Day One Announces Positive Initial Data from Pivotal FIREFLY-1 Trial of Tovorafenib (DAY101) in Relapsed Pediatric Low-Grade Glioma

June 12, 2022

Data show an overall response rate (ORR) of 64% and clinical benefit rate (CBR) of 91% in the first 22 evaluable patients treated with monotherapy tovorafenib

Topline results from the full FIREFLY-1 trial population expected in Q1 2023

Day One plans to initiate a pivotal Phase 3 clinical trial of tovorafenib in front-line pediatric low-grade glioma (pLGG), with first patient dosed expected in Q3 2022

Company to host conference call and webcast tomorrow, June 13, at 8:00 a.m. Eastern Time

SOUTH SAN FRANCISCO, Calif., June 12, 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 positive initial data from the first 22 Response Assessment for Neuro-Oncology ("RANO")-evaluable patients enrolled in the ongoing, open-label, single-arm, pivotal Phase 2 FIREFLY-1 clinical trial. FIREFLY-1 is evaluating tovorafenib (DAY101) as once-weekly monotherapy in patients aged 6 months to 25 years with relapsed or progressive pLGG, which is the most common brain tumor diagnosed in children and for which there are no approved therapies and there is no standard of care. The primary endpoint of the FIREFLY-1 trial is ORR by RANO criteria as assessed by blinded independent central review. 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. FIREFLY-1 is being conducted in collaboration with the Pacific Pediatric Neuro-Oncology Consortium (PNOC) and is designed to support the potential regulatory approval of tovorafenib.

Initial data from the first 25 patients enrolled in the trial demonstrate:

- 64% ORR and 91% CBR (partial response/unconfirmed partial response + stable disease) in the 22 RANO-evaluable patients:
    - 14 partial responses (13 confirmed responses and 1 unconfirmed response)
    - 6 patients with stable disease
- All patients with stable disease (n=6) were noted to have tumor shrinkage, ranging between 19% and 43%
- Responses were observed in patients with both BRAF fusions and BRAF V600E mutations who received prior MAPK-targeted therapy
- The median-time-to-response was 2.8 months
- A heavily-pretreated population, with a median of 3 prior lines of therapy (range: 1-9)
- All patients who responded remain on therapy (n=14) and no patients have discontinued treatment due to treatment-related adverse events.

Initial safety data, based on the first 25 patients, indicated monotherapy tovorafenib to be generally well-tolerated. The majority of adverse events (AEs) were grade 1 or 2 in nature; the most common (≥25% any grade) treatment related AEs were increase in blood creatine phosphokinase, rash, and hair color changes. Treatment-related AEs of grade 3 or greater occurred in nine patients (36%).

"These initial findings underscore the potential of tovorafenib monotherapy to become a significant and transformative new option for relapsed/progressive pLGG, a pediatric brain tumor with no approved treatments today," said Samuel Blackman, M.D., Ph.D., co-founder and chief medical officer of Day One. "With the registrational cohort fully enrolled, patient follow-up is ongoing, and we look forward to the topline data from the complete study population in the first quarter of 2023. Based on these positive initial data, we plan to begin the pivotal Phase 3 FIREFLY-2 clinical trial evaluating tovorafenib as a front-line therapy in pLGG to evaluate whether tovorafenib can provide benefit early in the disease development."

"These initial data demonstrate significant anti-tumor activity in children with relapsed/progressive pLGG, including children who are refractory to available therapies. Pediatric low-grade glioma is a truly challenging disease in which children face years of aggressive regimens that can carry a long-term impact on learning, cognition, and quality of life," said Roger Packer, M.D., senior vice president, Center for Neuroscience and Behavioral Medicine, and director, Brain Tumor Institute, Children's National Hospital.

Day One plans to present additional interim trial results from FIREFLY-1 at an upcoming medical conference in the second half of 2022. Day One anticipates releasing topline results for the full FIREFLY-1 pivotal study population in the first quarter of 2023. If the data are supportive, Day One expects to submit a new drug application (NDA) to the United States Food and Drug Administration (FDA) in the first half of 2023.

