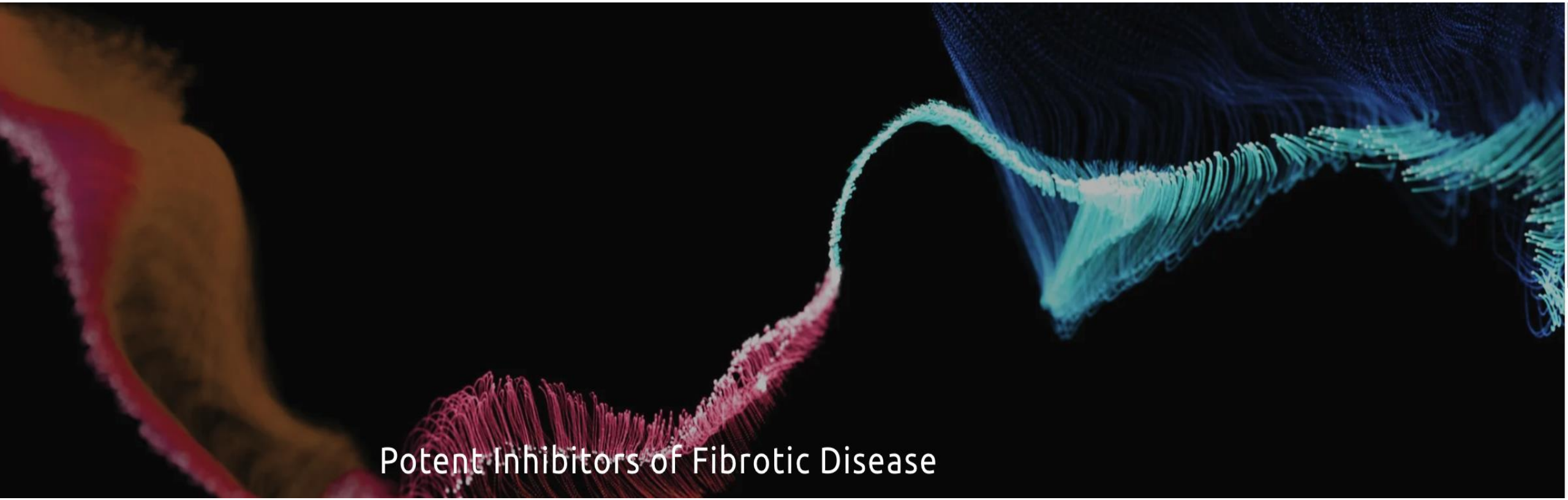
Shc Blockers for lung fibrosis



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Buto

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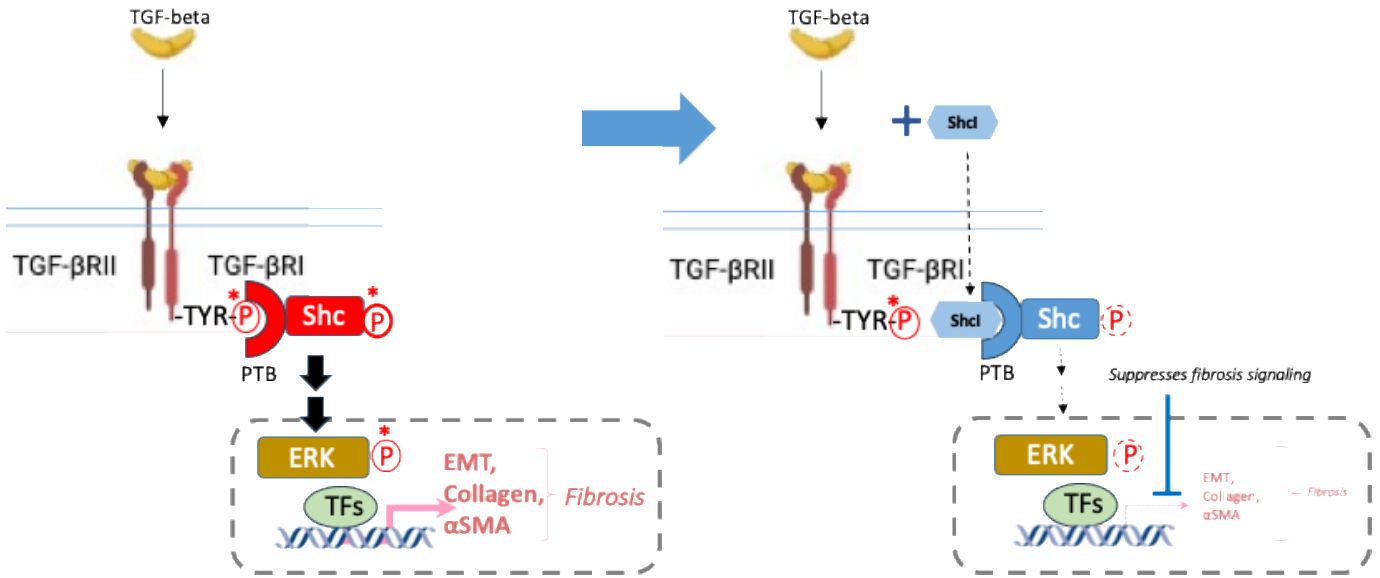
Buto Investment Highlights

- Fibrosis therapy is a major unmet need with TAM > $6B/yr.
- Buto uniquely develops First-In-Class Shc Inhibitors (ShcIs) to address tissue fibrosis.
- Buto has 4 proprietary methods to to move faster on ShcIs than the competition.
- Buto owns composition of matter patents on New Chemical entity ShcI scaffolds B-301 and others.
- ShcI B-301 outperforms nintedanib and pirfenidone by wide margins.
- ShcI B-301 reduces tissue fibrosis in lungs of man and mouse.
- ShcI B-301 therapeutic efficacy occurs at 25mg/kg, no side effects until > 300mg/kg.
- Lead candidate B-240 is 100X more potent than B-301 and has good PK.



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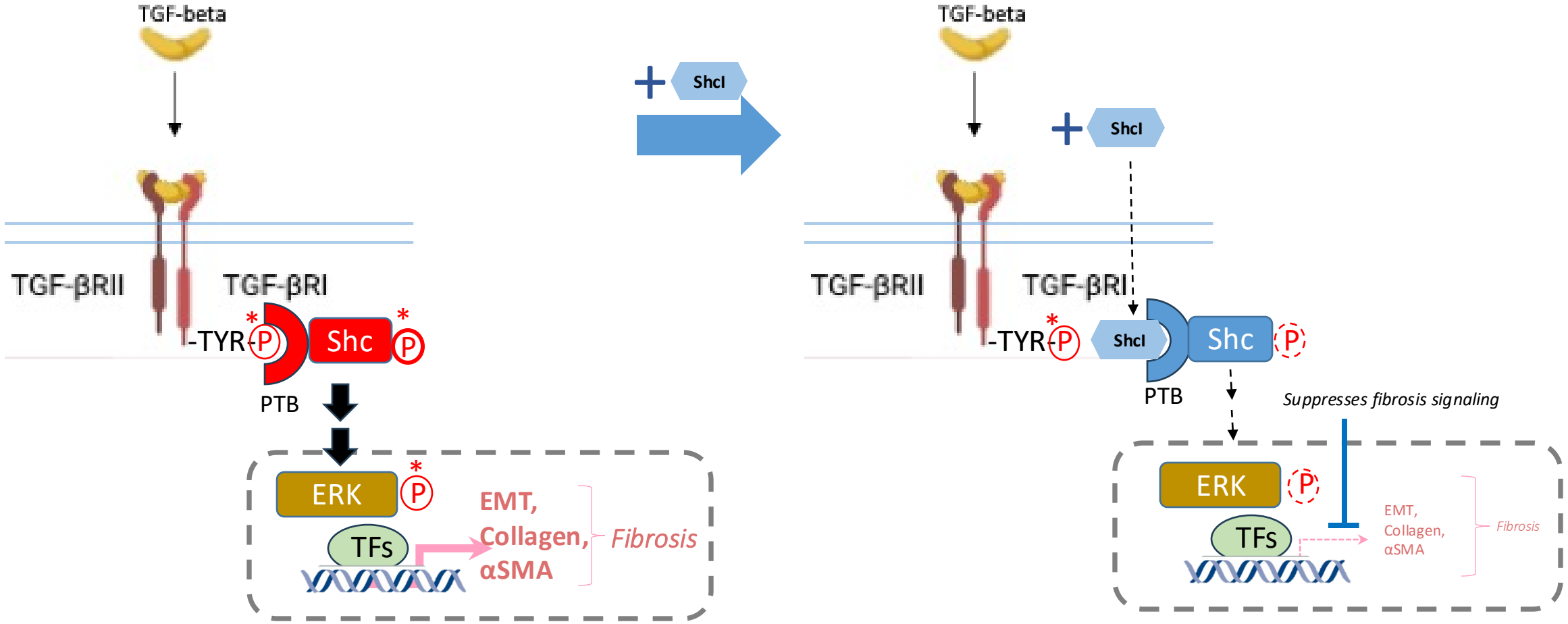
MoA: Shc activation is an important fibrotic mechanism; ShcI's block Shc activation and suppress fibrosis



