

2688MO

A phase I/II trial of FOG-001, a first-in-class direct β -catenin:TCF4 inhibitor - Safety and preliminary antitumor activity in patients with desmoid tumors

G.M. Cote¹, M. Cecchini², K.P. Papadopoulos³, M.M. Khushman⁴, M. Pelster⁵, J. Rodon⁶, S. Kummar⁷, R. Yaeger⁸, S. Sharma⁹, A. Wells¹⁰, M. Tipps¹⁰, A. Garofalo¹⁰, L.V. Akella¹⁰, Z. Yu¹⁰, X. Han¹⁰, L. Strong¹⁰, M.H. Nguyen¹⁰, K. Orford¹⁰, S.J. Klempner¹¹

¹ Hematology and Oncology, Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, United States of America, ² Yale University School of Medicine - Yale Cancer Center, New Haven, United States of America, ³ Department of Clinical Research, START - South Texas Accelerated Research Therapeutics, San Antonio, United States of America, ⁴ Hematology-Oncology, Washington University School of Medicine in St. Louis - Siteman Cancer Center, St. Louis, Florida, United States of America, ⁵ Department of Oncology, SCRI - Sarah Cannon Research Institute, Nashville, United States of America, ⁶ Drug Development Department, The University of Texas MD Anderson Cancer Center - Main Building, Houston, United States of America, ⁷ Division of Hematology & Medical Oncology, OHSU Knight Cancer Institute - Center for Health and Healing Building 1 - South Waterfront, Portland, United States of America, ⁸ Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, United States of America, ⁹ Medical Oncology, Honor Health Cancer Care, Scottsdale, United States of America, ¹⁰ Clinical Development, Parabilis Medicines (formerly Fog Pharmaceuticals, Inc.), Cambridge, United States of America, ¹¹ Medical Oncology, Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, United States of America

Background

Wnt pathway-activating mutations (WPAMs) are highly prevalent in desmoid tumors, almost all of which harbor a WPAM in *APC* or *CTNNB1*. FOG-001 is a Helicon™ peptide that competitively inhibits the interaction between β -catenin and TCF transcription factors. Given the causal nature of WPAM mutations in desmoid tumors, targeting β -catenin offers a more direct and disease-relevant approach than γ -secretase inhibitors, which inhibit Notch signaling. We describe a first-in-human, phase 1/2, multicenter study of FOG-001 in patients (pts) with WPAM+ solid tumors, including desmoid tumors, or microsatellite-stable colorectal cancer. This abstract reports data from pts with desmoid tumors.

Methods

Eligibility for desmoid pts: histologically confirmed desmoid tumor with WPAM; ≥ 1 prior systemic therapy or treatment naïve but deemed appropriate for participation. Primary objectives include safety/tolerability of FOG-001. Secondary objectives include anti-tumor activity.

Results

As of March 31, 2025, 5 desmoid tumor pts have received FOG-001 at doses ranging from 72–480 mg/m². Median age 27 years; 40% male. One pt with familial adenomatous polyposis had *APC* mutation, with *CTNNB1* mutations in the other 4 pts; 3 pts had prior treatment with nirogacestat and progressed (n=2) or discontinued due to intolerability (n=1). FOG-001 demonstrated low PK variability and a dose-proportional increase in exposure. The most common (all-grade/grade ≥ 3) treatment-related adverse events were alopecia (4/0; reversible), AST increase (3/1; reversible), epistaxis (3/0), fatigue (3/0), nausea (3/0), and hyperbilirubinemia (3/1; asymptomatic and reversible). Two of 4 efficacy-evaluable desmoid pts, including 1 pt progressing on nirogacestat, achieved a partial response (PR; 50%) with treatment duration of 33–77 weeks; the remaining 2 (50%) pts had stable disease (with 10.8% and 20.4% tumor reduction), for a disease-control rate of 100%.

Conclusions

Preliminary data show that FOG-001 has acceptable tolerability in pts with desmoid tumors. Tumor reductions were seen in all pts, including a PR in a pt who progressed on prior nirogacestat. Dose expansion in a desmoid-specific cohort is currently ongoing.

Clinical trial identification

NCT05919264.

Editorial acknowledgement

Editorial assistance for this abstract was provided by Lee Miller (Miller Medical Communications). This work was funded by the study sponsor (Parabilis Medicines).

Legal entity responsible for the study

Parabilis Medicines.

Funding

Parabilis Medicines.

