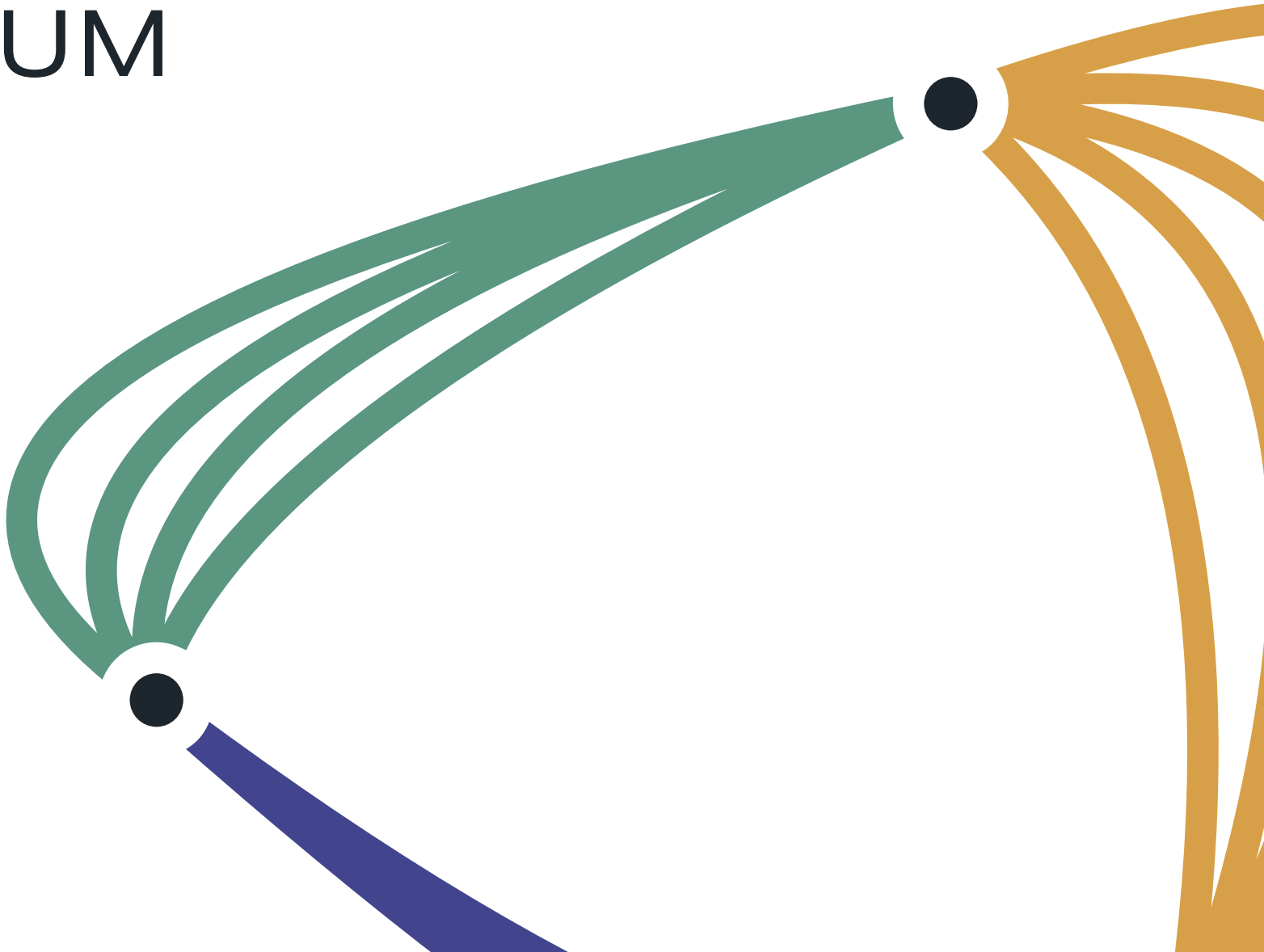
CONTINEUM
therapeutics

Corporate Presentation

November 2024



Legal Disclaimer

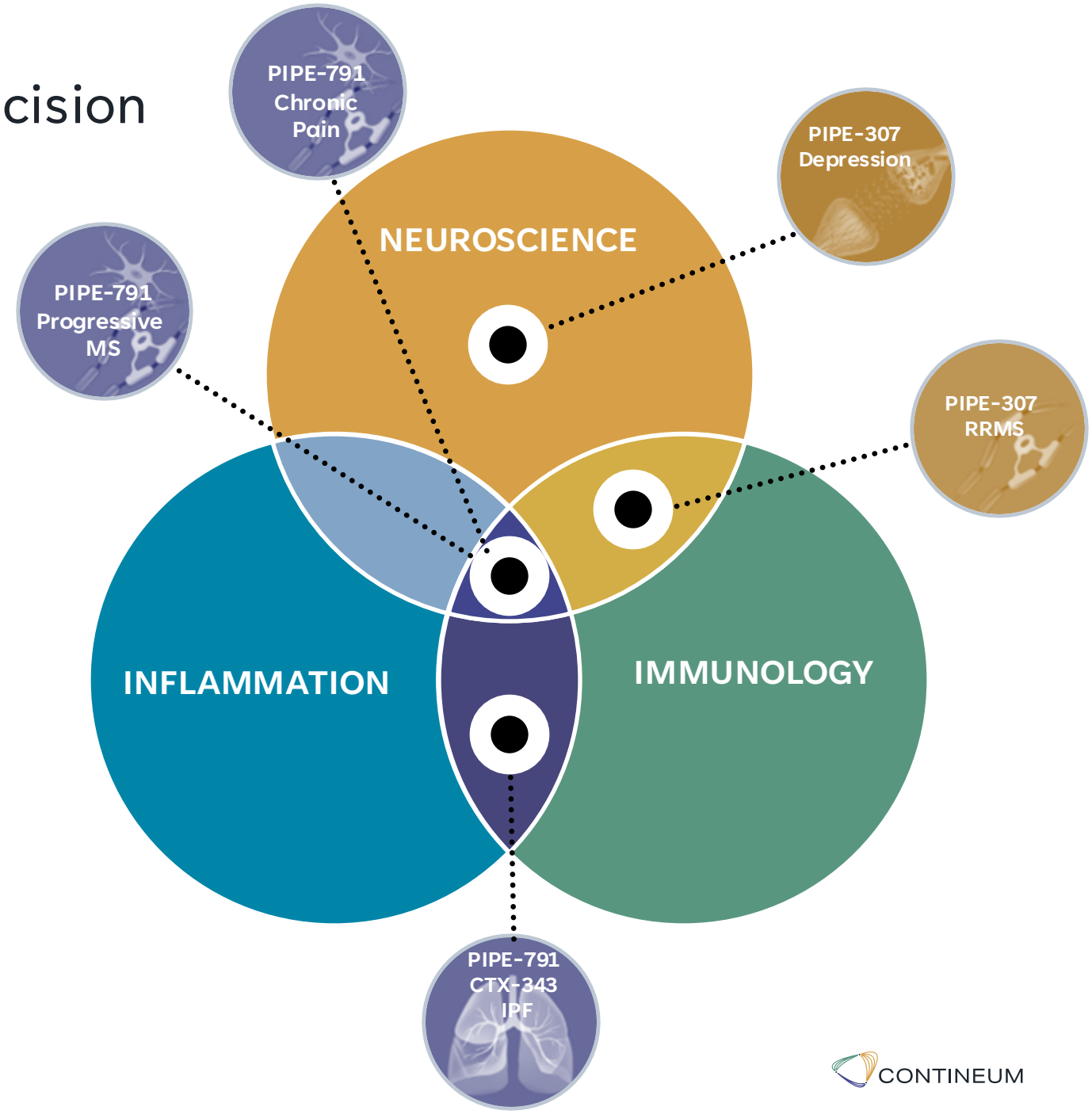
This presentation by Contineum Therapeutics, Inc. ("Contineum", "We" or "Our) contains forward-looking statements. All statements other than statements of historical facts contained in this presentation, including without limitation statements regarding our future results of operations and financial position, future revenue, timing, progress and expected results of our clinical trials and our product development efforts, business strategy, prospects, research and development costs, timing and likelihood of success, the size of the market opportunities, as well as plans and objectives of management for future operations, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that are in some cases beyond our control and may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. The words "anticipate," "believe," contemplate," "continue" "could," "estimate," "expect," "intend," "may," "might," "plan," "potential" "predict," "project," "should," "target," "will" or "would" or the negative of these terms or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. The forward-looking statements in this presentation are only predictions and represent our views as of the date of this presentation. Although we believe the expectations reflected in such forward-looking statements are reasonable, we cannot guarantee that the future results, advancements, discoveries, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. The forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, but not limited to: we are heavily dependent on the success of PIPE-791, our lead product candidate, and PIPE-307, both of which are in the early stages of clinical development, and neither of these drug candidates may progress through clinical development or receive regulatory approval, or, even if approved, may not be successfully commercialized; the results of earlier preclinical studies and clinical trials, including those conducted by third parties, may not be predictive of future results; the regulatory approval processes of the FDA and comparable foreign regulatory authorities are unpredictable, lengthy, and time-consuming and we or our partners may not obtain regulatory approval for our drug candidates; we may not be successful in our efforts to identify and develop additional drug candidates or identify additional indications for our drug candidates; we have incurred significant operating expenses since inception and we expect that our operating expenses will continue to significantly increase for the foreseeable future; we have a limited operating history, which may make it difficult to evaluate the prospects for our future viability; we will require significant additional capital to complete the development and commercialization of our drug candidates; our license agreement with an affiliate of Johnson & Johnson may not result in the successful development of PIPE-307; we may be unable to obtain, maintain and enforce intellectual property protection for our technology and drug candidates; we currently rely on third-party contract manufacturing organizations for the production of the raw materials and clinical supplies for our drug candidates; we rely on third parties to conduct our ongoing clinical trials of PIPE-791 and PIPE-307 and expect to continue to rely on third parties to conduct our future clinical trials; we face significant competition from biotechnology, pharmaceutical, and medical device companies; our drug candidates, even if approved, may fail to achieve market acceptance by physicians, patients, third-party payors, or others in the medical community necessary for commercial success; we expect to rely on third parties for sales, marketing and distribution of any drug candidates that receive regulatory approval; and we may seek to grow our business through in-licensing transactions or otherwise by acquiring drug candidates or complementary products, technologies or businesses. We discuss these and other risks and uncertainties in greater detail in the sections entitled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our periodic reports, including our most recent Form 10-Q for the period ended September 30, 2024, filed with the SEC on November 6, 2024 and other filings that we make with the SEC from time to time. Accordingly, readers should not rely upon forward-looking statements as predictions of future events. Except as required by applicable law, we undertake no obligation to update publicly or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements. We operate in a very competitive and rapidly changing environment. New risks emerge from time to time, and it is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances described in this presentation may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements contained in this presentation.

