August 8, 2021

Dear InSitu Biologics Shareholders,

Every so often, the InSitu Biologics Team is acutely reminded why our mission of providing an opioid-free solution for patients experiencing post-operative pain is so critical.

US Overdose Deaths Soared to All-Time High in 2020 – A 30 percent rise in fatalities was driven by opioids

Our Team and Investors are very passionate about addressing the opioid epidemic that continues to burden our society and particularly harms the young, who are often exposed to opioids through painful surgeries.

The summer has been very productive – we received positive pre-clinical animal study results on our lead product (INSB200™), had positive regulatory interactions with the FDA, further developed our manufacturing capabilities, and made progress towards future funding of the Company.

With the completion of recent multi-species animal studies, the number of InSitu animal study subjects has grown to over 265. In rat and canine model comparisons with Exparel® (our main competitor in peripheral nerve block), INSB200™ delivered both superior upfront nerve block and extended-release results, all while using a safer drug molecule.

- Compared to Exparel®, INSB200™'s upfront nerve block is **11x greater (rat)** and **24x greater (dog)**
- Extended-release pain control **lasts 3x longer** than Exparel® (72+ hours vs ~24 hours)
- Drug delivery capability is up to **4.8x greater** than Exparel®
- INSB200™'s drug molecule (ropivacaine) has **safer toxicity** characteristics and **better preserves motor function** than Exparel®'s drug molecule (bupivacaine)

Our growing body of pre-clinical animal work continues to confirm the superior potential of INSB200™ to be both safer and more effective than Exparel®.

In late July we requested a pre-investigational new drug (pre-IND) meeting with the FDA and submitted a detailed Company packet to the Agency. FDA granted us the pre-IND exchange, confirmed receipt of our packet, and will provide us a response by September 7th. The pre-IND process is a precursor to a formal IND submission, which we have planned for 2022. Receiving IND approval by the FDA will clear the path for us to begin human clinical trials.

We are working closely with our development and manufacturing partner, Lifecore Biomedical, to ensure that INSB200™ is manufactured safely, consistently, and is of the highest quality. FDA has mandatory requirements that control the chemistry and manufacturing of drug products – our work with Lifecore will allow us to provide evidence of these important safety measures prior to starting human clinical trials.

Our partner investment bankers in our Series A funding round are busy introducing us to funding sources around the globe. Over the next few months, we expect to select a lead investor and form a syndicate to complete our Series A round, which will fund InSitu Biologics through the first phase of human clinical trials in 2022.

The InSitu Team is so grateful for the excellent progress we've made in 2021! We are confident in our abilities to overcome any hurdles, secure adequate funding, and continue the strong upward trajectory of the Company. Thank you again for being a vital component of our success!

As always, feel free to contact us at any time at info@insitubiologics.com.

Best regards,

Kevin Bassett
President and CEO
InSitu Biologics, Inc.