Provectus Biopharmaceuticals Announces Initiation of Phase 1b/2 Clinical Trial to Study PV-10 in Combination with Immune Check Point Inhibitor Pembrolizumab

Study could be a "Significant Step to Co-Development Transaction"

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KNOXVILLE, Tenn.--(BUSINESS WIRE)--Provectus Biopharmaceuticals, Inc. (NYSE MKT: PVCT, www.pvct.com), a clinical-stage oncology and dermatology biopharmaceutical company ("Provectus"), today announced it has completed development of the protocol for Phase1b/2 testing of its investigational cancer drug PV-10 in combination with pembrolizumab in patients with Stage IV melanoma. Pembrolizumab (also known as Keytruda®, a product of Merck and Co. Inc., NYSE: MRK) is an immune checkpoint inhibitor approved for treatment of patients with advanced or unresectable melanoma. PV-10 is Provectus's novel investigational drug for cancer that is injected into solid tumors (intralesional administration); it is currently undergoing Phase 3 clinical testing in patients with Stage III melanoma. Clinical testing under the new Phase 1b/2 protocol is expected to commence before the end of the year.

The combination protocol enables initial clinical testing of concepts at the center of a patent held by Provectus, U.S. Patent number 9,107,887, which Pfizer, Inc. (PFE) jointly owns. Specifically, the patent covers the use of PV-10 in combination with systemic inhibitors of immune system down-regulation, such as anti-CTLA-4, PD-1 and PD-L1 immune checkpoint inhibiting antibodies. Pembrolizumab is an anti-PD-1 antibody. Pre-clinical testing of PV-10 used in combination with these important classes of drugs demonstrated potential importance for treatment of advanced cancers.

The FDA granted accelerated approval to pembrolizumab in September 2014, making it the first FDA-approved anti-PD-1 immune checkpoint inhibitor. Because pembrolizumab is already FDA-approved, Provectus can commence this study with or without assistance of a partner.

The Phase 1b/2 study will incorporate a modest sized single arm Phase 1b component of 24 subjects with expedited safety and efficacy end points. This is designed to support expansion to a larger randomized Phase 2 component. Combined, these two arms will enable assessment of the potential safety and clinical benefit of PV-10 when used with pembrolizumab for treatment of advanced melanoma.

Dr. Eric Wachter, CTO of Provectus, stated, "The primary end point of tolerability in the Phase 1b portion of the study, combined with assessment of progression free survival (PFS) and objective response rate (ORR) by RECIST criteria as key secondary endpoints, assessed over a 15 week treatment interval, establish a basis for determining whether to proceed to the larger, randomized Phase 2 portion of the study. We will use an adaptive design for powering Phase 2 based on preliminary results from Phase 1, and estimate this portion of the study to require at least 120 subjects, with a primary endpoint of PFS and key secondary endpoint of ORR. In both portions of the study, pembrolizumab will be administered every three weeks for up to 24 months, as is standard of care; PV-10 will be administered on the same schedule for the first 15 weeks to all of the subject's skin lesions. Subjects in Phase 1b will receive both PV-10 and pembrolizumab, whereas in Phase 2

subjects will be randomized to PV-10 + pembrolizumab or pembrolizumab alone."

Pete Culpepper, CFO and COO of Provectus, noted, "This study is both scientifically and commercially important to Provectus. Scientifically, combination therapy in cancer treatment is a rapidly maturing area, where rational combination of agents is replacing the empirical approaches of the past. Commercially, this is the second of three steps that we hope will significantly strengthen our hand in negotiating a co-development transaction with an immunotherapy-focused partner. Our joint patent with Pfizer was the first; this study is the second; and the third is our immune mechanism of action clinical study, which is underway at the Moffitt Cancer Center and which has completed recruitment."

The mechanism of action study's preliminary clinical findings, reported last year, showed that the immunologic effects of tumor ablation with PV-10 may be complementary to immune checkpoint inhibition. Companion pre-clinical testing of PV-10 in murine models of melanoma, also reported last year, showed that the therapeutic effects of PV-10 and immune checkpoint inhibition are increased when the two are used in combination.

The cost of pembrolizumab is reimbursed so it is not paid for by Provectus and the remaining cost of this study is budgeted with existing cash on hand of the Company.

For further details on the protocol visit https://www.clinicaltrials.gov/ct2/show/NCT02557321

About Provectus Biopharmaceuticals, Inc.

Provectus Biopharmaceuticals, Inc., specializes in developing oncology and dermatology therapies. PV-10, its novel investigational drug for cancer, is designed for injection into solid tumors (intralesional administration), thereby reducing potential for systemic side effects. Its oncology focus is on melanoma, breast cancer and cancers of the liver. The Company has received orphan drug designations from the FDA for its melanoma and hepatocellular carcinoma indications. PH-10, its topical investigational drug for dermatology, is undergoing clinical testing for psoriasis and atopic dermatitis. Provectus has completed Phase 2 trials of PV-10 as a therapy for metastatic melanoma, and of PH-10 as a topical treatment for atopic dermatitis and psoriasis. Information about these and the Company's other clinical trials can be found at the NIH registry, www.clinicaltrials.gov. For additional information about Provectus, please visit the Company's website at www.pvct.com or contact Porter, LeVay & Rose, Inc.

FORWARD-LOOKING STATEMENTS: This release contains "forward-looking statements" as defined under U.S. federal securities laws. These statements reflect management's current knowledge, assumptions, beliefs, estimates, and expectations and express management's current views of future performance, results, and trends and may be identified by their use of terms such as "anticipate," "believe," "could," "estimate," "expect," "intend," "may," "plan," "predict," "project," "will," and other similar terms. Forward-looking statements are subject to a number of risks and uncertainties that could cause our actual results to materially differ from those described in the forward-looking statements. Readers should not place undue reliance on forward-looking statements. Such statements are made as of the date hereof, and we undertake no obligation to update such statements after this date.

Risks and uncertainties that could cause our actual results to materially differ from those described in forward-looking statements include those discussed in our filings with the Securities and Exchange Commission (including those described in Item 1A of our Annual Report on Form 10-K for the year ended December 31, 2014) and the following:

- our determination, based on guidance from the FDA, whether to proceed with or without a partner with the fully enrolled phase 3 trial of PV-10 to treat locally advanced cutaneous melanoma and the costs associated with such a trial if it is necessary to complete (versus interim data alone);

- our determination whether to license PV-10, our investigational drug product for melanoma and other solid tumors such as cancers of the liver, if such licensure is appropriate considering the timing and structure of such a license, or to commercialize PV-10 on our own to treat melanoma and other solid tumors such as cancers of the liver;
- our ability to license PH-10, our investigational drug product for dermatology, PH-10, on the basis of our phase 2 atopic dermatitis and psoriasis results, which are in the process of being further developed in conjunction with mechanism of action studies; and
- our ability to raise additional capital if we determine to commercialize PV-10 and/or PH-10 on our own, although our expectation is to be acquired by a prospective pharmaceutical or biotech concern prior to commercialization.

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