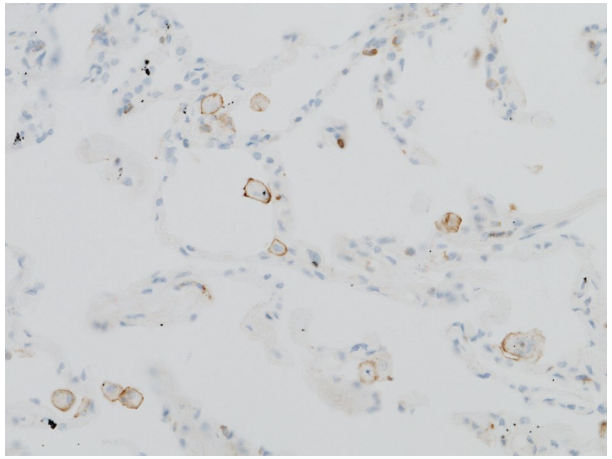


Byrne et al. J Exp Med 2020

ERJ OPEN RESEARCH
RESEARCH LETTER
J.M. OLDHAM ET AL.

Airway soluble CSF1R predicts progression in patients with idiopathic pulmonary fibrosis



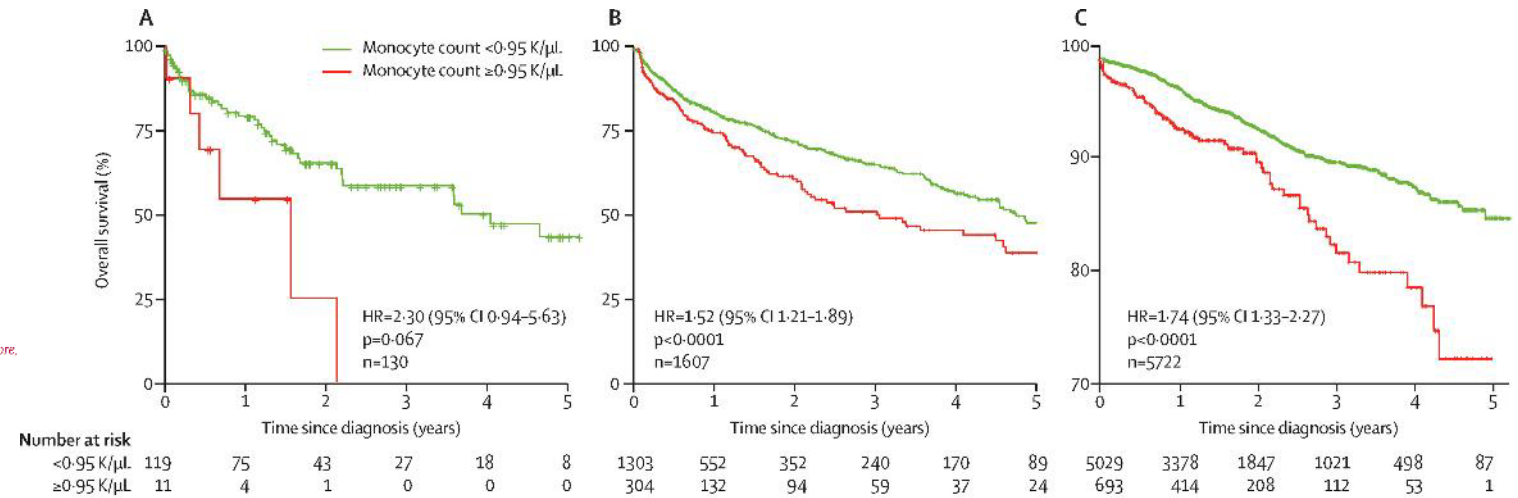


Oldham et al ERJOR 2022

Higher monocyte levels are associated with shorter survival in IPF and other fibrotic diseases

Increased monocyte count as a cellular biomarker for poor outcomes in fibrotic diseases: a retrospective, multicentre cohort study

Madeleine K D Scott, Katie Quinn, Qin Li, Robert Carroll, Hayley Warsinske, Francesco Vallania, Shirley Chen, Mary A Carns, Kathleen Aren, Jiehuan Sun, Kimberly Kolaris, Jungwha Lee, Jessika Baral, Jonathan Krapski, Hongyu Zhao, Erica Herzog, Fernando J Martinez, Bethany B Moore, Monique Hinchcliff, Joshua Denny, Naftali Kaminski, Jose D Herazo-Maya, Nigam H Shah, Purvesh Khatri**



D

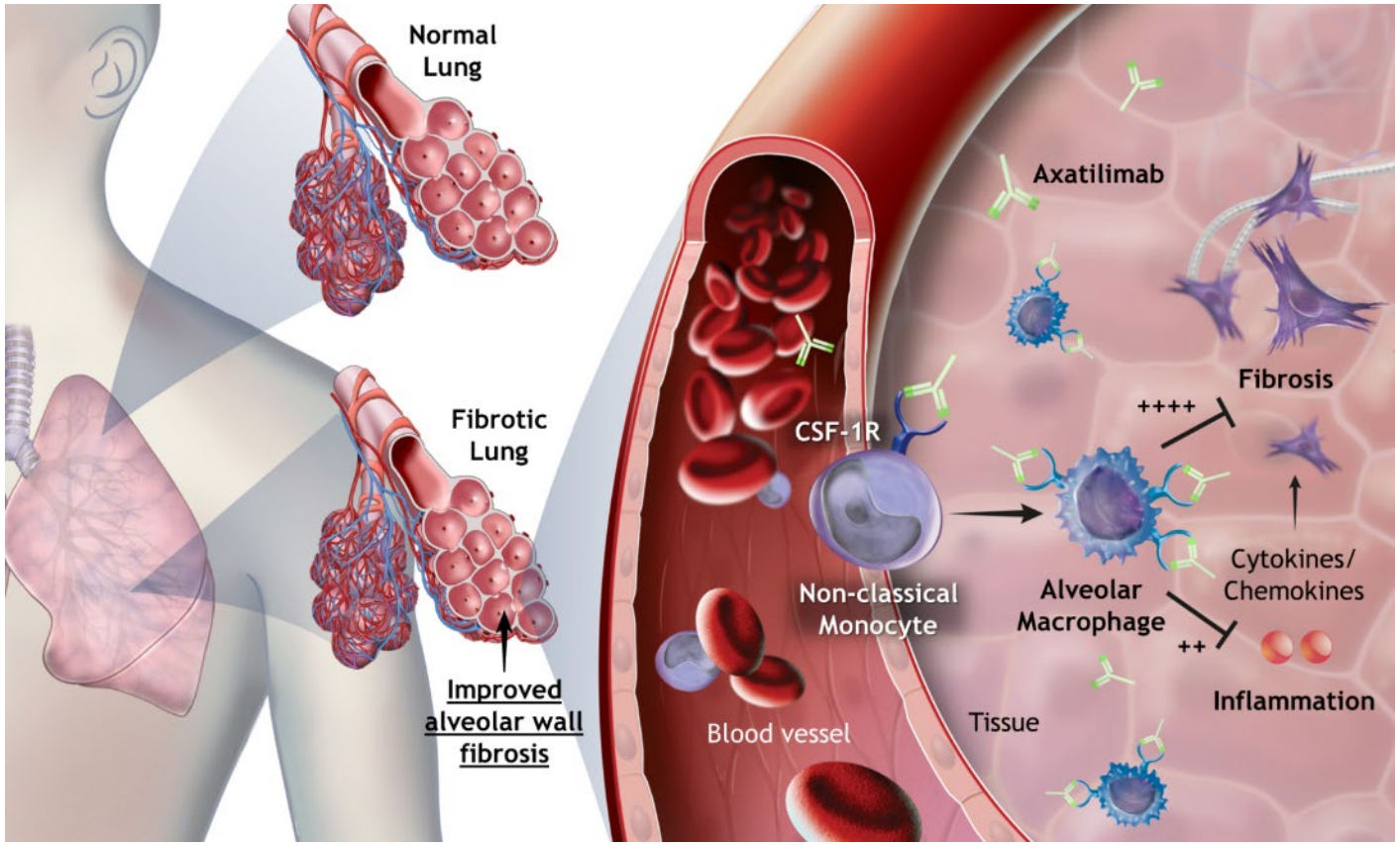
Cohort	n (%)	GAP index staging	95% CI (GAP index)	p	HR for FVC-adjusted monocyte count	95% CI (FVC-adjusted monocyte count)	p	HR for GAP-adjusted monocyte count	95% CI (GAP-adjusted monocyte count)	p
COMET	36 (80%)	1·42	0·77–2·63	0·26	2·67	0·97–7·40	0·06	2·62	0·94–7·27	0·06
Stanford	130 (100%)	1·74	1·34–2·25	<0·0001	2·43	1·00–5·91	0·05	1·87	0·76–4·61	0·17
Northwestern SSc-ILD	365 (100%)	1·65	1·35–2·02	<0·0001	2·39	1·06–5·38	0·04	1·90	0·83–4·34	0·13
Summary	**531**	**1·66**	**1·43–1·94**	<0·0001	**2·47**	**1·48–4·15**	**0·0063**	**2·06**	**1·22–3·47**	**0·0068**

Syndax

Scott et al. Lancet Respir Med 2019.

