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Moleculin Announces Additional Positive Interim Results from Phase 1/2 Clinical Studies of Annamycin in Acute Myeloid Leukemia

No evidence of cardiotoxicity to date; 40% of 10 patients dosed at ≥120 mg/m² demonstrate efficacy; trial progresses in Europe to 210 mg/m²

HOUSTON, Dec. 4, 2019 /PRNewswire/ -- Moleculin Biotech, Inc., (Nasdaq: MBRX) ("Moleculin" or the "Company"), a clinical stage pharmaceutical company with a broad portfolio of drug candidates targeting highly resistant tumors, today announced additional positive interim safety and efficacy data from one of the Company's two ongoing open label, single arm Phase 1/2 studies of Annamycin for the treatment of relapsed or refractory acute myeloid leukemia ("AML").

The Phase 1 portion of these clinical trials, which are described in more detail later in this press release, is designed to establish the safety of Annamycin and to determine the Recommended Phase 2 Dose to be used in the Phase 2 portion of the trials. While the Primary Endpoint of the Phase 1 portion is safety, a Secondary Endpoint is the assessment of efficacy generally defined as an improvement in bone marrow biopsy results sufficient to qualify patients for a potentially curative bone marrow transplant. The Company cautions not to place undue reliance on interim results.

The third cohort in Poland receiving a single dose of 180 mg/m^2 in the Phase 1 dose escalation portion of the trial was completed with no adverse events and the trial will continue to the next cohort of 210 mg/m^2. In the US trial, one patient has completed treatment in the second cohort at 120 mg/m^2. This brings the total number of patients treated and evaluated at or above 120 mg/m^2 to 10. An additional patient in the US has begun treatment at 120 mg/m^2 but has yet to complete post-treatment evaluation. The interim results for these 10 patients are 1 CRi (defined as a complete response with incomplete recovery of white blood cells and/or platelets) and 2 partial responses ("PRs" or where bone marrow blasts are reduced 50% and to below 25%). One additional patient was bridged to bone marrow transplant ("BT") based on a sufficient reduction in bone marrow

blasts, bringing the total to 4 out of 10 patients at or above 120 mg/m^2 who have demonstrated efficacy.

In the latest cohort in Poland, 1 of the 3 patients treated at 180 mg/m^2 had a PR sufficient to qualify for a potentially curative bone marrow transplant. The results for all 3 patients were reviewed by the Safety Review Committee, which determined that no drug-related adverse events were observed that would prevent advancing the trial to the next higher dose level of 210 mg/m^2. To date in the European trial, only one adverse event related to Annamycin has been reported; a patient experienced grade 2 mucositis (which resolved to grade 1 within 2 days). In the Company's parallel US clinical trial, one new patient (the first of cohort #2) achieved a "morphologically leukemia free state" or MLFS, which also constitutes a CRi, after receiving a single dose of 120 mg/m^2.

We refer to Annamycin as a "next generation anthracycline," because it is designed to provide enhanced therapeutic benefits when compared with traditional anthracyclines (like doxorubicin) while reducing the potential for unwanted cardiotoxicity, or damage to the heart. This design intent has previously been validated with preclinical toxicology studies in animal models (as required by FDA) demonstrating Annamycin has little to no cardiotoxicity when compared with doxorubicin. Of the 14 patients treated thus far in both trials, none has shown any evidence of cardiotoxicity. This includes 7 patients in Poland who were treated at levels above the US maximum allowable cumulative anthracycline dose level (550 mg/m^2), a limitation not imposed on our trial in Europe. If upheld in further studies, this lack of toxicity could be an important differentiator between Annamycin and the currently approved anthracyclines, for which cardiotoxicity is a well-known treatment limitation.

For example, a recent review published in Cardiovascular Drugs and Therapy (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5346598/) reported that 65% of patients who received the equivalent of 550 mg/m^2 of doxorubicin (a current standard of care anthracycline) exhibited sub-clinical cardiotoxicity, defined as a reduction in left ventricular ejection fraction >10% points to a value <50%. Of the 5 patients mentioned above who were treated in our European trial above 550 mg/m^2, no evidence of cardiotoxicity was detected. The same published review also suggested that a better long-term indicator of cardiotoxicity may be the measurement of an increase in a biomarker called Troponin. When measured as an early biomarker of cancer therapy-related cardiotoxicity, Troponin rise occurs consistently in 21% - 40% of patients after treatment with current standard of care anthracycline chemotherapy and, per the published review, such an increase in Troponin is associated with an increased risk of heart disease later in life. Of the 14 patients treated thus far in both of our Annamycin clinical trials, none has shown an increase in Troponin levels.

