Day One Announces Topline Data from Pivotal Phase 2 FIREFLY-1 Trial Demonstrating Meaningful Responses with Tovorafenib (DAY101) in Recurrent or Progressive Pediatric Low-Grade Glioma

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- *Overall response rate (ORR) of 64% and clinical benefit rate (CBR) of 91% in 69 heavily-pretreated, RANO-evaluable patients*
- *Median duration of 8.4 months on therapy as of September 28, 2022, with 77% of patients remaining on treatment*
- *Additional data to be presented at a medical meeting in the second quarter of 2023*
- *New Drug Application submission planned for first half of 2023*

SOUTH SAN FRANCISCO, Calif., Jan. 08, 2023 (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 topline results from the ongoing, open-label, pivotal Phase 2 FIREFLY-1 trial evaluating the investigational agent, tovorafenib (DAY101), as a monotherapy in recurrent or progressive pediatric low-grade glioma (pLGG). Pediatric low-grade glioma is the most common brain tumor diagnosed in children and for which there is no standard of care, and for which there are no approved therapies for the majority of patients. Additional data will be submitted for presentation at an upcoming medical meeting in the second quarter of 2023.

The primary endpoint of the FIREFLY-1 trial is overall response rate (ORR) by Response Assessment for Neuro-Oncology (RANO) criteria as assessed by blinded independent central review. Topline results as of September 28, 2022 include:

Among 69 RANO-evaluable patients:

- 64% ORR and 91% clinical benefit rate (complete response + partial response/unconfirmed partial response + stable disease)
    - 4% (n=3) confirmed complete responses
    - 59% (n=41) partial responses (31 confirmed and 10 unconfirmed)
    - 28% (n=19) patients with stable disease
- 86% (n=59) of patients had a BRAF fusion alteration, for which there are no approved systemic therapies, while the remaining 14% (n=10) had a BRAF mutation

Safety data, based on 77 treated patients, indicated monotherapy tovorafenib to be generally well-tolerated. The most common side effects reported related to tovorafenib were change in hair color (75%), increased creatine phosphokinase (64%), anemia (46%), fatigue (42%) and maculopapular rash (42%).

Among a total of 77 treated patients:

- Participants were heavily pretreated, with a median of three prior lines of systemic therapy (range: 1-9)
- The median duration of tovorafenib treatment was 8.4 months, with 77% (n=59) of patients on treatment at the time of the data cutoff
- Nearly 60% (n=46) of patients had already received at least one prior MAPK inhibitor prior to study participation

“The responses we’ve observed in the FIREFLY-1 study with weekly monotherapy tovorafenib in children with recurrent or progressive low-grade gliomas are very encouraging,” said Samuel Blackman, M.D., Ph.D., co-founder and chief medical officer of Day One. “As tovorafenib progresses in the clinic, we want to thank the patients, their families, the clinical investigators, and the advocates who have chosen to participate in the FIREFLY-1 clinical trial and support the development of a potential new treatment for children in need of new therapeutic options.”

FIREFLY-1 is evaluating tovorafenib as once-weekly monotherapy in patients aged 6 months to 25 years with recurrent or progressive pLGG. The trial is being conducted in collaboration with the Pacific Pediatric Neuro-Oncology Consortium (PNOC) and is designed to support the potential regulatory approval of tovorafenib.

“Based on the efficacy and safety profile of tovorafenib observed to date from the FIREFLY-1 trial population, we plan to submit a New Drug Application in the first half of this year that will include additional follow up from the full study population,” said Jeremy Bender, Ph.D., chief executive officer of Day One. “We look forward to continuing our discussions with regulatory authorities with the hope of bringing this therapy to children in need of new options as soon as possible.”

In addition to FIREFLY-1, Day One is expanding the development of tovorafenib as a front-line therapy for patients newly

diagnosed with pLGG. The global, Phase 3, registrational FIREFLY-2/LOGGIC clinical trial is evaluating once-weekly monotherapy tovorafenib in newly-diagnosed patients with pLGG harboring a known activating RAF alteration.

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.

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 potential 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. Due to the indolent nature of pLGG, patients generally 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 325 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 recurrent or progressive 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 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 and Phase 3 clinical trial for tovorafenib as designed, any expectations about safety, efficacy, timing and ability to complete clinical trials, release data results 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 global business or macroeconomic conditions, including as a result of the COVID-19 pandemic, inflation and rising interest rates 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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