Disclosure

G.M. Cote: Financial Interests, Personal, Other, Grant reviewing activity honorarium: Gilead Therapeutics; Financial Interests, Personal, Other, Honorarium: BioAtla; Financial Interests, Personal, Advisory Board: Chordoma Foundation, Ikena Oncology, C4 Therapeutics, Daiichi Sankyo, Parabilis; Financial Interests, Steering Committee Member, Site PI and Steering Com. member: PharmaMar; Financial Interests, Institutional, Local PI: Macrogenics, Repare Therapeutics, Foghorn, SMP Oncology, Rain Therapeutics, Inhibrx, Kronos, Bavarian Nordic, Pyxis; Financial Interests, Institutional, Funding, Funding for clinical trial, IST PI: Eisai; Financial Interests, Institutional, Funding, Funding for clinical trial. PI for IST: Merck Serono, Jazz Pharmaceuticals; Financial Interests, Institutional, Local PI, Local PI. See honorarium above: BioAtla; Financial Interests, Institutional, Local PI, Site PI. See also ad board: Ikena Oncology, C4 Therapeutics; Non-Financial Interests, Advisory Role, Medical Advisory Board: The EHE Foundation. M. Cecchini: Financial Interests, Personal, Advisory Board, Honoraria for advisory board: Eisai Co, Agios Pharmaceuticals, Dava Oncology, Bayer Pharmaceuticals, Seattle Genetics, Macrogenics, Taiho, Daiichi Sankyo, AstraZeneca; Financial Interests, Personal, Advisory Board: Agenus, Elevate Oncology, Regeneron, Loxo@Lily, Incendia Therapeutics, BeiGene, AbbVie, Modifi Bio, Parabalís, Wren Therapeutics, Incyte; Financial Interests, Institutional, Coordinating PI: AstraZeneca, Medilink; Financial Interests, Institutional, Local PI: Genentech, AbbVie, Parabalís, Beigene, Elevation Oncology, Janssen, Astellas, Boehringer Ingelheim, BioAtla, Ipsen, 858 Therapeutics, Arcus Biosciences, Famewave, Kymab, Daiichi Sankyo, Merck Serono, Bayer, Mirati Therapeutics, IGM Biosciences, Transcenta, Jacobio, Repare Therapeutics, Merck, NGM. K.P. Papadopoulos: Financial Interests, Personal, Speaker, Consultant, Advisor: Turning Point Therapeutics, AADI; Financial Interests, Personal, Funding: AbbVie, Daiichi Sankyo, Regeneron, Amgen, Incyte, Merck, 3D Medicines, Syros Pharmaceuticals, Mersana, MabSpace Biosciences, Jounce Therapeutics, Bayer, Anheart Therapeutics, F-star, Linnaeus Therapeutics, Mirati Therapeutic, Tempest Therapeutics, Treadwe. M.M. Khushman: Financial Interests, Personal, Speaker, Consultant, Advisor: Mueres, TriSalus Life Sciences, Cardinal Health, Bristol Myers Squibb, AbbVie, Exelixis, Elevar Therapeutics; Financial Interests, Personal, Speaker's Bureau: Caris Life Sciences; Financial Interests, Personal, Stocks or ownership: Cardiff Oncology; Financial Interests, Personal, Funding: AbbVie, FOGPharma, IgM Biosciences, Tori Biotherapeutics. M. Pelster: Financial Interests, Institutional, Other, Consulting: AstraZeneca, CytomX, Ipsen, Pfizer, Arcus Biosciences, Elevation Oncology, EMD Serono, Jazz Pharmaceuticals, Curio Science, Kura Oncology, Takeda; Financial Interests, Institutional, Local PI: Agenus, Arcus Biosciences, Astellas, BeiGene, BioNTech, Bristol Myers Squibb, Codiak Biosciences, Eisai, Gilead, HiberCell, Immune-Onc Therapeutics, Leap Therapeutics, Novartis, OncXerna Therapeutics, Panbela Therapeutics, Revolution Medicines, Surface Oncology, SQZ Biotechnologies, Translational Genomics, TransThera Sciences, ZielBio, 1200 Pharma, Actuate Therapeutics, Compass Therapeutics, CytomX, Elevation Oncology, Exelixis, Impact Therapeutics, Tachyon Therapeutics, AbbVie, Affini-T Therapeutics, Elicio, Fate