



## **Day One Announces Preliminary Phase 1 Results for DAY101 in Pediatric Low-Grade Glioma, Receipt of Breakthrough Therapy Designation (BTD) and New Phase 2 Study**

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In PNOC014, an ongoing Phase 1 Pacific Pediatric Neuro-Oncology Consortium (PNOC) network study sponsored by the Dana-Farber Cancer Institute, nine patients under 18 years of age with relapsed low-grade glioma have been treated with DAY101.

- Of the eight patients 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. The median time to response for these patients was only 10.5 weeks, and the most common side effects were skin rash and hair color changes.
- The US Food and Drug Administration (FDA) has granted DAY101 BTD for the treatment of pediatric patients with advanced low-grade glioma harboring RAF alteration. The FDA has also granted DAY101 Orphan Drug Designation for the treatment of malignant glioma.
- Day One is starting a global, single-arm, monotherapy, registration-enabling Phase 2 study of DAY101 for children and young adults with recurrent or progressive BRAF-altered low-grade gliomas.

South San Francisco, November 19, 2020: Day One Biopharmaceuticals, a company driven to develop promising new oncology therapies for both children and adults living with cancer, announced interim results from PNOC014, an ongoing Phase 1 investigator-sponsored study conducted by Dana-Farber and the Pacific Pediatric Neuro-Oncology Consortium (PNOC) of DAY101 in children with radiographically recurrent/progressive low-grade gliomas and other MAP kinase pathway activated tumors.

DAY101 is an investigational agent designed as an oral, once-weekly, brain-penetrant pan-RAF kinase inhibitor and is being developed by Day One for children and adults living with cancer. Over 250 patients have received DAY101 in clinical trials thus far. Early studies have demonstrated evidence of anti-tumor activity in adult and pediatric populations with specific genetic alterations in the RAS/MAP kinase pathway.

Preliminary results from PNOC014 were presented at the 25th Annual Scientific Meeting and Education Day of the Society for Neuro-Oncology, held virtually November 19-22, 2020 (CTNI-19) and can be viewed [in this link](#) by any registered attendee. The objective of the PNOC014 study is to assess the pharmacokinetics, safety and preliminary efficacy of DAY101 in children with recurrent or progressive pediatric low-grade gliomas and other RAS/RAF/MEK/ERK pathway activated tumors. Preliminary data from the nine patients in the first three dose escalation cohorts receiving once-weekly oral DAY101 were reviewed. Linear PK and predominantly grade 1-2 dermatological side effects were observed, including one grade 3 elevation in a muscle enzyme called creatinine phosphokinase or CPK. No grade 4 adverse events have been reported based on these preliminary data. A maximum tolerated dose has not been reached. Tumor response was assessed by an independent radiologic reviewer.

"We found in an independent analysis of the nine patients treated in the ongoing Phase 1 study that the majority had responses or stable disease based upon Response Assessment for Neuro-Oncology (RANO) criteria," says Dr. Karen D. Wright, Senior Physician at Dana-Farber and Assistant Professor of Pediatrics at Harvard Medical School and principal investigator and author of the Phase 1 study.

DAY101 has been granted BTD by the FDA for the treatment of pediatric patients with an advanced low-grade glioma 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. The BTD is designed to speed the development and regulatory review of new medicines that are intended to treat a serious condition and that have shown encouraging early clinical results, which demonstrate substantial, meaningful improvement over available medicines and where there is significant unmet medical need. The FDA granted this designation based on all of the available clinical data from the DAY101 development program, including data from the PNOC014 study. As noted above, DAY101 has also received Orphan Drug Designation from the FDA for the treatment of malignant glioma.

"These preliminary Phase 1 data suggest that DAY101, a CNS penetrant inhibitor of BRAF and CRAF fusions and mutations, appears to be well-tolerated and may have meaningful anti-tumor activity in pediatric patients with low-grade glioma," says Dr. Samuel Blackman, founder and Chief Medical Officer of Day One Biopharmaceuticals. "Of the eight patients with a confirmed RAF-fusion, we observed that two patients achieved a complete response, three had a partial response, two achieved stable disease, and one experienced progressive disease, with a median time to response of 10.5 weeks. The observed complete responses, rapid onset of responses, and durability of responses observed thus far make us excited about the potential that

DAY101 may have for providing meaningful clinical improvements for pediatric patients with RAF-altered low-grade gliomas in the coming years.”

Pediatric low-grade glioma is the most common form of childhood brain cancer, with over a thousand new diagnoses each year in the U.S. RAF alterations, including BRAF mutations and RAF fusions, are the most common cancer-causing genetic mutations in pediatric low-grade gliomas. These genetic alterations are also found in multiple adult solid tumors. Low-grade glioma can impact a child’s health in many ways depending on tumor size and location, including vision loss and motor dysfunction. While most children with low-grade gliomas survive their cancer, children who do not achieve a cure following surgery face years of increasingly aggressive chemotherapy that can have lasting effects on learning, cognition, and quality of life. There are no FDA approved therapies for pediatric low-grade glioma, and current treatments are associated with significant acute and life-long adverse effects. As a result, the unmet medical need for these patients remains high.

The PNOC014 trial is supported by the PLGA Fund at the Pediatric Brain Tumor Foundation, the Team Jack Foundation, Team Nathan, Day One, the Takeda Pharmaceutical Company, Dana-Farber Cancer Institute (DFCI), and the National Cancer Institute of the National Institutes of Health under award number P50 CA 165962 as part of the prestigious SPORC grant for Targeted Therapies in Gliomas awarded to Dana-Farber and Brigham and Women’s Hospital under Dr.’s Tracey Batchelor and Mario Suva and for which Dr. Wright is co-Principal Investigator on project 1 with co-collaborators Dr. Michael Eck and Dr. Daphne Haas-Kogan.

“Day One is launching a global Phase 2 monotherapy trial concurrent with the ongoing Phase 1 trial, evaluating the efficacy and safety of DAY101 administered orally, once-a-week in pediatric patients with relapsed or progressive low-grade glioma harboring a BRAF-alteration. The study will be conducted in collaboration with PNOC, is called FIREFLY-1 and PNOC026, and is intended to support DAY101 registration,” noted Dr. Jeremy Bender, CEO of Day One. “Day One’s rapid clinical, manufacturing, and regulatory execution of the DAY101 program demonstrates the commitment of this capable team. Children with cancer and their families are waiting for more options.”

#### **About Day One Biopharmaceuticals**

Day One Biopharmaceuticals is committed to leading the development of promising new therapies in children and to improving the standard of care for patients of all ages living with cancer. Day One partners with leading clinical oncologists, families, and scientists to identify, acquire, and develop emerging cancer treatments that can help both children and adults living with cancer. The company raised a \$62M series A financing from Canaan, Access Biotechnology, and Atlas Venture. Through Day One and its collaborators, cancer drug development comes of age. For more information, please visit [www.dayonebio.com](http://www.dayonebio.com).

#### **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.

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