1019P

Phase 1 Study of BHV-1530, a First-in-Class FGFR3 ADC in Advanced Tumors

G. Falchook[1], M. Song[2], J. Merchan[3], G. Iyer[4], W. McKean[5], A. Spira[6], S. Sahota[7], D. Benjamin[8], G. Sonpavde[9], J. Russell[10], J. Peng[11], S. Coker[12], N. Khokhar[12], J. Rodon Ahnert[13]

[1]Sarah Cannon Research Institute (SCRI) at HCA HealthONE, Denver, CO, United States of America; [2] NEXT Oncology, Dallas, TX, United States of America; [3]University of Miami, Sylvester Comprehensive Cancer Center, Miami, FL, United States of America; [4]Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, United States of America; [5]Utah Cancer Specialists, START Mountain Region, West Valley City, UT; [6]Research Department, NEXT Oncology at Virginia Cancer Specialist, Fairfax, United States of America; [7]Department of Oncology, NEXT Oncology, Austin, TX, United States of America; [8]Medical Oncology, Hoag Family Cancer Institute, Newport Beach, CA, United States of America; [9]Advent Health Research Institute, Orlando, FL, United States of America; [10]Tennessee Oncology, Nashville, TN, United States of America; [11]Clinical Pharmacology, Biohaven Pharmaceuticals Inc, New Haven, CT, United States of America; [12]Oncology Clinical Development, Biohaven Pharmaceuticals Inc, New Haven, CT, United States of America; [13]Department of Drug Development, The University of Texas, MD Anderson Cancer Center, Houston, TX, United States of America

BACKGROUND

- BHV-1530 is a novel, FGFR3 targeting ADC with a novel, proprietary topoisomerase I inhibitor payload and a site-specific, highly stable conjugation.
- It is designed for enhanced efficacy and differentiated safety and has potential to synergize with checkpoint inhibitors.
- There are no other FGFR3 ADCs currently in clinical development or approved.
- Unlike small molecule inhibitors, BHV-1530 has the potential to address unmet need across a broader range of cancers, including tumors with activating FGFR3 alterations* as well as FGFR3 wild-type overexpression.

*activating FGFR3 alteration refers to activating mutations or fusions

Figure 1. BHV-1530 Structure

BHV-1530 is an FGFR3 targeting ADC consisting of a humanized FGFR3 antibody with high selectivity and affinity for FGFR3, with no detectable binding to FGFR1, FGFR2 or FGFR4. It also consists of a stable branched linker, and a novel, proprietary Topo1 inhibitor, Topolx, as a payload (DAR4).

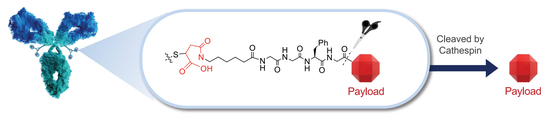
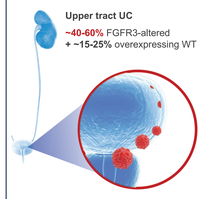


Figure 2. FGFR3 Alteration and Overexpression Prevalence

Frequency of FGFR3 Alterations and Overexpression in UC:



Upper tract UC
~40-60% FGFR3-altered
+ ~15-25% overexpressing WT

Non-muscle invasive UC
~60-70% FGFR3-altered
+ ~10-15% overexpressing WT

Muscle invasive UC
~20% FGFR3-altered
+ ~25-40% overexpressing WT

Metastatic UC
~25% FGFR3-altered
+ ~30% overexpressing WT

FGFR3 Alterations and Overexpression also seen in:

HSNCC
~15-20% FGFR3-altered in HPV+ HSNCC
+ up to 50% overexpressing WT

NSCLC
~1-2% FGFR3-altered
+ up to 30% overexpressing WT

Other
~1-5% FGFR3-alterations in other cancers

Alteration and overexpression rates from published literature; ranges reflect variability across cohorts and disease grade/stage.
HNSCC, head and neck squamous cell carcinoma; **NSCLC**, non-small cell lung cancer; **UC**, urothelial cancer; **WT**, wild type.