Market & Industry Data

This presentation contains estimates, projections and other information concerning our industry, our business and the markets for our product candidates, including data regarding the estimated size of such markets and the incidence of certain medical conditions. We obtained the industry, market and similar data set from our internal estimates and research, including surveys and studies we have sponsored and/or conducted, and from published studies from third parties, including governmental agencies. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

Pioneering the NI&I Field with Precision

- Sizeable markets in IPF, depression, MS and chronic pain with high unmet medical need
- Multiple shots on goal for both clinical-stage assets
- Valuable J&J partnership on PIPE-307 focused on RRMS and depression
- Robust patent estate protects pipeline through 2040 and beyond
- Recently completed IPO; strong proforma cash balance of $213.9M as of Q3 2024



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Balanced Development Pipeline and Targeted Discovery Platform

Drug Candidate	Mechanism	Program	Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Worldwide Rights
PIPE-791	LPA1R Antagonist	IPF*						CONTINEUM therapeutics
PIPE-791	LPA1R Antagonist	PPMS/SPMS*						
PIPE-791	LPA1R Antagonist	Pain**						CONTINEUM therapeutics
CTX-343	LPA1R Antagonist	Peripheral						CONTINEUM therapeutics
PIPE-307	M1R Antagonist	RRMS						Johnson&Johnson
PIPE-307	M1R Antagonist	Depression						Johnson&Johnson

* Single Phase 1b PET clinical trial of PIPE-791 for the potential treatment of IPF and Progressive MS.
** Exploratory Phase 1b, randomized, double-blind, placebo-controlled, crossover, multi-center study is expected to begin in the first quarter of 2025.

LPA1R Antagonism and PIPE-791 in Idiopathic Pulmonary Fibrosis

LPA1R: An Important Target for Pulmonary Fibrosis

Rationale & Unmet Need

- IPF is a **rare, irreversible, progressive interstitial lung disease** with unknown etiology
- Prognosis for **overall survival is worse than many forms of cancer**
- **Current therapies have limitations** related to side effects, tolerability, moderate efficacy and multi-daily dose regimens
- Levels of LPA are elevated in the lungs of IPF patients
- **Clinical validation** confirmed in IPF with LPA1R antagonist BMS-986278

~130K
Patients with IPF in the US

~3M
Patients with IPF Worldwide

~60-80%
Patients Dying From Respiratory Failure[1]

2
FDA-Approved Therapies for IPF

0
Approved Drugs Halt Progression of IPF

~$4B
Esbriet and Ofev Combined Sales in 2022[2]

[1] Within five years of diagnosis. Clin Respir J. 2022;16:84–96
[2] Boehringer Ingelheim press release March 29, 2023; Roche Holdings, Inc. Annual Report 2022

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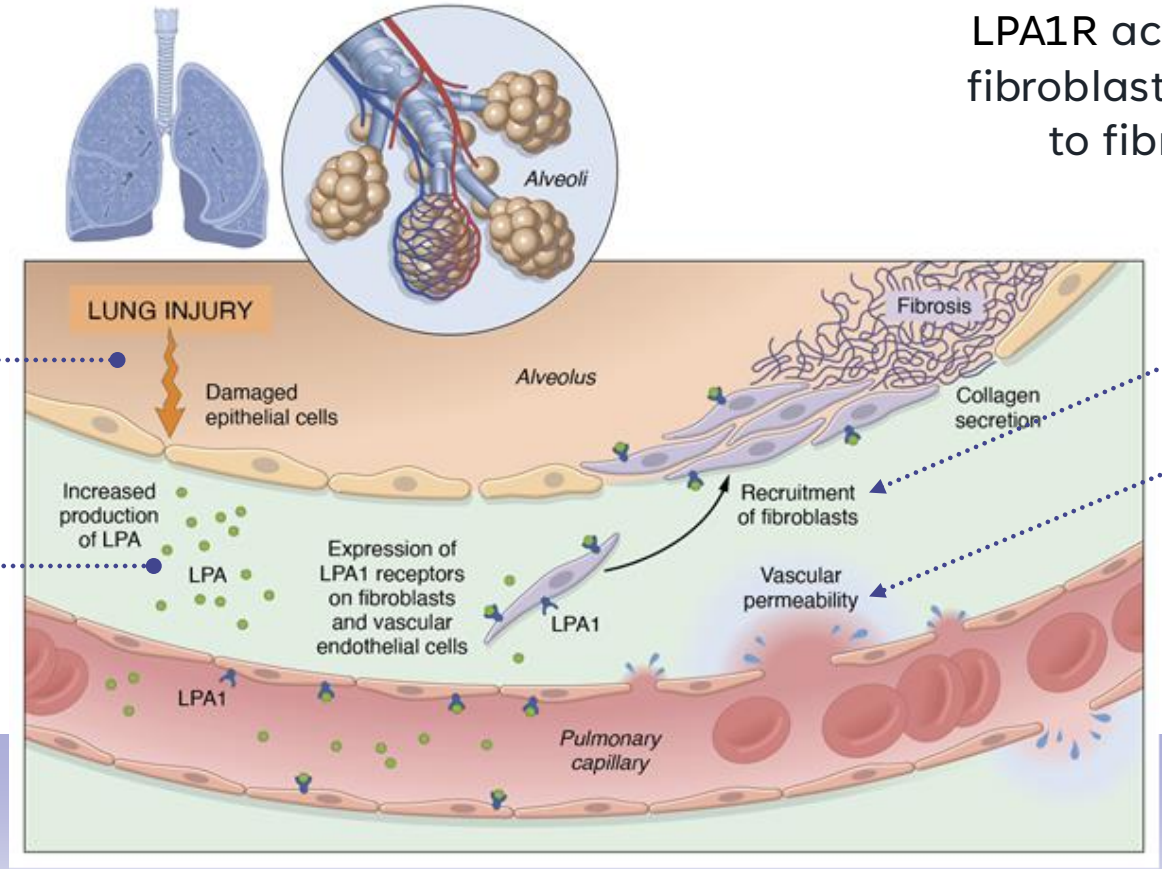
The Role of LPA1R in the Initiation and Progression of Pulmonary Fibrosis

LPA production and LPA1R expression increases following injury

LPA is elevated in the broncho-alveolar washings of IPF patients



LPA1R activation promotes recruitment of fibroblasts and collagen secretion leading to fibrosis and restrictive lung disease

LPA-induced endothelial barrier breakdown promotes further inflammation

Blocking the LPA1R inhibits several steps in the fibrosis pathway

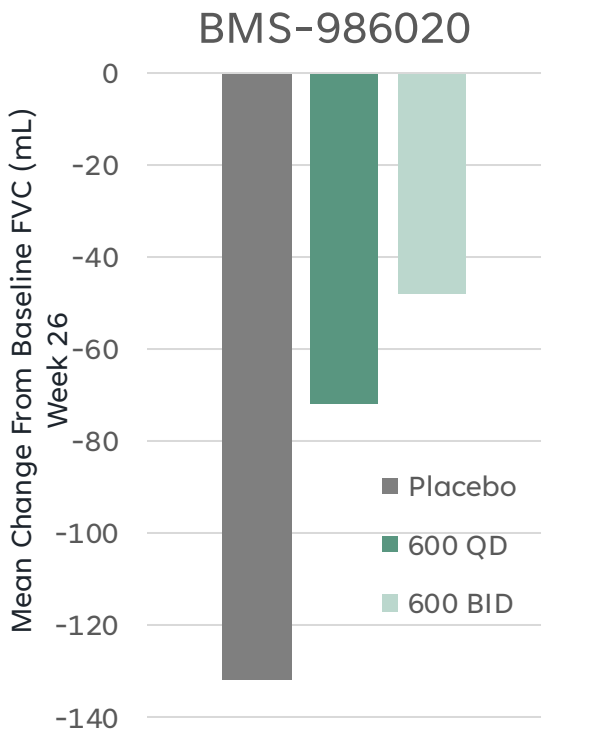
LPA1R Is a Clinically Validated Target in IPF

- Two LPA1R antagonists (BMS-986020 and BMS-986278) were shown to slow the rate of FVC decline in 26-week, placebo controlled, studies in patients with IPF
- Patients on BMS-986020 developed hepatobiliary toxicity that was later shown to be related to an off-target activity
- BMS-986278 was developed to minimize this off-target toxicity
- BMS-986278 60 mg BID required for efficacy
  → **opportunity for an improved compound, given once daily**

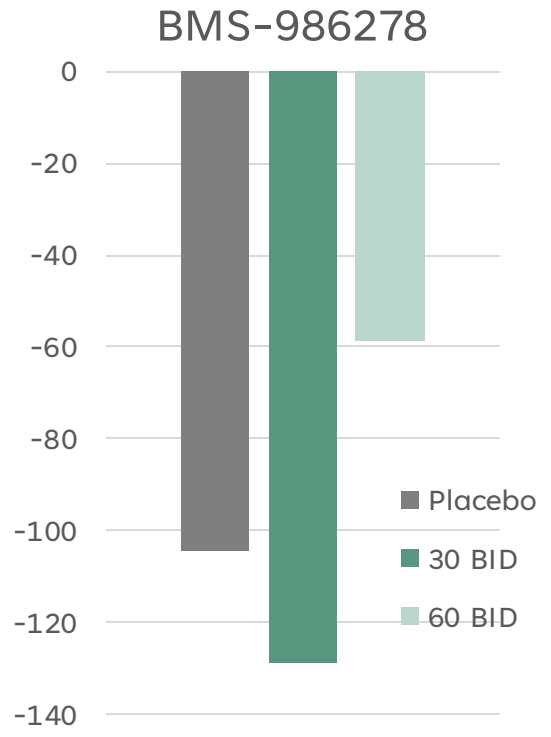
BMS Phase 2 Pulmonary Fibrosis PoC Studies*

Compound	Indication	# of Patients	Study Length (weeks)
BMS-986020	IPF	143	26
BMS-986278	IPF	276	26
BMS-986278	PPF	123	26

*Based on publicly available data (clinicaltrials.gov)