Expanding Development of Tovorafenib in Front-Line pLGG

Based on these initial FIREFLY-1 data, Day One plans to expand the development of tovorafenib as a front-line therapy for patients newly diagnosed with pLGG. The global, pivotal Phase 3, registrational clinical trial ("FIREFLY-2/LOGGIC") will evaluate once-weekly monotherapy tovorafenib in newly-diagnosed patients with pLGG. The FIREFLY-2/LOGGIC study is designed to evaluate the efficacy and safety of tovorafenib in patients with newly-diagnosed pLGG harboring a known activating BRAF alteration. The study is a randomized, monotherapy, open-label trial aiming to enroll

approximately 400 patients aged 6 months to 25 years across approximately 100 sites globally, including in the U.S., Europe and Asia. Participants will be randomized to either tovorafenib (Arm 1) or an investigator's choice of one of three standard of care chemotherapy options (Arm 2). The primary endpoint will be the ORR based upon RANO criteria as reported by Blinded Independent Central Review. Secondary endpoints will include safety, progression-free survival, duration of response, functional outcomes, and quality of life measures.

Day One will conduct the FIREFLY-2/LOGGIC trial in collaboration with the Low-Grade Glioma in Children (LOGGIC) consortium, a group of internationally recognized experts in pLGG research, and an extensive network of pediatric oncology centers, including Hopp Children's Cancer Center Heidelberg (KiTZ), the German Cancer Research Center (DKFZ) and the Brain Tumor Group of the European Society for Paediatric Oncology (SIOPE BTG). Day One expects to dose the first patient in FIREFLY-2/LOGGIC trial in the third quarter of 2022.

Conference Call and Webcast Information
Day One will host a conference call and webcast tomorrow, June 13, 2022, at 8:00 a.m. Eastern Time. To participate by telephone, please dial 844-713-6132 (Domestic) or 1-213-320-2543 (International). The conference ID number is 3568447. The webcast will be made available for replay on the Company's website beginning approximately two hours after the event and will be available for 30 days following the live presentation.

About Pediatric Low-Grade Glioma
Pediatric low-grade glioma (pLGG) is the most common brain tumor diagnosed in children, accounting for 30% – 50% of all central nervous system tumors. BRAF wild-type fusions are the most common cancer-causing genomic alterations in pediatric low-grade gliomas. These genomic alterations are also found in several adult and pediatric solid tumors. Currently approved BRAF inhibitors are only active in tumors harboring BRAF V600 mutations, exhibit limited activity in brain tumors, and cannot be used in patients harboring BRAF fusions.

Pediatric low-grade glioma can impact a child's health in many ways depending on tumor size and location, including vision loss and motor dysfunction. There are no approved therapies for pLGG, and current treatment approaches are associated with significant acute and life-long adverse effects. While most children with pLGG survive their cancer, children who do not achieve remission following surgery may face years of increasingly aggressive therapies that can have lasting effects on learning, cognition, and quality of life. Due to the indolent nature of pLGG, patients receive multiple years of systemic therapy.

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 the Pacific Pediatric Neuro-Oncology Consortium
The Pacific Pediatric Neuro-Oncology Consortium (PNOC) is an international consortium with study sites within the United States, Canada, Europe and Australia dedicated to bringing new therapies to children and young adults with brain tumors.

About Day One Biopharmaceuticals
Day One Biopharmaceuticals is a clinical-stage biopharmaceutical company that believes when it comes to pediatric cancer, we can do better. We put kids first and are developing targeted therapies that deliver to their needs. 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 (DAY101), is an investigational, oral, brain-penetrant, highly-selective type II pan-RAF kinase inhibitor. The Company's 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 DAY101 as designed, any expectations about safety, efficacy, timing and ability to complete clinical trials, release data results and to obtain regulatory approvals for DAY101 and other candidates in development, and the ability of DAY101 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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