Actinium Pharmaceuticals, Inc.
Form 424B5
April 17, 2019

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Filed Pursuant to Rule 424(b)(5)
Registration No. 333- 216748

SUBJECT TO COMPLETION, DATED April 17, 2019

Preliminary Prospectus Supplement

(To Prospectus Dated October 24, 2017)

Shares Common Stock

Warrants to Purchase Shares Common Stock

We are offering shares of our common stock and warrants to purchase up to shares of our common stock. Each share of our common stock is being sold together with a warrant to purchase of a share of our common stock. Each full warrant will have an exercise price of $ per share and will be exercisable during the period commencing on April , 2019 and ending on April , 2021. The shares of our common stock and warrants are immediately separable and will be issued separately, but will be purchased together in this offering. The shares of our common stock issuable from time to time upon exercise of the warrants are also being offered pursuant to this prospectus supplement and the accompanying prospectus.

Our common stock is presently traded on the NYSE American under the symbol “ATNM.” On April 17, 2019, the last reported sale price of our common stock was $0.50 per share. There is no established trading market for the warrants and we do not expect a market to develop. In addition, we do not intend to apply for the listing of the warrants on any national securities exchange or other trading market. Without an active trading market, the liquidity of the warrants will be limited.

Investing in the common stock involves risks. See “Risk Factors” beginning on page S-7 of this prospectus supplement.

	Per Share and Related Warrant	Total

Public offering price	$	$

Underwriting discounts and commissions(1)	$	$

Proceeds, before expenses, to us	$	$

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(1) We have agreed to reimburse the underwriters for certain expenses. See “Underwriting.”

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the securities against payment on or about April , 2019.

Sole Book-Running Manager

William Blair

The date of this prospectus supplement is April , 2019

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About this Prospectus Supplement

This prospectus supplement and the accompanying prospectus form a part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission utilizing a "shelf" registration process. This document is in two parts. The first part is the prospectus supplement, which describes the specific terms of this offering. The second part, the accompanying prospectus, provides more general information about the securities we may offer from time to time, some of which may not apply to the securities offered by this prospectus supplement. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. Before you invest, you should carefully read this prospectus supplement, the accompanying prospectus, all information incorporated by reference herein and therein, and the additional information described under "Where You Can Find More Information" on page S-21 of this prospectus supplement. These documents contain information you should consider when making your investment decision. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent that any statement that we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus or any documents incorporated by reference therein, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus and such documents incorporated by reference therein.

Neither we nor the underwriters have authorized any other person to provide you with any information that is different. We are offering to sell, and seeking offers to buy, our securities only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the securities in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and/or the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the securities and the distribution of this prospectus supplement and/or the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

Unless the context otherwise requires, references in this prospectus supplement to “we”, “us” and “our” refer to Actinium Pharmaceuticals, Inc.

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Prospectus Supplement Summary

This summary highlights selected information about our company, this offering and information appearing elsewhere in this prospectus supplement, in the accompanying prospectus, in the documents we incorporate by reference and in any free writing prospectus that we have authorized for use in connection with this offering. This summary is not complete and does not contain all the information that you should consider before investing in our securities. You should read this entire prospectus supplement and the accompanying prospectus carefully, including the “Risk Factors” contained in this prospectus supplement, the accompanying prospectus and the financial statements and the notes thereto incorporated by reference in this prospectus supplement and the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering, before making an investment decision. This prospectus supplement may add to, update or change information in the accompanying prospectus.