Adapted from Palmer et al., Chest, 2018



Adapted from Corte et al., ATS, 2023

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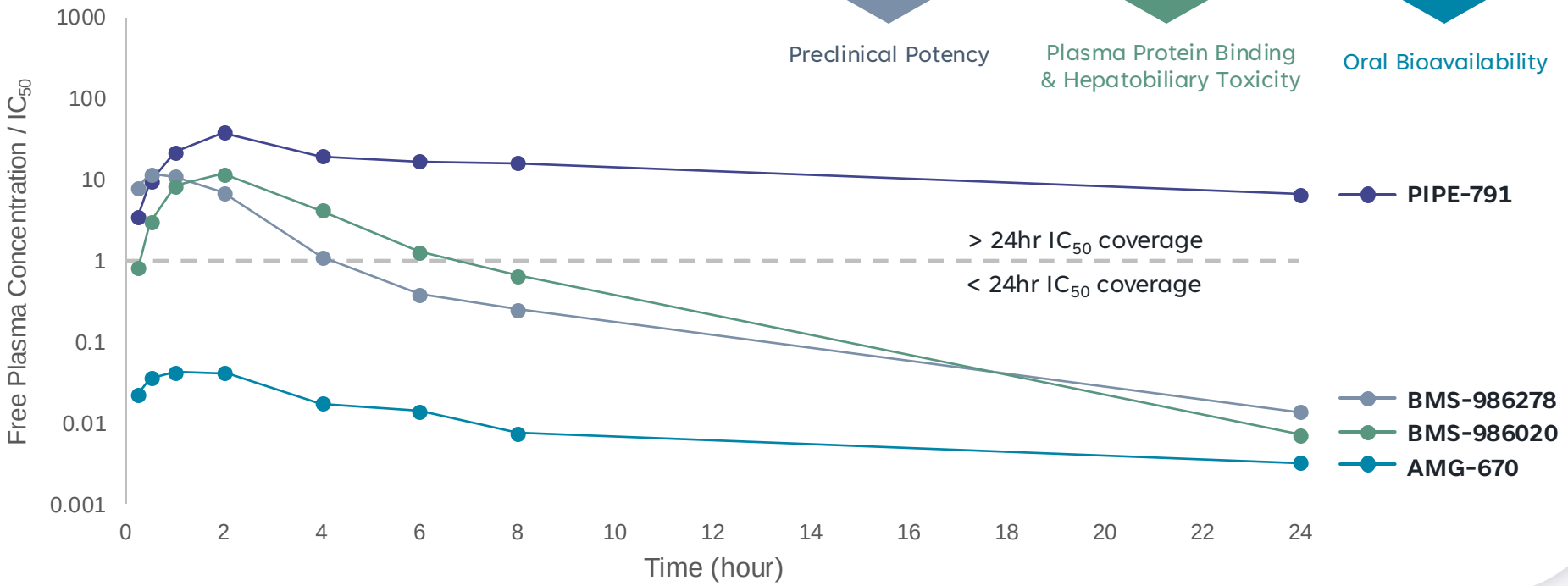
PIPE-791 Versus Other LPA1R Antagonists in Development

	PIPE-791	BMS-986278	BMS-986020	AMG-670
hLPA (Ca^{2+} flux) IC_{50}	9.9 nM	80 nM	2.0 nM	9.2 nM
Plasma protein binding, % Free (rodent)	5.7	15	0.2	0.07
Oral bioavailability %F	78%	138%	64%	4.7%
Stage of development	Phase 1	Phase 3	Phase 2 (terminated)	Phase 2

Preclinical Potency

Plasma Protein Binding & Hepatobiliary Toxicity

Oral Bioavailability



PIPE-791 has demonstrated high oral bioavailability and low plasma protein binding, which we believe will lead to increased PIPE-791 receptor exposure with low dosing

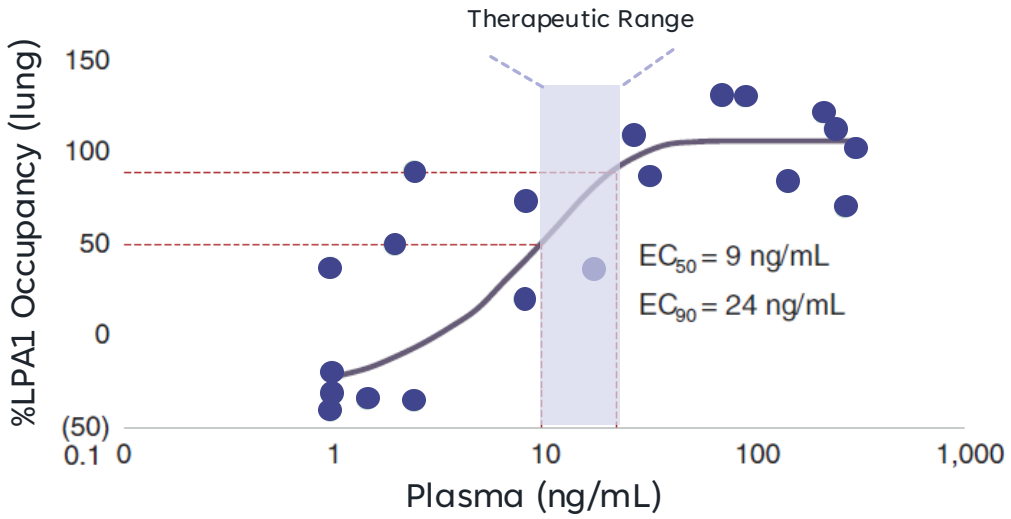
PIPE-791 – *In vitro* and *In vivo* pharmacology

Target Coverage for Antifibrotic Effect

Summary of *In Vitro* Pharmacology

Properties	*In Vitro* Profile
Radioligand binding Ki (nM)	0.752
K_{off} (min^{-1})	0.00133
LPA1 Ca^{2+} mobilization (nM, 24h)	9.9

In Vivo Lung LPA1R Occupancy



- PIPE-791 is a selective LPA1R antagonist with *in vitro* long receptor off rate
- PIPE-791 demonstrated dose-dependent lung LPA1R occupancy with once daily oral dosing
- Therapeutic concentration range - EC_{50} of 9 ng/mL → EC_{90} = 24 ng/mL
- Clinically translatable model to establish target-occupancy relationship to de-risk dose selection

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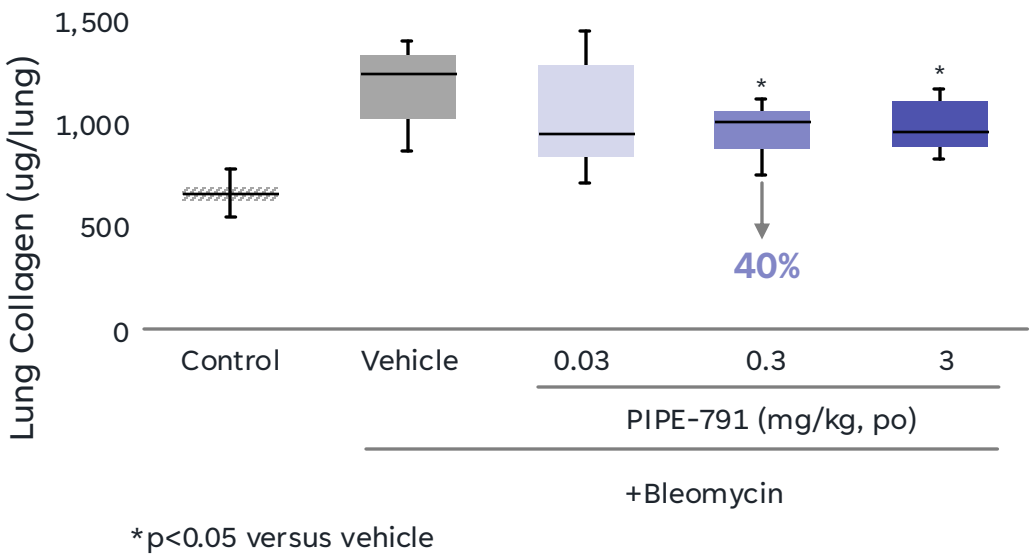
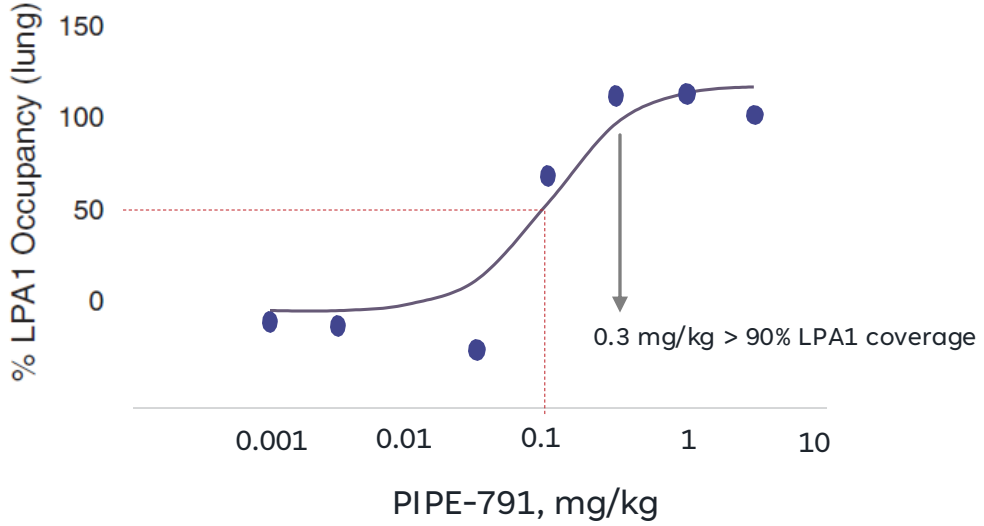
PIPE-791 – Bleomycin-induced *In Vivo* Lung Fibrosis Model

Total Pulmonary Collagen



LPA1R Occupancy Effect Relationship



- PIPE-791 treatment reduced injury-induced lung collagen, increased survival, and normalized body weights
- Maximal effect observed using 0.3 mg/kg with once daily dosing, representing high LPA1 lung occupancy

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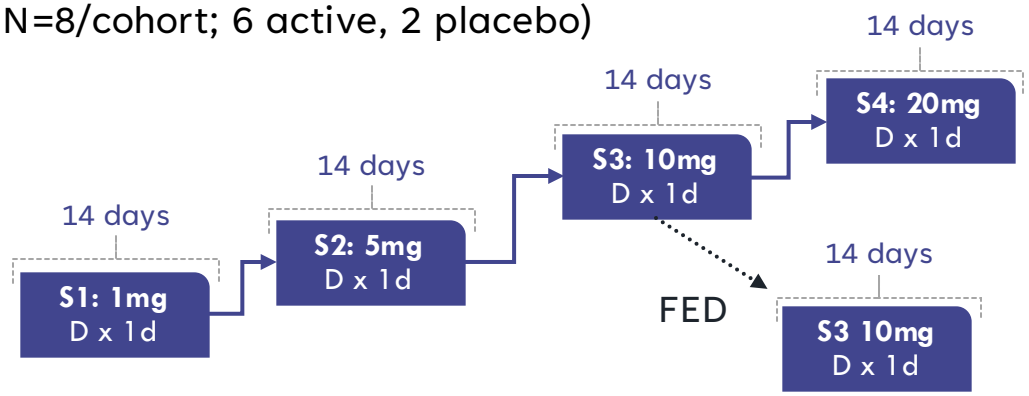
Phase 1 Healthy Volunteer Study Schema and Adverse Events