Axatilimab targets a novel and potentially complementary pathway in IPF

Axatilimab is a CSF1R-blocking antibody targeting monocyte-derived alveolar macrophages



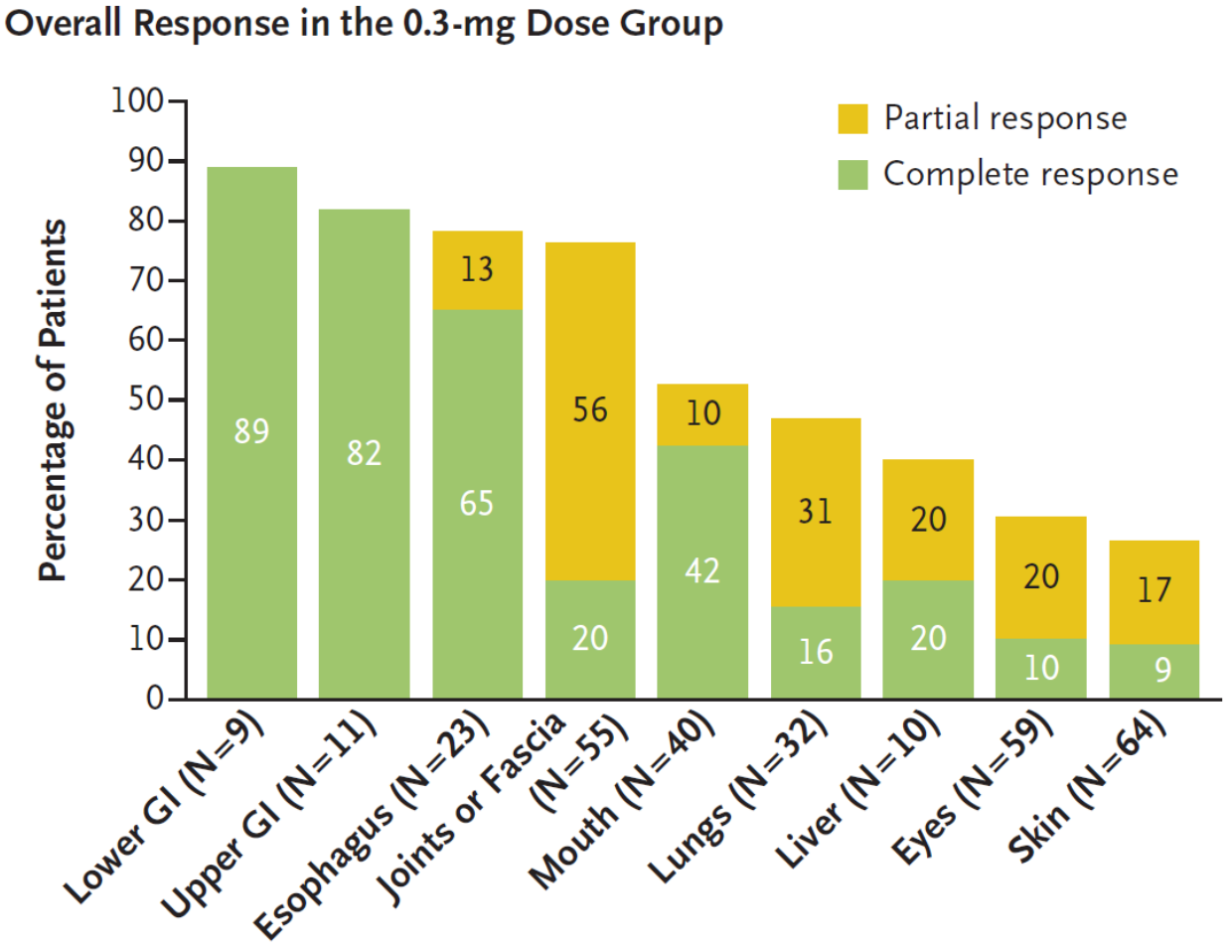
Axatilimab has shown strong activity across multiple organs in cGVHD

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Axatilimab in Recurrent or Refractory Chronic Graft-versus-Host Disease

D. Wolff, C. Cutler, S.J. Lee, I. Pusic, H. Bittencourt, J. White, M. Hamadani, S. Arai, A. Salhotra, J.A. Perez-Simon, A. Alousi, H. Choe, M. Kwon, A. Bermúdez, I. Kim, G. Socié, S. Chhabra, V. Radojcic, T. O'Toole, C. Tian, P. Ordentlich, Z. DeFilipp, and C.L. Kitko, for the AGAVE-201 Investigators*



Wolff et al. NEJM 2024.

Safety profile observed in cGVHD highlights axatilimab's combination potential

The NEW ENGLAND JOURNAL of MEDICINE

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Axatilimab in Recurrent or Refractory Chronic Graft-versus-Host Disease

D. Wolff, C. Cutler, S.J. Lee, I. Pusic, H. Bittencourt, J. White, M. Hamadani, S. Arai, A. Salhotra, J.A. Perez-Simon, A. Alousi, H. Choe, M. Kwon, A. Bermúdez, I. Kim, G. Socié, S. Chhabra, V. Radojcic, T. O'Toole, C. Tian, P. Ordentlich, Z. DeFilipp, and C.L. Kitko, for the AGAVE-201 Investigators*

Table 2. Safety Overview.*

Adverse Event	0.3-mg Dose Group (N=79)	1-mg Dose Group (N=81)	3-mg Dose Group (N=79)
	number of patients (percent)		
Any adverse event	76 (96)	80 (99)	78 (99)
Grade ≥3	39 (49)	49 (60)	56 (71)
Serious	30 (38)	33 (41)	38 (48)
Fatal	1 (1)	7 (9)	6 (8)
Any grade event in ≥20% of any dose group			
Aspartate aminotransferase level increased	11 (14)	31 (38)	43 (54)
Blood creatine kinase level increased	9 (11)	26 (32)	49 (62)
Lipase level increased	9 (11)	21 (26)	39 (49)
Amylase level increased	3 (4)	10 (12)	34 (43)
Blood lactate dehydrogenase level increased	11 (14)	22 (27)	32 (41)
Alanine aminotransferase level increased	10 (13)	18 (22)	31 (39)
Periorbital edema	2 (3)	19 (23)	23 (29)
Fatigue	18 (23)	16 (20)	21 (27)
γ-Glutamyltransferase level increased	8 (10)	16 (20)	21 (27)
Covid-19	13 (16)	18 (22)	11 (14)
Diarrhea	13 (16)	18 (22)	7 (9)
Blood alkaline phosphatase level increased	5 (6)	4 (5)	17 (22)
Headache	15 (19)	14 (17)	16 (20)
Any grade infection	58 (73)	59 (73)	55 (70)
Any grade key infection or reactivation			
Covid-19	15 (19)	19 (23)	14 (18)
Pneumonia	9 (11)	12 (15)	8 (10)
Aspergillus	0	3 (4)	0
Cytomegalovirus	0	1 (1)	2 (3)
Epstein–Barr virus	0	0	4 (5)
Any grade infusion-related reaction	6 (8)	4 (5)	1 (1)
Any grade ≥3 event in ≥5% of any dose group			
Pneumonia	8 (10)	7 (9)	5 (6)
Blood creatine kinase level increased	1 (1)	6 (7)	12 (15)
Covid-19	3 (4)	5 (6)	5 (6)
Hypertension	3 (4)	5 (6)	4 (5)
γ-Glutamyltransferase level increased	1 (1)	2 (2)	4 (5)
Lipase level increased	1 (1)	1 (1)	4 (5)
Periorbital edema	0	1 (1)	5 (6)
Any serious event in ≥5% of any dose group			
Covid-19	2 (3)	4 (5)	5 (6)
Pneumonia	7 (9)	8 (10)	4 (5)
Any adverse event leading to dose interruption	30 (38)	34 (42)	25 (32)
Any adverse event leading to dose reduction	5 (6)	6 (7)	13 (16)
Any adverse event leading to discontinuation of axatilimab	5 (6)	18 (22)	14 (18)†

Syndax

Wolff et al. NEJM 2024.

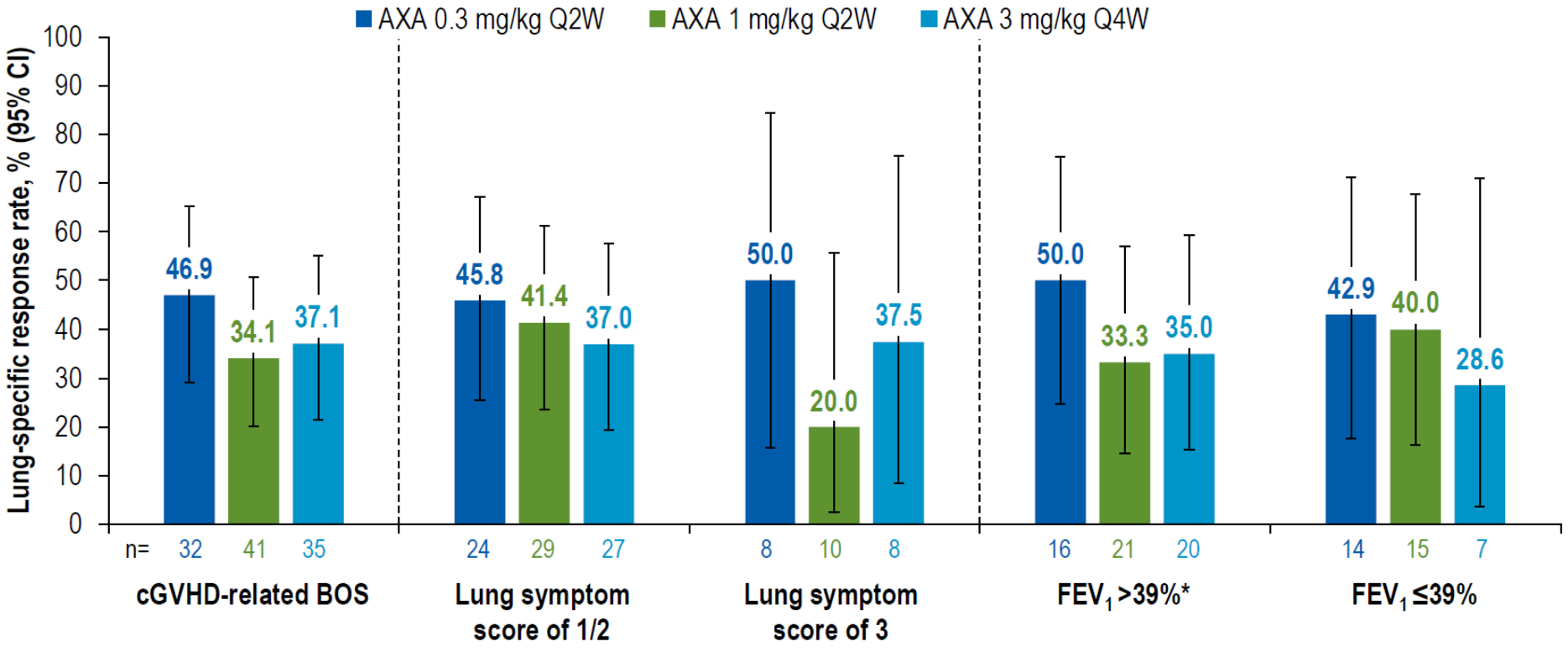
Data in cGVHD-related bronchiolitis obliterans syndrome (BOS) shows axatilimab has antifibrotic activity in the lung