"The interim data from our early-stage clinical trials of Annamycin continues to meet or exceed our expectations, from both a safety and efficacy perspective," commented Walter Klemp, Moleculin's Chairman and CEO. "We believe the activity we are seeing – with 40% of patients treated at or above 120 mg/m^2 responding with CRi's, PR's and/or bridging to a potentially curative bone marrow transplant – is encouraging, especially since we have yet to reach a maximum tolerable dose. Although the data is preliminary, we are excited by the results to date, and to continue moving forward. Importantly, recruitment continues to be much faster in Europe than in the US. We believe this is because Europe has imposed

fewer regulatory constraints on the level of anthracycline dosing allowed and because there are far fewer competing AML clinical trials in Poland, where our clinical testing sites are located."

"We should also point out," Mr. Klemp continued, "that there are two particularly important aspects of our development program that distinguish the potential prospects for Annamycin. First, we are studying the potential benefits of Annamycin in all AML patients, not just a subset of the AML population based on a particular gene mutation or other biomarker. Second, Annamycin is being investigated not as an adjuvant to other therapies, but as a single agent to treat relapsed or refractory AML patients, primarily as a bridge to transplant. We also believe the absence of cardiotoxicity, if it is borne out, would be especially important for pediatric patients, in addition to possibly suggesting Annamycin as an attractive alternative to currently approved anthracyclines for treating cancers beyond AML."

Dr. Robert Shepard, Moleculin's Chief Medical Officer for Annamycin added: "Although it is still early and the data are preliminary, I believe we may see that Annamycin has significant activity against relapsed and refractory AML. To have a 40% response rate this early in the dose-escalating process is very encouraging. And if the product ultimately is shown to have little or no cardiotoxicity – as the preliminary data suggest – there is a real potential for Annamycin to become the first approved anthracycline without a dose-limiting cardiovascular risk. The use of anthracyclines for induction therapy in acute leukemia is often, and unfortunately, limited if such treatment would put them over what is currently considered the 'lifetime maximum' anthracycline exposure (or 'maximum cumulative dose'). However, authorities in the EU took into account Annamycin's apparent lack of cardiotoxicity and have allowed us to demonstrate this in patients whose treatment would exceed this maximum cumulative dose. In fact, 7 of the 9 patients treated to date in Europe substantially exceeded that lifetime maximum based on their treatment with Annamycin and, of course, have shown no cardiotoxicity."

Study Design

The Company is studying Annamycin in both the US and Europe in open label, single arm clinical trials to assess the safety and efficacy of Annamycin for the treatment of adults with relapsed or refractory acute myeloid leukemia. The US and European trials have the same study design, consisting of a Phase 1 intended to establish a "Recommended Phase 2 Dose" ("RP2D"), to which the studies will then proceed. The Phase 1 studies provide for escalating doses in cohorts of 3 patients each, with each successive cohort receiving the next higher dose level until "dose limiting toxicities" prevent further increases. Cohorts 1, 2 and 3 in Poland received a dose of 120, 150 and 180 mg/m^2, respectively, and the results now permit moving to 210 mg/m^2. Cohort 1 in the US started at 100 mg/m^2, and the results supported moving to 120 mg/m^2, at which 1 patient has now been treated and evaluated as having achieved a "morphologically leukemia free state" or MLFS, which also constitutes a CRi. Because one patient in US cohort 1 did not complete the evaluation protocol, a fourth patient was added to complete that cohort. Once the Company establishes an RP2D, the intent is for each trial to advance to a Phase 2 arm planned to assess the safety and efficacy of Annamycin in 21 additional patients.

The data reported here is preliminary as collected by independent CRO site monitors per standard practice and is subject to subsequent quality assurance review.

