149 Fifth Ave, Suite 500
New York, NY 10010

Protagenic Therapeutics, Inc. Update

May 26, 2017

Dear Fellow Shareholders,

In the eight months since our last update letter in September 2016, we have advanced our programs towards a potential IND filing, filed a Registration Statement on Form S-1 with the SEC on behalf of certain stockholders who purchased Series B Preferred Stock in our private placement, and explored the expansion of our development program into a second main therapeutic area – addiction cessation therapy. In addition, we are exploring non-dilutive funding opportunities.

As reported previously, our most advanced drug candidate, PT00114, continues to show encouraging signals to potentially treat depression and anxiety, as well as other mood and addiction-related diseases. A chronic anxiety efficacy study is one of the two new studies we recently initiated. This study is being conducted for us at a contract research organization (CRO) in Europe. Our objective is to independently validate the activity of PT00114. Our analysis of the outcomes data received so far indicates beneficial effects of TCAP in reducing stress-related behaviors in a set of well-established rodent behavior tests known the "chronic social defeat" model. These studies demonstrated that PT00114 modulates behavioral responses under stress conditions in rodents. We are encouraged by these results.

A second study, aimed at demonstrating efficacy of PT00114 in treating pathologic drug addiction, is underway at another CRO, which we selected because it is a leader in the neuroscience space, particularly in behavioral studies of addiction. In a previous study, we saw that PT00114 reduced cocaine seeking activity in stressed rodents. Once replicated, the cocaine studies will be followed by those designed to demonstrate that PT00114 may have the potential to ameliorate drug seeking activity in an opiate model of addiction.

We anticipate that our current efforts will result in an IND submission to the FDA in the first half of 2018 if both efficacy and toxicology studies have a positive outcome. Upon a successful IND submission and acceptance by the FDA, we anticipate being able to commence Phase I clinical trials in 2018.

In summary, last year we completed a reverse merger and a private financing, and since then have been executing our plan to move us closer to our expected filing of an IND application with the FDA. Our R&D team is carrying out the steps to accomplish these tasks, including outsourcing our most recent preclinical efficacy studies. In parallel, we continue to add to our intellectual property estate and will strategically add to our IP portfolio over time. We are motivated by our progress to date and for the potential of our novel lead compound to change the way mood disorders are treated.

Garo H. Armen, Ph.D.
Chairman of Protagenic Therapeutics, Inc.

Notes:
As previously announced, Atrinsic, Inc. completed a reverse merger with Protagenic Therapeutics, Inc. on February 12, 2016. The resulting company adopted the name Protagenic Therapeutics, Inc. on June 17, 2016. Neuroactive peptide drug development is the sole line of business for the ongoing company.

This shareholder letter shall not constitute an offer to sell or the solicitation of an offer to buy any securities. This shareholder letter is being issued pursuant to and in accordance with Rule 135c under the Securities Act of 1933, as amended.

About Protagenic Therapeutics, Inc.
Protagenic Therapeutics, Inc. (OTCQB: PTIX) is a pre-clinical biopharmaceutical company endeavoring to develop first-in-class neuro-active peptides into human therapeutics to treat anxiety, treatment-resistant depression, and other disorders. For more information, please visit http://www.protagenic.com. (This website contains stale information and does not appear to include XBRL and SEC filings)

Cautionary Statement Relating to Forward - Looking Information for the Purpose of "Safe Harbor" Provisions of the Private Securities Litigation Reform Act of 1995

This letter contains forward-looking statements which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Statements contained in this letter, other than statements of historical fact, constitute "forward-looking statements." The words "expects," "believes," "anticipates," "estimates," "may," "could," "intends," "potential," "possible," "might," "look forward," and similar expressions are intended to identify forward-looking

statements. The forward-looking statements in this letter do not constitute guarantees of future performance. Investors are cautioned that statements in this letter which are not strictly historical statements, including, without limitation, statements regarding the development of the Company's IND-enabling trials, constitute forward-looking statements. Such forward-looking statements are subject to a number of risks and uncertainties that could cause actual results to differ materially from those anticipated. These risks and uncertainties include, but are not limited to, risks associated with: market conditions; our capital position; our ability to compete with larger, better financed pre-clinical biopharmaceutical companies; our anticipated timing for preclinical development, regulatory submissions, commencement and completion of clinical trials and product approvals; interpretations of current laws and the passages of future laws; our dependence on product candidates, which are still in an early development stage; our limited operating history; our ability to raise additional capital through the sale of shares of our common stock; our ability to obtain, maintain and protect intellectual property rights; the risk of litigation regarding our intellectual property rights or the rights of third parties; our ability to internally develop new inventions and intellectual property; our reliance on our license agreement with the University of Toronto; our ability to retain key executives; our lack of a sales and marketing organization and our ability to commercialize products, if we obtain regulatory approval; our ability to hire and retain skilled personnel; acceptance of our business model by investors; the accuracy of our estimates regarding expenses and capital requirements; our ability to adequately support growth; and other risks detailed in our filings with the SEC, including our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K. These forward-looking statements speak only as of the date made. We assume no obligation or undertaking to update any forward-looking statements to reflect any changes in expectations with regard thereto or any change in events, conditions or circumstances on which any such statement is based. You should, however, review additional disclosures we make in our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K filed with the SEC.