Diffusion Pharmaceuticals Inc.

May 12, 2017

Dear Diffusion Stockholders,

January 2016 marked the transition of privately held Diffusion Pharmaceuticals LLC into publicly traded Diffusion Pharmaceuticals Inc. through a reverse merger with the former RestorGenex Corporation. While 2016 presented challenges, the Company has weathered the storm and is sailing into a promising 2017. Our initial plan moving into 2016 was to raise a secondary public offering in the then-robust public biotech financing market, leveraging Diffusion's successful Phase 2 clinical trial of trans sodium crocetinate (TSC) in glioblastoma brain cancer (GBM) and our new status as a public company. The funds would be used to launch the TSC Phase 3 registration clinical trial in GBM, as well as advance TSC's uses in other cancers such as pancreatic and brain metastases, and explore its uses in non-oncology indications such as stroke. Unfortunately, around the time we became a publicly-traded entity, the 2015 biotech "boom" turned into an historically severe financing "bust" that persisted through 2016. The many investment banks with whom we were in discussions advised us at the time that our planned capital raise was not feasible under existing market conditions.

While remaining vigilant to opportunities to raise capital in the public and private markets, we embarked on a plan which consisted of 1) conserving and "stretching" our cash on hand (approximately $8.5 million following the merger), without compromising company operations; 2) progressing our Phase 3 ready GBM program, with an emphasis on optimizing the Phase 3 study design and meeting FDA requirements for Phase 3 clinical testing and drug manufacturing, and 3) raising Diffusion's profile in its new public marketplace, which we accomplished by up-listing our stock from OTC to NASDAQ, recruiting a high-profile public biotech figure to Diffusion's Board of Directors, establishing a prestigious new scientific advisory board and growing our patent estate.

Our search for financing culminated in the successful completion of our $25 million Series A Preferred Stock offering which closed in March of 2017. This Series A Preferred financing was oversubscribed, demonstrating a continuing demand by an accessible segment of potential investors. As reflected in the accompanying Proxy Statement, the Company is seeking stockholder approval for a Series B Preferred round this summer to acquire the additional financial resources needed to commence the TSC Phase 3 GBM clinical trial described below and progress our other programs. I urge you to approve this financing, thus keeping the Company on track to launch its critical Phase 3 trial of TSC in GBM patients later this year.

During the months leading up to the Series A offering, we continued preparations for the Phase 3 trial. After our End-of-Phase 2 FDA meeting, the Agency required us to complete two critical steps prior to the beginning of our planned Phase 3 trial, which were 1) to successfully complete a battery of extended toxicology studies in both dogs and rats to support our planned Phase 3 human dosing schedule, and 2) to participate in a separate meeting with the FDA in which they would review our manufacturing processes for the Phase 3 clinical and commercial quantities of TSC. These steps are now complete thanks to the exceptional efforts of the Diffusion

operational team, who successfully executed two demanding technical programs to the levels of FDA-required quality.

Meanwhile, the Diffusion clinical operations team focused on optimizing the design and cost of the TSC GBM Phase 3 study. Our Phase 2 study showed a 37% increase in overall survival at two years in the TSC-treated group compared to historical controls, and our original Phase 3 study design was targeted at reproducing or exceeding this result in a larger number of patients in a randomized, controlled trial. During 2016 and into 2017 we revisited this design strategy with the goal of decreasing the number of patients (and thus the cost), while increasing our probability of a successful outcome. One way to do this was to focus the patient population in the Phase 3 study toward that sub-segment of Phase 2 patients which had shown the strongest positive responses.

Our revised strategy targets the use of TSC in that subset of newly diagnosed GBM patients who are considered by their medical team to be inoperable, often because of their tumor's location in the brain. In our Phase 2 trial we had allowed the enrollment of such inoperables – comprising 25% of the study total -- and the results in that sub-group showed a nearly four times increase in the likelihood of their survival at two years compared to the inoperable patients in the untreated control group, which we believe is a highly meaningful signal. Our theory for this result is that because the vasculature surrounding the tumor remains undisturbed by surgery, TSC may be better able to help drive re-oxygenation of hypoxic tumor tissue, permitting our drugs' novel mechanism of action to more effectively enhance radiation and/or chemotherapy. We believe focusing on this patient sub-group in Phase 3 should provide real cost savings by reducing the needed number of patients from over 400 to around 230, while the strength of the Phase 2 efficacy signal should make the showing of significant clinical gain in Phase 3 more likely.

Another benefit of targeting the inoperable GBM population is that these patients are largely excluded from other GBM clinical trials with whom we might otherwise be competing for patients, highlighting the unmet need and desperate plight of these patients, and potentially lessening our recruitment challenges. Clinicians have agreed with this revised strategy and we are now working with the medical community, our contracting vendor/partners and the FDA to finalize the applicable protocol and start the study later this year.

Our other targeted oncology indications – pancreatic cancer and brain metastases – have been the focus of internal program development (in the form of manufacturing, FDA interaction and protocol design), as well as partnering discussions with various parties, both US and international, regarding possible strategic relationships that could provide resources useful in progressing these programs. We feel that partnering may be an advantageous way to carry these programs forward, and discussions are continuing.

As for our non-oncology programs, we are currently in discussions with doctors from UCLA and the University of Virginia, with whom we have established a joint team dedicated to developing a program to test TSC in the treatment of stroke.

In November of 2016, we achieved an up-list of the Company's stock from the OTC to the NASDAQ marketplace. This NASDAQ up-list greatly increases the number of investors now

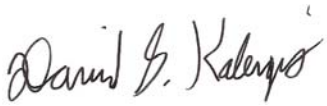
eligible to invest in Diffusion and provides a level of credibility above our previous position as an over-the-counter stock. While our NASDAQ listing also subjects us to additional levels of regulatory authority, we believe these complexities are worth it to place our breakthrough TSC small molecule platform onto a sound financial structure that can meet the challenges of Phase 3 clinical trials and ultimate commercialization.

During 2016, the Company added a high profile biotech figure, Mr. Isaac Blech, to its Board of directors, and established a new scientific advisory board featuring experts in a range of unmet medical needs characterized by hypoxia. A significant US patent was allowed and we also were featured in a number of scientific publications/abstracts in prestigious scientific venues, particularly in the areas of GBM and emergency medicine. More information on all of these developments is available in the press release section of our Website at www.diffusionpharma.com.

In closing, I want to extend my sincere thanks to all our investors for your continued support. The Diffusion team remains fully committed to advancing the clinical development of TSC for the improved treatment of life-threatening unmet medical needs, fulfilling the promise of our breakthrough therapeutic and providing a significant return to our stockholders.

I encourage you to read the enclosed Proxy Statement and related materials and vote on the proposals contained therein. I also look forward to seeing many of you at our Annual Meeting in Charlottesville on June 15, 2017

Sincerely,



David G. Kalergis
Chairman and CEO

THIS LETTER IS NOT AN OFFER TO SELL OR THE SOLICITATION OF AN OFFER TO BUY SHARES OF OUR PREFERRED STOCK, SHARES OF OUR COMMON STOCK OR ANY OTHER SECURITIES.

To read the complete 2017 10-K filing please visit

http://investors.diffusionpharma.com/Doc/Index?did=40490418