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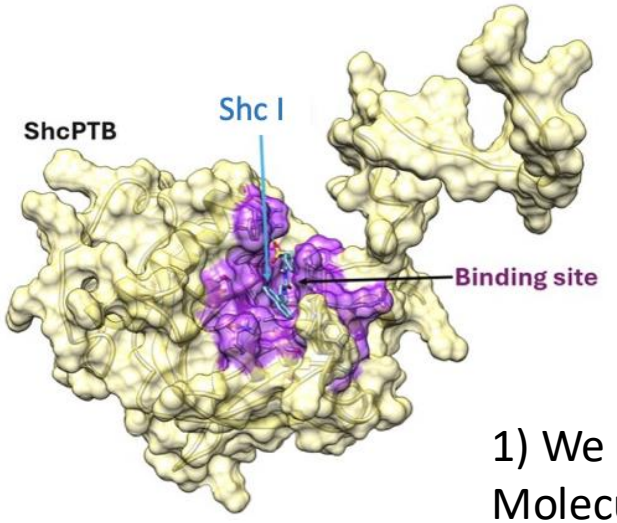
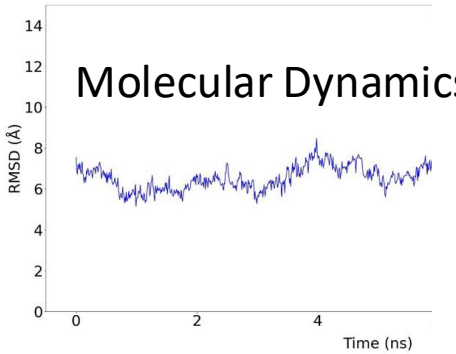
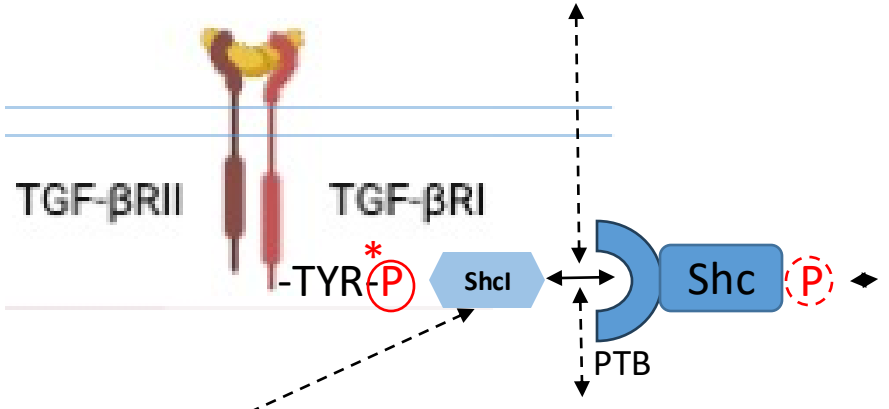
Buto's competitive edge: we can predict ShcI potency through 4 proprietary assays





1) We understand ShcI binding to PTB by Molecular Dynamics and Docking



4) We assay ShcI's potency by reduction of active phospho-Shc *in vitro* & *in vivo* and that activity correlates with #1, 2 & 3.

3) We assay ShcI's potency to block TYR-P ← → ShcPTB interaction and they correlate with #1 & 2.

2) We've measured binding affinities of 53 ShcIs to Shc by SPR and they correlate with computational methods

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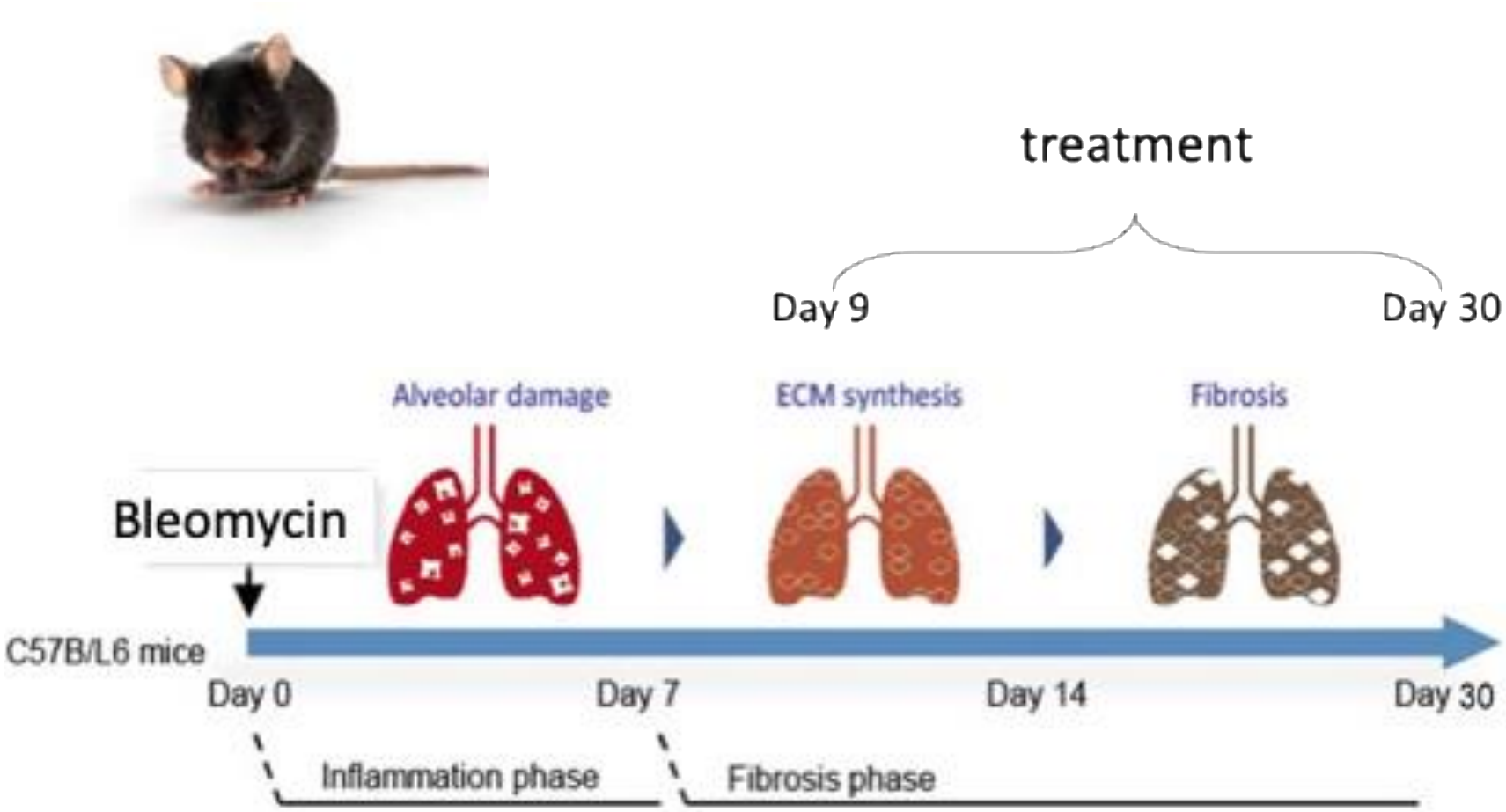
Lung fibrosis in Mice—bleomycin model



