

Peter Dogterom<sup>1</sup>, Khalid Abd-Elaziz<sup>1</sup>, Wytze Aalbers<sup>1</sup>, Theodore E. Liston<sup>2</sup>, Lisa Manna<sup>2</sup>, Mark Matson<sup>2</sup>  
and William Korinek<sup>2</sup> <sup>1</sup>QPS Netherlands, <sup>2</sup>Astrocyte Pharmaceuticals, Groton, CT, USA

## BACKGROUND

AST-004 is a small molecule being developed by Astrocyte Pharmaceuticals. AST-004 acts via a novel cerebroprotective mechanism, namely the activation of adenosine A1 and A3 receptors (A1R and A3R) expressed on astrocytes, leading to enhanced mitochondrial energy production, and the promotion of multiple intrinsic healing mechanisms. AST-004 has been identified in human CSF and is a blood-brain barrier penetrant.

## METHODS

- ▶ Double blind placebo-controlled adaptive study design in healthy volunteers
- ▶ Enrolled 24 subjects
- ▶ Open label cohort with CSF collection, multiple timepoints
- ▶ AST-004 loading dose infused over 10 min followed by continuous infusion over 6 hrs
- ▶ Predefined plasma exposure with mean  $C_{max}$  of  $\geq 2500$  ng/mL (this exceeds efficacy exposures seen preclinically)

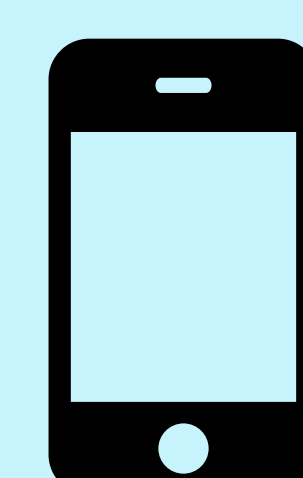
## RESULTS and CONCLUSIONS:

Following dosing regimens were given:

Cohort	n on active	loading dose (mg)	maintenance dose (mg/hr)
1a	3	100	30
2a	3	100	80
3a	3	130	130
4a	3	130	180
4b	3	130	180
5a	4	130	180

- ▶ All treatments were safe and well tolerated
- ▶ PK of AST-004 was dose proportional
- ▶ Final dose: fast steady state safely reaching highest plasma and CSF concentrations of 3642.18 and 231.40 ng/ml, respectively
- ▶ Data confirms AST-004 plasma and CSF concentrations associated with significant preclinical efficacy can be safely achieved in humans and will advance to additional testing of safety and efficacy in Phase 2 clinical studies

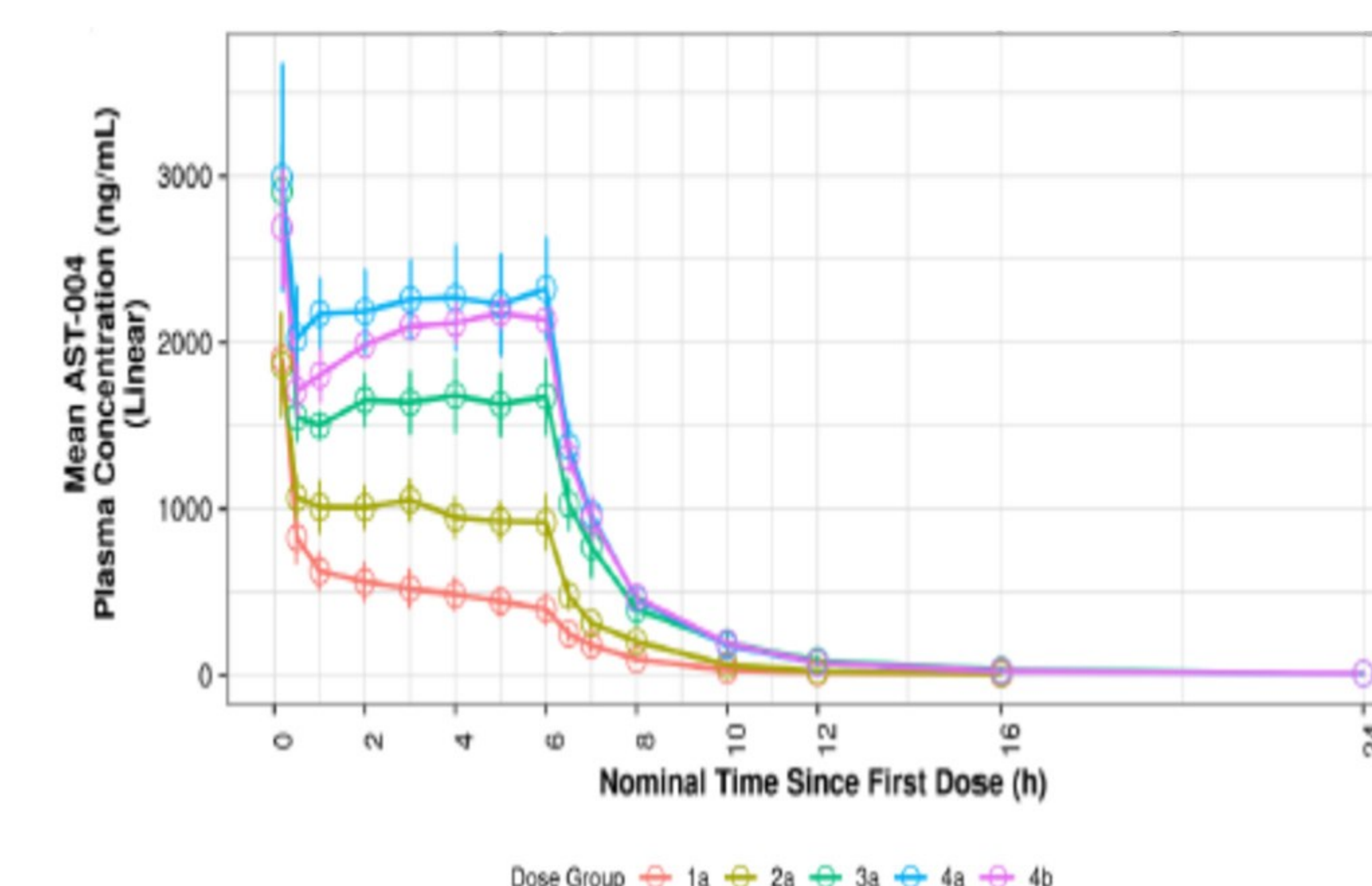
**AST-004, a novel cerebroprotective agent, is safe and well tolerated in healthy volunteers at plasma and CSF exposures associated with pre-clinical efficacy**



