Day One Announces Three Year Follow-Up Data From OJEMDA™ (tovorafenib) Phase 2 FIREFLY-1 Trial at the 2025 Society for Neuro-Oncology (SNO) Annual Meeting

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Updated data expands clinically meaningful results available from FIREFLY-1 pivotal trial

77% of patients who entered the treatment-free observation period following OJEMDA treatment remained off therapy for at least 12 months

The median time to next treatment (TTNT) following initiation of OJEMDA exceeded 3.5 years

BRISBANE, Calif., Nov. 24, 2025 (GLOBE NEWSWIRE) -- Day One Biopharmaceuticals, Inc. (Nasdaq: DAWN) ("Day One" or the "Company"), a biopharmaceutical company dedicated to developing and commercializing targeted therapies for people of all ages with life-threatening diseases, today announced three-year results from the OJEMDA pivotal Phase 2 FIREFLY-1 trial in an oral presentation at the 30th Annual Meeting & Education Day of the Society for Neuro-Oncology .

New data from the ongoing FIREFLY-1 trial (Arm 1), with an updated median study duration of 40.6 months (data cutoff June 6, 2025), are described below. Primary trial results, including trial eligibility, patient demographics, efficacy and safety have been previously reported (Kilburn, et al. *Nature Medicine 2024)*.

"We are excited by these updated three-year data showing that patients taking tovorafenib were able to spend meaningful time off therapy, with the option to retreat as needed," said Elly Barry, MD, Chief Medical Officer of Day One. "These findings highlight the potential for a treatment approach to help support patients through the long-term course of their disease and further support our view that tovorafenib has the potential to become the second line standard of care in pLGG."

In 76 evaluable patients from Arm 1, 44 (58%) completed 26 or more cycles of treatment (approximately 24 months). Amongst the key primary endpoints, the overall response rate was 53% (40/76), the median duration of response was 19.4 months (95% CI [13.8-27.2]), and the time to response was 5.4 months (range [1.6-17.5]). The pre-specified secondary study endpoint of Progression Free Survival was evaluated by Response Assessment in Pediatric Neuro-Oncology Low-Grade Glioma. The median was 16.6 (10.9–22.0) months.

Exploratory analyses were also undertaken to further assess the clinical impact of tovorafenib in the same study population. Among these analyses:

- The median time-to-next-treatment (defined as the time from the date of the first dose of tovorafenib to the start of the first subsequent anticancer treatment, or date of death) was 42.6 months (95% CI [36.7-NE]).
- 39 patients entered a treatment-free observation period:
    - 77% (30/39) were treatment-free for a minimum of 12 months.
    - Median treatment-free interval, measured from the end of tovorafenib primary treatment to the start of the next subsequent anticancer treatment or death, was not reached.
    - Tumor rebound was minimal in the first 6 months off therapy, with 31% of patients experiencing a ≥25% increase in tumor size from the last scan prior to the last dose.
    - Eight patients received retreatment with tovorafenib:
        - The median retreatment duration was 9 months (all patients remained on therapy at the time of data cutoff).
        - The median maximum percentage change in tumor reduction was –38.3%.

"These three-year data showed that patients were able to maintain disease control during extended periods off therapy, with the option to reinitiate tovorafenib treatment if clinically indicated," said Dr. Cassie Kline, Director of Clinical Research in the Division of Neuro-Oncology at the Children's Hospital of Philadelphia. "This approach has the potential to offer patients and their families meaningful time away from treatment."

In this updated three-year analysis, no new safety signals were identified. Grade 3 or higher adverse events most commonly reported (≥ 5% of patients) were decreased growth velocity, anemia, blood creatine phosphokinase increased, maculopapular rash, alanine aminotransferase increased.

Tovorafenib is approved by the U.S. Food and Drug Administration for the treatment of pediatric patients 6 months of age and older with relapsed or refractory pediatric low-grade glioma (pLGG) harboring a BRAF fusion or rearrangement.

About tovorafenib

Tovorafenib (known as OJEMDA™ in the U.S.) is a Type II RAF kinase inhibitor mutant BRAF V600, wild-type BRAF, and wild-type CRAF kinases. Tovorafenib is indicated for the treatment of patients 6 months of age and older with relapsed or refractory pediatric low-grade glioma (LGG) harboring a BRAF fusion or rearrangement, or BRAF V600 mutation. This indication is approved under accelerated approval based, in part, on response rate and duration of response according to multiple response assessment criteria: Response Assessment in Neuro-Oncology High-Grade Glioma (RANO-HGG) criteria, Response Assessment in Pediatric Neuro-Oncology Low-Grade Glioma (RAPNO LGG) criteria, and Response Assessment for Neuro-Oncology Low-Grade Glioma (RANO LGG) criteria. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Tovorafenib is under evaluation as a therapy for patients aged 6 months to 25 years with pLGG harboring BRAF fusion or rearrangement, or BRAF V600 mutation requiring front-line treatment (Phase III FIREFLY-2/LOGGIC).