Axatilimab in Patients With Lung Chronic Graft-Versus-Host Disease and Related Bronchiolitis Obliterans Syndrome: Results From the AGAVE-201 Study

Amandeep Salhotra, MD,[1] Valkal Bhatt, PharmD,[2] Britnie Thomas, PhD,[2] Shuyuan Lou, PhD,[2] Vedran Radojcic, MD,[3] Zachariah DeFilipp, MD[4]

[1]City of Hope National Medical Center, Duarte, CA, USA; [2]Incyte
[3]Syndax Pharmaceuticals, Inc., New York, NY, USA; [4]Massachu

American Thoracic Society International Conference; May 17–21, 2025; San Fra



Salhotra et al. Axatilimab in Patients With Lung Chronic Graft-Versus-Host Disease and Related Bronchiolitis Obliterans Syndrome: Results From the AGAVE-201 Study. Oral presentation at ATS 2025.

MAXPIRe is a robust Phase 2 trial of axatilimab in IPF

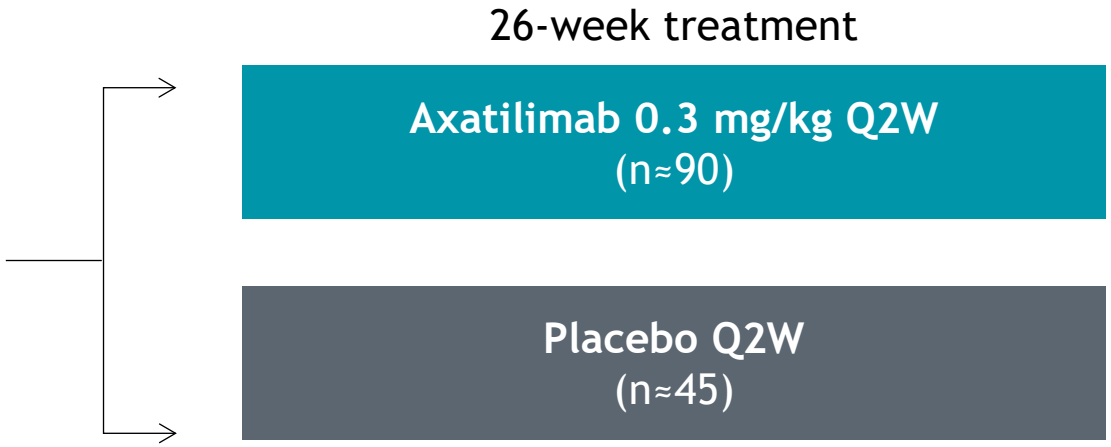
Randomized, double-blind, placebo-controlled, multi-center international trial

MAXPIRe
IPF CLINICAL TRIAL

Key eligibility criteria:

- ≥40 yrs of age
- HRCT confirming IPF diagnosis
- FVC ≥45% of predicted normal (PN)
- FEV_1/FVC ≥0.7
- DL_{CO} ≥30% and ≤90% PN
- Stable background use of pirfenidone or nintedanib allowed

(N≈135)



Randomized 2:1 to axatilimab or placebo; stratified by background antifibrotic therapy (pirfenidone, nintedanib, or none)

PRIMARY ENDPOINT:

- Annualized rate of decline in FVC over 26 weeks (ml)

SECONDARY ENDPOINTS:

- Disease progression, SGRQ (quality of life measures), change in FVC % predicted, DL_{CO}

Syndax

ClinicalTrials.gov ID: NCT06132256; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; SGRQ, St. George's Respiratory Questionnaire; DL_{CO}, diffusion capacity for carbon monoxide; HRCT, high-resolution computed tomography

Summary

- IPF is a deadly and progressive disease
- Current therapies slow but do not prevent progression of fibrosis
- There is an increasing drive to combine therapies in IPF
- CSF-1R positive macrophages play an important role in fibrogenesis
- Axatilimab has been shown to be effective in GVHD – a disease of small airway fibrosis
- The MAXPIRe trial will provide important proof-of-concept in IPF

Q&A - Axatilimab

Michael A. Metzger
Chief Executive Officer and Director

Nick Botwood, MBBS
Head of R&D and Chief Medical Officer

Peter Ordentlich, PhD
Chief Scientific Officer and Founder

Toby M. Maher, MD, PhD
Professor of Clinical Medicine and Director of Interstitial Lung Disease, Keck Medical School of University of Southern California

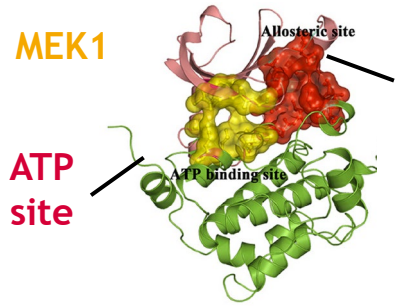
Expanding our pipeline into EGFRm NSCLC with SNDX-4321

Nick Botwood, MBBS
Head of Research & Development and Chief Medical Officer

Allosteric inhibitors are increasingly reshaping the standard of care for difficult-to-treat cancers

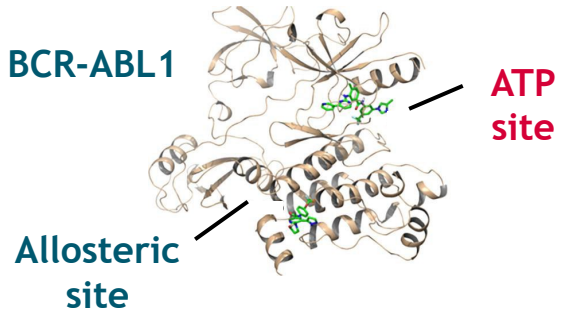
Melanoma

Trametinib (Mekinist)



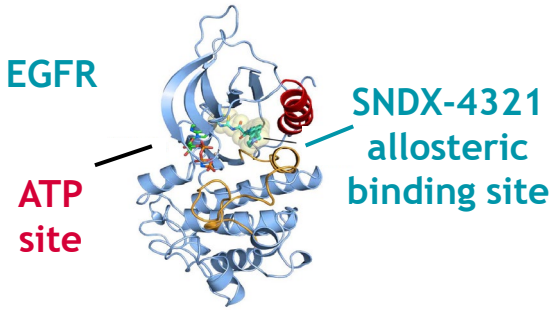
Chronic myeloid leukemia

Asciminib (Scemblix)



EGFRm NSCLC

SNDX-4321



2013 — 2021 — Future

Allosteric inhibitors bind to non-active sites rather than the ATP-binding site on tyrosine kinases; their binding induces a conformational change that 'locks' the kinase in an inactive state

Allosteric approaches can modulate kinase activity with high specificity, optimizing on-target efficacy while reducing off-target toxicity

Syndax

Zhu et al. Int J Mol Sci 2020; Schoepfer et al. J Med Chem 2018.

Syndax aims to address significant unmet needs in EGFRm NSCLC with a novel approach

Currently approved and investigational drugs primarily target the EGFR ATP-binding site

3rd gen approved EGFRi

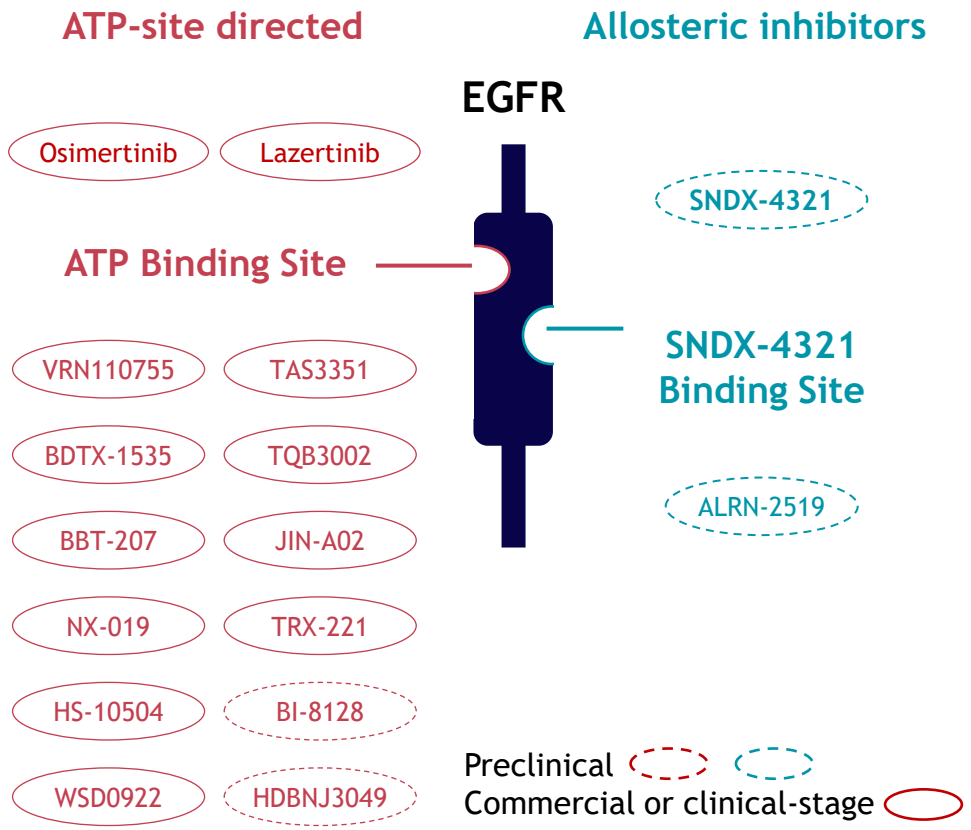
- Reduced benefit for patients with L858R, CNS metastases, or atypical activating mutations

