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CTNI-52. SURVIVAL OUTCOMES IN RECURRENT GLIOBLASTOMA (GBM) PATIENTS TREATED WITH A SINGLE INTRA-TUMORAL ADMINISTRATION OF BIZAXOFUSP, AN IL-4R-TARGETING TOXIN, IN A PHASE IIB TRIAL:
John Sampson1, Achal Singh Achrol2, Manish Aghi1, Krystof Bankiewicz4, Martin Bexon1, Steven Brenn5, Andrew Brenner1, Sajeel Chowdhary1, Melissa Coello1, Annick Desjardins6, Benjamin Ellingson7, John Floyd8, Seunggu Han9, Santosh Kesari11, Yael Mardor12, Fahar Merchant13, Rosemina Merchant13, Dina Randazzo24, Michael A. Vogelbaum12, Frank Vrioni16, Eva Wembacher-Schroeder17, Minh D. To18, Miroslaw Zabek19, and Nicholas Butowski19; 1Duke University, Durham, USA, 2Loma Linda University Medical Center, Loma Linda, USA, 3University of California, San Francisco, San Francisco, USA, 4Ohio State University College of Medicine, Columbus, USA, 5Medicenna Therapeutics, Toronto, Canada, 6University of Pennsylvania, Philadelphia, USA, 7UT Health San Antonio Mays Cancer Center, San Antonio, TX, USA, 8Boca Raton Regional Hospital, Boca Raton, USA, 9Duke University Medical Center, Durham, USA, 10Department of NeuroOncology, Moffitt Cancer Center, Tampa, FL, USA, 11Brainlab AG, Munich, Germany, 12Maxoivan Bronowski Hospital, Warsaw, Poland, 13University of California San Francisco, San Francisco, USA

BACKGROUND: Bizaxofusp (MDNA35) is an IL-4R-targeting toxin in development for recurrent (r)GBM, a universally fatal disease with mOS of 6-9 months. IL-4R is overexpressed in GBM and surrounding tumor microenvironment, with high expression associated with poor clinical outcome. Method: Efficacy and safety were evaluated in a single-arm, open-label, multi-center Phase 2 study using convection-enhanced delivery of Bizaxofusp. The primary endpoint of mOS was compared to results from a blinded eligibility-matched external control arm (ECA). OS was defined as time from relapse to death/censor. IL-4R expression was determined by immunohistochemistry of available archival tumor tissues from both arms.

RESULTS: Bizaxofusp showed an acceptable safety profile at doses of up to 240 µg. Forty-four subjects were treated with Bizaxofusp per protocol; 81 ECA subjects met the eligibility criteria of the study. The Bizaxofusp group had a significantly longer mOS (12.85 months compared to 7.7 months for ECA; HR: 0.62; 95% CI: 0.42-0.89). Amongst the unmethylated MGMT and high IL-4R sub-groups, subjects treated with Bizaxofusp had significantly longer mOS when compared to the ECA. Eleven patients (25%) treated with Bizaxofusp survived ≥ 24 months; 3 patients were still alive (29.9, 32.8 and 40.1 months) at last follow-up. High IL-4R expression was associated with improved survival (mOS, 15.8 versus 9.8 months; HR: 0.7; 95% CI: 0.39-1.46) at all doses. However at high doses (180 µg) subjects with low IL-4R expression had significantly longer survival versus low dose Bizaxofusp (mOS, 15.4 versus 9.1 months; HR: 0.28; 95% CI: 0.09-0.91), CONCLUSION: In patients with rGBM, a single treatment of Bizaxofusp resulted in significantly improved OS compared to eligibility-matched ECA. High-dose Bizaxofusp was equally effective irrespective of IL-4R expression. A Phase 3 registration trial will use a novel hybrid design with a propensity-matched ECA comprising two-thirds of the control arm, setting a new precedent for GBM clinical trials.