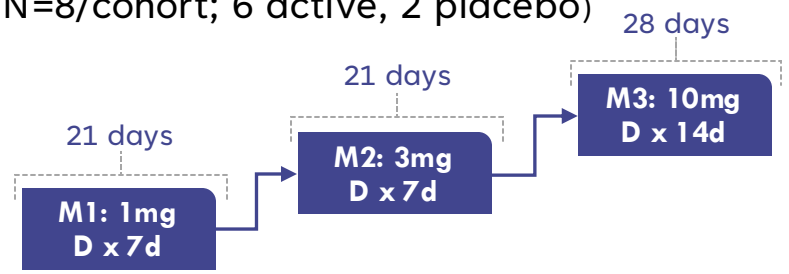
Single ascending dose cohorts

(N=8/cohort; 6 active, 2 placebo)



Multiple ascending dose cohorts

(N=8/cohort; 6 active, 2 placebo)



- SAD4 PK >> predicted pharmacologically active range
- MAD3 extended to 14d to confirm steady-state

Treatment emergent AEs reported in ≥ 2 subjects

AE (# of subjects)	Placebo	SAD1	SAD2	SAD3	SAD4	MAD1	MAD2	MAD3
Abdominal pain		1	1					
Nasal congestion				1				1
URI			1					2
Rhinitis				1				1
Headache	1		1		3	1		
Back pain				1	2			

- No dose-limiting AEs or toxicity
- No notable changes/pattern in clinical laboratory, ECG/telemetry, or vital signs
- Database locked: Feb 2024

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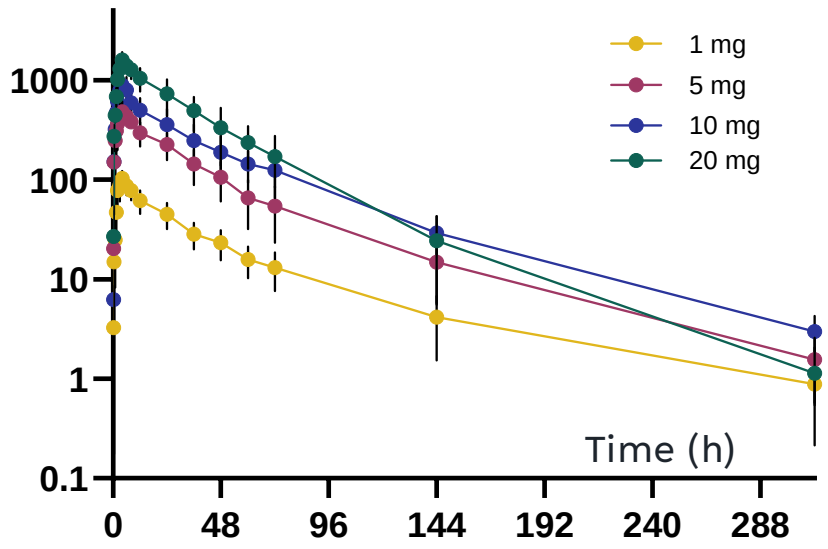
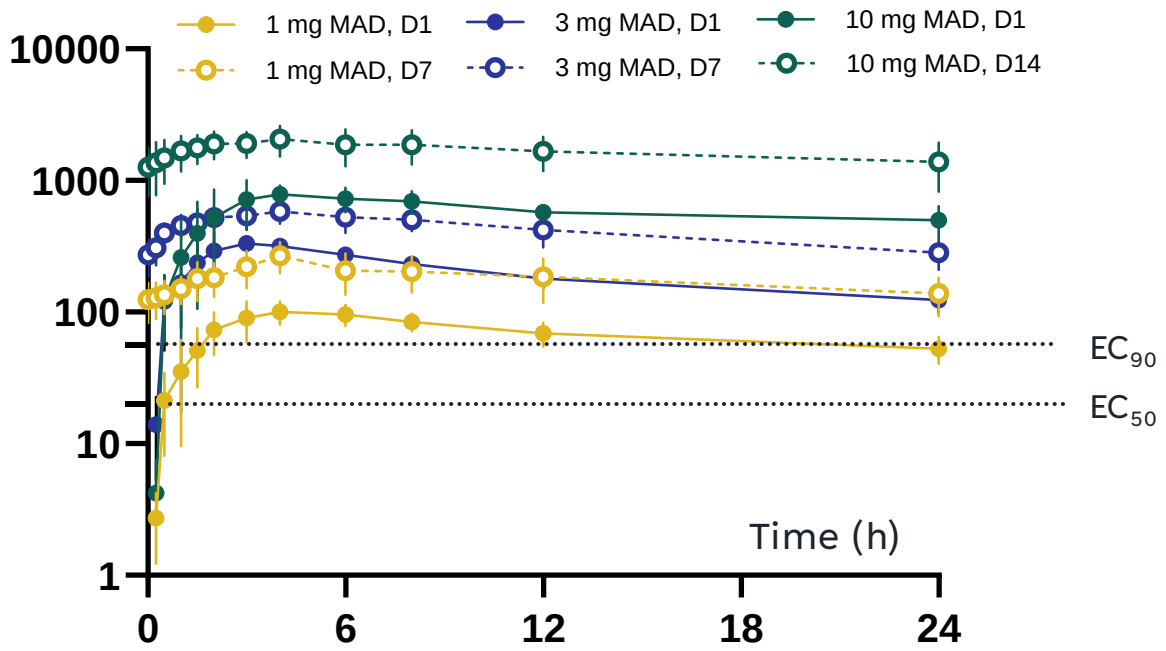
PIPE-791 Phase 1 SAD and MAD Cohort PK Profiles

SAD: Mean plasma concentration (ng/ml) through Day 14 [semi-log]



- SAD PK linear and dose-proportional
- $T_{1/2}$ SAD 1-4 cohorts: 55, 45, 42, 31 hours
- FED state: No overall change in AUC24; slightly delayed T_{max} and reduced C_{max}

MAD: Mean 24-hour plasma concentration (ng/ml) through Day 7 (MAD1 and MAD2) and Day 14 MAD3 [semi-log]



- EC_{50} and EC_{90} receptor occupancy (based on preclinical studies) reached at 24-hour trough after single 1 mg dose

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PIPE-791: Clinical Development and PoC Plans in Pulmonary Fibrosis

2023-2024

Phase 1 SAD/MAD/FED Healthy Volunteer Trial
Randomized, double-blind, placebo-controlled
(n = 56)

STUDY OBJECTIVES:

Primary:
Safety and tolerability

Secondary:
Pharmacokinetics

2024

Phase 1b
Lung PET Study (n = 6-8)
(MHRA authorized)

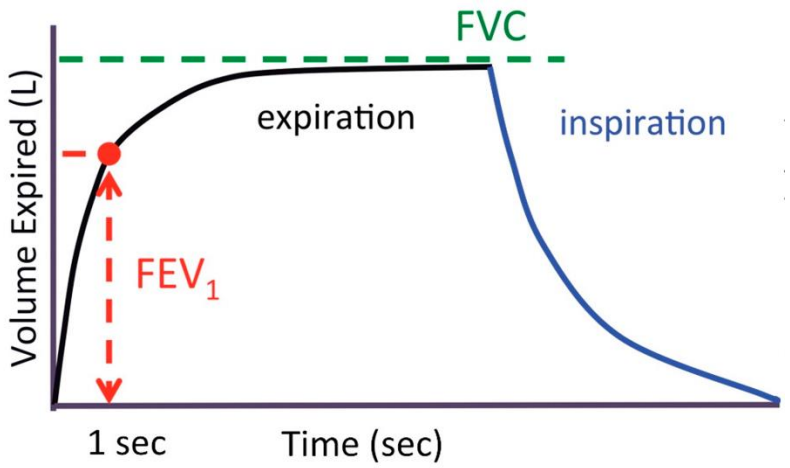
STUDY OBJECTIVES:

Primary:
PK/RO relationship

2025

Phase 2 DB-RCT Dose-Ranging
Idiopathic pulmonary fibrosis
Primary: Change in FVC from Baseline to 6m
(pending FDA IND authorization)

Spirometry: Forced vital capacity



*GLP tox NOAEL 1000 mg/kg/day; chronic GLP tox ongoing

*Visual representation of FVC test

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LPA1R Antagonism and PIPE-791 in Progressive MS

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Progressive MS Is an Area of Significant Unmet Need

Rationale & Unmet Need

- MS is a chronic, immune-mediated disease of the CNS characterized by **neuroinflammation and demyelination** leading to continued **worsening of clinical disability**
- Within the CNS, the LPA1R is enriched in glial cells including microglia and oligodendrocytes
- LPA is elevated in the CSF of patients with MS
- PIPE-791 potentially promotes remyelination and reduces neuroinflammation
- Very limited treatment options for patients with Progressive MS

~2.8M

Patients with MS Globally

>750K

Patients with Progressive MS Globally

~15%

Newly Diagnosed Patients Have PPMS[1]

~50-70%

Patients with RRMS Progress to SPMS[2]

[1]As of 2020 [2]within 10-15 years

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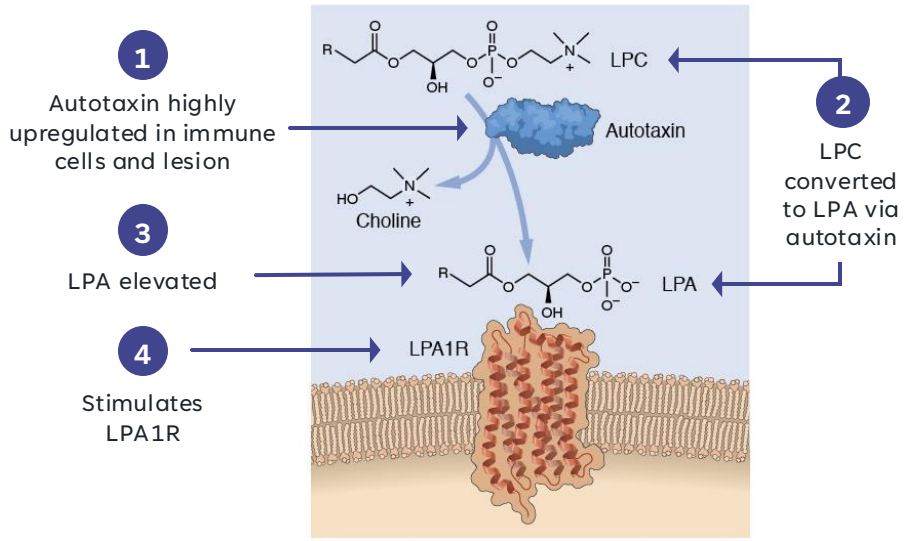
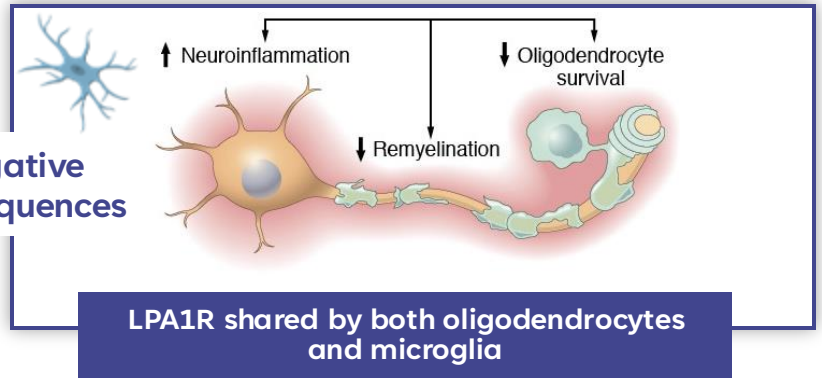
LPA1R: Key Regulator of Remyelination and Neuroinflammation





