FOR IMMEDIATE RELEASE

Protagenic Therapeutics Receives FDA Pre-IND Feedback Supporting New IND for PT00114 in Generalized Anxiety Disorder

FDA raises no objection to the Company's planned Phase 1 program design, dose-escalation approach, or CMC and nonclinical packages; IND submission remains on track for the fourth quarter of 2026

NEW YORK, NY –August 20, 2026— (ACCESS Newswire) - Protagenic Therapeutics, Inc. (OTCQB: PTIX), a clinical-stage biopharmaceutical company developing novel peptide-based treatments for stress-related neuropsychiatric disorders, today announced that it has received written responses from the U.S. Food and Drug Administration (FDA) to its Type B pre-Investigational New Drug (pre-IND) meeting request for PT00114, the Company's leading investigational neuropeptide product candidate, for the treatment of generalized anxiety disorder (GAD).

In its written responses, FDA identified no clinical hold issues and raised no objection to the overall design of the Company's planned three-part Phase 1 program, including its dose-escalation approach and safety review governance, and did not identify deficiencies that it indicated would preclude submission of an IND. FDA also indicated that the Company's proposed potency and comparability strategy, together with its chemistry, manufacturing, and controls (CMC) and nonclinical packages, appear reasonable to support an IND submission.

The new IND builds directly on PT00114's completed Phase 1 single ascending dose and multiple ascending dose studies, which were conducted outside the United States. In those studies, PT00114 was reported to be well tolerated across all dose levels studied, with no serious adverse events reported. These studies were conducted in a limited number of healthy volunteers outside the United States and were not conducted under an IND. FDA's guidance allows the Company to carry this clinical experience forward into a US clinical development program in GAD, incorporating refined CMC specifications and expanded dose cohorts into the upcoming submission.

Based on this feedback, Protagenic plans to submit the IND before the end of 2026 and is targeting first patient dosing in the first half of 2027, pending FDA review and clearance.

According to the National Institute of Mental Health, generalized anxiety disorder affects approximately 6.8 million adults in the United States in a given year. No new medicine has been approved by FDA specifically for GAD in nearly two decades, and many patients do not achieve an adequate response to first-line treatment.

"FDA's feedback gives us a clear path to submitting a new IND for PT00114 in generalized anxiety disorder, and it reflects the clinical and manufacturing groundwork our team has completed to date," said Bill Nichols Jr., President of Protagenic Therapeutics. "In preclinical studies, PT00114 has been observed to act directly on the brain's stress response system rather than simply blunting symptoms, and we believe that mechanism, if confirmed in clinical trials, could represent a meaningfully different approach for a patient population this large and this underserved. Submitting this IND is our next milestone, and we look forward to continuing to work with FDA."

About PT00114 PT00114 is Protagenic's lead clinical asset, a first-in-class investigational neuropeptide targeting the teneurin C-terminal associated peptide (TCAP) pathway for the treatment of stress-related neuropsychiatric disorders. PT00114 has completed single ascending dose and multiple ascending dose Phase 1 studies in healthy volunteers outside the United States, in which it was reported to be well tolerated with no serious adverse events reported. Preclinical studies of PT00114 have shown activity in validated animal models of anxiety, depression, substance use, and post-traumatic stress. PT00114 is an

investigational product candidate that has not been approved for any use by FDA or any other regulatory authority, and its safety and efficacy have not been established.

About Generalized Anxiety Disorder Generalized anxiety disorder is a common and often chronic psychiatric condition characterized by persistent, excessive worry that interferes with daily functioning. Current standard-of-care treatments, including SSRIs, SNRIs, and benzodiazepines, are associated with delayed onset of action, incomplete response, and tolerability or dependence concerns, underscoring the need for treatments with novel mechanisms of action.

About Protagenic Therapeutics, Inc. Protagenic Therapeutics, Inc. (OTCQB: PTIX) is a clinical-stage biopharmaceutical company dedicated to developing novel peptide-based treatments for stress-related neuropsychiatric disorders. The Company is headquartered in New York, NY.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements may be identified by words such as "anticipate," "believe," "could," "estimate," "expect," "intend," "may," "plan," "potential," "target," "will," "would," and similar expressions, and include, among others, statements regarding the implications of FDA's pre-IND written responses; the Company's plans to submit a new IND; the anticipated timing of the IND submission, FDA review, and first patient dosing; the design, initiation and conduct of the planned Phase 1 program; the sufficiency of the Company's CMC, nonclinical and potency and comparability packages; the relevance of prior ex-U.S. clinical experience; and PT00114's mechanism of action and therapeutic potential in GAD.

These statements are not guarantees of future performance and are based on management's current expectations and assumptions, which are subject to substantial known and unknown risks and uncertainties that could cause actual results to differ materially, including, among others: the risk that FDA's pre-IND advice is non-binding and that FDA may raise additional questions, request additional data, impose a clinical hold, or otherwise delay or prevent the planned program; the Company's ability to complete IND-enabling CMC, manufacturing and nonclinical activities on the anticipated timeline or at all; the risk that results from prior ex-U.S. studies in healthy volunteers, and from preclinical animal models, are not predictive of results in U.S. clinical trials or in patients with GAD; risks relating to clinical trial design, site activation, patient enrollment, retention and data integrity; the Company's need for substantial additional capital, its history of losses, and the substantial doubt about its ability to continue as a going concern described in its filings; risks relating to reliance on third-party manufacturers, contract research organizations and collaborators; risks relating to intellectual property protection and competition; risks associated with the Company's status as an OTCQB-quoted company, including limited trading liquidity, price volatility and dilution from future financings; and the other risks and uncertainties described under "Risk Factors" in the Company's Annual Report on Form 10-K for the fiscal year ended [ ] and in the Company's subsequent Quarterly Reports on Form 10-Q and Current Reports on Form 8-K filed with the Securities and Exchange Commission, which are available at www.sec.gov.

Because the Company's common stock may be considered "penny stock," the statutory safe harbor for forward-looking statements under the Private Securities Litigation Reform Act of 1995 may not be available to the Company, and the Company therefore also relies on the protections afforded by the "bespeaks caution" doctrine. Forward-looking statements speak only as of the date of this press release, and the Company undertakes no obligation to update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.

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