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# Moleculin Announces Successful Completion of US Phase 1 AML Trial of Annamycin

**No evidence of cardiotoxicity; preliminary assessment shows efficacy in 2 out of 6 patients; Company updates interim Phase 1 trial results in Europe**

HOUSTON, Feb. 3, 2020 /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 that its open label, single arm US Phase 1 trial met its primary objective of demonstrating the safety of Liposomal Annamycin ("Annamycin") in treating relapsed or refractory acute myeloid leukemia ("AML"). The Company also announced an update on interim enrollment, safety and efficacy data in its parallel Phase 1 trial in Europe, which continues with dose escalation, thus far without safety concerns.



## **Safety of Annamycin in AML Patients**

The US Phase 1 trial met its primary endpoint, demonstrating the safety of Annamycin in treating AML when delivered to patients at or below the lifetime maximum anthracycline dose established by the FDA. The primary safety signal was the absence of cardiotoxicity (potential damage to the heart), a serious and often treatment-limiting issue prevalent with currently approved anthracyclines. This was determined by echocardiograms, as well as cardiac health biomarkers, principally blood troponin levels, which are considered an indicator of potential long-term heart damage. The data showed no cardiotoxicity in any of the 6 patients evaluated in the US Phase 1 trial. Additionally, there were no unexpected serious adverse events and no dose limiting toxicities at any dose tested.

## **Preliminary Evidence of Effectiveness**

Although the primary objective of the Phase 1 trial was to evaluate safety, the study also gathered data to support a preliminary assessment of the product's potential efficacy. Among other things, the study recorded complete response (CR), partial response (PR), event-free survival, overall survival (Kaplan-Meier), and time to and duration of

remission/response. Based on these criteria, efficacy was seen in 2 of the US patients, even though the drug was dosed at what was expected to be sub-therapeutic levels. The evidence of efficacy consisted of 1 patient who achieved a "morphologically leukemia-free state," which the protocol defined as a CR with incomplete recovery of platelets or neutrophils (CRi), and another patient who had a substantial remission of leukemia cutis (a somewhat rare leukemia symptom), from diffuse to 3 small lesions.

Moleculin Chairman and CEO Walter Klemp commented, "To see this kind of activity this early is very encouraging, especially since Phase 1 trials are primarily designed to demonstrate safety, not efficacy, and the dosing was therefore at a level we expected to be sub-therapeutic, based on previous data. We also are pleased because Annamycin is being studied as a single agent, not in combination with any other drugs. We believe this is potentially significant, because our clinical advisors believe the vast majority of relapsed or refractory AML patients do not respond to single agents. Although this is very early data from a small sample size, we are especially encouraged because the dosing was well below our anticipated recommended Phase 2 dose. We look forward to the potential validation of these results in further study and believe that, if the level of activity experienced in the US trial can be demonstrated in a larger patient population, we may be well-positioned to seek accelerated approval from the FDA. FDA has already granted Fast Track designation, which recognizes that Annamycin shows the potential to address unmet medical needs, which can include providing efficacy comparable to available therapies while avoiding toxicity associated with the existing treatment."

### **European Phase 1 Trial**

The Company is conducting a very similar Phase 1 trial in Europe, but with dose escalation beyond what FDA permitted in the US. To date, 11 patients have been dosed in Europe, and the study has shown similar safety outcomes, including no cardiotoxicity in any patient. To date, only one adverse event related to Annamycin has been reported in the European trial; a patient experienced grade 2 mucositis that resolved to grade 1 within 2 days.

The European patients have been dosed at levels ranging from 120 mg/m<sup>2</sup> to 210 mg/m<sup>2</sup>, with 2 patients now having been enrolled in the fourth cohort in Europe receiving a single dose of 210 mg/m<sup>2</sup>. Between the US and European studies, 14 AML patients have been evaluated after receiving Annamycin at or above 120 mg/m<sup>2</sup>. When they entered the study, 9 of the 14 patients were considered relapsed and 5 were considered refractory. Although reduction in bone and circulating blasts has been seen in both relapsed and refractory AML patients, each of the 5 patients where efficacy endpoints were met was a relapsed patient. The efficacy-related data for those patients (which includes the 2 US patients mentioned above) include:

- One patient had a CRi, which the protocol defined as a complete response with incomplete recovery of white blood cells and/or platelets;
- Two patients had PRs (partial responses, meaning that bone marrow blasts were reduced 50% and to below 25%);
- One patient had a substantial remission of their somewhat rare leukemic symptom known as leukemia cutis; and
- One patient was bridged to bone marrow transplant (BT) based on a sufficient reduction in bone marrow blasts.

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 17 patients treated and fully evaluated thus far in both trials, including those treated below 120 mg/m<sup>2</sup>, none has shown any evidence of cardiotoxicity. This includes 9 patients in Poland who were treated at levels above the US maximum allowable lifetime cumulative anthracycline dose level (550 mg/m<sup>2</sup>), a limitation not imposed on our trial in Europe. If confirmed 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<sup>2</sup> 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%. In the 5 patients mentioned above who were treated in our European trial above 550 mg/m<sup>2</sup>, 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 17 patients treated thus far in both of our Annamycin clinical trials, none has shown an increase in troponin levels.

## **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 Europe received a dose of 120, 150 and 180 mg/m<sup>2</sup>, respectively, and the results have permitted moving to Cohort 4 with dosing at 210 mg/m<sup>2</sup>, in which 2 of the 3 patients have been enrolled and treated. Cohort 1 in the US started at 100 mg/m<sup>2</sup>, and the results supported moving to Cohort 2 at 120 mg/m<sup>2</sup> which has now been fully recruited, treated, and evaluated. Beyond this dose level patients would receive greater than the lifetime maximum anthracycline dose of 550 mg/m<sup>2</sup> allowed by the FDA. Once the Company establishes an RP2D, the intent is 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. 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.

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<sup>2</sup>, as exceeding this dose level would require the patient to exceed the established lifetime maximum exposure to anthracyclines (presuming all anthracyclines are cardiotoxic). 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 visit <http://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, whether the level of activity and lack of toxicity experienced in the Company's current trials can be demonstrated in a larger patient population, whether the patient safety data gained from the Company's European trial will assist in the FDA's review of Annamycin's cardiac safety, the willingness of the FDA

to waive their lifetime maximum allowable anthracycline limit with regard to Annamycin, 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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