Progenics Pharmaceuticals to Initiate a Basket Trial by Year End to Support an Expanded Label for AZEDRA® (iobenguane I 131) in Multiple MIBG Avid Neuroendocrine Tumors

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NEW YORK, June 20, 2019 (GLOBE NEWSWIRE) -- Progenics Pharmaceuticals, Inc. (NASDAQ:PGNX), ("Progenics" or the "Company"), an oncology company developing innovative targeted medicines and artificial intelligence to find, fight and follow cancer, today announced that the Company has reached alignment with the U.S. Food and Drug Administration (FDA) on the clinical development plan to pursue a tissue agnostic indication to support an expanded label for AZEDRA (iobenguane I 131) for the treatment of patients with unresectable or metastatic neuroendocrine tumors (NETs) who are MIBG avid. Following a Type B meeting with the FDA, the Company plans to conduct a basket study that will evaluate AZEDRA in patients with NETs that are MIBG avid, including gastroenteropancreatic neuroendocrine tumors (GEP-NETs) and other NETs, with a dosing regimen that potentially enables outpatient administration. AZEDRA is the first and only approved therapy in the U.S. for the treatment of adult and pediatric patients 12 years and older with iobenguane (MIBG) scan positive, unresectable, locally advanced or metastatic pheochromocytoma or paraganglioma who require systemic anticancer therapy.

NETs are a group of rare tumors of neural crest origin, most commonly found in the gastrointestinal or respiratory tracts, although they may also be found in the central nervous system, thyroid gland, skin, breast, colon, and urogenital system, including prostate cancer, among other locations. NETs overexpress the norepinephrine reuptake transporter on their cell surface. MIBG is a known substrate for the transporter and, therefore, MIBG avidity can be used to enrich for patients who are most likely to respond to AZEDRA therapy. NETs are considered rare tumors, although the incidence has continued to increase in the last 10-15 years, with approximately 12,000 patients being diagnosed in the U.S. each year.

"Following our productive discussions with the FDA, we have a clear path forward to expand the reach of AZEDRA to patients with other MIBG avid NETs who have failed or are ineligible for available therapies which represents a very high unmet need," said Mark Baker, Chief Executive Officer of Progenics. "Should this trial support an expanded label, we believe there is the potential to increase by many multiples the size of the commercial market of AZEDRA. We expect to initiate our AZEDRA basket study by the end of the year, reinforcing our commitment to rapidly advance our portfolio of life-saving radiopharmaceutical oncology treatments."

"In an effort to expedite late stage oncology drug development, FDA has recently provided guidance on a type of trial design that tests a single drug in different tumor types defined by genetic or other biomarkers," said Asha Das, MD, Chief Medical Officer. "We have received strong interest from key opinion leaders in using this study design to evaluate AZEDRA in multiple NET subtypes defined by MIBG avidity, especially with a dosing regimen that potentially enables outpatient administration."

The basket study is expected to enroll approximately 120 patients at sites in the U.S. Progenics plans to initiate the study by the end of 2019.

About AZEDRA

Indication

AZEDRA® (iobenguane I 131) is indicated for the treatment of adult and pediatric patients 12 years and older with iobenguane scan positive, unresectable, locally advanced or metastatic pheochromocytoma or paraganglioma who require systemic anticancer therapy.

Important Safety Information

Warnings and Precautions:

Risk from Radiation Exposure: AZEDRA contributes to a patient's overall long-term radiation exposure. Long-term cumulative radiation exposure is associated with an increased risk for cancer. These risks of radiation associated with the use of AZEDRA are greater in pediatric patients than in adults. Minimize radiation exposure to patients, medical personnel, and household contacts during and after treatment with AZEDRA consistent with institutional good radiation safety practices and patient management procedures.
Myelosuppression: Among the 88 patients who received a therapeutic dose of AZEDRA, 33% experienced Grade 4 thrombocytopenia, 16% experienced Grade 4 neutropenia, and 7% experienced Grade 4 anemia. Five percent of patients experienced febrile neutropenia. Monitor blood cell counts weekly for up to 12 weeks or until levels return to baseline or the normal range. Withhold and dose reduce AZEDRA as recommended in the prescribing information based on severity of the cytopenia.
Secondary myelodysplastic syndrome, leukemia, and other malignancies: Myelodysplastic syndrome (MDS) and acute leukemias were reported in 6.8% of the 88 patients who received a therapeutic dose of AZEDRA. The time to development of MDS or acute leukemia ranged from 12 months to 7 years. Two of the 88 patients developed a non-hematological malignancy.
Hypothyroidism: Hypothyroidism was reported in 3.4% of the 88 patients who received a therapeutic dose of AZEDRA. Initiate thyroid-blocking medications starting at least 1 day before and continuing for 10 days after each AZEDRA dose to reduce the risk of hypothyroidism or thyroid neoplasia. Evaluate for clinical evidence of hypothyroidism and measure thyroid-stimulating hormone (TSH) levels prior to initiating AZEDRA and annually thereafter.
Elevations in blood pressure: Eleven percent of the 88 patients who received a therapeutic dose of AZEDRA experienced a worsening of pre-existing hypertension defined as an increase in systolic blood pressure to ≥160 mmHg with an increase of 20 mmHg or an increase in diastolic blood pressure to ≥ 100 mmHg with an increase of 10 mmHg. All changes in blood pressure occurred within the first 24 hours post infusion. Monitor blood pressure frequently during the first 24 hours after each therapeutic dose of AZEDRA.
Renal toxicity: Of the 88 patients who received a therapeutic dose of AZEDRA, 7% developed renal failure or acute kidney injury and 22% demonstrated a clinically significant decrease in glomerular filtration rate (GFR) measured at 6 or 12 months. Monitor renal function during and after treatment with AZEDRA. Patients with baseline renal impairment may be at greater risk of toxicity; perform more frequent assessments of renal function in patients with mild or moderate impairment. AZEDRA has not been studied in patients with severe renal impairment.
Pneumonitis: Fatal pneumonitis occurred 9 weeks after a single dose in one patient in the expanded access program. Monitor patients for signs and symptoms of pneumonitis and treat appropriately.
Embryo-fetal toxicity: Based on its mechanism of action, AZEDRA can cause fetal harm. Verify pregnancy status in females of reproductive potential prior