4th gen investigational EGFRi

- Primarily target osimertinib on-target resistance (C797S), limiting benefit to a small population

Bispecific antibodies and ADCs

- Limited by significant toxicities and route of administration



SNDX-4321, a mutant-selective, allosteric EGFR inhibitor

- **Allosteric approach allows for:**
  - ✓ **'Double drugging'** of the target (may enhance efficacy and delay resistance)
  - ✓ **High selectivity** (supports combinability + tolerability)
- **First- and best-in-class potential**
- **Broad therapeutic window** expected
- **Oral** administration

Note: This is an illustrative figure that does not depict every approved or investigational therapy targeting EGFRm NSCLC.
EGFRi, EGFR inhibitor

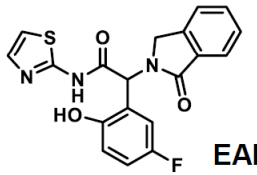
SNDX-4321, a mutant-selective, allosteric EGFR inhibitor for non-small cell lung cancer (NSCLC)

Michael J. Eck, MD, PhD
Professor, Department of Cancer Biology, Dana-Farber Cancer Institute
Professor, Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School

Disclosure statement: Dr. Eck is a paid consultant to Syndax and a co-developer/inventor of SNDX-4321 and related technology licensed to Syndax by the Dana-Farber Cancer Institute. Dr. Eck has received and may receive in the future income from licensing fees, milestone and royalty payments via Dana-Farber's royalty sharing policy.

SNDX-4321 builds on Dana-Farber Cancer Institute's pioneering work on allosteric EGFR inhibitors

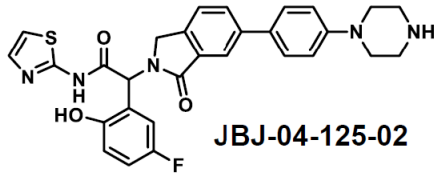
Overcoming EGFR(T790M) and EGFR(C797S) resistance with mutant-selective allosteric inhibitors



EAI045

Nature 2016, 534, 129

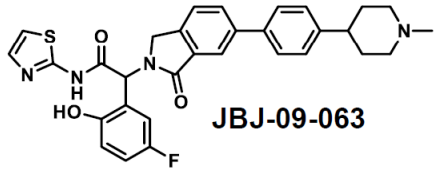
Single and Dual Targeting of Mutant EGFR with an Allosteric Inhibitor



JBJ-04-125-02

Cancer Disc 2019, 9, 926

An allosteric inhibitor against the therapy resistant mutant forms of EGFR in non-small cell lung cancer



JBJ-09-063

Nat Cancer. 2022, 3, 402

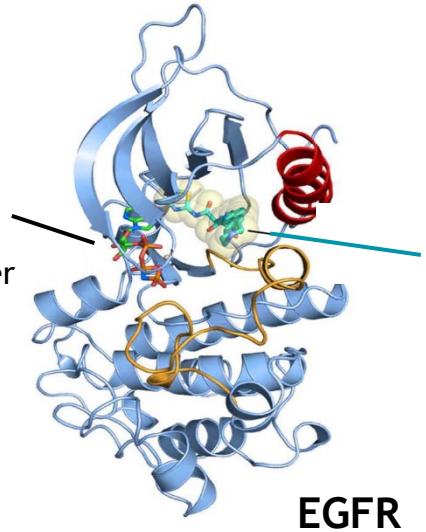
SNDX-4321 mutant-selective allosteric EGFR inhibitor

SNDX-4321:

- Binds at a pocket adjacent to the active (ATP) site that is only accessible with L858R and certain other EGFR mutations
- Structurally distinct from published compounds and addresses their key liabilities (prior compounds were potent and selective, but lacked suitable PK and chemical properties)
- Developed specifically for L858R with or without acquired resistance mutations

ATP site

(binding site for osimertinib + other EGFR inhibitors)

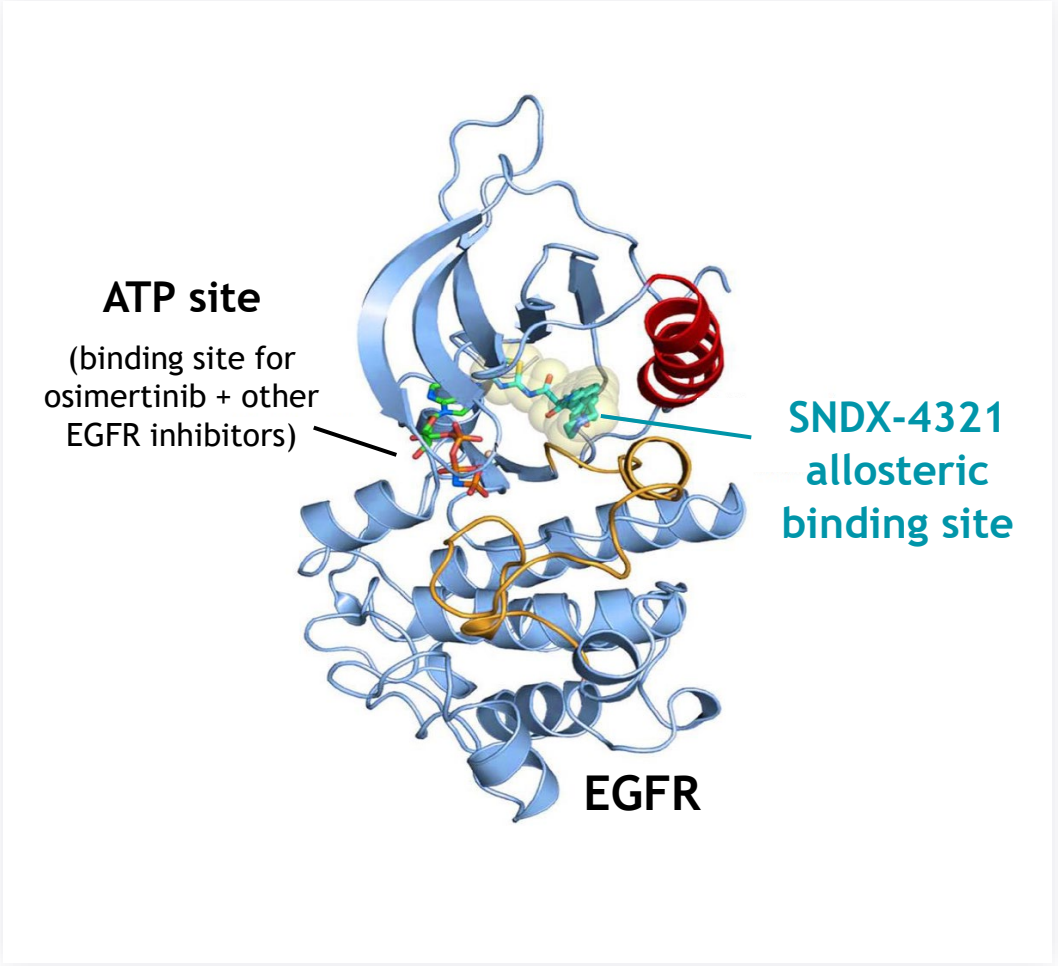


SNDX-4321 allosteric binding site

EGFR

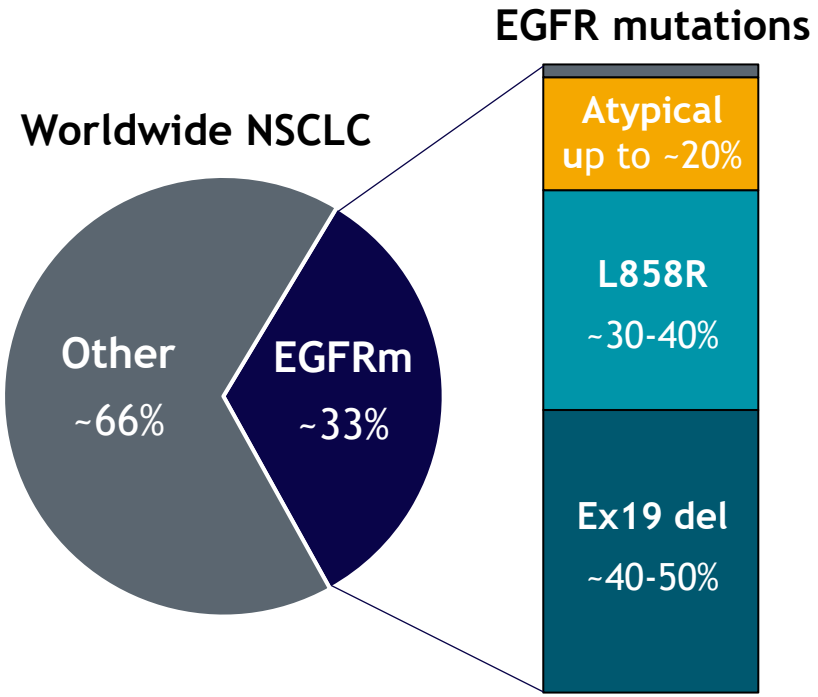
SNDX-4321 has the potential to advance the Tx paradigm for EGFRm NSCLC