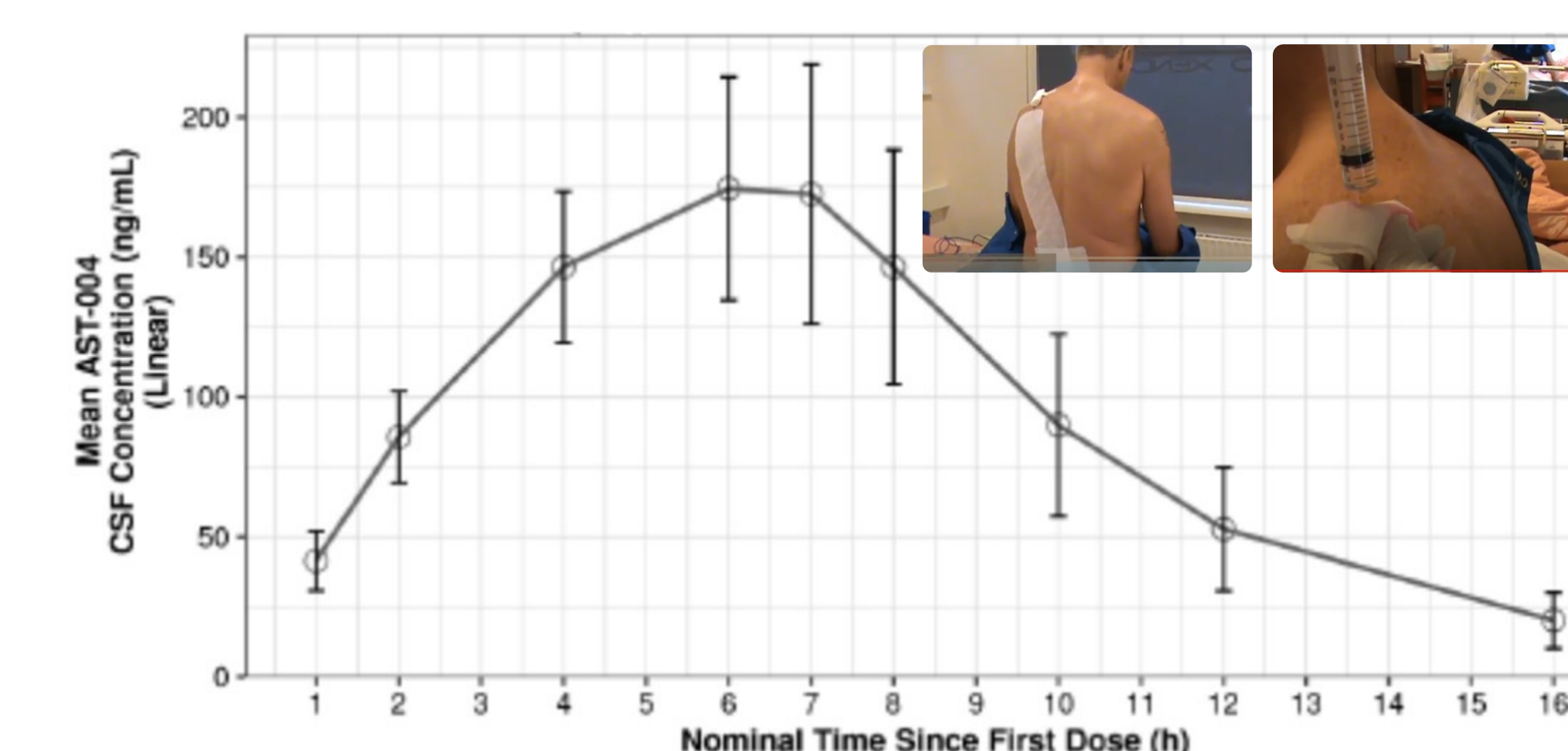
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Arithmetic mean AST-004 plasma concentration – time profiles



Arithmetic mean AST-004 CSF concentration – time profile (CSF cohort)



Arithmetic mean AST-004 plasma concentration – profile (CSF cohort)