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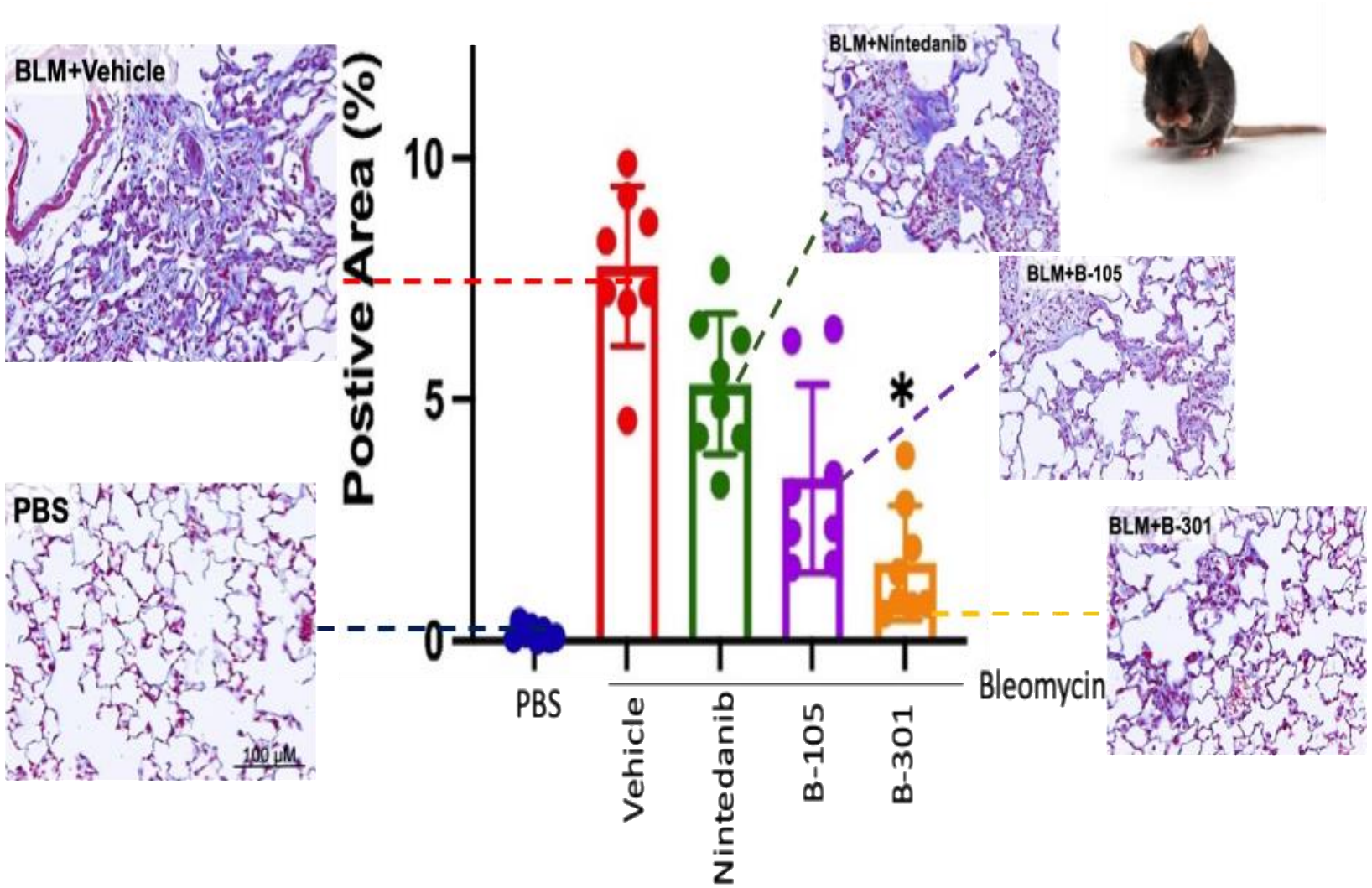
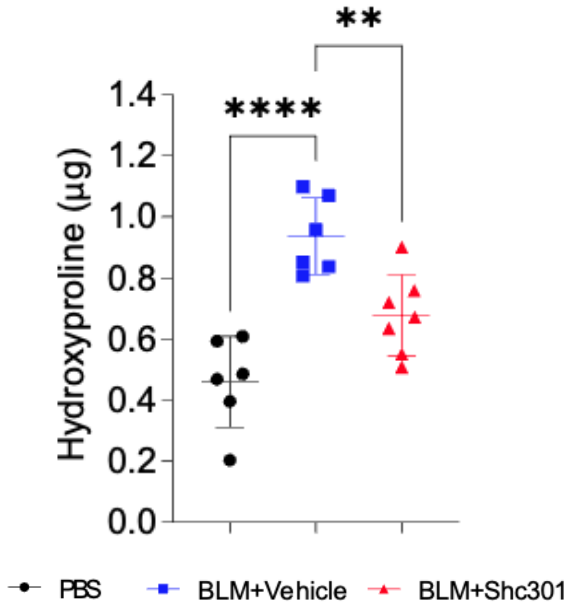
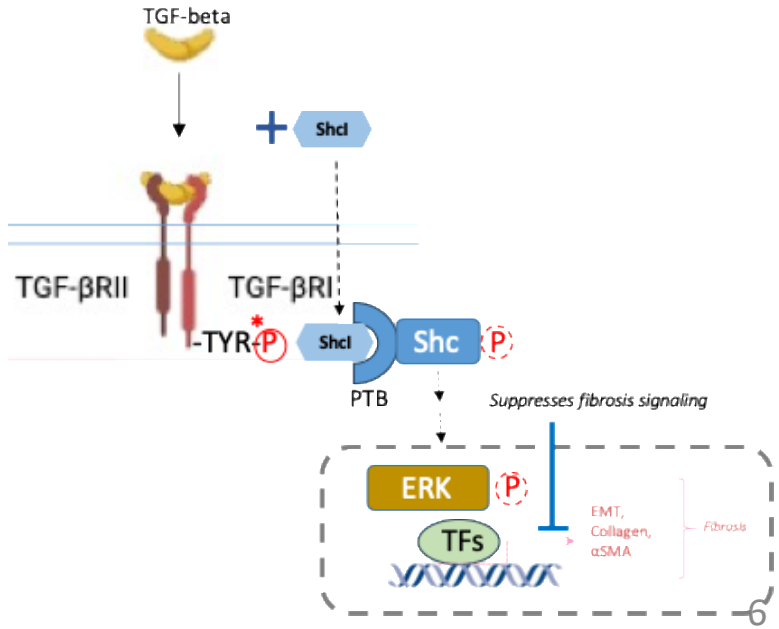
B-301 Reduces Lung Fibrosis Staining by Masson's Trichrome more than isodosed BI's Nintedanib







