Online Supplement
Recombinant Alpha-1 Antitrypsin–Fc Fusion Protein INBRX-101 in Adults With Alpha-1 Antitrypsin Deficiency: A Phase 1 Study

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Supplementary Table 1. Approving Independent Ethics Committees or Institutional Review Boards (IRB) at Study Sites

Site number	Principal investigator	Site	Approving committee
101	Brantly	University of Florida College of Medicine	WIRB
102	Campos	University of Miami Miller School of Medicine	WIRB
103	Kueppers	Temple University – of the Commonwealth System of Higher Education	Temple University IRB
108	Brown	Indiana University	Indiana University IRB
109	Devine	The University of Texas Health Science Center at Tyler	The University of Texas Health Science Center at Tyler – IRB
110	Kuhn	UC Davis Health	UC Davis Medical Center
111	Farah	Hannibal Clinic	WIRB
301	Mahadeva	University of Cambridge	Edgbaston Research Ethics Committee
302	Turner	University Hospital Birmingham NHS Foundation Trust	University Hospital Birmingham NHS Foundation Trust
303	Hopkinson	Royal Clinical Research Facility, 1st Floor Fulham	West Midlands – Edgbaston Ethics Committee

		Wing	
401	Cole	New Zealand Clinical Research	Heath and Disability Ethics Committee
402	Chang	Waikato District Health Board	Heath and Disability Ethics Committee
403	Veale	New Zealand Respiratory and Sleep Institute	Heath and Disability Ethics Committee

WIRB, Western Institutional Review Board.

Supplementary Table 2. AEs Related to Infusion as Determined by the Investigator

Preferred term, n (%)	Part 1 (n=24)	Part 2 (n=18)
Blood pressure increased	2 (8.3)	2 (11.1)
Pruritus	2 (8.3)	1 (5.6)
Urticaria	1 (4.2)	1 (5.6)
Chest discomfort	1 (4.2)	0
Back pain	1 (4.2)	0
Dizziness	0	1 (5.6)
Dysesthesia	0	1 (5.6)
Paresthesia	0	1 (5.6)
Flushing	0	1 (5.6)
Infusion-related reaction[a]	0	1 (5.6)

AE, adverse event.

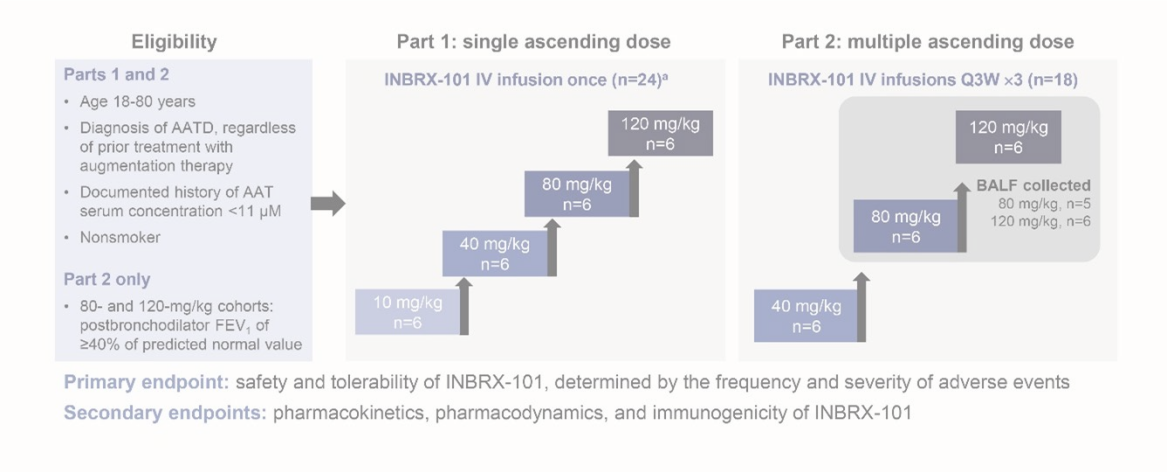
[a] Verbatim term: “back pain during infusion.”

Supplementary Table 3. Descriptive Statistics of INBRX-101 PK Parameters in Part 2

PK parameter	INBRX-101 dose cohort		
	40 mg/kg Q3W × 3 (n=6)	80 mg/kg Q3W × 3 (n=6)	120 mg/kg Q3W × 3 (n=6)
C_{max}, mean (SD), μM	7.8 (0.95)	17.4 (1.95)	23.5 (6.71)
T_{max}, median (range), days	0.042 (0.02-0.08)	0.021 (0.02-1.00)	0.031 (0.02-0.08)
Observed AUC_{inf}, mean (SD), day•μM	315.5 (19.40)	647.4 (133.66)	892.1 (119.02)
Half-life lambda z, mean (SD), days	15.7 (1.81)	16.8 (3.77)	18.2 (3.02)

AUC_{inf}, area under the plasma drug concentration-time curve to infinity; C_{max}, maximum concentration; PK, pharmacokinetic; Q3W, every 3 weeks; T_{max}, time to C_{max}.