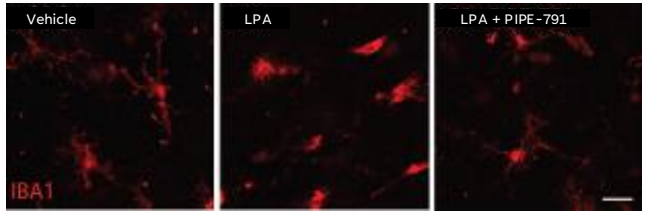
Negative Consequences

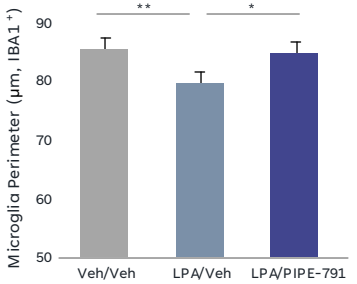
LPA1R shared by both oligodendrocytes and microglia

Blocking LPA1R Reduces Neuroinflammation and Promotes Remyelination – Demonstration in *Ex Vivo* Slice Cultures

REDUCED NEUROINFLAMMATION

PIPE-791 inhibits microglia activation

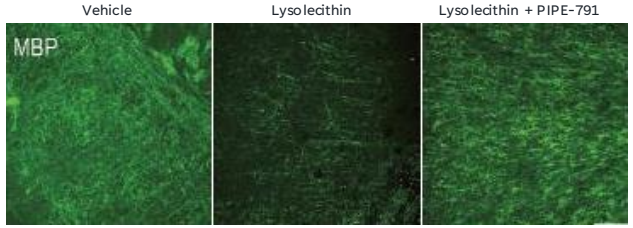


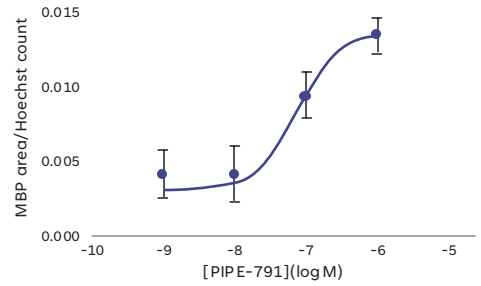


*p<0.05, **p<0.01

REMYELINATION

PIPE-791 promotes remyelination in an *ex vivo* brain slice





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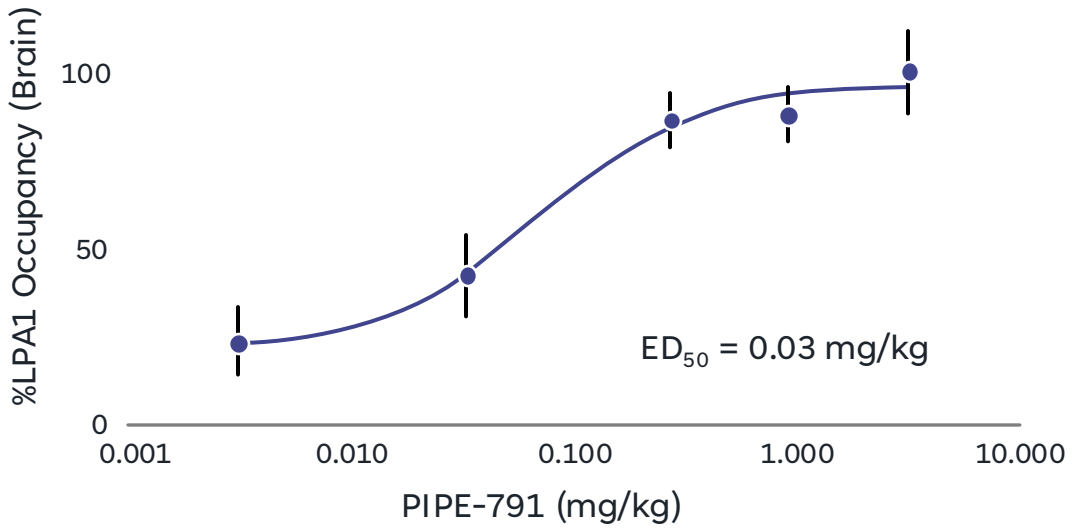
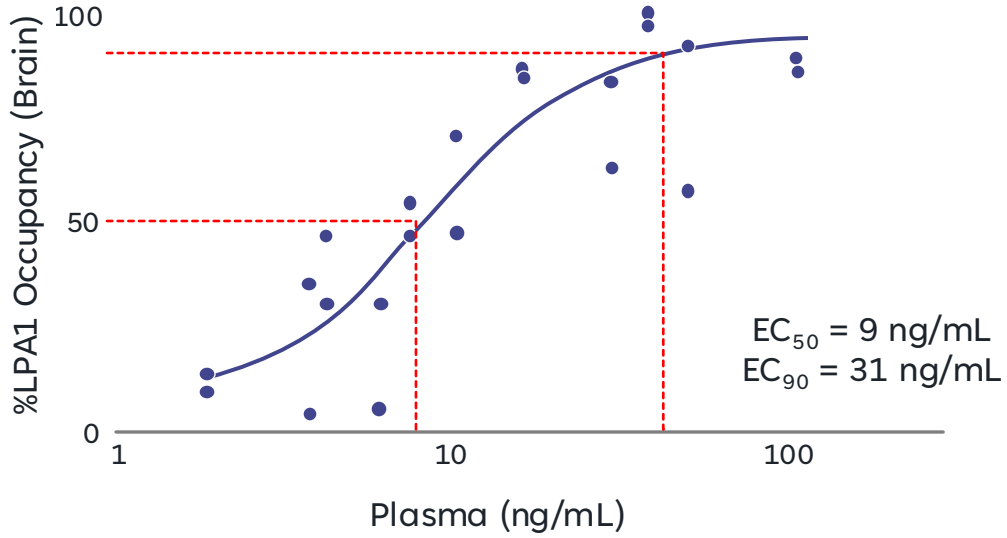
PIPE-791 *In Vivo* LPA1R Receptor Occupancy

Dose Occupancy Relationship



Plasma Occupancy Relationship



- PIPE-791 showed dose-dependent CNS LPA1R receptor occupancy with once daily oral dosing
- Correcting for plasma protein binding in rodents (96.6%), the resulting unbound EC_{50} is estimated to be 0.7 nM

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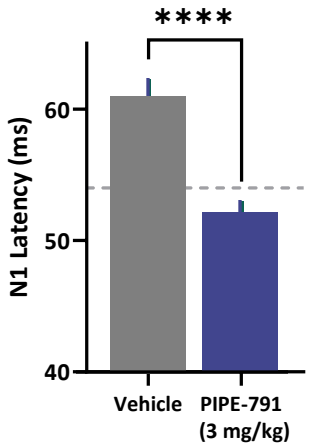
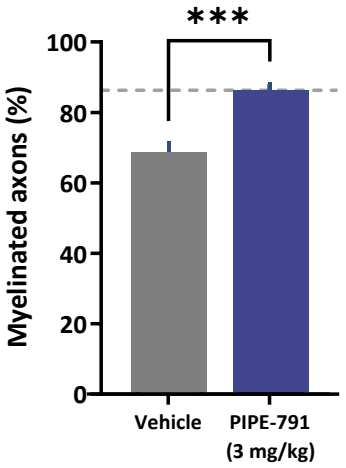
PIPE-791 Promotes Functional Remyelination and Reduces Neuroinflammation *In Vivo*

Mouse EAE Model

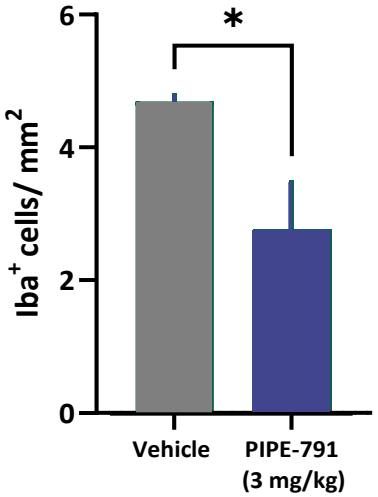
Restored VEP-Latency



Increased Myelination



Reduced Neuroinflammation



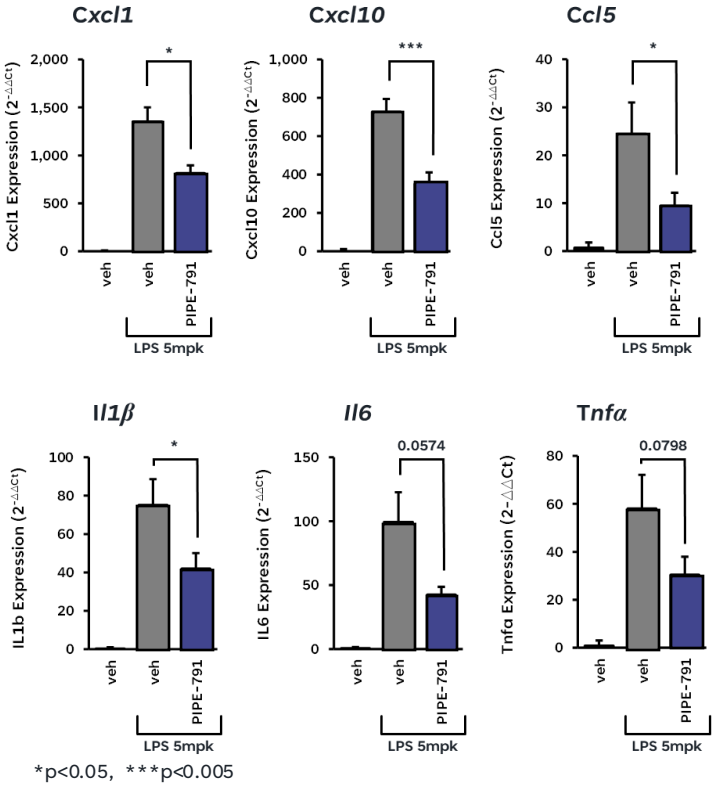
VEP-latency = **translatable clinical endpoint:** retinal to visual cortex speed