Therapeutics, Fog Pharmaceuticals, GSK, Jazz Pharmaceuticals, Kura Oncology, Neogene, Roche, SeaGen, Takeda, Artios Pharma. J. Rodon: Financial Interests, Personal, Advisory Board: Ellipses Pharma, iOnctura SA, Aadi Bioscience, Envision Pharma, Molecular Partners, Mekanistic, Amgen; Financial Interests, Personal, Other, Consultancy: Clarion Healthcare, Debiopharm, Cullgen, Pfizer, Macrogenics, Oncology One, Columbus Venture Partners, Sardona Therapeutics, Avoro Capital Advisors, Vall d'Hebron Institute of Oncology/Ministero De Empleo Y Seguridad, Chinese University of Hong Kong, Boxer Capital, LLC, Tang Advisors, LLC, Alnylam Pharmaceuticals, BridgeBio Pharma; Financial Interests, Personal, Other, Consultancy/Advisory Board: Monte Rosa Therapeutics, Merus N.V., Incyte; Financial Interests, Institutional, Other, Clinical Research: Novartis, Spectrum Pharmaceuticals, Symphogen, BioAtla, Pfizer, GenMab, CytomX, Kelun-Biotech, Takeda-Millennium, GSK; Financial Interests, Institutional, Other, Research Funding: Blueprint Medicines, Black Diamond, Merck Sharp & Dohme; Financial Interests, Institutional, Research Grant, Research Funding/Clinical Research: Hummingbird, Yingli; Financial Interests, Institutional, Research Grant, Research Funding: Vall d'Hebron Institute of Oncology/Cancer Core Europe; Financial Interests, Institutional, Research Grant, Clinical Research: Bicycle Therapeutics, Taiho, Roche Pharmaceuticals, Merus, Curis, AadiBioscience, Nuvation, ForeBio, BioMed Valley Discoveries, Loxo Oncology, Cellestia, Deciphera, Ideaya, Amgen, Tango Therapeutics, Mirati, Linnaeus Therapeutics, Bayer, Hutchinson MediPharma; Other, Other: VHIO/Ministero De Empleo Y Seguridad Social; Other, Travel: European Society for Medical Oncology, Loxo Oncology. S. Kummar: Financial Interests, Personal, Speaker, Consultant, Advisor: Bayer, Mundipharma, Harbour BioMed, SpringWorks Therapeutics, Gilead Sciences, Mirati Therapeutics, Cadila Pharmaceuticals, Oxford BioTherapeutics, Genome Insight, Seagan, BPGBio, XY One Therapeutics, GI Innovation, AADI, MOMA Therapeutics, Daiichi Sankyo; Financial Interests, Personal, Other, Travel: Bayer; Financial Interests, Personal, Stocks/Shares: PathomIQ, Arxeon Therapeutics, Fortress Biotech; Financial Interests, Personal, Funding: Bristol Myers Squibb, Pfizer, Incyte, Taiho Pharmaceutical, Bayer, Astex Pharmaceuticals, Seagen, Amgen, Genome & Company, Moderna Therapeutics, ADC Therapeutics, ORIC Pharmaceuticals, Elevation Oncology, Vincerox Pharma, Day One Therapeutics, Transcenta. R. Yaeger: Financial Interests, Personal, Advisory Board: Eli Lilly, Mirati Therapeutics, Merck, Erasca, Revolution Medicine; Financial Interests, Personal, Invited Speaker: Zai Lab; Financial Interests, Institutional, Local PI: Mirati Therapeutics, Boehringer Ingelheim, Pfizer, Revolution Medicine, Parabilis; Financial Interests, Institutional, Research Grant: Boundless Bio; Other, DSMB member: CytoDyn. S. Sharma: Financial Interests, Personal, Speaker, Consultant, Advisor: Barricade Therapeutics, Elevar Therapeutics, Purple Biotech, Novelty Nobility, Tisch Cancer Institute; Financial Interests, Personal, Other, Co-Founder / Chief Medical Officer: Stingray Therapeutics, Black Canyon Bio; Financial Interests, Personal, Other, Equity founder: Bonneville Bio, LLC. A. Wells: Financial Interests, Personal, Full or part-time Employment: Bristol Myers Squibb, Fog Pharmaceuticals; Financial Interests, Personal, Stocks or