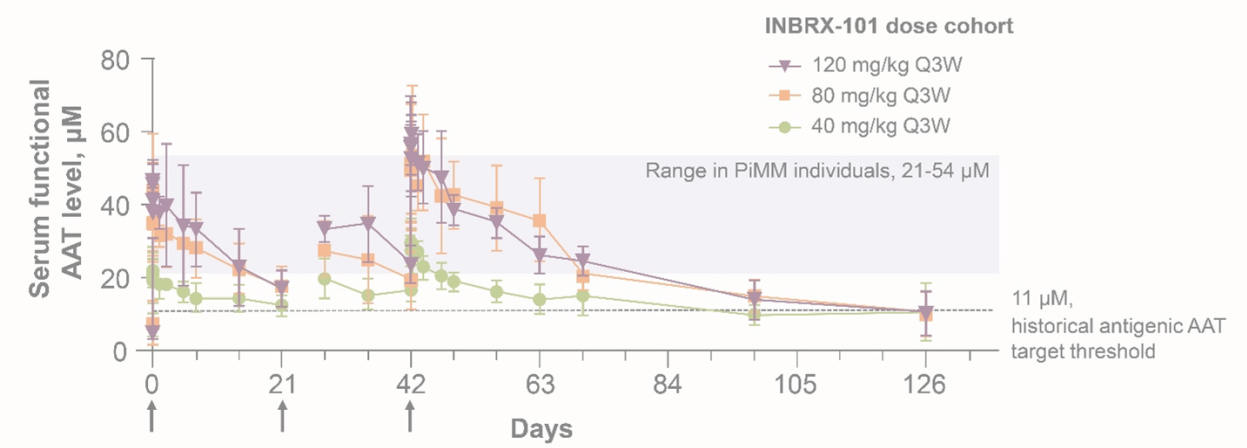
Supplementary Figure 1. Study Design



[a] Patients in part 1 could continue in the study to participate in part 2; patients were monitored for a minimum of 12 weeks after study drug administration before they entered part 2. Patients could participate in part 2 without having participated in part 1.

AAT, alpha-1 antitrypsin; AATD, alpha-1 antitrypsin deficiency; BALF, bronchoalveolar lavage fluid; FEV_1, forced expiratory volume in 1 second; IV, intravenous; Q3W, every 3 weeks.

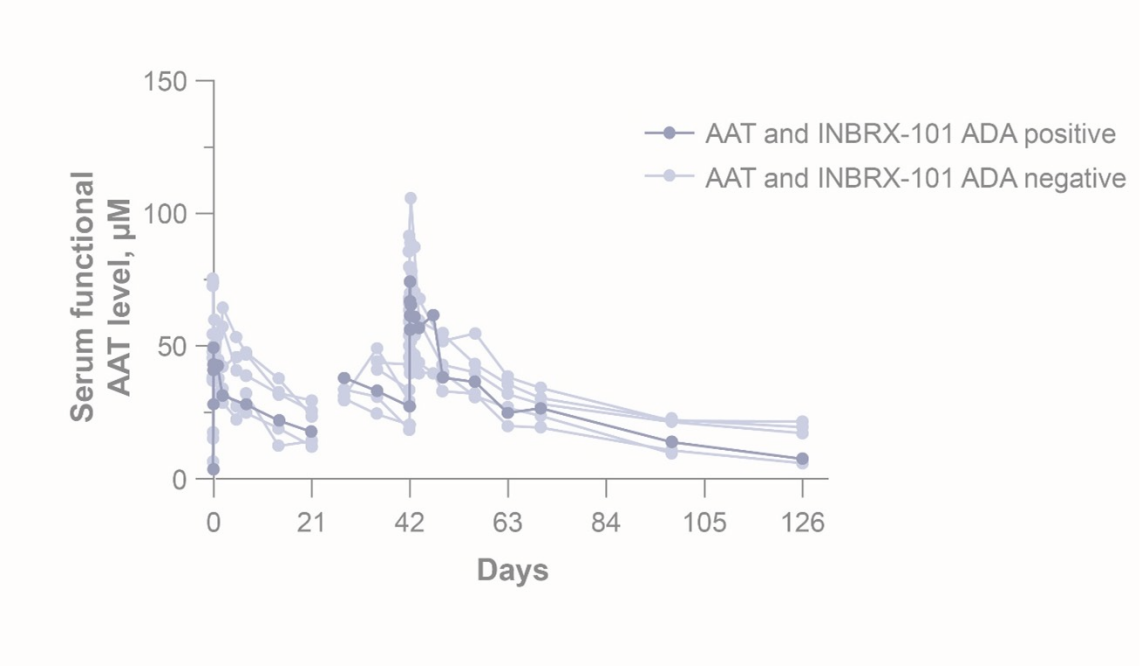
Supplementary Figure 2. Serum Functional AAT PK Profiles in Part 2 in Patients With a PiZZ Genotype



Arrows indicate dosing. Patients were assessed weekly from day 7 to day 42 to reduce patient burden. No PK samples were collected immediately following the second dose (day 21). The normal range shown in the plot was determined in 65 healthy volunteers with the PiMM genotype.[1]

AAT, alpha-1 antitrypsin; PK, pharmacokinetic; Q3W, every 3 weeks.

Supplementary Figure 3. Serum Functional AAT Levels in Patients With or Without ADAs Against INBRX-101 and AAT



Patients were administered INBRX-101 at a dose of 120 mg/kg Q3W. Patients were assessed weekly from day 7 to day 42 to reduce patient burden. No PK samples were collected immediately following the second dose (day 21).

AAT, alpha-1 antitrypsin; ADA, antidrug antibody; Q3W, every 3 weeks.

References

1. Veale A, Farah H, Mahadeva R, et al. Recombinant AAT-Fc fusion protein INBRX-101 achieves normal serum AAT levels in patients with alpha-1 antitrypsin deficiency (AATD). *Eur Respir J.* 2022;60(suppl 66):3599.