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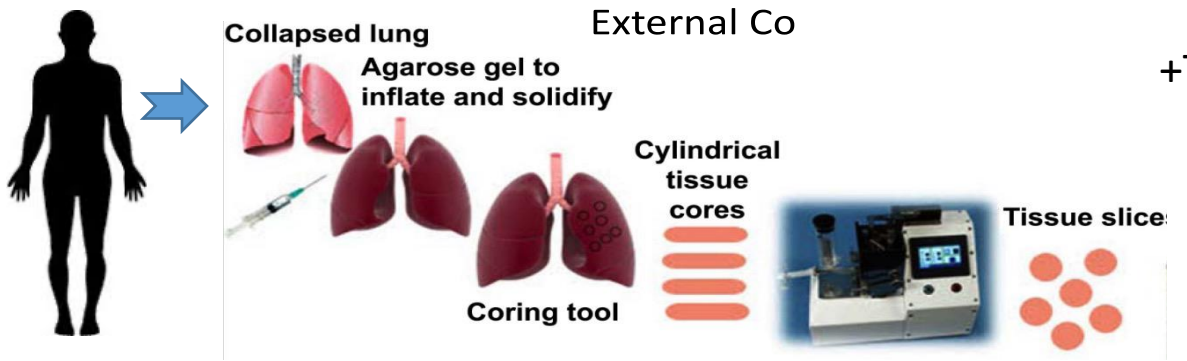
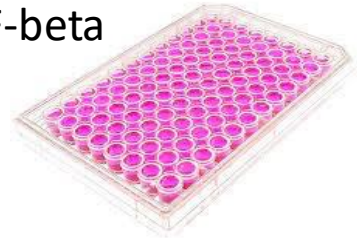
Shc301's IC50 for hydroxyproline inhibition is ~100-fold lower than Pirfenidone's in human lung



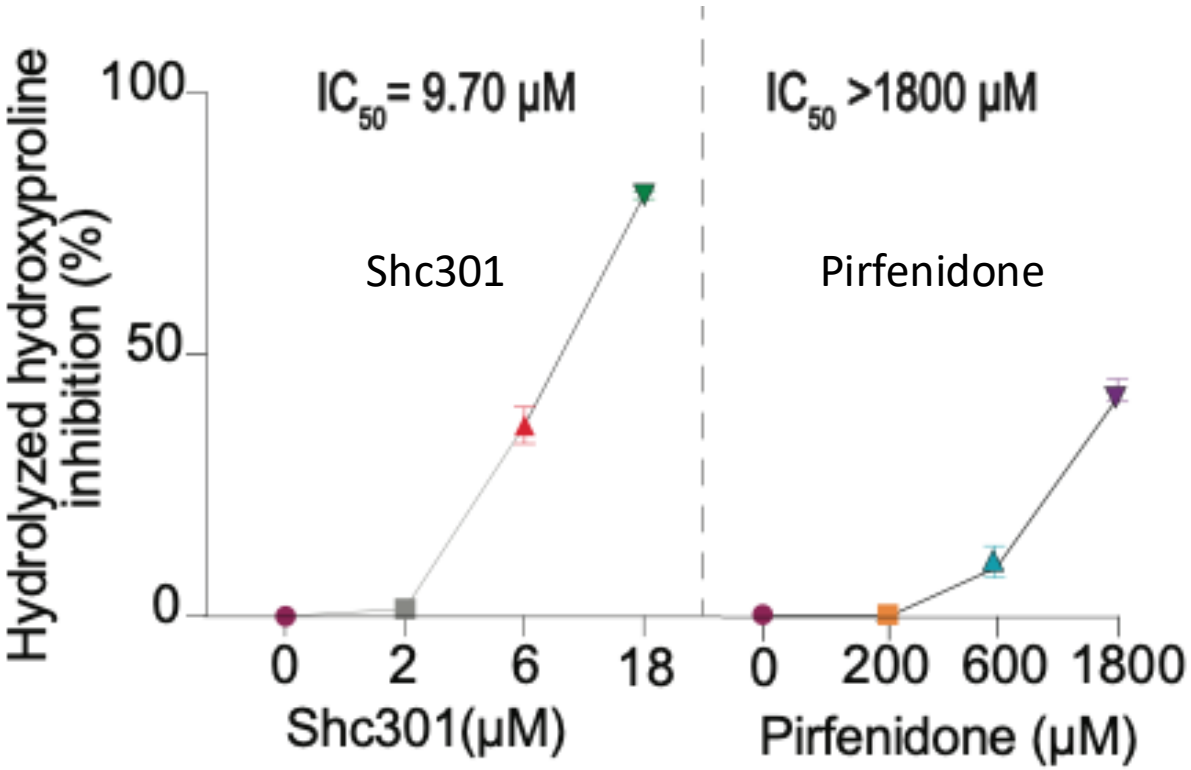
External Co

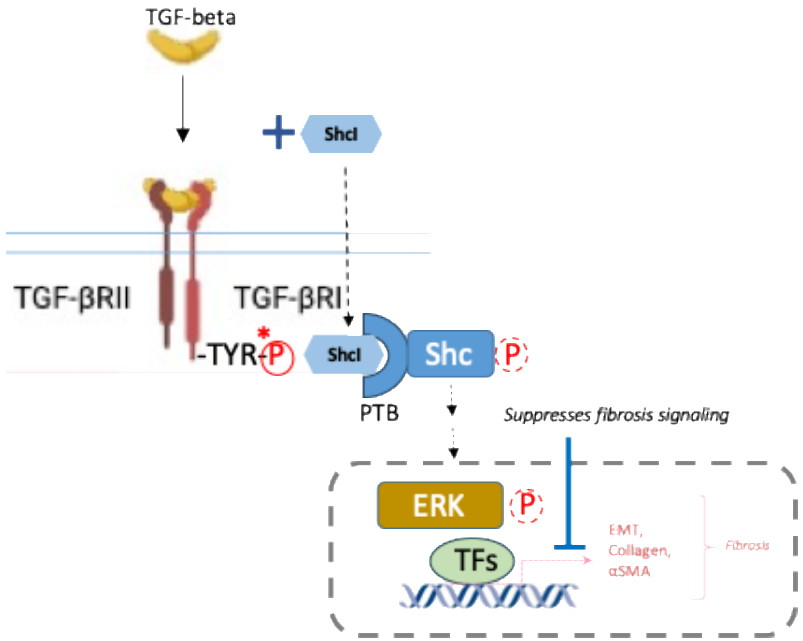
+TGF-beta



HTS assay of fibrotic proteins

Therefore Shc301 is 100X more anti-fibrotic than standard-of-care lung fibrosis drug