1. Müller, D. C., Murtha, A. J., Bacon, J. V. W., et al. (2026). Prospective multicenter study of cfDNA versus tumor tissue guiding FGFR-targeted therapy in metastatic urothelial cancer. Nature Communications, 17(1). Article 3263. https://doi.org/10.1038/s41467-026-69927-7. **2.** Hammerman PS, Hayes DN, Grandis JR. Therapeutic insights from genomic studies of head and neck squamous cell carcinomas. Cancer Discov. 2015 Mar;5(3):239-44. doi: 10.1158/2159-8290.CD-14-1205. Epub 2015 Feb 2. **3.** Zhou Z, et al. Targeting FGFR in non-small cell lung cancer: implications from the landscape of clinically actionable aberrations of FGFR kinases. Cancer Biol Med. 2021 Jun 15;18(2):490–501. **4.** Moes-Sosnowska et al. Fibroblast growth Factor Receptor 1-4 Genetic Aberrations as Clinically Relevant Biomarkers in Squamous Cell Lung Cancer. Front Oncol. 2022.

OBJECTIVES

The primary objective is to evaluate safety and tolerability of BHV-1530 monotherapy. The secondary objectives include the evaluation of pharmacokinetics and preliminary efficacy. A combination with an anti-PD1 is being studied in a second portion of the study.

STUDY DESIGN

- BHV-1530-101 (NCT06874335) is an ongoing Phase 1 first-in-human trial of BHV-1530 Q3W in participants with advanced solid tumors.
- Eligible patients were ≥18 years of age and had an advanced or metastatic urothelial cancer (UC) of the urinary tract, non-small cell lung cancer (NSCLC), head and neck squamous cell carcinoma (HNSCC) of the oral cavity, hypopharynx, oropharynx, nasopharynx, larynx and sinonasal tract.
- Other patients with advanced or metastatic solid tumors with a documented activating FGFR3 alteration were also eligible.

Figure 3. BHV-1530 Q3W: Monotherapy Dose Escalation Schema

RESULTS

Enrollment

- As of 18-Sept-2026, 17 participants were enrolled and received BHV-1530 Q3W at DL1 (1mg/kg, n=3), DL2 (2mg/kg, n=4), DL3 (3.3mg/kg, n=3), DL4 (5mg/kg, n=3) and DL5 (7mg/kg, n=4).
- **Table 1** provides details of the participants demographics and baseline characteristics.

Table 1. Baseline Demographics

Demographic Characteristics	BHV-1530 Q3W (n=17)
Age, y, median (min, max)	66.0 (28, 74)
Gender, n (%)	
Male	10 (58.8)
Female	7 (41.2)
Histology, n (%)	
Urothelial cancer (UC)	4 (23.5)
Activating FGFR3 alteration	3 (75)
Head and neck squamous cell carcinoma (HNSCC)	2 (11.8)
Activating FGFR3 alteration	1 (50)
Non-small cell lung cancer (NSCLC)	2 (11.8)
Activating FGFR3 alteration	0
Others	9 (52.9)
Activating FGFR3 alteration	4 (44.4)
Prior line of therapy for advanced/metastatic disease, median (min, max)	2 (1, 6)
ECOG PS 0, n (%) / **1**, n (%)	8 (47.1) / 9 (52.9)
Prior *EV, P (UC only), n (%)	4 (100)
Prior anti-FGFR3 therapy	1

*EV, P: Enfortumab vedotin, pembrolizumab

Safety

- The maximum tolerated dose (MTD) was not reached by the clinical cut off (CCO), with dose escalation ongoing.
- No dose-limiting toxicities, treatment-related serious adverse events or treatment emergent deaths have been reported.
- Only one participant discontinued treatment due to an AE. This was due to Grade 2 increased lacrimation and Grade 2 blurry vision. This participant had blurry vision at baseline.
- Interstitial lung disease/pneumonitis was not reported in any participant.
- Treatment emergent adverse events, (TEAEs) occurred in 17 pts (100%) and were mostly Grade 1-2, including nausea (41.2%) and fatigue (35.3%).
- There were no cases of AEs frequently associated with FDA-approved pan-FGFR inhibitors, including hyperphosphatemia, nail dystrophy or central serous retinopathy.
- Hematologic and gastrointestinal events were reported at low rates.
- See **Table 2** for a summary of TEAEs reported ≥ 10% of pts in the study.