Remyelination in mouse EAE model

Microglia accumulation – marker of local **neuroinflammation**

**** p<0.001; *** p<0.005; * p<0.05.

LPS Challenge Model



*p<0.05, ***p<0.005

Brain penetrant PIPE-791 reduces LPS-induced neuroinflammatory markers

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PIPE-791: Clinical Development and Early PoC Plans in Multiple Sclerosis

2023

Phase 1 SAD/MAD/FED Healthy Volunteer Study
Randomized, double-blind, placebo-controlled
(n = 56)

STUDY OBJECTIVES:

Primary:
Safety and tolerability

Secondary:
Pharmacokinetics

2024

Phase 1b
Brain PET Study (n = 6-8)
(MHRA authorized)

STUDY OBJECTIVES:

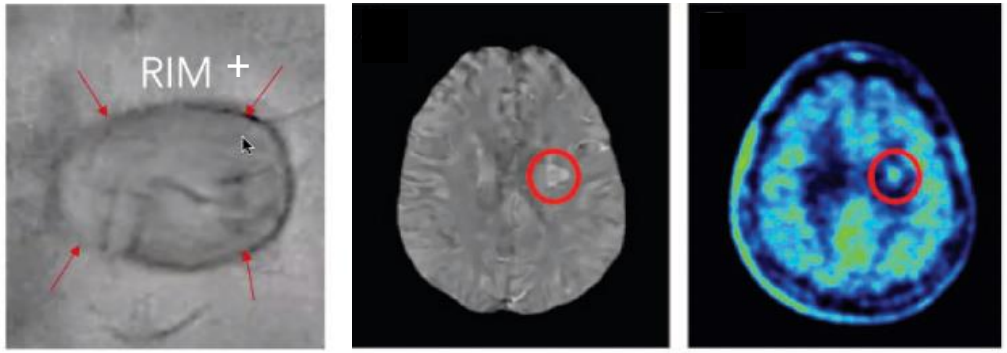
Primary:
PK/RO relationship

*GLP tox NOAEL 1000 mg/kg/day; chronic GLP tox ongoing

2025

Phase 2 DB-RCT Dose-Ranging
Progressive MS: PPMS/SPMS
Primary: Change in neuro-inflammatory imaging biomarkers under consideration
(pending FDA authorization)

Illustrative examples of paramagnetic lesions by MRI QSM and TSPO activity by PET PK11195



Paramagnetic lesion by MRI

Quantitative susceptibility mapping (QSM)

PK11195 PET

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LPA1R Antagonism and PIPE-791 in Chronic Pain

LPA1R: An Exploratory First Step in Chronic Pain

Rationale & Unmet Need

- **FDA authorization of IND for PIPE-791 for the treatment of chronic pain** – two separate indications (osteoarthritis and chronic back pain)
- **Exploratory Phase 1b**, randomized, double-blind, placebo-controlled, crossover, multi-center study is expected to **begin in the first quarter of 2025**
- LPA pathways have been specifically implicated in the neuropathic components of preclinical pain models and clinical biomarker studies
- **Potentially differentiated**, non-opioid treatment option for patients

~33M

Patients with osteoarthritis in the US[1]

15%-25%

OA patients with neuropathic pain

~45M

Patients with chronic low back pain in US[1]

20%-55%

Chronic low back pain patients with neuropathic pain

Current pharmacologic treatments include NSAIDs, antidepressants, steroid injections and opioids

[1]As of 2020

CTX-343 for Peripheral Fibrotic Diseases

IND submission expected in 2025

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CTX-343 – *In vitro* and *In vivo* pharmacology

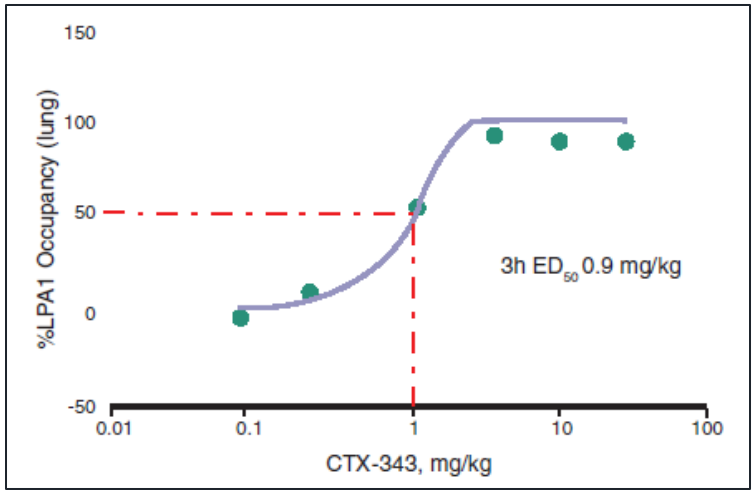
Target Coverage for Antifibrotic Effect

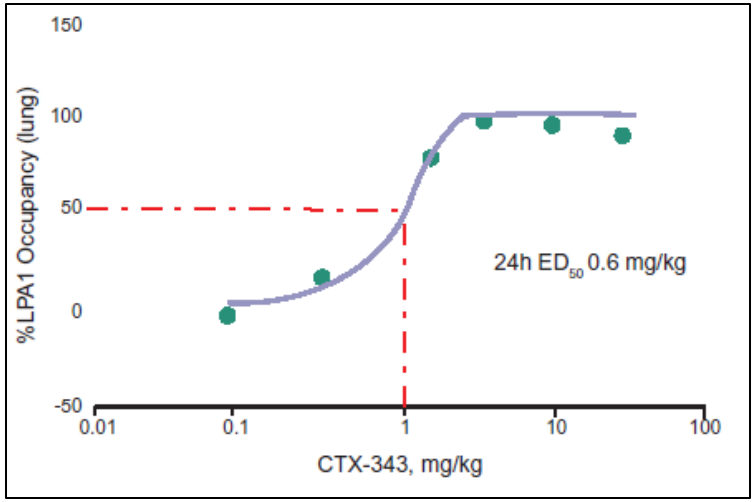
Summary of *In Vitro* and *In Vivo* Properties

Properties	*In Vitro* Profile
Radioligand binding Ki (nM)	5.56 (IC_{50}: 19.5)
K_{off} (min^{-1})	0.00036
LPA1 Ca^{2+} mobilization (nM)	48.1
Rodent $K_{p,uu}$ @ 2h	0.05

- CTX-343 is a potent, peripherally restricted LPA1R antagonist with *in vitro* long receptor off rate, slow *in vivo* clearance and high oral bioavailability
- CTX-343 shows a dose-dependent LPA1R receptor occupancy at 3- and 24-hours after a single dose

In Vivo Lung LPA1R Occupancy





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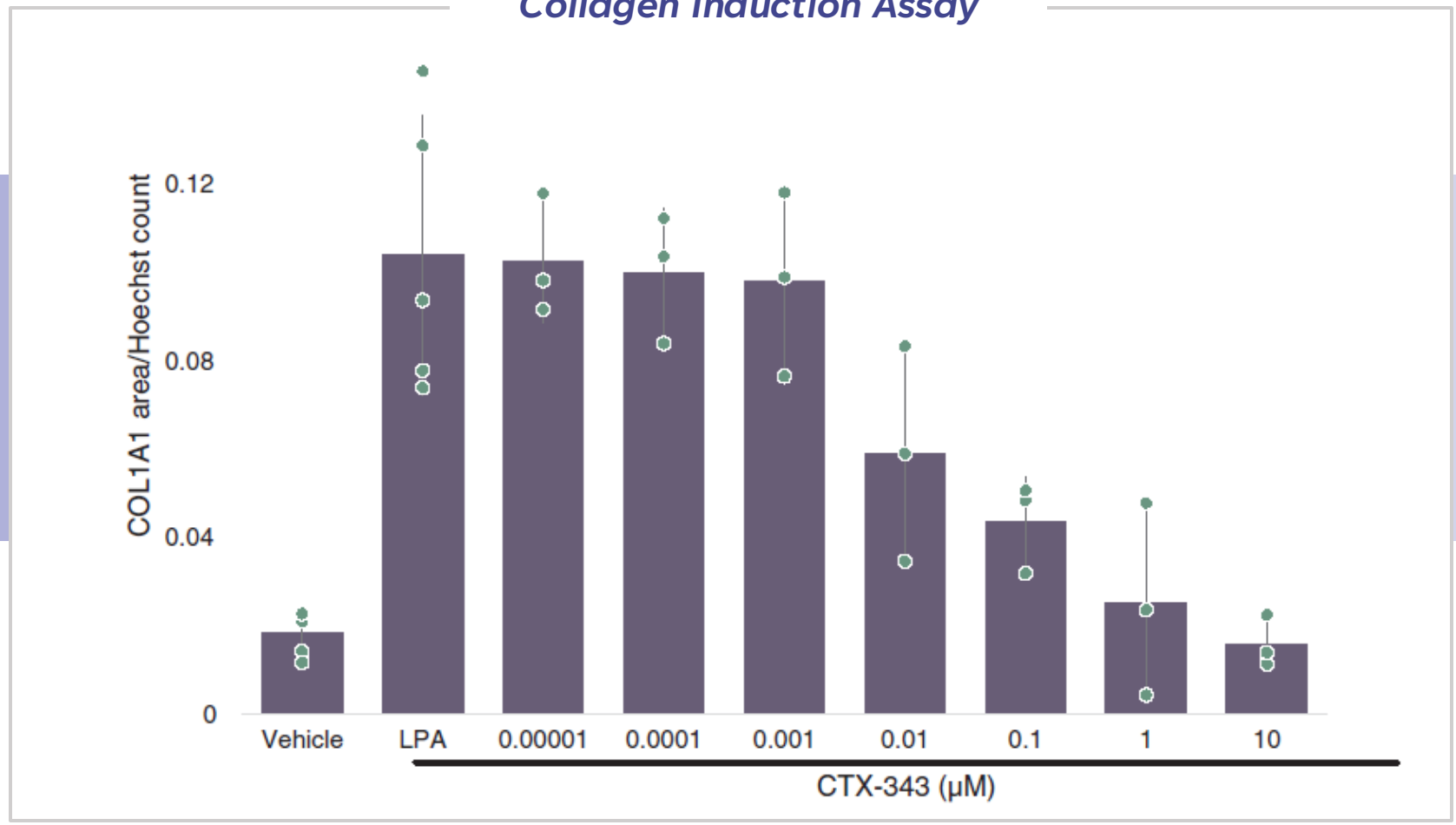
CTX-343 Inhibits LPA1-Induced Fibroblast Collagen Production



