Day One Announces First Patient Dosed in FIREFLY-1 Pivotal Phase 2 Clinical Trial of DAY101 in Pediatric Progressive Low-Grade Glioma

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- FIREFLY-1 is designed to support regulatory registration of DAY101 in pediatric low-grade glioma (pLGG), which is the most common form of childhood brain cancer and has no approved therapies
- DAY101 is an oral, brain-penetrant, highly-selective type II pan-RAF kinase inhibitor with demonstrated evidence of anti-tumor activity in pLGG

SOUTH SAN FRANCISCO, CA, May 11, 2021 – Day One Biopharmaceuticals, a clinical-stage biopharmaceutical company dedicated to developing and commercializing targeted therapies for patients of all ages with genetically defined cancers, today announced that the first patient has been dosed in FIREFLY-1, a Phase 2 clinical trial evaluating the safety and efficacy of DAY101 in pediatric, adolescent and young adult patients with recurrent or progressive low-grade glioma harboring a known BRAF alteration. Pediatric low-grade glioma (pLGG) is the most common form of childhood brain cancer and has no approved targeted therapeutics. The trial is being conducted in collaboration with the Pacific Pediatric Neuro-Oncology Consortium (PNOC) and is designed to support the regulatory approval of DAY101.

DAY101 is an oral, brain-penetrant, highly-selective type II pan-RAF kinase inhibitor designed to target a key enzyme in the MAPK signaling pathway. Dysregulation of the MAPK pathway has been shown to occur in many cancers. In pLGG, BRAF wild-type fusions are the most common cancer-causing genomic alterations. DAY101 has been granted Breakthrough Therapy designation by the U.S. Food and Drug Administration (FDA) for the treatment of patients with pLGG harboring an activating RAF alteration who require systematic therapy and who have either progressed following prior treatment or who have no satisfactory alternative treatment options.

“Treating the first patient in FIREFLY-1 is an important milestone for Day One and underscores our critical mission of advancing innovative targeted therapies for people of all ages living with cancer,” said Jeremy Bender, Ph.D., chief executive officer of Day One. “Children with low-grade glioma often face surgery and years of increasingly aggressive therapies that can have lasting effects on learning, cognition, and quality of life. We look forward to working closely with PNOC to complete this trial, which has the potential to make DAY101 the first approved therapy for pLGG and the first approved pan-RAF inhibitor.”

“Studies have demonstrated that DAY101 has high brain distribution and exposure, thus potentially benefiting patients with brain tumors such as pLGG,” said Samuel Blackman, M.D., Ph.D., co-founder and chief medical officer of Day One. “The FIREFLY-1 pivotal trial follows initial data from the Phase 1 PNOC014 study in nine children with pLGG, which indicated that DAY101, as monotherapy, has potent anti-tumor activity, rapid onset of responses, and was well tolerated. We believe DAY101 has the potential to become an important treatment advance for pediatric patients with RAF-altered low-grade gliomas.”

About FIREFLY-1
FIREFLY-1 is a pivotal Phase 2, multicenter, open-label study designed to evaluate the safety and efficacy of DAY101 in patients aged 6 months to 25 years with relapsed or progressive low-grade glioma harboring a known activating BRAF alteration. The study aims to enroll approximately 60 patients, who will receive oral DAY101 at a dose of 420 mg/m2 once weekly. The primary endpoint will be overall response rate (ORR), defined as the proportion of patients with best overall confirmed response rate based upon Response Assessment for Neuro-Oncology (RANO) criteria. Secondary and exploratory endpoints include the overall response rate based on Response Assessment in Pediatric Neuro-Oncology (RAPNO) criteria and volumetric analyses, event free survival, safety, functional outcomes, and quality of life measures.

Additional information about FIREFLY-1 may be found at ClinicalTrials.gov, using Identifier NCT04775485.

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 mutations in pediatric low-grade gliomas. These genomic alterations are also found in several adult 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 a cure following surgery 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 DAY101
DAY101 is an oral, brain-penetrant, highly-selective type II pan-RAF kinase inhibitor designed to target a key enzyme in the MAPK signaling pathway. Studies have shown DAY101 has high brain distribution and exposure in comparison to other MAPK pathway inhibitors, thus potentially benefiting patients with primary brain tumors or brain metastases of solid tumors. DAY101 is a type II RAF inhibitor that selectively inhibits both monomeric and dimeric RAF kinase, which broadens its potential clinical application to treat an array of RAF-altered tumors.

DAY101 has been studied in over 250 patients, and as a monotherapy demonstrated good tolerability and encouraging anti-tumor activity in pediatric and adult populations with specific MAPK pathway-alterations.

In November 2020, Day One announced preliminary results from PNOC014, an ongoing Phase 1 Pacific Pediatric Neuro-Oncology Consortium (PNOC) network study with DAY101 sponsored by the Dana-Farber Cancer Institute, in patients under 18 years of age with relapsed low-grade glioma. Preliminary results demonstrated that of the eight patients in the study with RAF fusions, two patients achieved a complete response by Response Assessment for Neuro-Oncology (RANO), three had a partial response, two achieved prolonged stable disease, and one experienced progressive disease. DAY101 also demonstrated a tolerable safety profile.

DAY101 has been granted Breakthrough Therapy designation by the U.S. Food and Drug Administration (FDA) for the treatment of patients with pLGG harboring an activating RAF alteration who require systemic therapy and who have either progressed following prior treatment or who have no satisfactory alternative treatment options. In addition, DAY101 has received Orphan Drug designation from the FDA for the treatment of malignant glioma.

Day One is conducting a pivotal Phase 2 trial (FIREFLY-1) of DAY101 in pediatric, adolescent and young adult patients with pLGG. Day One also plans to study DAY101 alone or in combination with other agents that target key signaling nodes in the MAPK pathway, such as the Company's MEK inhibitor pimasertib, in patient populations where various RAS and RAF alterations are believed to play an important role in driving disease.

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, Israel, 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 dedicated to developing and commercializing targeted therapies for patients of all ages with genetically defined cancers. Day One was founded to address a critical unmet need: children with cancer are being left behind in a cancer drug development revolution. Our name was inspired by the "The Day One Talk" [1] that physicians have with patients and their families about an initial cancer diagnosis and treatment plan. We aim 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, DAY101, is an oral, highly-selective type II pan-RAF kinase inhibitor, and is being evaluated in a pivotal Phase 2 clinical trial (FIREFLY-1) in pediatric, adolescent and young adult patients with recurrent or progressive low-grade glioma (pLGG). The Company's pipeline also includes the investigational agent pimasertib, a clinical-stage, oral, highly selective small molecule inhibitor of mitogen-activated protein kinase kinases 1 and 2 (MEK). Through Day One and its collaborators, cancer drug development comes of age. Day One is based in South San Francisco. For more information, please visit www.dayonebio.com.

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 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.

[1]Jennifer W. Mack and Holcombe E. Grier; Journal of Clinical Oncology 2004 22:3, 563-566

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