Table 2. TEAEs: BHV-1530 Q3W in ≥ 10% of pts

		BHV-1530 Q3W (n=17)
AE (N/%)	**All Grades**	**Grade ≥3**
Nausea	7 (41.2)	0
Fatigue	6 (35.3)	0
Abdominal pain	4 (23.5)	0
Diarrhoea	3 (17.6)	1 (5.9)
Dyspepsia	2 (11.8)	0
Vomiting	2 (11.8)	0
Pruritus	2 (11.8)	0
Rash	2 (11.8)	0
Rash maculo-papular	2 (11.8)	0
Dyspnoea	2 (11.8)	0
Pulmonary embolism	2 (11.8)	0
Anaemia	2 (11.8)	0
Lymphopenia	2 (11.8)	1 (5.9)
Dizziness	2 (11.8)	0

Efficacy

- All pts, n=17, dose range 1mg/kg through 7mg/kg, were efficacy evaluable as of the CCO.
- **Of the 6-efficacy evaluable pts with an activating FGFR3 alteration, 5 (83.3%) had tumor reduction at doses ≥ 3.3 mg/kg and 3 (50%) had a confirmed objective response, see Figure 4.**
- Overall, confirmed responses were observed in 3 (17.6%) pts; in UC (n=2), and HNSCC (n=1). Any tumor reduction was observed in 8 (47.1%) pts. The disease control rate (DCR) was 64.7%.
- Nine pts continue on study treatment at time of CCO.
- All patients with UC and with a response were post-EV, P; responses also seen post-FGFR TKI, supporting mechanistic independence from prior ADC and TKI therapy.

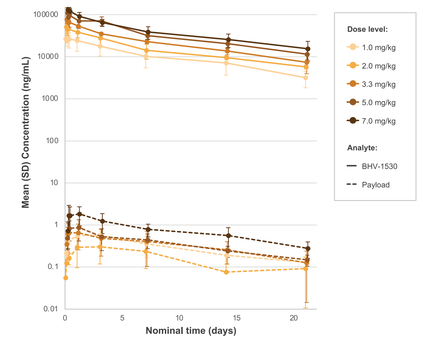
Pharmacokinetics

- BHV-1530 (ADC) serum concentrations (Cmax and AUC) increased in an approximately dose-proportional manner.
- The unconjugated payload serum concentrations were low, with a payload-to-ADC AUC molar ratio <1%, indicating that the ADC was highly stable in circulation, see **Figure 5**.
- There was modest accumulation (<=54%) for both ADC and payload at steady-state versus Cycle 1 (data not shown) which supports Q3W dosing.

Figure 4. Waterfall Plot of Best Percent Change from Baseline in Patients with Activating FGFR3 Alterations

G/GEA, gastric/gastric esophageal adenocarcinoma; **VSCCS**, verrucous squamous cell carcinoma of skin

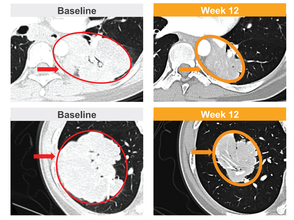
Figure 5. Mean (SD) BHV-1530 (ADC) & Payload Concentration-Time Plot for Cycle 1



CASE NARRATIVE

- 28 yo female, urothelial cancer with **FGFR3-TACC3 fusion** and **V555L gatekeeper mutation** with metastasis to lung and thoracic lymph node. The patient was **heavily pre-treated:** 4 prior lines, including Padcev®, Keytruda® and **2 FGFR TKIs (Balversa®, vepugratinib)**.
- Patient had a deepening response on treatment and remains on study with **confirmed PR beyond 6 months** and is tolerating study drug with mild treatment related nausea and no FGFR related toxicity.