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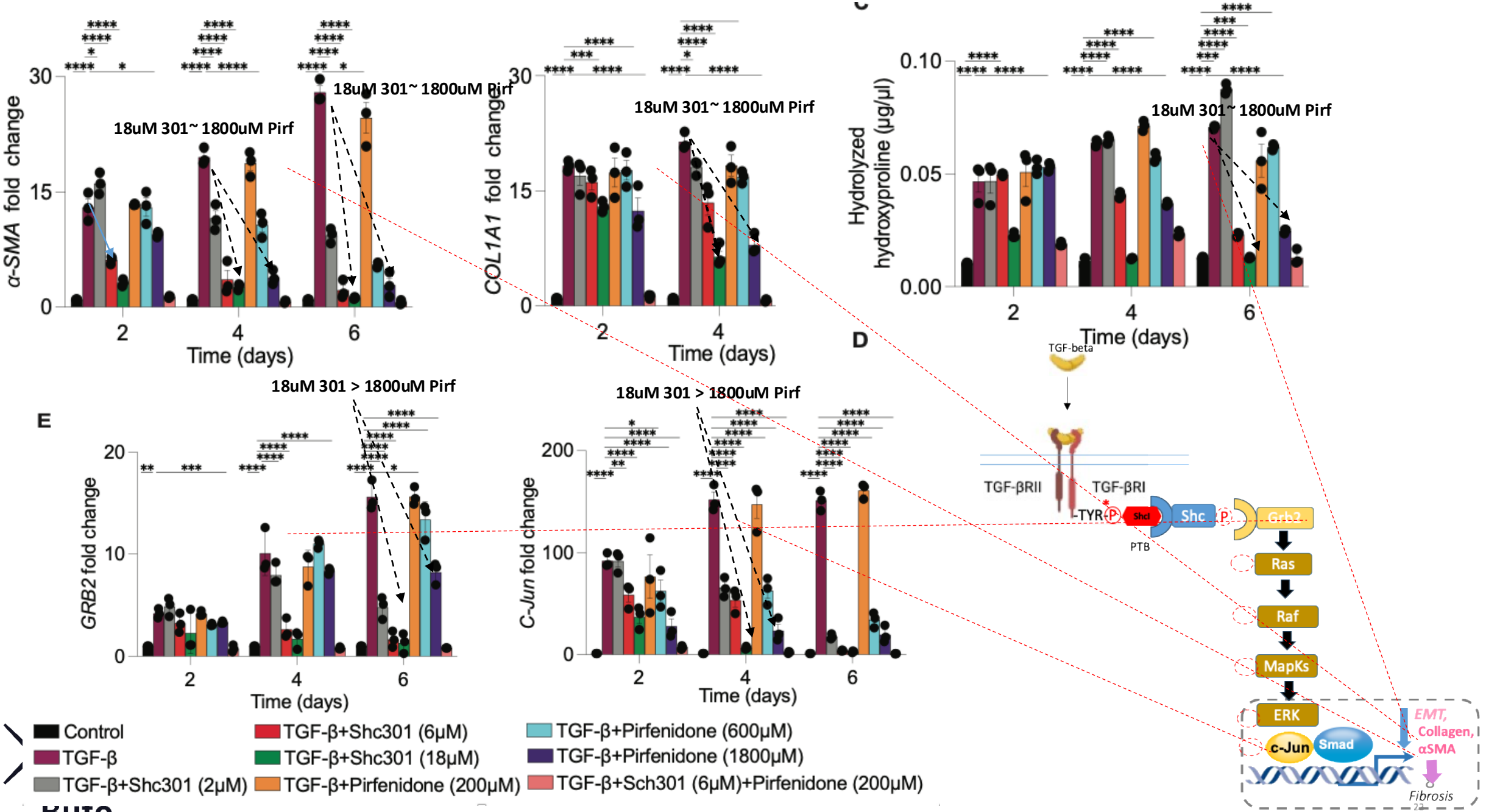
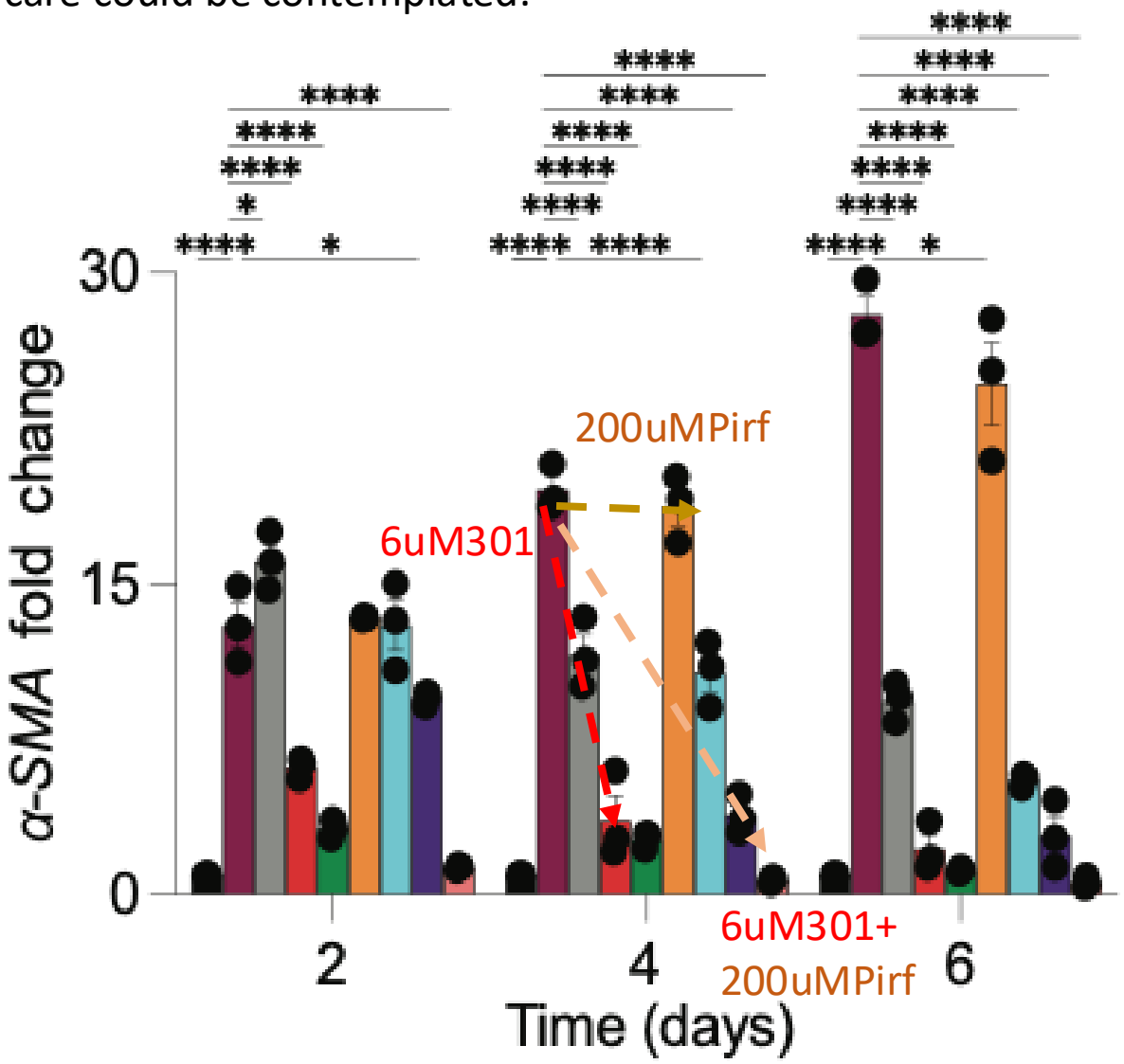
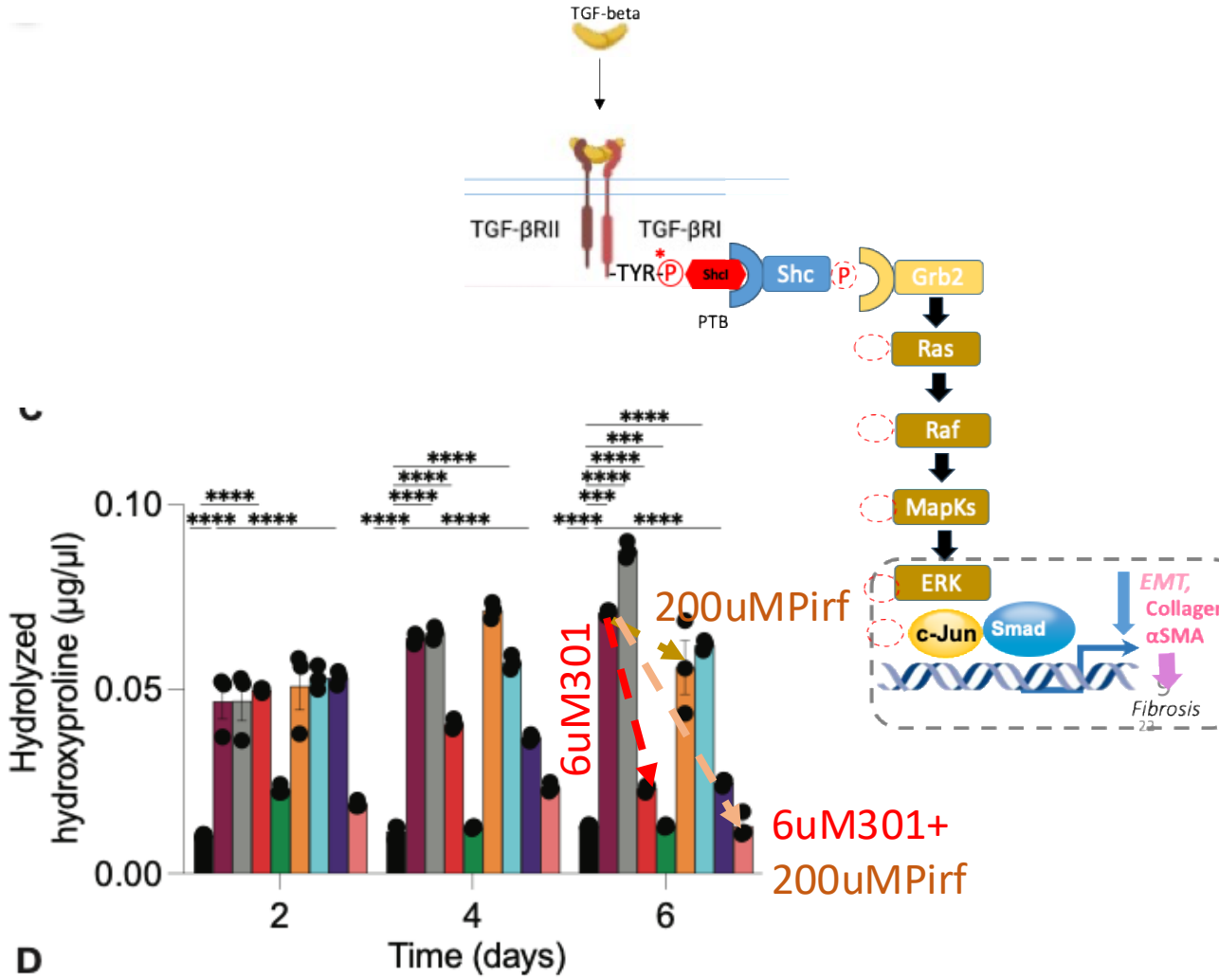
Shc 301 is 100-fold more anti-fibrotic than pirfenidone in TGF-beta treated human lung slices: 18uM301 = 1800uM Pirfenidone