- Excellent selectivity, oral bioavailability, and brain penetration
- Efficacy in multiple tumor models as a single-agent or in combination with osimertinib, and in intracranial model
- **Allosteric mechanism provides multiple benefits:**
  - ✓ **Ability to co-bind with ATP-site inhibitors enables 'double drugging',** which could enhance efficacy and delay resistance
  - ✓ **Improved selectivity** for mutant vs. wild-type EGFR may improve safety
  - ✓ **Single-agent activity could enable treatment of osimertinib-resistant cancers** and patients who progress after frontline therapy



Significant unmet needs remain in EGFRm NSCLC despite recent advances

- ~200,000 people are diagnosed with NSCLC annually in the U.S. alone[1]
- **Worldwide ~1/3 of NSCLC patients have EGFR mutations[2]**
  - The most common EGFR mutations are exon 19 deletions and L858R point mutations
- Osimertinib +/- chemotherapy is the most frequently used treatment for EGFR-mutated (EGFRm) NSCLC with an exon 19 deletion or L858R mutation



While three generations of EGFR inhibitors have transformed the SOC, significant unmet needs remain for patients with L858R mutations, CNS disease, atypical mutations, or resistance to osimertinib

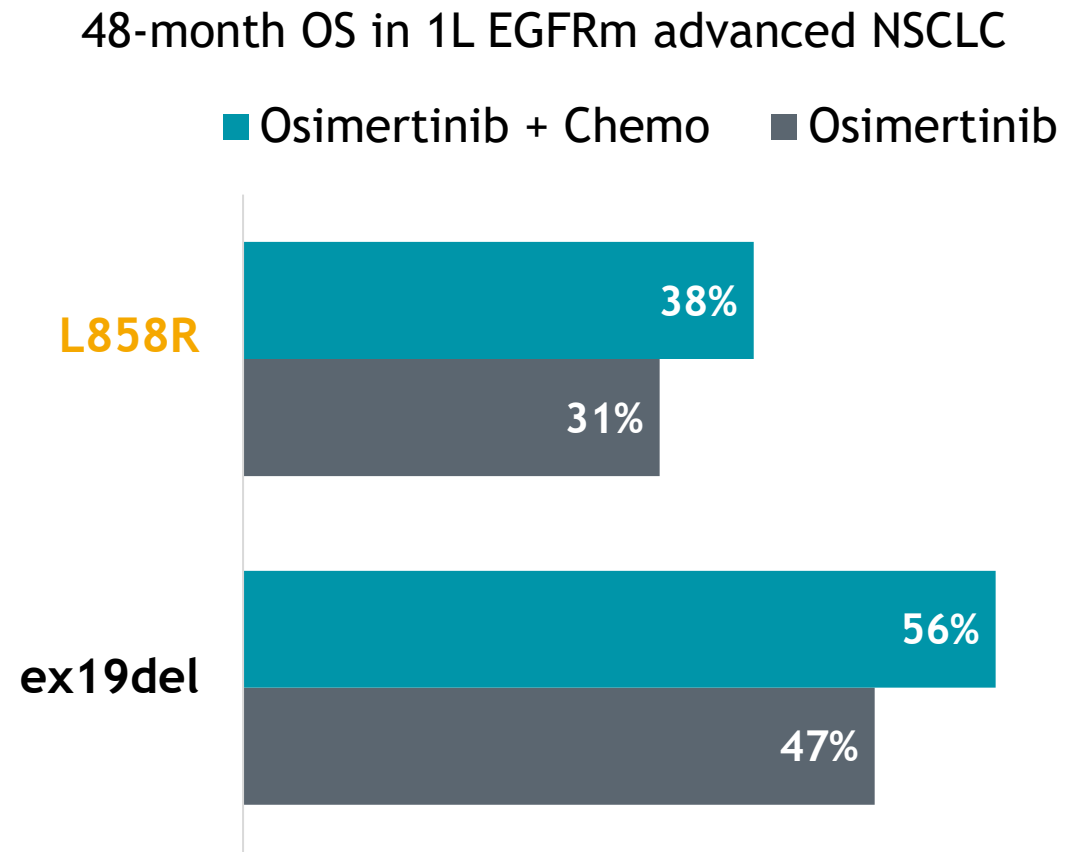
1. American Cancer Society. Key Statistics for Lung Cancer. Last revised January 13, 2026; 2. Li et al. Oncol Rep 2017; 3. Chen et al. J Med Chem 2018.

SNDX-4321 has the potential to address several areas of high unmet need in EGFRm NSCLC

	UNMET NEEDS	SNDX-4321 PROFILE
1	Patients with L858R have poorer outcomes than those with ex19 deletions	High activity as a single agent and in combination with osimertinib in L858R models
2	Patients with CNS metastases fare worse than those without	Highly CNS penetrant; demonstrated efficacy in intracranial model
3	Patients with atypical mutations have poorer outcomes than those with classical mutations	Preclinical data show activity against certain atypical mutants
4	Resistance emerges to osimertinib and all other 3rd gen EGFR inhibitors	Unique binding site - no single mutation confers resistance to both SNDX-4321 and osimertinib

1 Patients with L858R NSCLC have poorer outcomes than those with ex19del

FLAURA2 showed that even with the addition of chemotherapy, L858R patients continue to have shorter OS than ex19del patients

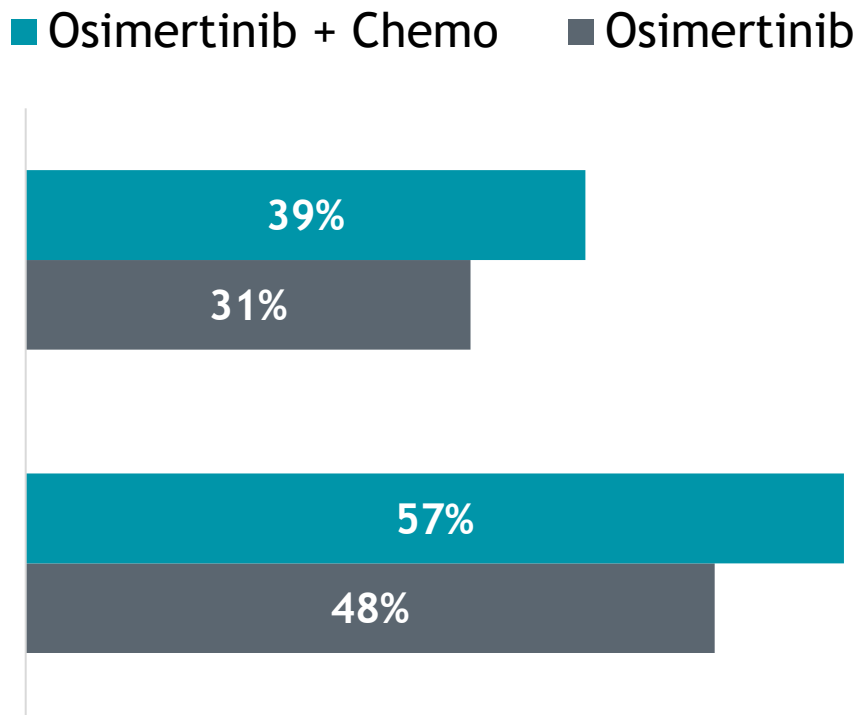


Jänne et al. NEJM 2026.

2 EGFRm NSCLC patients with CNS metastases fare worse than those without

FLAURA2 showed that even with the addition of chemotherapy, patients with CNS metastases continue to have shorter OS than those without

48-month OS in 1L EGFRm advanced NSCLC



~40% of patients have CNS metastases at time of initial diagnosis

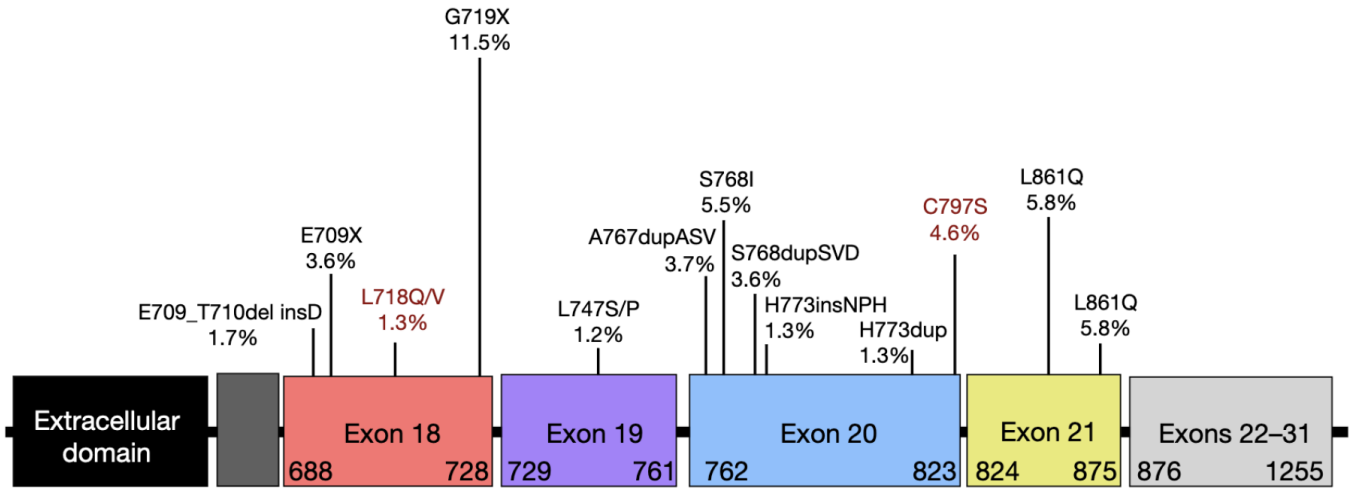
(Includes both L858R and ex19del patients)

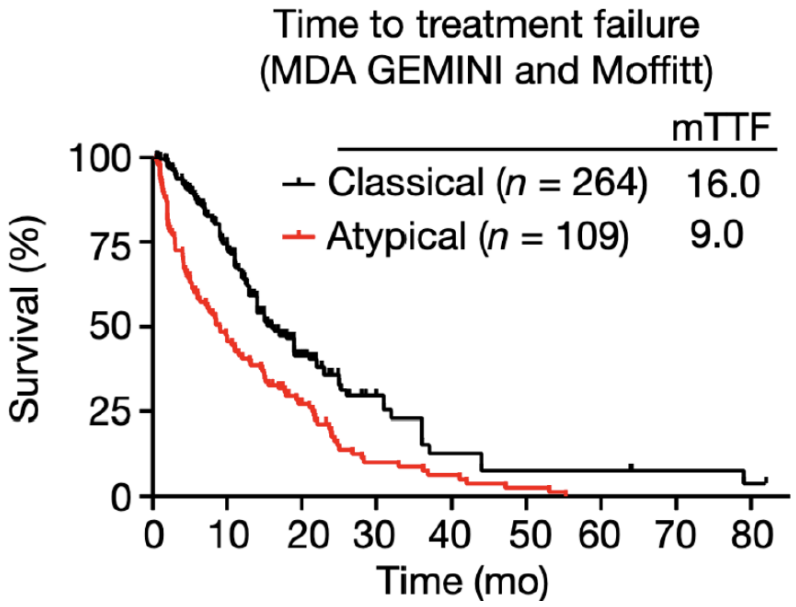
Jänne et al. NEJM 2026.

