Day One Announces First Patients Dosed in Phase 1b/2 Combination Study with Tovorafenib (DAY101) and Pimasertib in RAF-altered Solid Tumors

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Phase 1b/2 combination study, FIRELIGHT-1, to leverage insights from pediatric development to evaluate potential synergistic effects of the two candidates among adolescents and adults

SOUTH SAN FRANCISCO, Calif., May 23, 2022 (GLOBE NEWSWIRE) -- Day One Biopharmaceuticals (Nasdaq: DAWN), a clinical-stage biopharmaceutical company dedicated to developing and commercializing targeted therapies for people of all ages with life-threatening diseases, today announced the first patients have been dosed in sub-study 2 of FIRELIGHT-1, a Phase 1b/2 clinical trial evaluating tovorafenib (DAY101) in combination with pimasertib in adolescent and adult patients with recurrent, progressive, or refractory solid tumors with MAPK pathway aberrations.

Tovorafenib is an investigational, oral, brain-penetrant, highly-selective type II pan-RAF kinase inhibitor and pimasertib is an investigational, oral, highly-selective small molecule inhibitor of mitogen-activated protein kinases 1 and 2 (MEK-1/-2). Both investigational therapies are designed to target key enzymes in the MAPK signaling pathway.

“The MAPK pathway is one of the most commonly dysregulated cancer signaling pathways. A growing body of preclinical data indicates that the combination of a type II RAF inhibitor and a MEK inhibitor may have synergistic activity against tumors bearing a variety of different MAPK pathway alterations. We are excited to expand the development of both tovorafenib and pimasertib and further characterize the potential of combination therapy in adolescent and adult patients with treatment-resistant MAPK pathway-altered solid tumors,” said Samuel Blackman, M.D., Ph.D., co-founder and chief medical officer of Day One. “Extending our research into the combination setting in adult and adolescent patients is a logical next step as it allows us to build on tovorafenib’s monotherapy activity and uncover its full therapeutic potential in tumors with unaddressed MAPK alterations.”

The Phase 1b portion of the multi-center, open-label umbrella study will evaluate the safety of combining tovorafenib once weekly with pimasertib in approximately 25 adolescent and adult patients (≥ 12 years of age) to determine optimal dosing. Secondary and exploratory endpoints evaluate duration to response, progression-free survival, and time to response. The Phase 2 portion will evaluate the efficacy and safety of the optimal dose combination from Phase 1b across one or more genomically-defined expansion cohorts. Additional information may be found at ClinicalTrials.gov, using Identifier NCT04985604.

About Tovorafenib
Tovorafenib is an investigational, oral, brain-penetrant, highly-selective type II pan-RAF kinase inhibitor designed to target a key enzyme in the MAPK signaling pathway, which is being investigated in primary brain tumors or brain metastases of solid tumors. Tovorafenib has been studied in over 250 patients to date. Currently tovorafenib is under evaluation in a pivotal Phase 2 clinical trial (FIREFLY-1) among pediatric, adolescent and young adult patients with pediatric low-grade glioma (pLGG), which is an area of considerable unmet need with no approved therapies. Tovorafenib is also being evaluated alone or as a combination therapy for adolescent and adult patient populations with recurrent or progressive solid tumors with MAPK pathway aberrations (FIRELIGHT-1). Tovorafenib has been granted Breakthrough Therapy and Rare Pediatric Disease designations by the U.S. Food and Drug Administration (FDA) for the treatment of patients with pLGG harboring an activating RAF alteration. Tovorafenib has also received Orphan Drug designation from the FDA for the treatment of malignant glioma, and from the European Commission (EC) for the treatment of glioma.

About Pimasertib
Pimasertib is an investigational, oral, highly selective, small molecule inhibitor of mitogen-activated protein kinases 1 and 2 (MEK-1/-2) within the MAPK signaling pathway. Pimasertib has been dosed in over 850 patients to date for various tumor types. Preclinical data indicates that the combination of a MEK inhibitor, such as pimasertib, and a type II RAF inhibitor, such as tovorafenib, has synergistic anti-tumor activity.

Day One is conducting a Phase 1b/2 study (FIRELIGHT-1) to evaluate the safety, tolerability, and preliminary efficacy of combining pimasertib with tovorafenib in adolescent and adult patients (≥12 years of age) with recurrent, progressive, or refractory solid tumors with MAPK pathway aberrations.

About Day One Biopharmaceuticals
Day One Biopharmaceuticals is a clinical-stage biopharmaceutical company developing targeted therapies for patients of all ages with life-threatening diseases. Day One was founded to address a critical unmet need: the dire lack of therapeutic development in pediatric cancer. The Company’s name was inspired by the “The Day One Talk” that physicians have with patients and their families about an initial cancer diagnosis and treatment plan. Day One aims to re-envision cancer drug development and redefine

what's possible for all people living with cancer—regardless of age—starting from Day One.

Day One partners with leading clinical oncologists, families, and scientists to identify, acquire, and develop important emerging cancer treatments. The Company's lead product candidate, tovorafenib, is an investigational, oral, brain-penetrant, highly-selective type II pan-RAF kinase inhibitor and the pipeline also includes pimasertib, an investigational, oral, highly-selective small molecule inhibitor of mitogen-activated protein kinases 1 and 2 (MEK-1/-2). Day One is based in South San Francisco. For more information, please visit www.dayonebio.com or find the company on LinkedIn or Twitter.

Cautionary Note Regarding Forward-Looking Statements
This press release contains "forward-looking" statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995, including, but not limited to: Day One's plans to develop cancer therapies, expectations from current clinical trials, the execution of the Phase 2 clinical trial for tovorafenib (DAY101) as designed, any expectations about safety, efficacy, timing and ability to complete clinical trials and to obtain regulatory approvals for tovorafenib and other candidates in development, and the ability of tovorafenib to treat pLGG or related indications.

Statements including words such as "believe," "plan," "continue," "expect," "will," "develop," "signal," "potential," or "ongoing" and statements in the future tense are forward-looking statements. These forward-looking statements involve risks and uncertainties, as well as assumptions, which, if they do not fully materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements.

Forward-looking statements are subject to risks and uncertainties that may cause Day One's actual activities or results to differ significantly from those expressed in any forward-looking statement, including risks and uncertainties in this press release and other risks set forth in our filings with the Securities and Exchange Commission, including Day One's ability to develop, obtain regulatory approval for or commercialize any product candidate, Day One's ability to protect intellectual property, the potential impact of the COVID-19 pandemic and the sufficiency of Day One's cash, cash equivalents and investments to fund its operations. These forward-looking statements speak only as of the date hereof and Day One specifically disclaims any obligation to update these forward-looking statements or reasons why actual results might differ, whether as a result of new information, future events or otherwise, except as required by law.

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