Day One Announces Updated FIREFLY-1 Data for Tovorafenib and Completion of Rolling NDA Submission to FDA for Relapsed or Progressive Pediatric Low-Grade Glioma (pLGG)

September 11, 2023

Overall response rate (ORR) greater than 50% across three assessment criteria

Median duration of tovorafenib treatment of 15.8 months as of June 5, 2023, with 66% of patients remaining on treatment

FDA filing decision expected by mid-November

BRISBANE, Calif., Sept. 11, 2023 (GLOBE NEWSWIRE) -- Day One Biopharmaceuticals (Nasdaq: DAWN) (“Day One” or the “Company”), a clinical-stage biopharmaceutical company dedicated to developing and commercializing targeted therapies for people of all ages with life-threatening diseases, today announced the recently completed submission of the rolling New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) for tovorafenib as a monotherapy in relapsed or progressive pediatric low-grade glioma (pLGG). The Company anticipates the FDA will file the rolling NDA by mid-November 2023.

pLGG is the most common brain tumor diagnosed in children, with patients suffering profound tumor and treatment-associated morbidities that can impact their life trajectory over the long term. For the majority of patients in the relapsed setting, there is no standard of care and no approved therapies.

“We believe that tovorafenib, if approved, could change the treatment landscape for children living with this chronic and relentless disease,” said Jeremy Bender, Ph.D., chief executive officer of Day One. “The NDA submission of tovorafenib is a significant milestone for Day One and an important step towards bringing a potential new targeted therapy to children with brain cancer.”

The Company initiated the rolling submission of the NDA in May 2023 based on data from the FIREFLY-1 trial with a data cutoff as of December 22, 2022. An updated Clinical Study Report (CSR) was submitted to the FDA with an additional six months of safety and efficacy data through June 5, 2023.

FIREFLY-1 is an open-label, pivotal Phase 2 trial, which treated a total of 137 patients across two study arms. Arm 1 evaluated tovorafenib in 77 patients as a once-weekly monotherapy in patients aged 6 months to 25 years with relapsed or progressive pLGG. The primary endpoint of the trial is ORR by Response Assessment for Neuro-Oncology High-Grade Glioma (RANO-HGG) criteria. Secondary endpoints include ORR by Response Assessment in Pediatric Neuro-Oncology Low-Grade Glioma (RAPNO-LGG), progression-free survival (PFS), duration of response (DOR), time to response, clinical benefit rate and safety. The NDA submission also includes an exploratory analysis of ORR by Response Assessment for Neuro-Oncology Low-Grade Glioma (RANO-LGG). All data have been assessed by a blinded Independent Review Committee (IRC).

Updated FIREFLY-1 Data Demonstrate Consistent and Durable Response

New data from the FIREFLY-1 trial, with a data cutoff of June 5, 2023, are described below. Detailed data will be presented at an upcoming medical conference.

RANO-HGG (n=69 evaluable) data, the primary endpoint of the trial:

- 67% ORR (complete response (CR) + partial response (PR))
- 93% clinical benefit rate (CBR) (CR + PR + stable disease (SD))
    - 17% (n=12) CR
    - 49% (n=34) PR
    - 26% (n=18) SD
- At the time of data cutoff, the median duration of response (DOR) based on RANO-HGG criteria was 16.6 months (95% CI: 11.6, not estimable)

Among a total of 77 treated patients:

- The median duration of tovorafenib treatment was 15.8 months, with 66% (n=51) of patients on treatment at the time of data cutoff

Safety data, based on the 137 patients treated in both Arm 1 and Arm 2 of FIREFLY-1, indicated monotherapy tovorafenib to be generally well-tolerated. The vast majority of adverse events were Grade 1 or Grade 2, with most common side effects reported related to tovorafenib being change in hair color (76%), fatigue (44%), maculopapular rash (41%), dry skin (33%), and dermatitis acneiform (30%). The most commonly reported treatment-related lab abnormalities were CPK elevation, LDH elevation, anemia, hypophosphatemia and AST elevation. Nearly all of the lab abnormalities had no clinical manifestations and did not require clinical intervention or change in study treatment.

The NDA submission also included the evaluation of responses by RAPNO-LGG and RANO-LGG. Those results include:

RAPNO-LGG (n=76 evaluable) data, a key secondary endpoint of the trial:

- 51% ORR (CR + PR + minor response (MR))
- 82% CBR (CR+ PR + MR + SD)
    - 37% (n=28) PR
    - 14% (n=11) MR
    - 30% (n=23) SD
- At the time of data cutoff, the median DOR based on RAPNO-LGG criteria was 13.8 months (95% CI: 11.3, not estimable)

RANO-LGG (n=76 evaluable) data, an exploratory analysis of the trial:

- 53% ORR (CR + PR + MR)
- 83% CBR (CR + PR + MR + SD)
    - 26% (n=20) PR
    - 26% (n=20) MR
    - 30% (n=23) SD
- At the time of data cutoff, the median DOR based on RANO-LGG criteria was 14.4 months (95% CI: 11.0, not estimable)

Tovorafenib was granted Rare Pediatric Disease Designation for relapsed or progressive pLGG and, as such, may qualify for receipt of a priority review voucher, if tovorafenib is approved by the FDA in this indication. Based on Day One's current operating plan, management believes it has sufficient capital resources to fund anticipated operations into 2026.

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 systems tumors. BRAF wild-type fusions are the most common cancer-causing genomic alterations in pLGG. These genomic alterations are also found in severe 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 the vast majority of patients with 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 FIREFLY-1
FIREFLY-1 is evaluating tovorafenib as once-weekly monotherapy in patients aged 6 months to 25 years with relapsed or progressive pLGG harboring a known activating BRAF alteration. The trial is being conducted in collaboration with the Pacific Pediatric Neuro-Oncology Consortium (PNOC). The primary endpoint is overall response rate (ORR), defined as the proportion of patients with confirmed response based upon RANO-HGG criteria. Secondary and exploratory endpoints include the overall response rate based on RAPNO-LGG criteria, RANO-LGG criteria and volumetric analyses, progression-free survival, safety, functional outcomes, and quality of life measures. RANO-HGG, RANO-LGG and RAPNO-LGG are assessed by blinded independent central review. Additional information about FIREFLY-1 may be found at ClinicalTrials.gov, using Identifier NCT04775485.

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 Tovorafenib
Tovorafenib is an investigational, oral, brain-penetrant, highly-selective type II 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 relapsed or progressive pLGG, which is an area of considerable unmet need with no approved therapies for the vast majority of patients. 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 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, is an investigational, oral, brain-penetrant, highly-selective type II 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 Brisbane, California. For more information, please visit www.dayonebio.com or find the Company on LinkedIn or X/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 trials for tovorafenib as designed, any expectations about safety, efficacy, timing and ability to complete clinical trials, release data results, the ability of Day One to obtain regulatory approvals for tovorafenib and other candidates in development, including the acceptance by the FDA of Day One's NDA submission for tovorafenib, 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. 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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