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Monopar Announces Clinical and Preclinical Program Updates

- *Validive Phase 2b/3 VOICE trial now open at 43 sites; active and enrolling in US and EU*
- *Open-label Phase 1b camsirubicin trial: early signs of clinical benefit observed*

WILMETTE, Ill., Feb. 15, 2022 (GLOBE NEWSWIRE) -- Monopar Therapeutics Inc. (Nasdaq: MNPR), a clinical-stage biopharmaceutical company focused on developing proprietary therapeutics designed to extend life or improve the quality of life for cancer patients, today announced program updates across its pipeline and anticipated 2022 highlights.

Program Developments

Validive – International Phase 2b/3 VOICE Clinical Trial, Actively Recruiting

Severe oral mucositis (SOM) is a painful and debilitating ulceration of the mucosal membranes of the mouth caused by the chemoradiotherapy used to treat patients with oropharyngeal cancer. SOM prevents these patients from being able to drink and/or eat, and can increase hospitalization rates, cause interruption or termination of chemoradiotherapy before completion of treatment, and cause aspiration induced lung injury. SOM results in significant short- and long-term negative impacts on clinical outcomes and quality of life. There is no FDA-approved preventative or treatment option for the estimated >40,000 newly diagnosed individuals with oropharyngeal cancer in the US who may receive chemoradiation each year and are at-risk of developing SOM. Recent trials show that the majority of oropharyngeal cancer patients receiving chemoradiotherapy will develop SOM.

Validive is a once daily self-administered mucoadhesive tablet designed to prevent SOM in oropharyngeal cancer patients who receive chemoradiotherapy. Monopar is evaluating Validive in this patient population in the international Phase 2b/3 VOICE study. Updated highlights of this trial include:

- 43 clinical sites opened to date, active and enrolling patients in both the US and Europe
- Interim analysis is currently anticipated to be reached in mid-2022. Further, based on timely findings extracted from public reporting of recently completed SOM trials, the Company is presently evaluating potential enhancements to and exact timing of the interim analysis

Camsirubicin – Phase 1b Dose-Escalation Trial, Actively Recruiting

Advanced soft tissue sarcoma (ASTS) is a diverse type of cancer that typically develops in the connective tissue of the body and which has metastasized (spread) or is not amenable

to surgery. The average life expectancy from time of diagnosis for patients with ASTS is about 12 to 15 months. Doxorubicin is the current 1st line standard of care treatment for most types of ASTS.

Doxorubicin is FDA approved in 14 different types of cancers including soft tissue and bone sarcomas; metastatic stomach, ovarian, thyroid, lung, and breast cancer; acute myeloid and lymphoblastic leukemia; Hodgkin and non-Hodgkin lymphoma; and neuroblastoma, and is one of the most widely used cancer drugs around the world. It is a drug that becomes more effective at higher doses. Unfortunately, due to the potential development of irreversible heart damage, patients stop doxorubicin treatment once a certain cumulative lifetime dose limit threshold is reached. Dosing higher than this lifetime limit sharply increases the rate of irreversible heart damage. As a result, even if patients are responding to treatment, they discontinue doxorubicin treatment typically after only 6 to 8 cycles of doxorubicin.

Monopar is developing a novel proprietary analog of doxorubicin called camsirubicin. Camsirubicin has been designed to retain the anti-cancer activity while avoiding the irreversible heart damage that is seen with doxorubicin. The hypothesis behind the use of camsirubicin is straightforward: modifying doxorubicin in order to reduce cardiac damage could enable higher and longer dosing, resulting in better patient outcomes. The preclinical, Phase 1, and Phase 2 camsirubicin data generated to date support the potential to treat patients with high doses per cycle and for longer periods of time. No irreversible heart damage has been seen to date in any of the camsirubicin clinical trials.