Tovorafenib was granted Breakthrough Therapy and Rare Pediatric Disease designations by the FDA for the treatment of patients with pLGG harboring an activating RAF alteration, and it was evaluated by the FDA under priority review. Tovorafenib has also received Orphan Drug designation from the FDA for the treatment of malignant glioma and from the European Commission for the treatment of glioma.

For more information, please visit www.ojemda.com.

About Pediatric Low-Grade Glioma

Pediatric low-grade glioma (pLGG) is the most common brain tumor with an estimated US incidence of 1,100 and Europe incidence of 700 children per year who are eligible for front-line systemic therapy.[i, ii] BRAF is the gene most commonly altered in pLGG, which include two primary types of BRAF alterations – a BRAF gene fusion and BRAF point mutation. These BRAF alterations account for >50% of pLGG cases worldwide and until now there were no approved treatments for people with pLGG driven by BRAF fusions.[i, iii]

Pediatric low-grade gliomas can be chronic and relentless, with patients suffering profound side effects from both the tumor and the treatment, which may include chemotherapy and radiation. These side effects can impact their life over the long term, and may include muscle weakness, loss of vision, and difficulty speaking. This type of tumor has a high risk of progression, and many children with pLGG require long-term treatment. While most children with pLGG survive their cancer, children who do not achieve a complete resection following surgery may face years of increasingly aggressive treatment.

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 Pediatric Neuro-Oncology Consortium (PNOC). The pivotal and ongoing Phase 2 FIREFLY-1 study evaluated the safety and efficacy of tovorafenib in 137 relapsed or refractory BRAF-altered pLGG patients, who had received at least one line of prior therapy, across two study arms. Arm 1 (n=77) was used for the efficacy analyses and Arm 2 provided safety data for an additional 60 patients, initiated to enable access to tovorafenib once Arm 1 had fully recruited.

At the time of data cutoff on May 10, 2024, the major efficacy outcome measure was overall response rate (ORR) of 53% (40/76), determined by blinded independent central review based on RAPNO-LGG (Response Assessment in Pediatric Neuro-Oncology) criteria. Median duration of response (DOR) was 18 months (12.0, 22.8) and median time to response (TTR) was 5.4 months (range 1.6, 17.5). The most common adverse reactions (≥30%) were rash, hair color changes, fatigue, viral infection, vomiting, headache, hemorrhage, pyrexia, dry skin, constipation, nausea, dermatitis acneiform, and upper respiratory tract infection. Grade 3 or higher adverse reactions (≥5%) were rash, viral infection, and hemorrhage. Additional information about FIREFLY-1 may be found at ClinicalTrials.gov, using Identifier NCT04775485.

About the Pediatric Neuro-Oncology Consortium

The 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 believes when it comes to pediatric cancer, we can do better. The Company was founded to address a critical unmet need: the dire lack of therapeutic development in pediatric cancer. 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 targeted

cancer treatments. The Company's pipeline includes tovorafenib (OJEMDA™) and DAY301.

Day One is based in Brisbane, California. For more information, please visit www.dayonebio.com or find the Company on LinkedIn or X.

Day One uses its Investor Relations website (ir.dayonebio.com), its X handle (x.com/DayOneBio), and LinkedIn Home Page (linkedin.com/company/dayonebio) as a means of disseminating or providing notification of, among other things, news or announcements regarding its business or financial performance, investor events, press releases, and earnings releases, and as a means of disclosing material nonpublic information and for complying with its disclosure obligations under Regulation FD.

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 and commercialize cancer therapies, expectations from current and planned clinical trials, the execution of the Phase 2 and Phase 3 clinical trial for tovorafenib as designed, expectations with respect to the timing of Day One's Phase 1a/b clinical trial of DAY301, 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 and retain 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, changing interest rates, government shutdowns, cybersecurity incidents, significant political or regulatory developments or changes in trade policy, including tariffs, shifting priorities within the U.S. Food and Drug Administration and reduced funding to federal healthcare programs, global regional 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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[i] Ryall S, et al. Acta Neuropathol Commun. 2020;8(1):30.

[ii] Estimates of annual incidence and prevalence for addressable patient population in E.U. 4 + U.K. are based on Ipsen calculations from publicly available data (Eurostat, <25yo population; Global Burden of Disease 2019; Desandes et al. Incidence and survival of children with central nervous system primitive tumors in the French National Registry of Childhood Solid Tumors. Neuro Oncol. 2014 Jul;16(7):975-83. doi: 10.1093/neuonc/not309; Qaddoumi et al. Outcome and prognostic features in pediatric gliomas: a review of 6212 cases from the Surveillance, Epidemiology, and End Results database. Cancer. 2009 Dec 15;115(24):5761-70. doi: 10.1002/cncr.24663)

[iii] Traunwieser T, et al. Neurooncol Adv. 2020;2(1):vdaa094.