Astrocyte Pharmaceuticals 2023 Q4 Investor Update

To Astrocyte Pharmaceuticals Shareholders and Noteholders,

Astrocyte continues to make progress on multiple fronts and I'm pleased to provide everyone with the following updates. The confidential standard quarterly financial statements for Q3 2023 are available for shareholders upon request.

Astrocyte had its first formal interaction with the FDA in August, another key milestone! We conducted a Pre-IND Meeting that allowed us to ask the FDA a range of questions ahead of submitting our full Investigational New Drug (IND) application. "Meeting" is a bit of a misnomer as everything is handled with an exchange of written information: we submit a request and questions, and a ~100-page briefing book, and they send us their responses. Given we had already submitted much of our preclinical data to regulatory agencies in Hungary and the Netherlands, and they approved proceeding to human studies with AST-004, we expected favorable responses from the FDA as well.

Overall, the FDA answers to our questions were favorable and they did not request any additional animal or human studies before proceeding with a Phase 2 clinical study in the U.S. They did suggest three additional minor lab studies that would help our IND application: 1) a CYP liver induction study (while we had data showing AST-004 is very unlikely to have an effect, they prefer having a definitive study; we have now done this study, and it was negative as predicted and this data will be included in the IND), 2) a more advanced whole blood clot in vitro interaction study with tPA (we provided our prior in vitro study that showed AST-004 doesn't effect tPA's enzymatic activity, but the FDA wanted us to test that AST-004 doesn't effect tPA's ability to dissolve actual human blood clots; this study is in progress and the data is showing AST-004 has zero effect on tPA, and we will include this data in the IND), and 3) they

asked for additional information and justification on possible PEG-related impurities ethylene glycol and diethylene glycol (this labwork is still in progress at our manufacturing partner and we expect to have the data to make the additional justifications in December). When we have the data from all three studies, we will submit the IND to get the FDA's formal approval to move forward with a Phase 2 clinical study.

Second, while our updates are typically centered on Astrocyte, I feel compelled to speak to some recent news stories in the field of stroke research. This quarter has seen major setbacks for two of our most advanced competitors in stroke. First, in October, the company NoNO reported their results from two Phase 3 clinical studies in stroke patients. This article describes the findings, but overall their drug nerinetide did not show a benefit in stroke patients. In parsing the data, they think they may have seen some benefit from treating very early, and/or if they re-normalize and adjust all the data in a certain way, but it's clear that their approach does not have broad potential. Importantly for Astrocyte, there are several lessons learned from their clinical trial design, first and foremost of which is that they only treated slow-progressing stroke patients with good collateral blood circulation to the ischemic area (patients that do better with current care) – not a great design. They likely needed to do this because their drug has a half-life of ~90 seconds and isn't likely to reach the distressed ischemic tissue in need – not a great drug. Our planned Phase 2 stroke trial will focus on fast-progressing stroke patients with poor collateral circulation who do poorly with current care and have the most medical need (and who have the best chance for a good drug to show a treatment effect).

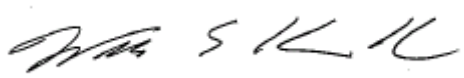
The other stroke company in the news is ZZ Biotech. The company had interesting Phase 2 data using their drug 3K3A-APC, and this summer started a 1,400 stroke patient Phase 3 clinical study, entirely funded by the NIH StrokeNet. This week there were some very serious allegations of misconduct relating to both the founding preclinical research (mostly conducted in the founder's lab) and the Phase 2 clinical trial. There will undoubtedly be further investigations into all their research and a likely halt to their Phase 3 study. While there can be bad actors in any industry, the Astrocyte team and I are all shocked by the story. I want to emphasize that the Astrocyte team, and all our collaborators and partners with whom we have worked in this space, have always and will always operate with the highest integrity. We have

systematically done the hard research to thoroughly characterize our drug, and most of our key studies conducted by third parties. We will continue to emphasize the professionalism of the Astrocyte team and our research in all interactions.

For those of you who follow the Astocyte X/Twitter account (@AstrocytePharma), you may have already seen these stories, but I wanted to be sure to highlight them for all of you. The New York Times did two major articles recently: the first on hidden wounds from U.S. soldiers firing long-range M777A2 howitzer cannons (article link here), and the second on hidden wounds in youth football injuries (article link here). As a warning, both articles are profoundly disturbing and heartbreaking. However, I do encourage you to read/watch them as they really help to emphasize the broad and serious impacts of repeated head injuries, and the substantial impact that AST-004 could have on many, many people's lives.

As many of us take a break during the upcoming Thanksgiving holiday to reflect on the aspects of our lives for which we are thankful, I would like to express my deep gratitude for the research conducted at Astrocyte. I am very thankful we have the opportunity to develop a treatment that could help so many people, for the professionalism and high integrity exhibited by our team, as well as the support we receive from all of you that enables us to advance this potentially life-saving medication!

With sincere thanks,



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