Business Overview

Actinium Pharmaceuticals Inc. is a clinical-stage, biopharmaceutical company focused on developing and potentially commercializing therapies for targeted conditioning prior to cell therapies such as a Bone Marrow Transplant, or BMT, or CAR-T, a type of cellular therapy that genetically alters a patient's own T cells to target and kill their cancer cells, and for other adoptive cell therapies. In addition, we are also developing potential therapies for targeting and killing cancer cells either as single agents or in combination with other drugs. Our targeted therapies are Antibody Radiation-Conjugates, or ARC's, that combine the targeting ability of a monoclonal antibody, or mAb, with the cell-killing ability of a radioisotope to deliver radiation internally in a precise manner to potentially generate more potent efficacy and with less toxicity than radiation that is delivered externally. We are developing two clinical stage ARC programs that target the antigens CD45 and CD33, respectively, which are currently being studied in several hematologic indications. We employ our ARC's at higher doses of radioisotope intensity for targeted conditioning prior to a BMT and at lower doses for targeted conditioning, which is also known as lymphodepletion, prior to CAR-T and other adoptive cell therapies. In addition, we are pursuing development of our ARC's at low doses in combination with other therapeutic modalities such as chemotherapy, targeted agents or immunotherapy and as a monotherapy. Our ARC-based clinical programs are underpinned by our AWE or Antibody Warhead Enabling technology platform where we have data in both liquid and solid tumors, intellectual property and know-how that we intend to use to create additional ARC's targeting new antigens with multiple radioisotopes such as actinium-225, or Ac-225, and iodine-131, or I-131. Our AWE technology platform is currently being utilized in a research collaboration with Astellas Pharma, Inc. centered on our technology for Ac-225.

Targeted Conditioning Pipeline

Our lead targeted conditioning product candidate is Iomab-B, an ARC that is comprised of the anti-CD45 mAb known as apamistamab or BC8 and the radioisotope I-131. CD45 is expressed on leukemia, lymphoma and nucleated immune cells with an average of 200,000 copies per cell but with minimal expression outside of the hematopoietic system. Iomab-B is currently being studied in the pivotal Phase 3 Study of Iomab-B in Elderly Relapsed or Refractory AML, or SIERRA, clinical trial for targeted conditioning prior to a BMT for patients with active, relapsed or refractory (r/r) Acute Myeloid Leukemia, or AML, who are over age 55. The SIERRA trial will compare outcomes of patients randomized to receive Iomab-B and a BMT (the study arm) to those patients randomized to receive physician's choice of salvage chemotherapy (the control arm). Salvage chemotherapy is also defined as conventional care, as no standard of care exists for this patient population. Patients who fail to achieve a CR or Complete Response on the control arm are ineligible to proceed to a BMT but the trial design permits these patients to cross over to the study arm if they meet the eligibility criteria. The primary endpoint of the SIERRA trial is durable Complete Remission, or dCR, of six months and the secondary endpoint is one-year Overall Survival, or OS. The SIERRA trial is currently active at 18 sites in the United States and Canada, which includes many of the leading BMT sites based on volume. We expect to complete enrollment of the SIERRA trial and have topline data that we believe will support the submission of a Biologics License Application, or BLA, with the FDA in 2020. If approved, we expect to launch Iomab-B commercially in the United States in 2020 or 2021. Our initial commercial launch would target the leading 50-100 BMT and medical centers that perform the vast majority of BMT's today.

Safety and feasibility data from the first 38 patients enrolled on the SIERRA trial, which represents 25% of the total of 150 patients to be enrolled in the trial, was presented in an oral presentation at the American Society

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of Hematology, or ASH, Annual Meeting in December 2018. It was reported that all patients initially randomized to the study arm that received a therapeutic dose of Iomab-B (18/18) received a BMT, with a median time to BMT of 28 days, and all patients achieved engraftment in a median time of 16 days despite a high median blast count of 30%. On the control arm, 4/19 patients received a BMT after receiving conventional care with a median time to BMT of 67 days and median blast count of 26%. Of the patients failing to achieve a CR with conventional care (15/19), 10 patients were eligible to cross over to the study arm. All cross over patients (10/10) received a BMT after receiving Iomab-B, with a median time to BMT of 66 days and all patients achieved engraftment in a median time of 17 days despite high median blast count of 45% at time of cross over. There was no (0/18) 100-day non-relapse mortality reported in the study arm, while 1 of 4 patients in the control arm and 1 of 10 cross over patients experienced 100-day non-relapse mortality.