Figure 7. Axial CT Images



CONCLUSION

Early results show that BHV-1530 has encouraging preliminary clinical activity in multiple tumor types for this first-in-class FGFR3 ADC. BHV-1530 is safe and well tolerated, with a differentiated safety profile. No FGFR class toxicities have been observed to date, which is attributed to binding specificity to FGFR3, and the low rates and severity of payload class toxicity is attributed to the low concentration of free payload in serum. Dose escalation is ongoing as monotherapy and in combination with an anti-PD1.

Disclosures:

Gerald Steven Falchook
Sarah Cannon Research Institute at HealthONE

Royalties: Wolters Kluwer (2014-present)
Advisory role: AbbVie (2022), Jubilant (2022), BostonGene (2022), Teon (2022), Merck (2022), Sanofi (2023), BridgeBio (2023), Beijing Avistone (2024)
Advisory role: None
Speakers honorarium for CME: Clinical Care Options (2024)
Travel: Sarah Cannon Research Institute (employer, at least once yearly), Amgen (2022), Synthonx/Sanofi (2022), GSK (2023), Cytiet (2023)

Research funding: Abbisko, ABL Bio, Abbvie, ADC Therapeutics, Acrotar, Acrivon Therapeutics, Agenus, Aileron, Alterome, Alink Biotherapeutics, Amgen, Arcus, ARMO/Eli Lilly, AriVent BioPharma, Arlos, Astellas, AstraZeneca, Avenzo, Axcynsis Therapeutics, Bayer, BeiGene, Beijing Avistone, Bioatla, Biohaven Pharmaceuticals, Bioinvent, Biomea Fusion, Bicycle, Black Diamond, Boehringer Ingelheim, Boundless, Centessa, Conjupro, Context Therapeutics, Crescent Biopharma, Crinetics Pharmaceuticals, Cytier, Cytomx, D3 Bio, Daiichi, Deciphera, Dren Bio, Dynamicure, Elkon, Eli Lilly, Epizyme, Erasca, Exelixis, Freenome, Fujifilm, Genentech, GlaxoSmithKline, GSK, GV20, Harbour BioMed, Hutchison MediPharma, IGM Biosciences, IDEAYA, Ikena, Immuneering, Immunitas, ImmuneGen/MacroGenics, Incyte, InSilico Medicine, Jacobio, Jazz, Jounce, Jubilant, Kinnta, Kumquat, Kura, LaxoBayer, Medlink, Merck, Metabomed, Mirati, ModeX, Molecular Templates, Nammi, Navire/BridgeBio, NGM Bio, NiKang, Normunity, Novartis, Novelwise Pharmaceuticals, Nuvalent, Nuvectis, Oncorus, Oncusp, OnKure, Pfizer, Phanes, PharmaMar, Pheast, Phronttine, PMV, Poseida, Prelude, PureTech, Pyramid, Pyxis, Quanta, RasCal, Regeneron, Relay, Rgenix, Ribon, Roche, Samumed, Sapience, Sarah Cannon Development Innovations, Seagen, Silicon/Stingthera, Simcha, Sinxomics, Sutro Biopharma, Synthonx/Sanofi, Systimmune, Tachyon, Takeda, Tallac, Tango, Tarus, Tarveda, Taska, Teneobio, Tesaro, TORL, Turning Point, Vironexis Biotherapeutics, Xencor, Zhuhai Yufan

Acknowledgements:

We thank the patients who volunteered to participate in this study and their caregivers for their invaluable time and commitment.
We also thank the investigators, their study team members for their participation in this study.
We thank our collaborators for helping in the execution of this study.

To download a copy of this poster, scan QR code.
Copies of this poster obtained through QR, AR and/or text key codes are for personal use only and may not be reproduced without written permission of the authors.

biohaven®