ownership: Bristol-Myers Squibb/Celgene. M. Tipps: Financial Interests, Personal, Full or part-time Employment: Parabilis Medicines; Financial Interests, Personal, Stocks/Shares: Parabilis Medicines. A. Garofalo: Financial Interests, Personal, Full or part-time Employment: Fog Pharmaceuticals; Financial Interests, Personal, Stocks or ownership: Fog Pharmaceuticals, Arvinas, Kymera, Arcus Biosciences. L.V. Akella: Financial Interests, Personal, Full or part-time Employment: Fog Pharmaceuticals, Parabilis Medicines; Financial Interests, Personal, Other, Travel, Accommodations, Expenses: Fog Pharmaceuticals, Parabilis Medicines; Financial Interests, Personal, Stocks/Shares: Fog Pharmaceuticals, Parabilis Medicines. Z. Yu: Financial Interests, Personal, Other, Travel, Accommodations, Expenses: Fog Pharmaceuticals; Financial Interests, Personal, Full or part-time Employment: Fog Pharmaceuticals; Financial Interests, Personal, Stocks/Shares: Fog Pharmaceuticals; Financial Interests, Personal, Royalties: Radius health, Inc. Treatment of breast cancer with AR agonist/SARM Constellation pharmaceuticals. Treatment of solid tumors with ARID1A mutation with EZH2 inhibitor. X. Han: Financial Interests, Personal, Full or part-time Employment: Parabilis Medicines; Financial Interests, Personal, Stocks/Shares: Parabilis Medicines. L. Strong: Financial Interests, Personal, Full or part-time Employment: Parabilis Medicines; Financial Interests, Personal, Stocks/Shares: Parabilis Medicines. M.H. Nguyen: Financial Interests, Full or part-time Employment: Fog Pharmaceuticals, Bristol-Myers Squibb/Celgene; Financial Interests, Other, Travel, Accommodations, Expenses: Fog Pharmaceuticals, Bristol-Myers Squibb/Celgene; Financial Interests, Stocks or ownership: Fog Pharmaceuticals, Bristol Myers Squibb/Celgene. K. Orford: Financial Interests, Institutional, Full or part-time Employment, Chief Medical Officer at FogPharmaceuticals, Inc.: FogPharma; Financial Interests, Personal, Stocks/Shares: FogPharma. S.J. Klempner: Financial Interests, Personal, Advisory Board, Stomach Cancer Advisory Board: Merck, Bristol Myers Squibb, Astellas, Daiichi Sankyo; Financial Interests, Personal, Advisory Board, One Time Advisory Board: Natera; Financial Interests, Personal, Advisory Board, Stomach Cancer consulting, ended in 1/2024: Novartis; Financial Interests, Personal, Advisory Board, Stomach cancer advisory board x1 in 1/2024, 1/2025: AstraZeneca; Financial Interests, Personal, Advisory Board, Stomach cancer advisory board x1 in 3/2024: I-Mab Therapeutics; Financial Interests, Personal, Advisory Board, Stomach cancer consulting, <\$1,500 USD in 2023: Taiho Oncology; Financial Interests, Personal, Advisory Board, Stomach cancer advisory board x1, 6/2024: Eisai; Financial Interests, Personal, Advisory Board, Steering committee for trial, one time gastric cancer advisory board: Amgen; Financial Interests, Personal, Advisory Board, One time advisory board, 1/2025: Gilead; Financial Interests, Personal, Advisory Board, One time gastric cancer advisory board, 2025: BeiGene; Financial Interests, Personal, Advisory Board, One time advisory board, 6/2024: Elevation Oncology; Financial Interests, Personal, Other, Consulting on gastric cancer: Signet Therapeutics; Financial Interests, Personal, Stocks/Shares, Early investor, company is not public: MBrace; Financial Interests, Institutional, Coordinating PI, National PI for trial: Leap Therapeutics; Financial Interests, Personal and Institutional, Local PI, Local PI for trial, also served on advisory board as noted above: Astellas; Financial Interests, Institutional, Local PI, Site PI for phase III trials: Arcus; Financial Interests, Personal and Institutional, Local PI, Site PI for trial, as disclosed above was a one-time advisory board participant, <\$5,000 USD: I-Mab; Financial Interests, Personal and Institutional, Local PI, Advisory board participation as disclosed above, local PI for clinical trial: AstraZeneca; Non-Financial Interests, Advisory Role, Medical-Scientific Advisory Board Member: Debbie's Dream Foundation; Non-Financial Interests, Advisory Role, Member of Scientific Advisory Board: Hope for Stomach Cancer; Non-Financial Interests, Other, Member of Gastric and Esophageal NCCN Guideline Committees: NCCN; Non-Financial Interests, Leadership Role, Co-chair NCI Esophagogastric Task Force, no compensation: NCI; Other, Participant in gastroesophageal CME activities, compensated, last in 3/2025: Research to Practice.