Diffusion Pharmaceuticals Inc.

DIFFUSION PHARMACEUTICALS INC.

2017 ANNUAL REPORT

FORM 10-K

Diffusion Pharmaceuticals Inc.

April 30, 2018

Dear Diffusion Stockholders,

In 2017, Diffusion Pharmaceuticals Inc. reached all of the milestone goals necessary for successful initiation of our Phase 3 clinical trial in newly diagnosed, inoperable GBM brain cancer patients. These goals were many and included clinical trial study design, obtaining FDA sign-off, study-drug manufacturing, vetting and selection of the various contract research organizations, and trial site selection involving interactions with the doctors and hospitals which actually provide the treatment and care for the patients in our Phase 3 trial.

Moving into a Phase 3 clinical trial on-time and in-budget is a remarkable accomplishment, for which I extend a warm thank you to the Diffusion staff and to Diffusion's investors, all of whom had a critical role in making this happen. Enrollment and dosing is continuing, along with the initiation of new study sites, as we work to complete enrollment of the first cohort of patients in the trial design and expand the study.

We were financially supported in these accomplishments by a private financing through the Maxim Group which generated gross proceeds of $25 million. Shortly after the close of the year, we raised an additional $12 million through a public offering conducted by H.C. Wainwright & Company LLC. These funds will be directed toward our Phase 3 GBM trial and other oncology programs, as well as toward exploration of promising non-oncology opportunities, such as stroke.

Following the public offering, our stock moved below the $1.00 per share price required by Nasdaq to retain our listing status. De-listing can be avoided, however, via a reverse stock split, which would have the effect of bringing the stock price above the required $1.00 per share mark. As reflected in the accompanying Proxy Statement, we are seeking stockholder approval for the flexibility to conduct such a reverse stock split later in the year, if necessary. I urge you to approve the Board of Directors' proposal authorizing a reverse stock split, protecting our ability to retain its Nasdaq listing.

Our other targeted oncology indications – pancreatic cancer and brain metastases – have been the focus of internal program development 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.

With our non-oncology programs, we continue to work with physicians from the University of Virginia, UCLA, and other institutions with whom we have established a joint team dedicated to developing a program to test TSC in the treatment of stroke. In January of this year an abstract titled "PreHospital Acute Stroke Therapy with Trans Sodium Crocetinate (PHAST-TSC)," was presented at the International Stroke Conference in Los Angeles. With input from authors affiliated with UVA, UCLA, University of Southern California, and Diffusion Pharmaceuticals Inc.,

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the abstract described the design and rationale for the planned Phase 2 PHAST-TSC study, highlighting the potential benefits of TSC in patients with acute ischemic or hemorrhagic stroke in a pre-hospital (ambulance) setting. We are eager to start this trial pending receipt of financing.

During 2017, we were extremely pleased to add Dr. Robert Ruffolo to our Board of Directors. Bob was formerly President of Research and Development at Wyeth Pharmaceuticals and Corporate Senior Vice President of Wyeth (now Pfizer). In addition, Biotech industry veteran Bill Hornung, previously with PTC Therapeutics, Elan Pharmaceuticals, The Liposome Company and Contravir Pharmaceuticals was named our Chief Business Officer. Also added to our team was Dr. Kimberly Driver, who became our Director of Finance.

A significant US patent was allowed in 2017, expanding coverage of the therapeutic use of TSC and other related compounds to five hypoxia-related conditions including congestive heart failure, chronic renal failure, acute lung injury (ALI), chronic obstructive pulmonary disease (COPD), and respiratory distress syndrome (RDS). Our patent estate currently includes the use of TSC in oncology, stroke, and neurodegenerative diseases such as Alzheimer's.

More information on all of these developments is available in the press release section of our website at www.diffusionpharma.com.

Again, 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 return to our stockholders.

I encourage you to read the enclosed Proxy Statement and related materials and vote in favor of the proposals contained therein. I also look forward to seeing many of you at our Annual Meeting in Charlottesville on June 14, 2018

Sincerely,

David G. Kalergis
Chairman and CEO