- CTX-343 inhibited LPA-induced COL1A1 in primary human lung fibroblasts with an IC50 of 10.2 nM

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PIPE-307, an M1R Antagonist, for Depression

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PIPE-307: Two Shots on Goal for CNS

DEPRESSION

~280M

Patients Globally

Approved therapeutics suffer from major limitations

- Many patients fail to respond to available therapies
- Approved therapies have pronounced side effects

RELAPSING-REMITTING MS

~2M

Patients Globally

>20 FDA-approved DMTs that are only partially effective

- Approved therapies decrease annual relapse rate
- Do not directly remyelinate nerve fibers or reduce clinical disability

Completed 2 Phase 1 Healthy Volunteer trials with no dose-limiting AEs and desired target engagement

PIPE-307 is a selective agent with an MoA that is clinically validated in two key CNS indications of high unmet need

Partnering Agreement with J&J for PIPE-307 – $1B+ Potential Payments

- Leverages Contineum's expertise in precision neuroregeneration
- Contineum is leading Phase 2 development in RRMS, for which a study (VISTA) was initiated in late 2023
- J&J has the right, in its sole discretion, to further develop or elect not to develop PIPE-307 for RRMS
- J&J plans to initiate Phase 2 trial in depression in 2H 2024

Johnson&Johnson
Innovative Medicine

Global development and license agreement for PIPE-307 in all indications

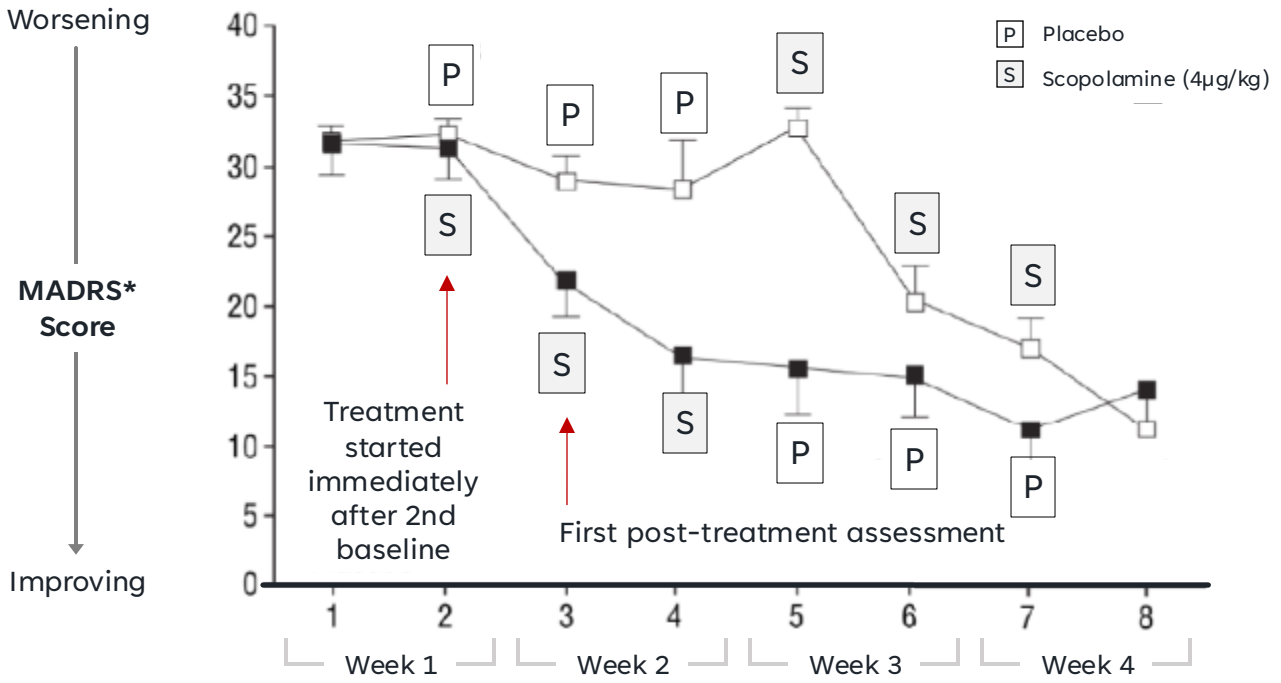
$50M upfront, $25M equity investment, milestones >$1B, and tiered royalties (low-double digit to high-teens)

Contineum has opt-in right to fund-part Phase 3 development costs in return for an increase in royalty rates

J&J commitment to precision neuroscience

Clinical Validation For Depression

Scopolamine vs Placebo: Antidepressant Proof-of-concept[1]



*MADRS – Montgomery-Asberg Depression Rating Scale [1]*Furey and Drevets, Arch Gen Psych 2006*

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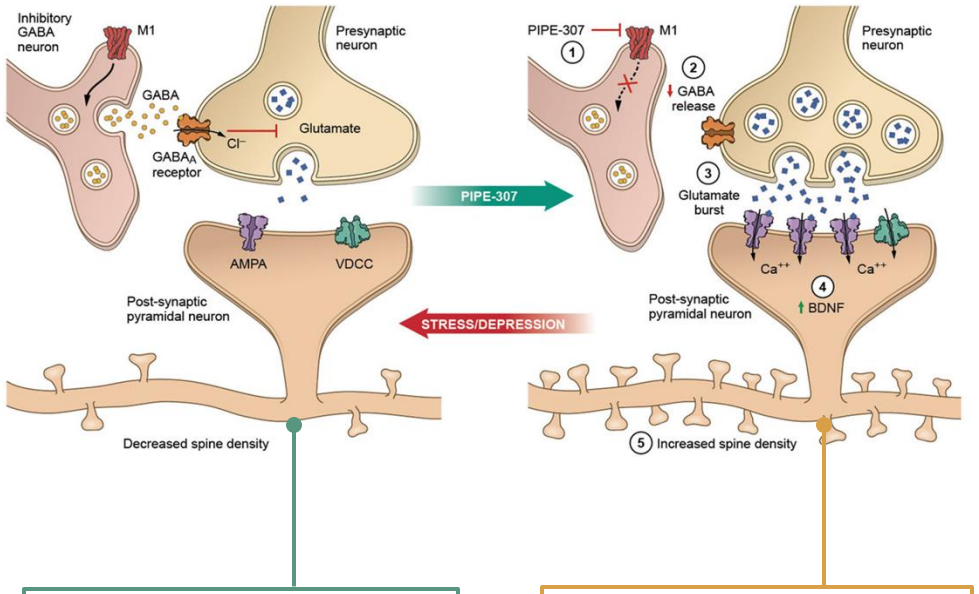
M1R Mechanistic Rationale And Preclinical Validation

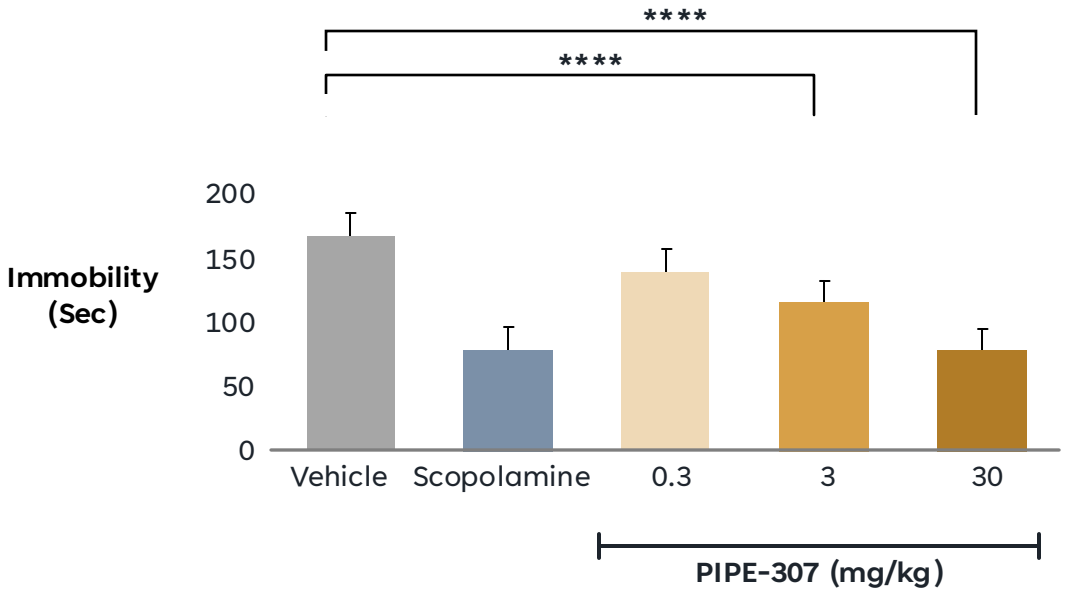
Blocking M1R Restores Synaptic Connectivity



DECREASED spine density
(fewer synaptic connections)

RESTORED spine density
(synaptogenesis)

Acute Dosing Paradigm



****p<0.0001 versus vehicle

Consistent with the literature, scopolamine decreases immobility time - this effect is mimicked by the selective M1R antagonist PIPE-307

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PIPE-307, an M1R Antagonist, for RRMS