to initiating AZEDRA. Advise females and males of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment with AZEDRA and for 7 months after the final dose. Advise males with female partners of reproductive potential to use effective contraception during treatment and for 4 months after the final dose.
Risk of infertility: Radiation exposure associated with AZEDRA may cause infertility in males and females. Radiation absorbed by testes and ovaries from the recommended cumulative dose of AZEDRA is within the range where temporary or permanent infertility can be expected following external beam radiotherapy.

Adverse Reactions:

The most common severe (Grade 3–4) adverse reactions observed in AZEDRA clinical trials (≥ 10%) were lymphopenia (78%), neutropenia (59%), thrombocytopenia (50%), fatigue (26%), anemia (24%), increased international normalized ratio (18%), nausea (16%), dizziness (13%), hypertension (11%), and vomiting (10%). Twelve percent of patients discontinued treatment due to adverse reactions (thrombocytopenia, anemia, lymphopenia, nausea and vomiting, multiple hematologic adverse reactions).

Drug Interactions:
Based on the mechanism of action of iobenguane, drugs that reduce catecholamine uptake or that deplete catecholamine stores may interfere with iobenguane uptake into cells and therefore interfere with dosimetry calculations or the efficacy of AZEDRA. These drugs were not permitted in clinical trials that assessed the safety and efficacy of AZEDRA. Discontinue the drugs listed in the prescribing information for at least 5 half-lives before administration of either the dosimetry dose or a therapeutic dose of AZEDRA. Do not administer these drugs until at least 7 days after each AZEDRA dose.

For important risk and use information about AZEDRA, please see Full Prescribing Information.

To report suspected adverse reactions, contact Progenics Pharmaceuticals, Inc. at 844-668-3950 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

About PROGENICS

Progenics is an oncology company focused on the development and commercialization of innovative targeted medicines and artificial intelligence to find, fight and follow cancer, including: therapeutic agents designed to treat cancer (AZEDRA®, 1095, and PSMA TTC); prostate-specific membrane antigen (“PSMA”) targeted imaging agent for prostate cancer (PyL™ and 1404); and imaging analysis technology (aBSI and PSMA AI). Progenics has two commercial products, AZEDRA, for the treatment of patients with unresectable, locally advanced or metastatic pheochromocytoma or paraganglioma (rare neuroendocrine tumors of neural crest origin) who require systemic anticancer therapy; and RELISTOR® (methylnaltrexone bromide) for the treatment of opioid-induced constipation, which is partnered with Bausch Health Companies Inc.

This press release contains projections and other "forward-looking statements" regarding future events. Statements contained in this communication that refer to Progenics' estimated or anticipated future results or other non-historical facts are forward-looking statements that reflect Progenics' current perspective of existing trends and information as of the date of this communication. Forward-looking statements generally will be accompanied by words such as "anticipate," "believe," "plan," "could," "should," "estimate," "expect," "forecast," "outlook," "guidance," "intend," "may," "might," "will," "possible," "potential," "predict," "project," or other similar words, phrases or expressions. Such statements are predictions only, and are subject to risks and uncertainties that could cause actual events or results to differ materially. These risks and uncertainties include, among others, the inherent uncertainty of outcomes in studies such as the planned basket study for AZEDRA, market acceptance for approved products; the risk that the commercial launch of AZEDRA may not meet revenue and income expectations; the cost, timing and unpredictability of results of clinical trials and other development activities and collaborations; the unpredictability of the duration and results of further regulatory discussions and requirements for the AZEDRA basket study; the possible impairment of, inability to obtain and costs of obtaining intellectual property rights; possible product safety or efficacy concerns, general business, financial, regulatory and accounting matters, litigation and other risks. More information concerning Progenics and such risks and uncertainties is available on its website, and in its press releases and reports it files with the U.S. Securities and Exchange Commission, including those risk factors included in its Annual Report on Form 10-K for the year ended December 31, 2018, as updated in its subsequent Quarterly Reports on Form 10-Q. Progenics is providing the information in this press release as of its date and, except as expressly required by law, Progenics disclaims any intent or obligation to update or revise any forward-looking statements, whether as a result of new information, future events or circumstances or otherwise.

Additional information concerning Progenics and its business may be available in press releases or other public announcements and public filings made after this release. For more information, please visit www.progenics.com. Information on or accessed through our website or social media sites is not included in the company's SEC filings.

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