Shc 301 at 6uM + Pirfenidone 200uM potentiates each other's anti-fibrotic effects, thus a co-dosing study alongside standard of care could be contemplated.





Control
TGF-β
TGF-β+Shc301 (2μM)
TGF-β+Shc301 (6μM)
TGF-β+Shc301 (18μM)
TGF-β+Pirfenidone (200μM)
TGF-β+Pirfenidone (600μM)
TGF-β+Pirfenidone (1800μM)
TGF-β+Sch301 (6μM)+Pirfenidone (200μM)

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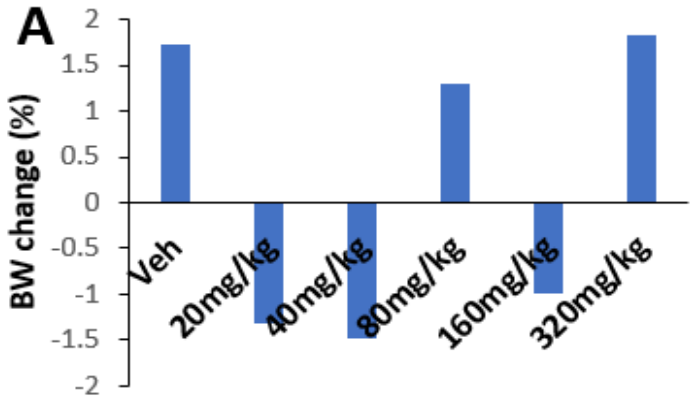
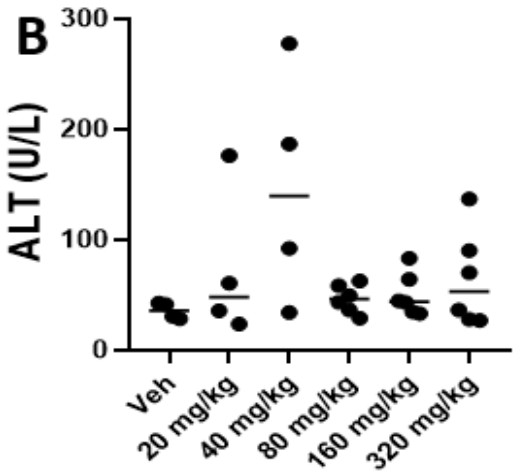
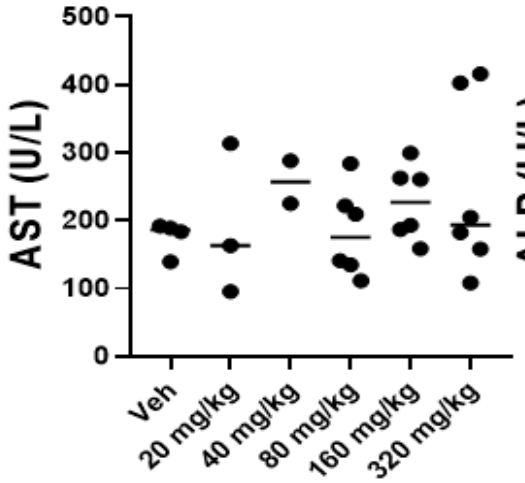
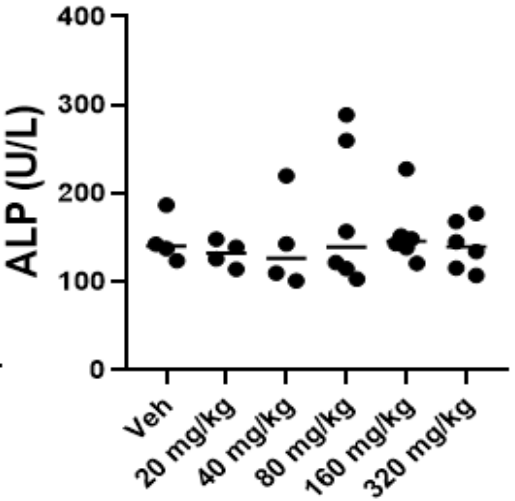
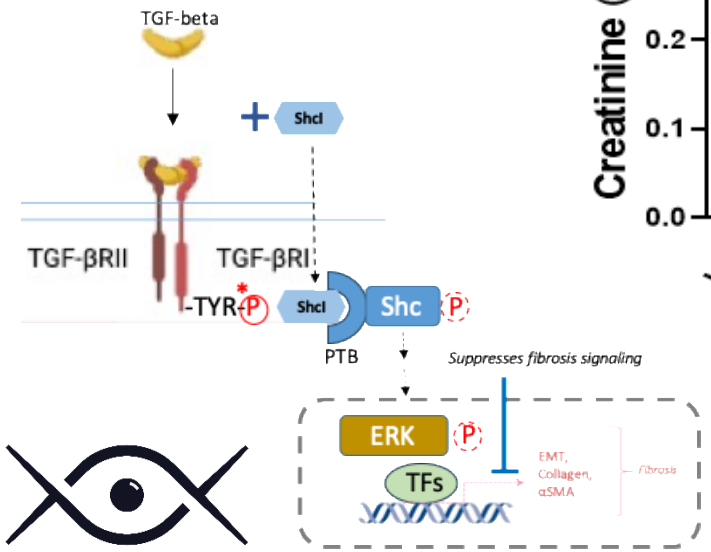
Safety: B-301 has therapeutic effect at 25 mpk, dosed 10X higher at 320mpk there is no weight loss, liver toxicity, or deaths