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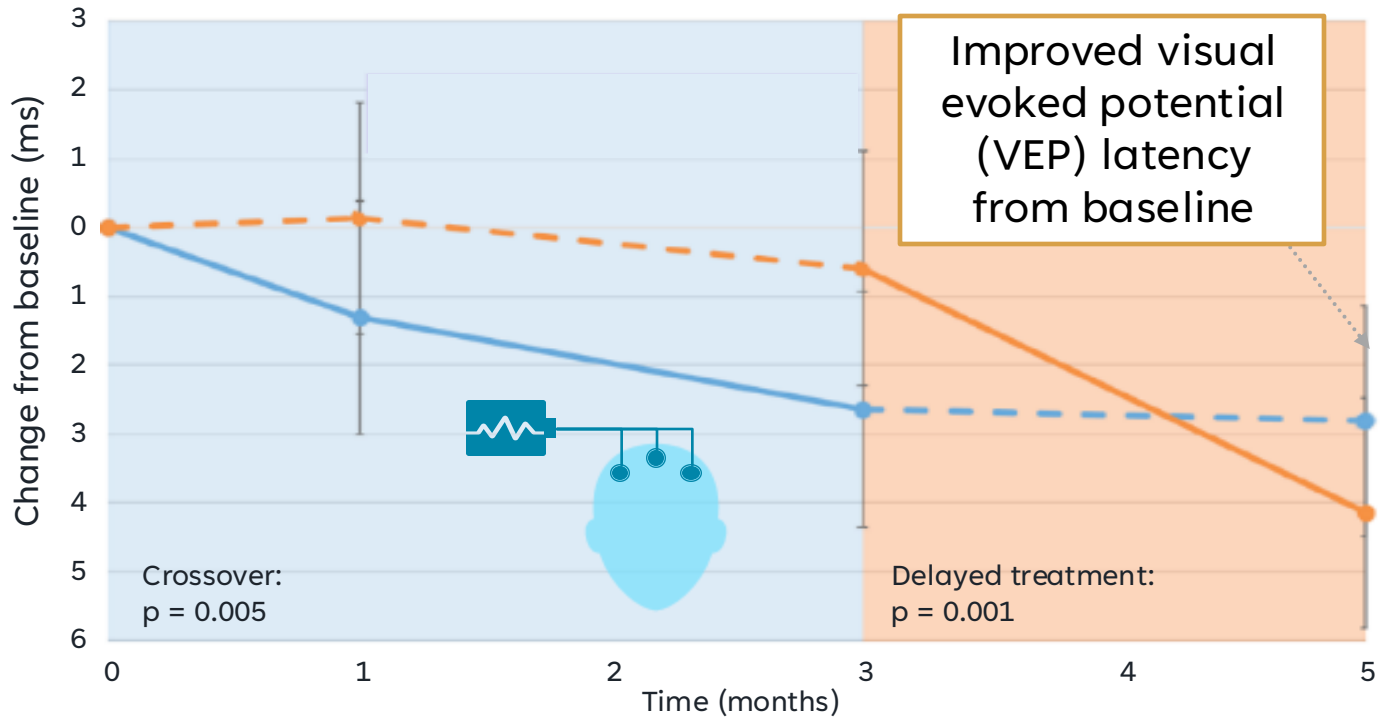
Clinical Validation For Remyelination

Phase 2 clemastine ReBUILD RRMS trial



- Statistically significant improvement in VEP latency in both crossover and delayed treatment cohorts
- Key validation for the potential for remyelination with PIPE-307

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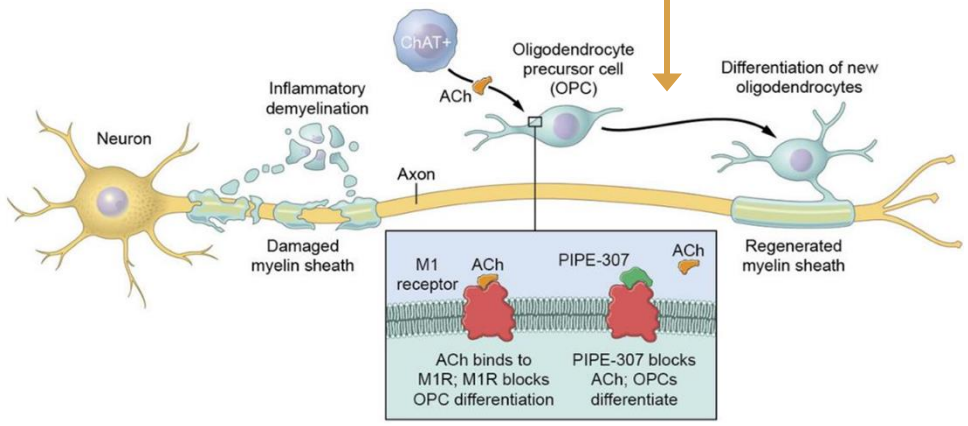
M1R Mechanistic Rationale And Preclinical Validation

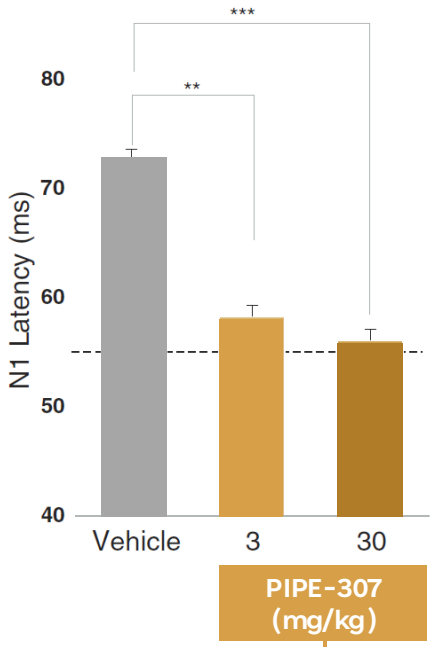
Blocking M1R Promotes Remyelination

Reactivating endogenous pathway

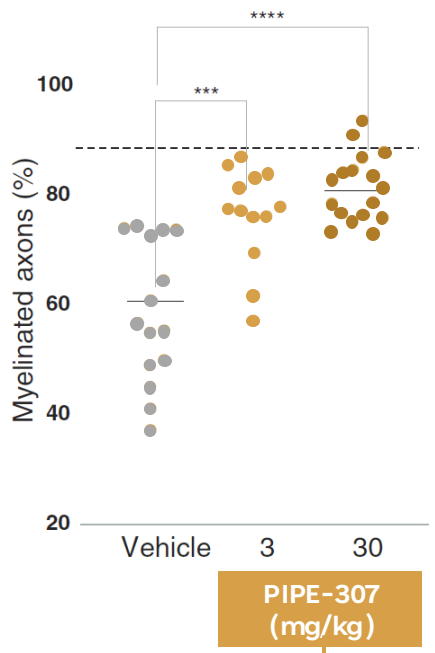


PIPE-307 Promotes Remyelination In Preclinical EAE Model

Restored VEP-Latency



Increased Myelination



**p<0.01, ***p<0.005 vs Vehicle treated

***p<0.001, ****p<0.0001, vs Vehicle treated

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PIPE-307: Phase 1 Healthy Volunteer Trials Support Both Indications

Phase 1 SAD/MAD Trial Results

Tolerability

- Well-tolerated across all dose cohorts
- No dose-limiting AEs or toxicity observed

Pharmacokinetics

- Linear and dose-proportional PK (c/w preclinical studies)

Exploratory

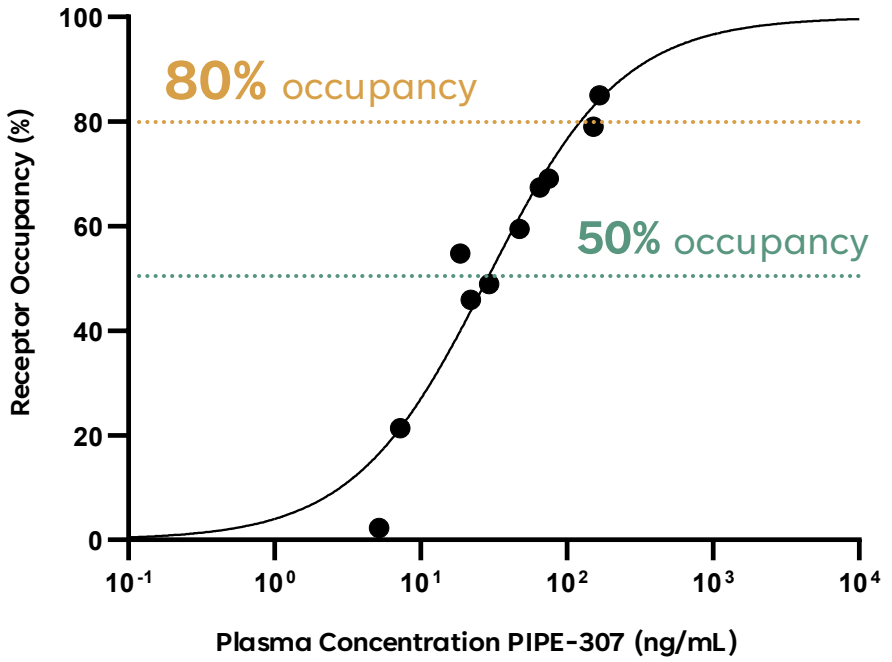
- Cognition: psychomotor, attention, learning, executive function
- No significant PK or dose-related effects on cognitive function

Phase 1 PET Trial Results

- Established brain receptor uptake and PK relationship at pharmacologically active doses for CNS indications
- Plasma PK at target receptor occupancy well-tolerated

PHASE 1 PET

Receptor occupancy (RO) vs plasma concentration



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VISTA: Phase 2 Randomized, Double-Blind Placebo-Controlled Trial in RRMS

Key Eligibility Criteria

- 18-50y patient with RRMS
- Diagnosis of MS < 10 y
- EDSS: 0-6.0
- Stable DMT therapy

VISTA

6m dose-ranging
Daily oral dosing
1:1:1 Randomization
n=168

- Placebo (n=56)
- PIPE-307 Dose A (n=56)
- PIPE-307 Dose B (n=56)

Primary Objectives

- **Safety and tolerability**
- **Low contrast letter acuity**

Key Secondary Objectives

- Symbol digit modalities test
- Timed 25-foot walk test
- 9-hole peg test
- MRI (MTR and DTI)
- Neurofilament light chain

Illustrative 2.5% Sloan Low Contrast Letter Acuity

- Captures disability outside EDSS
- Correlates with OCT, MRI, VEP, QoL
- Considered one of the most sensitive tests to detect a treatment effect

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Key Clinical Milestones

Catalyst-Rich 24 Months: Completed & Anticipated Clinical Milestones & Inflection Points

	2024		2025
PIPE-791	• Received Phase 1 Healthy Volunteers Clinical Data • MHRA Authorization to Commence Phase 1b PET Study • Receive Phase 1b PET Study Healthy Volunteer Clinical Data	✓ ✓	• Receive Phase 1b Brain & Lung PET Study Clinical Data • Complete Chronic tox & IND to support Ph2 PoC trials • Initiate Phase 2 IPF PoC Study • Initiate Phase 2 Progressive MS PoC Study • Initiate Phase 1b Chronic Pain Study
CTX-343	• Selected Development Candidate for **Peripherally-Restricted LPA1R Antagonist**	✓	• File IND for Peripherally-Restricted LPA1R Antagonist • Receive Phase 1 Healthy Volunteers Clinical Data
PIPE-307	• Initiated Phase 2 RRMS PoC Study • Initiate Phase 2 Depression PoC Study	✓	• Complete enrollment in Phase 2 RRMS PoC Study

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therapeutics

Corporate Presentation

November 2024