Day One Announces New FIREFLY-1 Data for Tovorafenib (DAY101) and Initiation of Rolling NDA Submission to FDA for Relapsed or Progressive Pediatric Low-Grade Glioma

June 4, 2023

Overall response rate (ORR) of 67% and clinical benefit rate (CBR) of 93% in 69 heavily pretreated RANO-HGG evaluable patients

The Company expects to complete rolling NDA submission in October 2023

Conference call and webcast today at 6:00 p.m. CT

BRISBANE, Calif., June 04, 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 new data from the registrational Phase 2 FIREFLY-1 trial evaluating the investigational agent tovorafenib (DAY101). These data were shared in an oral presentation today at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting. In addition, the Company announced that it has initiated a 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).

“We believe the data presented at ASCO for monotherapy tovorafenib demonstrate durable responses in children with relapsed pLGG who have limited treatment options,” said Jeremy Bender, Ph.D., chief executive officer of Day One. "Based on the strength of the safety and efficacy data we’ve observed to date, we believe tovorafenib has a compelling clinical profile. We’re looking forward to continuing our collaboration with the FDA as we submit the remainder of the data over the next several months.”

FIREFLY-1 Program Update

In May 2023, the Company initiated a rolling submission of the NDA to the FDA. The rolling submission allows Day One to submit portions of the regulatory application and have them reviewed by the FDA on an ongoing basis. The Company anticipates the rolling NDA submission of tovorafenib will be complete in October 2023 following submission of an amended clinical study report (CSR) that will include safety and efficacy data from a planned June 2023 data cutoff.

Updated FIREFLY-1 Data Presented at ASCO

FIREFLY-1, an open-label, pivotal Phase 2 trial, treated 77 patients and evaluated tovorafenib as a once-weekly monotherapy in patients aged 6 months to 25 years with relapsed or progressive pLGG (Arm 1). The primary endpoint of the FIREFLY-1 trial is overall response rate (ORR) by Response Assessment for Neuro-Oncology High-Grade Glioma (RANO-HGG) criteria as assessed by blinded independent central review. 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 study also includes an exploratory analysis of ORR by Response Assessment Neuro-Oncology Low-Grade Glioma (RANO-LGG).

New data from the FIREFLY-1 trial, with a data cutoff of December 22, 2022, were presented at ASCO by Dr. Lindsay Kilburn of Children’s National Medical Center.

Patient demographics in registrational Arm 1 (n=77):

- 83% (n=64) of patients had a BRAF fusion, for which there are no approved systemic therapies, while the remaining 17% (n=13) had a BRAF V600E mutation
- Participants were heavily pretreated, with a median of two prior lines of systemic therapy (range: 1-9) and 49% (n=38) of patients having 3 or more prior lines of therapy
- 60% (n=46) of patients had already received at least one prior MAPK inhibitor prior to study participation

RANO-HGG (n=69) data:

- 67% ORR by RANO-HGG, the primary endpoint of the trial
- 93% clinical benefit rate (complete response (CR) + partial response (PR) + stable disease (SD))
  - 6% (n=4) CR
  - 61% (n=42) PR, including 3 uPR
  - 26% (n=18) SD
- At the time of data cutoff, the median duration of response (DOR) based on RANO-HGG criteria was not yet reached (95% CI: 9.0 months, not estimable)

Among a total of 77 treated patients:

- The median duration of tovorafenib treatment was 10.8 months, with 74% (n=57) of patients on treatment at the time of data cutoff

Safety data, based on the 136 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 (71%), fatigue (50%), vomiting (43%), maculopapular rash (41%) and headache (39%). The most commonly reported lab abnormalities were CPK 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.

"We have observed tovorafenib as being well tolerated in children and is resulting in clinically meaningful responses in patients, many of whom have tumors which have progressed in spite of multiple prior therapies," said Dr. Lindsay Kilburn, Children's National Medical Center.

Additional Secondary and Exploratory Endpoint Analyses

The Company also shared the evaluation of responses by RAPNO-LGG and RANO-LGG. Those results include:

*RAPNO-LGG data (n=69):

- 51% (n=35) ORR by RAPNO-LGG
  - 25% (n=17) PR including 4 uPR
  - 26% (n=18) MR including 4 uMR
  - 36% (n=25) patients with SD
- The median time to response was 5.5 months for confirmed responses
- At the time of data cutoff, the median Independent Review Committee (IRC)-assessed DOR based on confirmed RAPNO-LGG responses is 12 months (95% CI: 11.2, not estimable)

**Pending adjudication*

RANO-LGG (n=76) data:

- 49% (n=37) ORR by RANO-LGG
  - 26% (n= 20) PR including 8 uPR
  - 22% (n= 17) MR including 2 uMR
  - 34% (n=26) patients with SD
- The median time to response was 4.2 months for confirmed responses
- At the time of data cutoff, the median IRC-assessed DOR based on confirmed RANO-LGG responses is 14.4 months (95% CI: 8.4, not estimable)

"When we look at the clinical activity of monotherapy tovorafenib in FIREFLY-1, we are seeing high rates of durable tumor reduction in this heavily pre-treated population, and a safety profile that allows for potential long-term dosing. For a patient population in which the goal of therapy has historically been prolonged disease stabilization, we are seeing meaningful responses across various assessment criteria," said Dr. Samuel Blackman, co-founder and head of research and development, Day One. "We look forward to following the data as we continue to collaborate with the FDA to complete our NDA submission and potentially bring a new medicine to these underserved children."

The presentation is accessible on the Day One investor website.

Conference Call and Webcast Information
Day One will host a conference call and webcast on June 4, 2023, at 6:00 p.m. CT. Participants can access the conference call live via webcast from the Investors & Media page of Day One's website. To participate via telephone, please register in advance at this link. Upon registration, all telephone participants will receive a confirmation email detailing how to join the conference call, including the dial-in number along with a unique passcode that can be used to access the call.

The webcast will be made available for replay on the Company's website 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 pLGG. 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 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 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 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 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 Brisbane, California. 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 trials 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 inflation, rising interest rates, instability in the global banking system, and geopolitical conflicts 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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