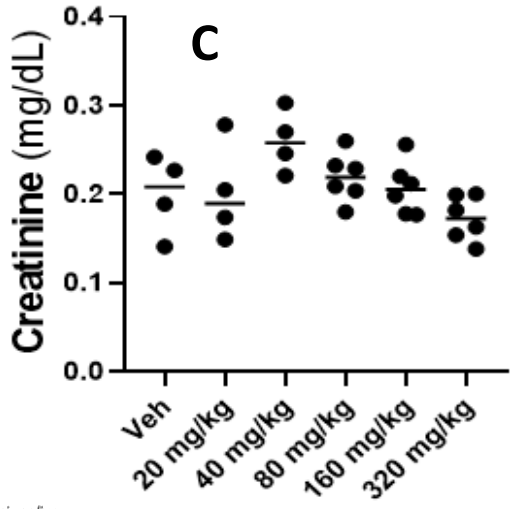


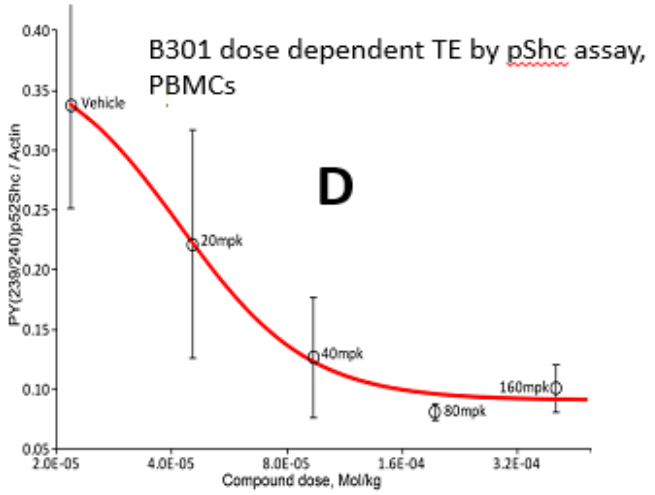


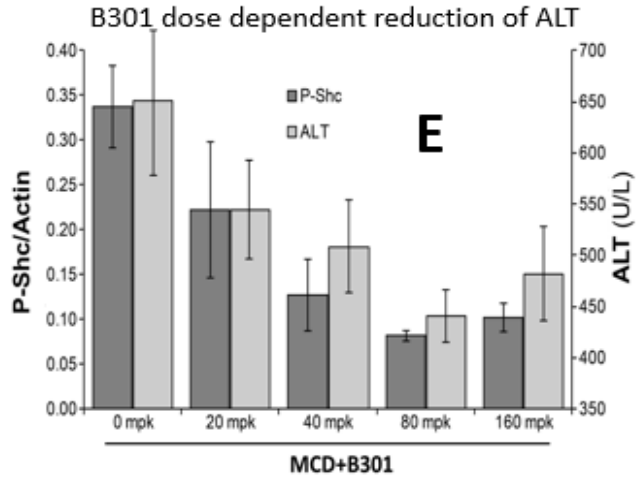












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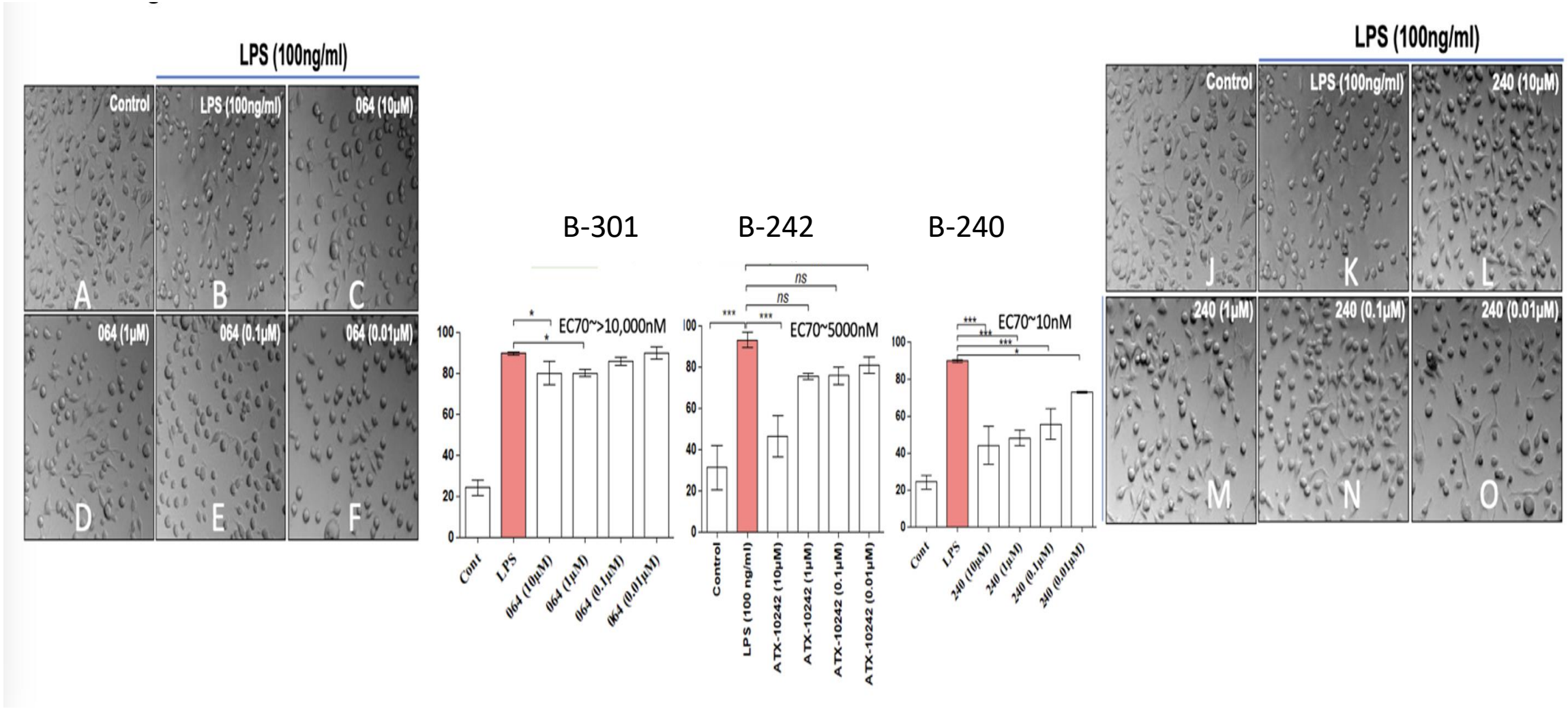
Buto modified B-301 to make molecule B-240, B-240 is 1000x more potent