3 Patients with atypical activating EGFR mutations have shorter time to treatment failure as compared with classical mutations

Atypical variants account for up to ~20% of EGFRm NSCLC (excluding exon20 insertions); most common atypical mutations are G719X, S768I, and L861Q

Frequency of atypical EGFR mutations >1%





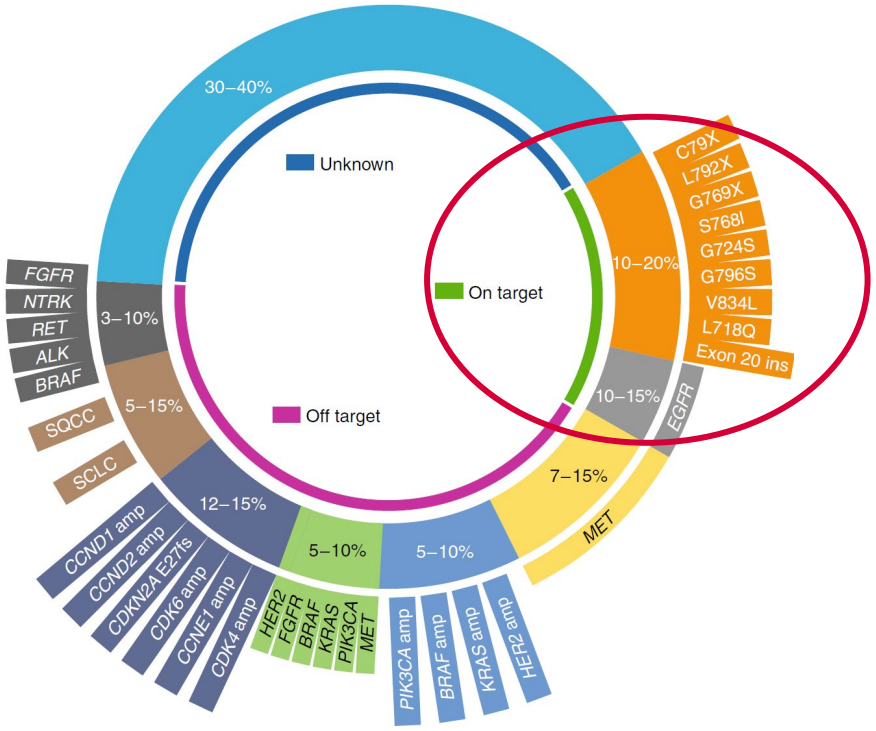
Syndax

Robichaux et al. Nature 2021.

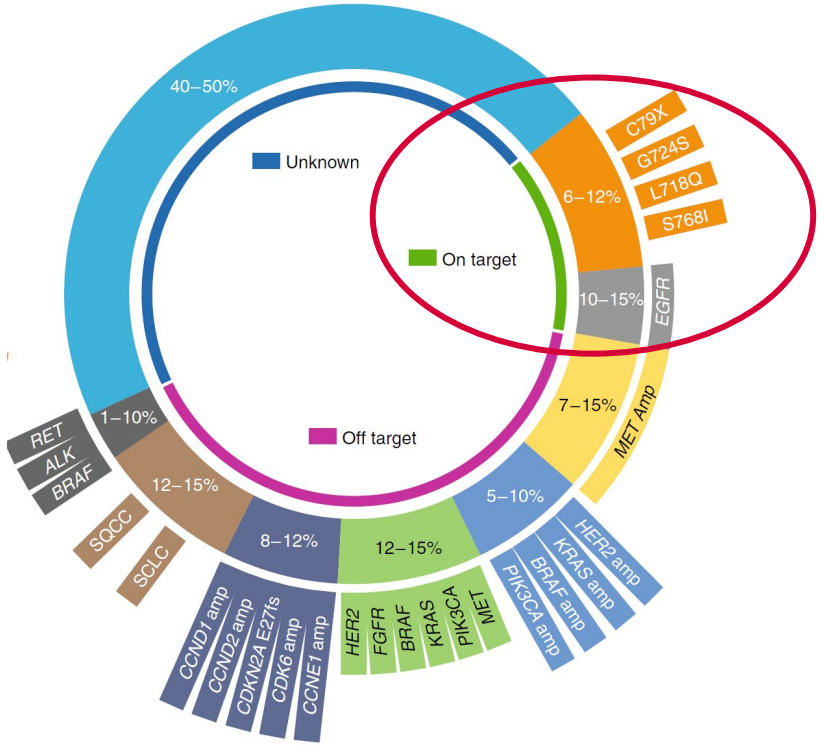
4 On-target mutations in EGFR confer resistance to osimertinib

C797S (most common), L718X, L792F, G796S and others

Up to ~20% after 2nd line Tx



Up to ~12% after 1st line Tx



EGFR mutation	*EGFR* amplification	*MET* amplification	Other acquired amplifications	Acquired mutations	Cell cycle gene alterations	Histological transformation	Fusion

Syndax

Passaro et al. Nat Cancer 2021.

SNDX-4321 is a mutant-selective and potent allosteric EGFR inhibitor

Preclinical studies show:

1. **Negligible activity against wild-type EGFR**
2. **Activity against L858R, with or without common resistance mutations to osimertinib** (e.g., C797S)
3. **Activity against certain atypical mutations** including L861Q, one of the most common atypical variants
4. No activity against exon 19 deletions or exon 20 insertions

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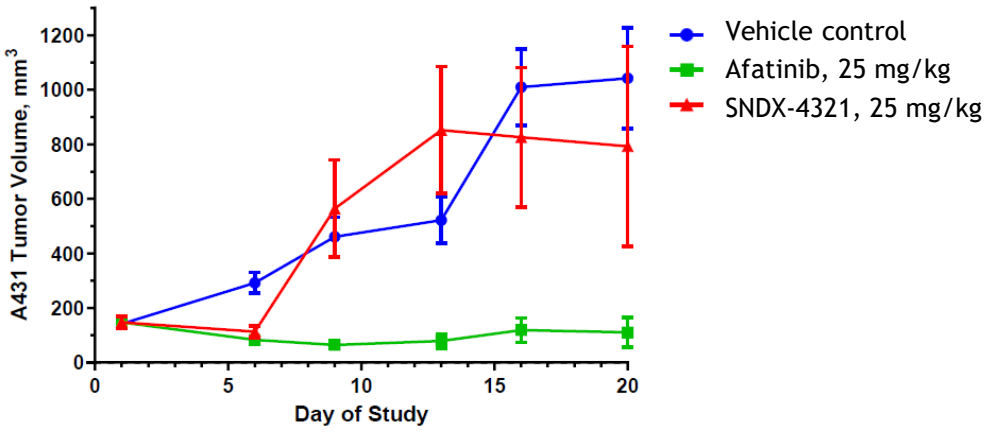
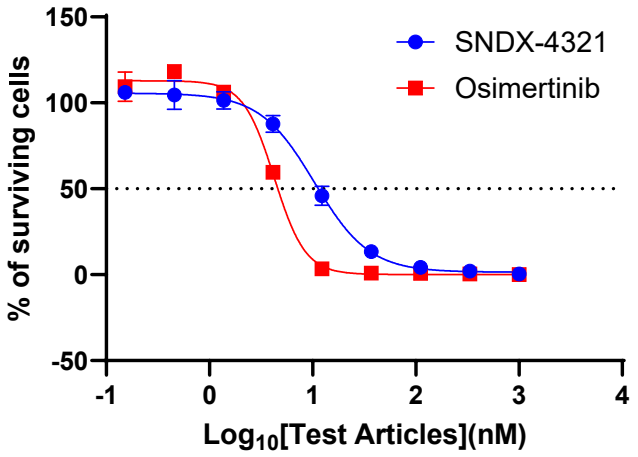
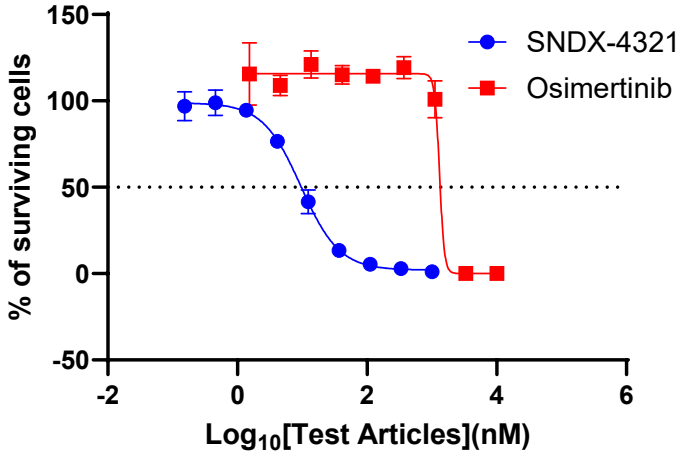
1. A431 (WT harboring tumor)



