



December 28, 2021

Dear InSitu Biologics Shareholders,

We recently shared a report that US overdose mortality surged to a record 93,000 fatalities in 2020. This tragic trend has continued, with more than 100,000 Americans dying of drug overdoses from May 2020 to April 2021. This [US News and World Report article](#) is particularly poignant for our Team, as it features InSitu Biologics' home state of Minnesota and the nearby college town of Mankato.

2021 has been an excellent year for InSitu Biologics – since our last update in August, we have the following accomplishments to celebrate:

- Received positive pre-IND feedback from the FDA in September which confirmed the strategy and regulatory path for our IND application later next year, paving the path to begin Phase I human clinical trials;
- Continuing development of our lead product, INSB200™, as our scientists refine the formulation for optimal performance and safety characteristics prior to human use;
- Gains in process development work with LifeCore Biomedical, our contract manufacturing partner, as we ensure INSB200™ can be manufactured consistently, meet strict standards required by the FDA and, most importantly, satisfy safety and efficacy requirements for our patients;
- Three new patent applications as we continue to bolster our intellectual property position and further protect our technology and trade secrets;
- Publication and presentation of INSB200™ data by our Chief Medical Officer (Mark Ereth, MD) at the American Society of Regional Anesthesiology fall meeting (with accompanying “[Best of Meeting](#)” award)
- Securement of exclusive worldwide rights to cancer therapeutics via sub-license of 17 Cleveland Clinic Foundation patents, allowing InSitu Biologics entrée into the drug delivery field for cancer; and
- Close of an additional \$3M in institutional funding (to bring our total 2021 raise to \$6.5M).

You may have noticed our updated insitubiologics.com website reflecting a broadening of our vision to include drug delivery of not only pain management products, but also cancer and eventually antibiotic drug delivery solutions.

As we approach 2022, we are as excited as ever about what lies ahead for InSitu Biologics. In January we will be moving into a new office in Oakdale, Minnesota, joining the [Incubology](#) community which caters to early-stage companies and offers world-class security, services, and amenities. We will continue our longstanding relationship with LifeCore Biomedical as we progress towards human trials and ensure a solid manufacturing footing. Our scientists are completing testing of INSB200™ that will optimize the balance between its performance and safety as we strive for the best pain management solution for post-operative patients. Our bankers will continue to introduce us to the best financing opportunities worldwide as we work towards closing our \$15M-\$20M series A round.

Businesses have been challenged in 2021 by constant supply chain disruptions and travel restrictions that prohibit critical face-to-face interactions – InSitu Biologics has been acutely affected by many of these pandemic-induced difficulties. Despite the Omicron variant sweeping across the world, we are very optimistic about the prospect of getting beyond the constant threat of COVID in the near future as we continue our work and progress towards our goals.

As always, we are so grateful for our investors and wish you and your families the happiest of Seasons Greetings! Please direct any questions/comments to info@insitubiologics.com for a timely response.

Best regards,

Kevin P. Bassett

Kevin Bassett
President and CEO