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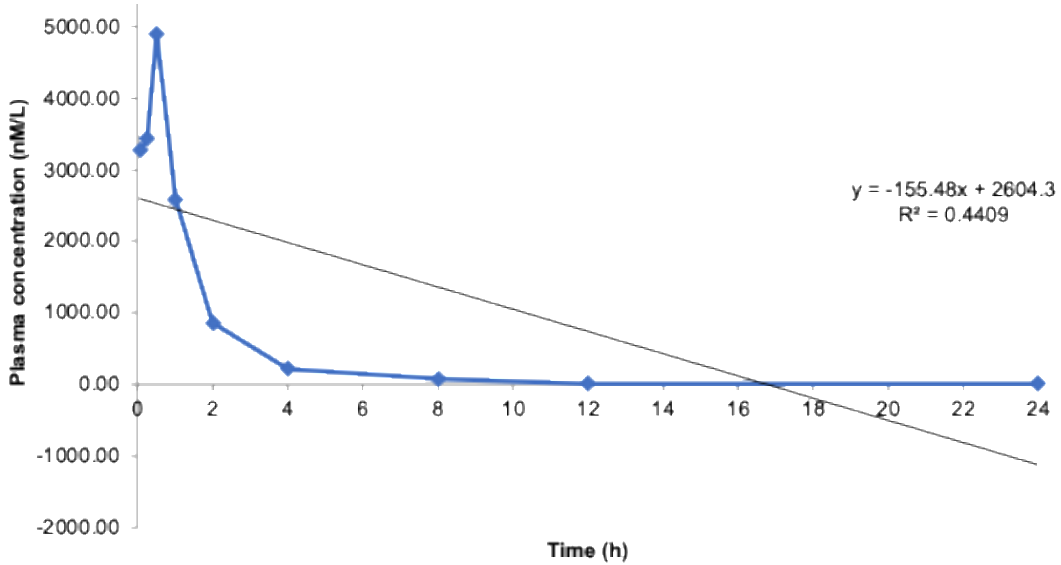
B-240 has good PK in mice, improved over its parent B-301

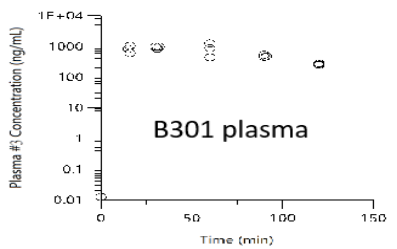


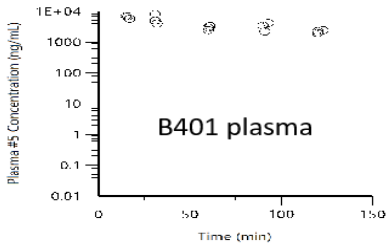
Calculated Concentration of sample (nM)	
T. Points (h)	Average Concentration
0.08	3278.01
0.25	3438.51
0.5	4901.13
1	2588.02
2	856.76
4	220.61
8	74.04
12	11.42
24	11.90

Parameters	Result
Cmax (nM)	4901
Tmax (h)	0.50
AUC (nM.h)	7186.00
T1/2 elimination (h)	2.76
Vd (ml)	805.89
CL (ml/h)	202.69
MRT (h)	2.01

Mice well tolerated the dose

Dose:30mg/Kg
Vehicle: 0.5%CMC
Species:Mice
Strain: C57BL/6





Compound#	Tissue	HL_Lambda_z	Tmax	Cmax	AUClast
		(min)	(min)	(ng/g) or (ng/mL)	(min*ng/g) or (min*ng/mL)
B301	Plasma	35.24	32	973.36	77807.53
B401	Plasma	33.5	15	6987.8	451287.24

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Buto seeks investment to bring its Shcl's to the clinic for lung fibrosis indications

ACTIVITY	BUDGET	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8
LEAD OPTIMIZATION	**$ 705,000**								
Medicinal Chemistry	$ 240,000	$ 40,000	$ 40,000	$ 40,000	$ 40,000	$ 40,000	$ 40,000		
Pharmacology (in-vitro/in-vivo_	$ 240,000	$ 40,000	$ 40,000	$ 40,000	$ 40,000	$ 40,000	$ 40,000		
PK/ADME	$ 100,000		$ 20,000	$ 20,000	$ 20,000	$ 20,000	$ 20,000		
Off-target profile	$ 125,000				$ 50,000		$ 75,000		
IND ENABLING	**$ 550,000**								
Process Chem/Scale up	$ 90,000						$ 30,000	$ 30,000	$ 30,000
Rat Oral BA and Dose Ranging PK	$ 50,000							$ 50,000	
Dog Oral BA and Dose Ranging PK	$ 250,000								$ 250,000
Complete ADME	$ 80,000							$ 40,000	$ 40,000
Complete Off-Target	$ 80,000							$ 40,000	$ 40,000
PRE-IND MEETING	**$ 125,000**								
Pre-IND Package	$ 75,000						$ 25,000	$ 25,000	$ 25,000
Reg Consultant	$ 25,000						$ 10,000	$ 15,000	
Tox Consultant	$ 25,000						$ 10,000	$ 15,000	
IP FILING	**$ 20,000**								
Provisional	$ 20,000						$ 20,000		
TOTAL	**$ 1,400,000**	$ 80,000	$ 100,000	$ 100,000	$ 150,000	$ 100,000	$ 270,000	$ 215,000	$ 385,000

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Summary

- Lung and Liver Fibrosis are unmet needs with high TAM.
- Buto uniquely develops First-In-Class ShcIs that have potent anti-fibrotic effects.
- Buto moves faster than competitors with 4 proprietary assays of ShcI potency for rapid drug development.
- Shc 301 reduces lung fibrosis in man and mouse, more potently than standard-of-care nintedanib and pirfenidone.
- Shc 301 has excellent ~10X therapeutic index.
- Buto improved B-301's potency >100X with molecule B-240, B-240 has good PK.
- Buto owns composition of matter patents on B-301 and many other New Chemical entity ShcI scaffolds.
- Buto seeks Investment /partnerships to develop B-240 as an anti-fibrotic clinical candidate.

Buto

Buto Team

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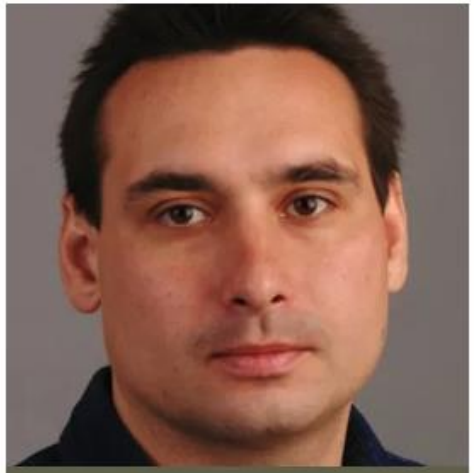
CEO

Sundeep Dugar, PhD

CSO



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Board Member

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