2. Ba/F3 EGFR L858R



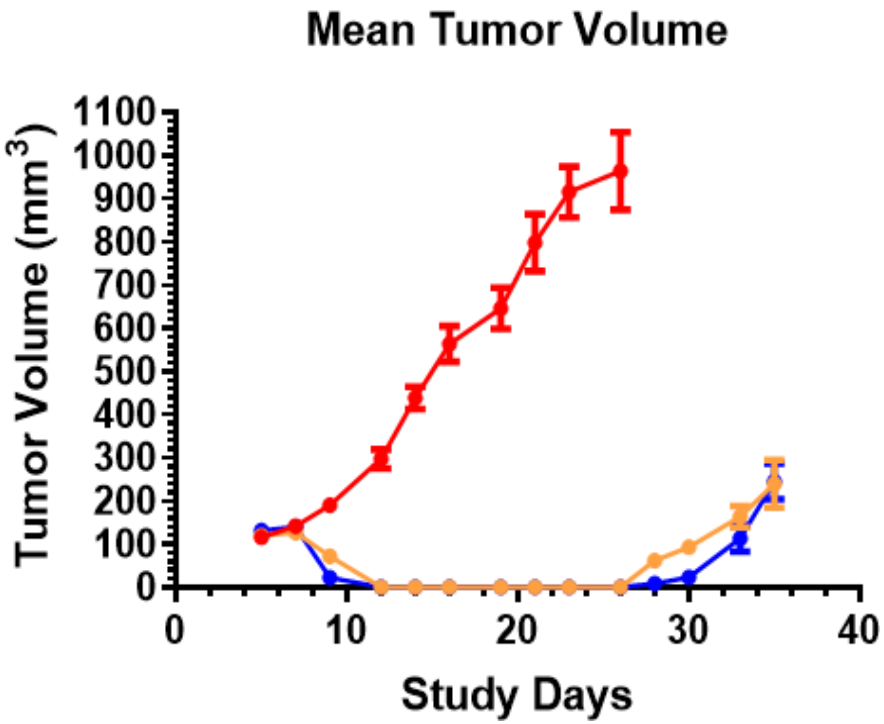
Ba/F3 EGFR L858R C797S



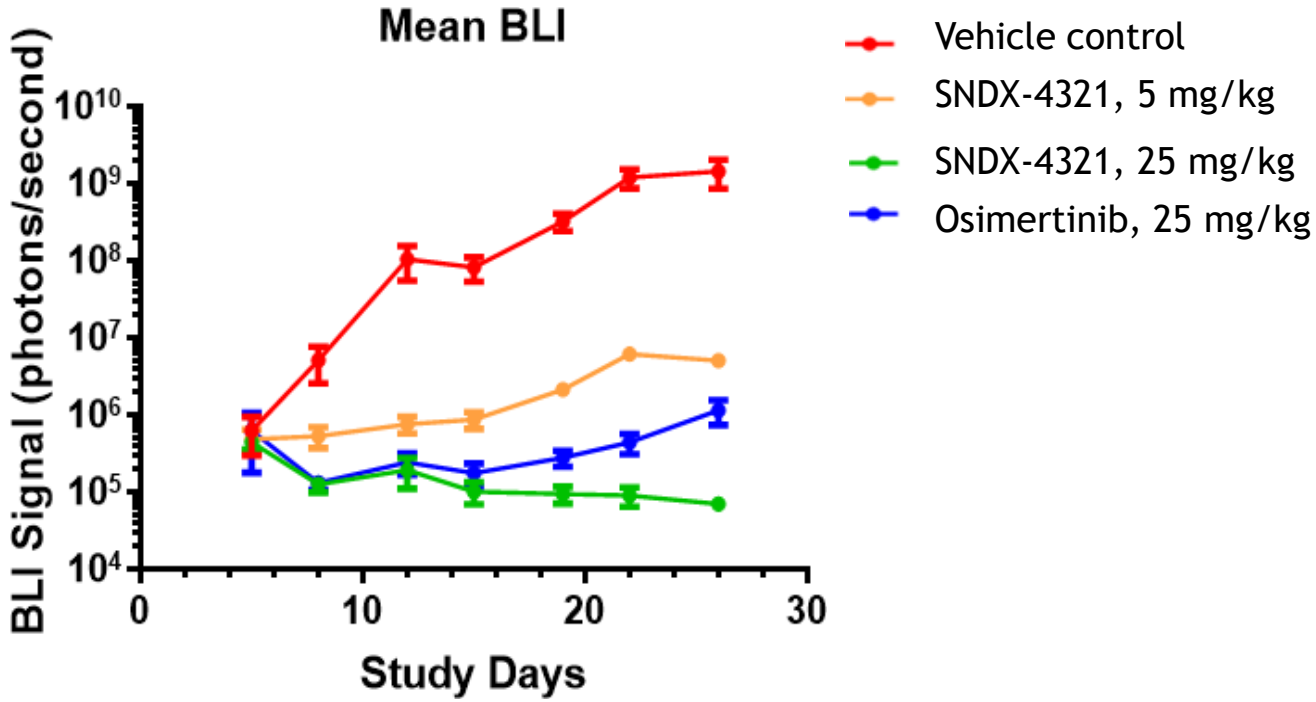
SNDX-4321 is effective in the CNS in intracranial xenograft model