Actimab-MDS is our second pivotal program for targeted conditioning. Actimab-MDS is an ARC comprised of the anti-CD33 mAb lintuzumab linked to the radioisotope Ac-225. CD33 is expressed in a majority of patients with MDS. Actimab-MDS is informed by prior experience with our CD33 ARC in multiple trials for patients with AML, MDS and for patients that have progressed from MDS to AML, which is also known as secondary AML. Data from these trials showed that our CD33 ARC had single-agent activity capable of producing CRs in certain patients at varying dose levels with minimal extramedullary toxicities. However, dose dependent myelosuppression was seen in many of these patients. Given this safety and efficacy profile, it was decided to pursue a trial in targeted conditioning in high-risk MDS patients with this ARC in combination with Reduced Intensity Conditioning, or RIC, regimens. RIC regimens are comprised of low doses of highly toxic chemotherapies such as fludarabine, cytarabine, busulfan and melphalan. Actimab-MDS is intended to enable targeted conditioning prior to a BMT in patients with MDS or Myelodysplastic Syndrome with poor or very poor cytogenetics, which is defined as having three or more chromosomal abnormalities. A BMT is the only curative treatment option for these patients. However, these patients have poor outcomes due to high relapse rates following a BMT. Based on our interactions with FDA to date, we believe that we will need to conduct a Phase 1 dose finding clinical trial that will be followed by a randomized trial that depending on the results observed may potentially serve as a pivotal trial to support the submission of a BLA. We are currently finalizing the protocol for the Phase 1 trial with the FDA, as well as the pathway to a pivotal trial. Subject to feedback from the FDA, we expect to initiate the Phase 1, single-arm trial in the first half of 2019 that is anticipated to enroll 7–18 patients, and expect to be able to initiate the randomized trial in the first half of 2020.

Our Iomab-ACT construct is a lower dose of Iomab-B (CD45 – I-131) that we are developing as a targeted conditioning or lymphodepletion agent prior to CAR-T and adoptive cell therapies. CD45 is an antigen expressed on many cells that are relevant to the mechanism of CAR-T therapies including lymphocytes, regulatory T cells and macrophages that have been associated with clinical responses that limit the safety and efficacy of these CAR-T therapies including Cytokine Release Syndrome, or CRS, neurotoxicity and durability of response. Some of these limitations may be attributable to the chemotherapy-based conditioning agents that are being used currently prior to CAR-T therapies. Actinium's Iomab-ACT program is highly differentiated when compared to Fludarabine and Cyclophosphamide or Flu/Cy or other chemotherapy-based regimens that are used as the standard of practice today for lymphodepletion prior to CAR-T. Unlike chemotherapy, Iomab-ACT is targeted in nature and due to this targeted effect, we expect can improve CAR-T cell expansion more efficiently, potentially resulting in responses that are more durable and also with reduced CAR-T related toxicities. Importantly, the Iomab-ACT program construct enables lymphodepletion through a single-dose, outpatient administration versus Flu/Cy or other chemotherapy-based lymphodepletion regimens that can require multiple infusions in an inpatient setting over several days. Because of this potentially superior profile, the Iomab-ACT construct could result in improved access to CAR-T therapy and better outcomes. Preclinical data from our Iomab-ACT program was accepted for poster presentation at the Transplantation and Cellular Therapy Meetings.

CD33 ARC Therapeutics and Combinations

We are applying our CD33-targeting ARC product candidate lintuzumab-Ac-225 to multiple hematologic indications, as CD33 is an antigen that has been found to be expressed in a majority of patients with AML and MDS and 25–35% of patients with Multiple Myeloma, or MM. Our CD33 development program is examining the construct at various dose levels and dosing regimens either alone or in combination in these various disease indications. We currently have multiple clinical trials ongoing, in startup phase, or in planning, to use our CD33 ARC in combination with other therapeutic modalities such as chemotherapy, targeted agents

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