The Company is currently enrolling patients in an open-label Phase 1b dose escalation trial in ASTS patients to evaluate higher doses of camsirubicin than have been used in the previous Phase 1 and Phase 2 trials. Although this Phase 1b is designed to determine the maximum tolerated dose of camsirubicin, given the historical dose-dependent anti-tumor response repeatedly demonstrated with doxorubicin, efficacy measurements are being tracked in these patients as the dose is increased. Updated highlights of this trial include:

- Phase 1b dose-escalation trial initiated in September 2021, with first patients dosed in October 2021
- First dose level completed in November 2021, with positive recommendation from trial safety review committee to proceed to next higher dose level
- Three patients already dosed at the second dose level, which is a higher dose level than tested in any prior camsirubicin clinical trial

“Early signs of clinical benefit are being observed with camsirubicin in this Phase 1b trial, which is quite encouraging. Two of three patients in the first dose level have stable disease, one of which has liver metastases and experienced fairly quickly a reduction in pain and improved liver function tests,” said Dr. Sant Chawla, Principal Investigator, Sarcoma Oncology Research Center in Santa Monica, CA. “The second cohort so far is also looking encouraging. We look forward to continuing to escalate the camsirubicin dose level to identify a new, higher recommended Phase 2 dose, and continuing to assess camsirubicin for evidence of antitumor activity.”

Radiopharmaceutical Platform and MNPR-101

Monopar and NorthStar Medical Radioisotopes have extended their 50/50

radiopharmaceutical partnership for 2022. This collaboration has generated a radioimmunotherapeutic candidate, MNPR-101-PCTA, that is being evaluated as a potential diagnostic and therapeutic agent in cancer and severe COVID-19. Updated highlights of this program include:

- Provisional composition of matter patents filed covering the Actinium-based radiopharmaceutical drug candidate (MNPR-101-PCTA-Ac-225)
- Peer-reviewed publications highlighting the utility of MNPR-101 and MNPR-101 fragment conjugates as uPAR-targeted imaging agents in numerous cancers
- Currently evaluating pathways to initiating a first-in-human study

MNPR-202

MNPR-202 is a novel analog of camsirubicin currently being evaluated in preclinical studies. It retains the same potentially non-cardiotoxic backbone as camsirubicin but has been modified at other positions, which may enable it to evade doxorubicin drug resistance mechanisms. Updated highlights of this program include:

- Entered collaboration and commenced work with Cancer Science Institute of Singapore to evaluate activity of MNPR-202 in preclinical models of multiple cancers
- Composition of matter patent covering MNPR-202 has been allowed in the US

Forward-Looking Statements

Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. The words “may,” “will,” “could,” “would,” “should,” “expect,” “plan,” “anticipate,” “intend,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue,” “target” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Examples of these forward-looking statements include statements concerning: that the VOICE trial’s Interim analysis is currently anticipated to be reached in mid-2022; that the VOICE trial continues to be active and enrolling patients in both the US and Europe; that modifying doxorubicin in order to reduce cardiac damage could enable higher and longer dosing of camsirubicin, resulting in better patient outcomes; that Monopar looks forward to continuing to escalate the camsirubicin dose level to identify a new, higher recommended Phase 2 dose, and continuing to assess camsirubicin for evidence of antitumor activity; that Monopar is currently evaluating pathways to initiating a first-in-human study of MNPR-101-PCTA-Ac-225; and that MNPR-202 may be able to evade doxorubicin drug resistance mechanisms. The forward-looking statements involve risks and uncertainties including, but not limited to: not successfully recruiting additional patients and initiating additional clinical trial sites for the VOICE clinical trial or the camsirubicin Phase 1b clinical trial within expected timeframes, if at all; that the VOICE clinical trial may not reach interim analysis by mid-2022, if at all; the Company’s inability to raise sufficient funds or engage a partner to complete the Phase 3 portion of the VOICE clinical trial and continue the camsirubicin clinical program beyond the Phase 1b clinical trial; that MNPR-101-PCTA-Ac-225 may not find a pathway to initiating a first-in-human study; that the preclinical work of MNPR-202 may not show meaningful results; and the significant general risks and uncertainties surrounding the research, development,

regulatory approval, and commercialization of therapeutics. Actual results may differ materially from those expressed or implied by such forward-looking statements. Risks are described more fully in Monopar's filings with the Securities and Exchange Commission. All forward-looking statements contained in this press release speak only as of the date on which they were made. Monopar undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made. Any forward-looking statements contained in this press release represent Monopar's views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date.

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