H1975 (L858R/T790M) dual subcutaneous/intracranial model, 21 days dosing, QD

Subcutaneous tumor implant

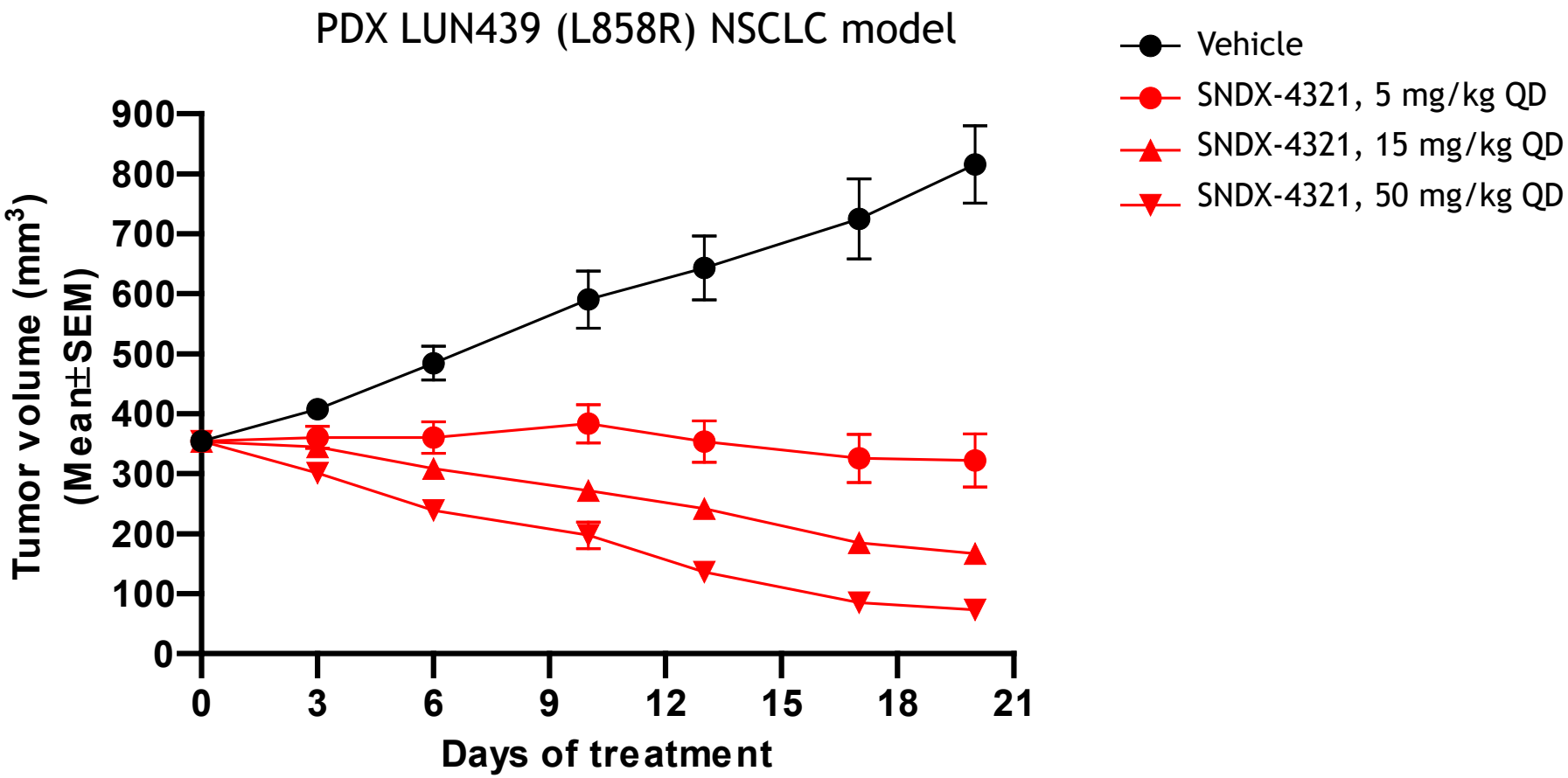


Intracranial tumor implants



SNDX-4321 is highly active as a single agent in L858R NSCLC PDX models

SNDX-4321 inhibits growth of L858R containing tumors in a dose-dependent fashion



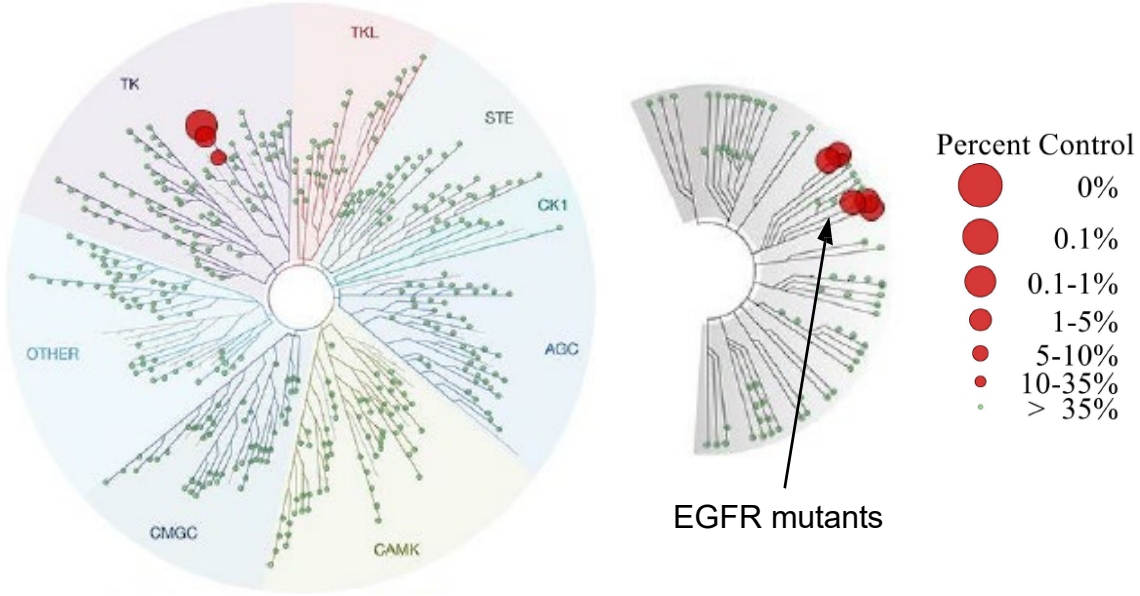
PDX, patient-derived xenograft

While SNDX-4321 is highly active as a single agent, the more significant opportunity is for combination therapy

Advantages of allosteric approach, especially for combination therapy:

- Bind outside ATP site, yielding excellent kinome-wide selectivity
- Better/different tox profile as compared with ATP-site inhibitors
- Distinct resistance mechanisms - retain activity against ATP-site mutations
- Potential for co-binding with ATP-site compound (e.g., 3rd gen EGFR inhibitor) to deliver enhanced efficacy and delay resistance

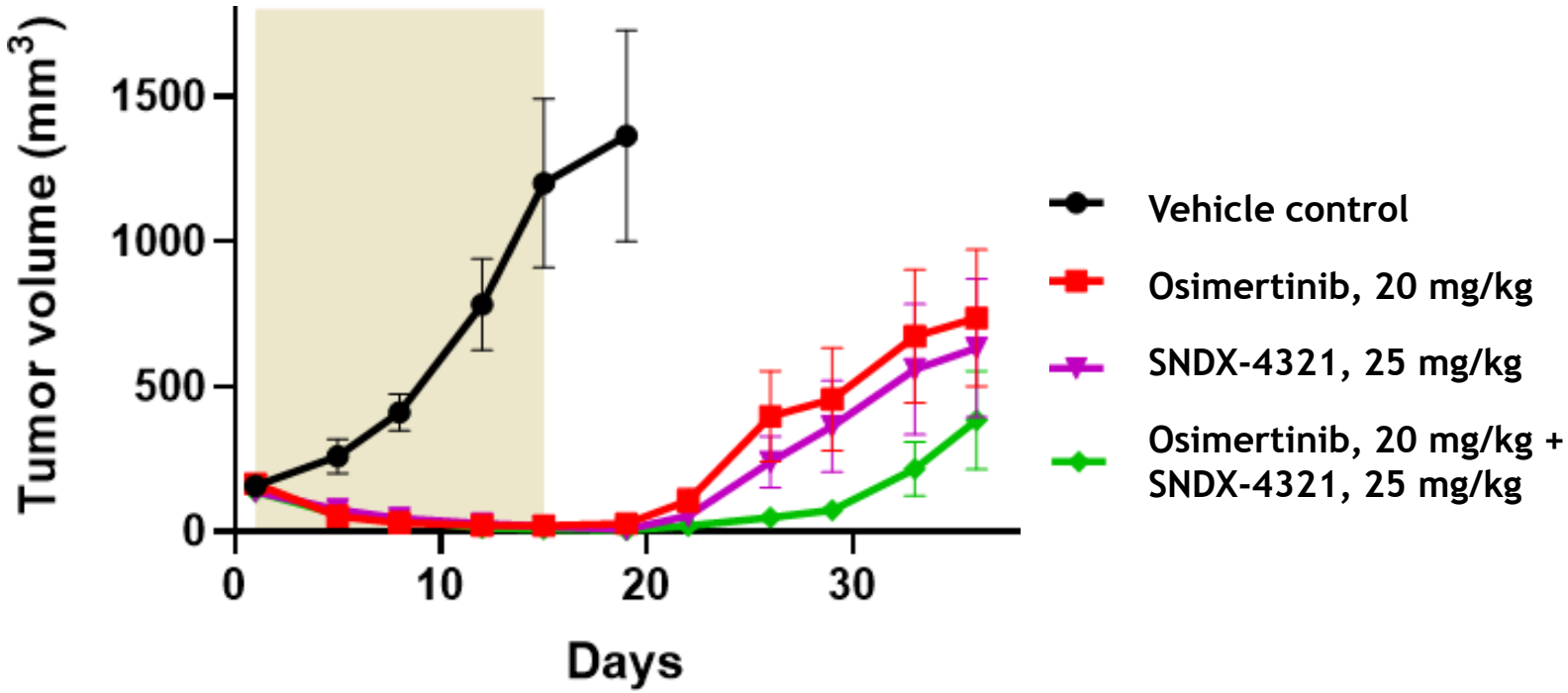
DiscoverX KinomeScan, SNDX-4321 @ 1µM



In vivo efficacy studies show benefit of combining SNDX-4321 with osimertinib

Delayed tumor regrowth and improved survival in H1975 (L858R/T790M) model

Dosed for 15 days, QD, then monitor for regrowth



- Combination of SNDX-4321 and osimertinib was well-tolerated
- Clear combination benefit in terms of delayed regrowth and survival

Summary – SNDX-4321

- **Novel, mutant-selective allosteric EGFR inhibitor that could address EGFRm NSCLC populations with significant unmet needs**, such as those with L858R mutations, CNS metastases, atypical mutations, or resistance to osimertinib

- **Highly active as a single agent and in combination with osimertinib** in L858R models with and without common resistance mutations

- **Allosteric approach makes SNDX-4321 an ideal combination partner** with osimertinib or other ATP-site directed EGFR inhibitors

  - Unique binding site – no single mutation confers resistance to both SNDX-4321 and osimertinib; not affected by ATP-site mutations that confer resistance to osimertinib

  - Lack of activity on wild-type EGFR and other kinases bode well for combinability

- **Highly CNS penetrant** with demonstrated efficacy in a brain metastasis model

- **Active against L861Q and other atypical mutations** in preclinical models

SNDX-4321 - Next steps

Nick Botwood, MBBS
Head of Research & Development and Chief Medical Officer

SNDX-4321 clinical development plan designed to efficiently generate safety and efficacy data that support allosteric approach in EGFRm NSCLC

Anticipated path forward

Demonstration of monotherapy activity anticipated in early 2028

Q&A - SNDX-4321

Michael A. Metzger
Chief Executive Officer and Director

Nick Botwood, MBBS
Head of R&D and Chief Medical Officer

Peter Ordentlich, PhD
Chief Scientific Officer and Founder

Michael J. Eck, MD, PhD
Professor, Department of Cancer Biology, Dana-Farber Cancer Institute; Professor, Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School

Closing remarks

Michael A. Metzger
Chief Executive Officer and Director

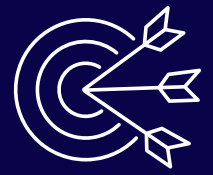
Syndax is delivering for patients and driving substantial long-term value

TRACK RECORD OF SUCCESS

Proven ability to translate scientific discoveries into novel therapies, with 3 FDA approvals between 2 drugs and thousands of patients treated

WORLD-CLASS R&D CAPABILITIES

Fully integrated biotech with deep expertise and strong partnerships with leading researchers



DEEP AND GROWING PIPELINE

Robust late- and early-stage pipeline with multiple near-term catalysts in 2H26 and blockbuster opportunities

SOLID FINANCIAL POSITION

Driving towards profitability with growing revenues; fully funded to advance late-stage trials and pipeline assets

Continued focus on driving revenue growth and pipeline progress, with multiple near-term catalysts and blockbuster opportunities

Anticipated milestones

Revuforj (revumenib) & SNDX-62122

Acute Leukemia

- Advance global enrollment in pivotal 1L trials of revumenib
- New 1L, maintenance, real-world, and R/R revumenib data in 2H26 + beyond
- Publish R/R NUP98r AML data in 4Q26

Myelofibrosis

- Initiate Ph 1/2 proof-of-principle trial with revumenib in 4Q26; initial data 2H27
- Submit IND and initiate Ph 1 SNDX-62122 trial in 2027

Niktimvo (axatilimab-csfr)

Chronic GVHD

- Ph 2 axatilimab + ruxolitinib data in 4Q26
- Ph 3 axatilimab + corticosteroid data early 2028

Idiopathic pulmonary fibrosis

- Ph 2 MAXPIRe data in 4Q26

SNDX-4321

EGFRm NSCLC

- Submit IND by YE 2026
- Initiate Ph 1 trial in 2027; initial data early 2028

2
Ph 2 readouts in 4Q26

Multiple
revumenib readouts in acute leukemia in 2H26 + beyond

4
assets in the clinic in 2027