We have been and intend to continue reporting top-line results by cohort in each trial, with each announcement also including an update on the other trial. Top-line results will include reporting of any drug-related adverse events ("AEs") and assessment of cardiotoxicity, including ECHO or MUGA scans measuring change in ejection fraction and measuring blood Troponin level, which is considered a biomarker for potential long-term cardiovascular impairment. To date, one patient experienced grade 2 mucositis (which resolved to grade 1 within 2 days) and no other drug-related AEs have been reported. Also, no loss of ejection fraction or rise in Troponin levels has been reported. Top-line results will also include the number of partial responses ("PRs"), complete responses ("CRs") and patients deemed capable of progressing to a potentially curative bone marrow transplant, which we term "bridge to transplant" ("BTs"), each of which is essentially a function of the magnitude of reduction in a patient's bone marrow blasts. For purposes of these clinical trials, a CR means that the patient's bone marrow blasts reduced to 5% or less (with CRi meaning a CR where there was incomplete recovery of white blood cell and/or platelet counts), a PR means the patient's bone marrow blasts reduced by 50% and resulted in a blast count of 25% or less, and a BT means patients are deemed capable of progressing to a potentially curative bone marrow transplant. To date, there has been 1 CRi in the US (@ 120 mg/m^2), 2 PRs in Europe (1 @ 120 mg/m^2 and 1 @ 180 mg/m^2) and 4 BTs (1 in the US and 3 in Europe).

The US trial also differs from the European trial in that the FDA would like to review safety data relating to cardiotoxicity from patients treated prior to advancing beyond 120 mg/m^2, as exceeding this dose level would require the patient to exceed the established lifetime maximum exposure to anthracyclines (presuming all anthracyclines are cardiotoxic). To date, 100% of all 14 patients treated in both the US and EU trials have shown no incidence of cardiotoxicity, including 7 patients out of 9 treated in Poland who exceeded the lifetime maximum anthracycline exposure level. The Company believes that the additional patient safety data gained from the European trial may also assist in the FDA's review of Annamycin's cardiac safety.

About Moleculin Biotech, Inc.

Moleculin Biotech, Inc. is a clinical stage pharmaceutical company focused on the development of a broad portfolio of oncology drug candidates for the treatment of highly resistant tumors. The Company's clinical stage drugs are: Annamycin, a Next Generation Anthracycline, designed to avoid multidrug resistance mechanisms with little to no cardiotoxicity being studied for the treatment of relapsed or refractory acute myeloid leukemia, more commonly referred to as AML, WP1066, an Immune/Transcription Modulator capable of inhibiting p-STAT3 and other oncogenic transcription factors while also stimulating a natural immune response, targeting brain tumors, pancreatic cancer and hematologic malignancies, and WP1220, an analog to WP1066, for the topical treatment of cutaneous T-cell lymphoma. Moleculin is also engaged in preclinical development of additional drug candidates, including additional Immune/Transcription Modulators, as well as compounds capable of Metabolism/Glycosylation Inhibition.

For more information about the Company, please visithttp://www.moleculin.com.

Forward-Looking Statements

Some of the statements in this release are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995, which involve risks and uncertainties. Forward-looking statements in this press release include, without limitation, the ability of the Company to successfully recruit patients to complete its clinical trials, the ability of Annamycin to show safety and efficacy in patients, and the ability for Annamycin to be an alternative to currently approved anthracyclines for treating cancers other than AML. Although Moleculin believes that the expectations reflected in such forward-looking statements are reasonable as of the date made, expectations may prove to have been materially different from the results expressed or implied by such forward-looking statements. Moleculin Biotech has attempted to identify forward-looking statements by terminology including "believes," "estimates," "anticipates," "expects," "plans," "projects," "intends," "potential," "may," "could," "might," "will," "should," "approximately" or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. These statements are only predictions and involve known and unknown risks, uncertainties, and other factors, including those discussed under Item 1A. "Risk Factors" in our most recently filed Form 10-K filed with the Securities and Exchange Commission ("SEC") and updated from time to time in our Form 10-Q filings and in our other public filings with the SEC. Any forward-looking statements contained in this release speak only as of its date. We undertake no obligation to update any forward-looking statements contained in this release to reflect events or circumstances occurring after its date or to reflect the occurrence of unanticipated events. The Company cautions investors not to place undue reliance on the interim results announced today.

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