BIORA™ Therapeutics

Solving Drug Delivery Challenges with Ingestible Drug-Device Combinations

14th Annual PODD Meeting

October 28, 2024

Innovating smart pill technologies to deliver the right dose to the right place, safely

BIORA™ Therapeutics

ISO 13485 CERTIFIED

NAVIcap™

TARGETED ORAL DELIVERY

Treatment at the site of disease in the GI tract could improve outcomes for people with IBD

BIOjet™

SYSTEMIC ORAL DELIVERY

Oral needle-free delivery of large molecules with liquid jet injection

Targeted delivery or collection of payload in GI tract

- Uses optical localization technology to track its location in GI tract
- IP protected utility for diagnostics, sampling and drug delivery; targeting any desired location of GI tract
- Over 800 devices have been assessed in animals and over 320 in humans
- First application is topical drug delivery to the colon for IBD

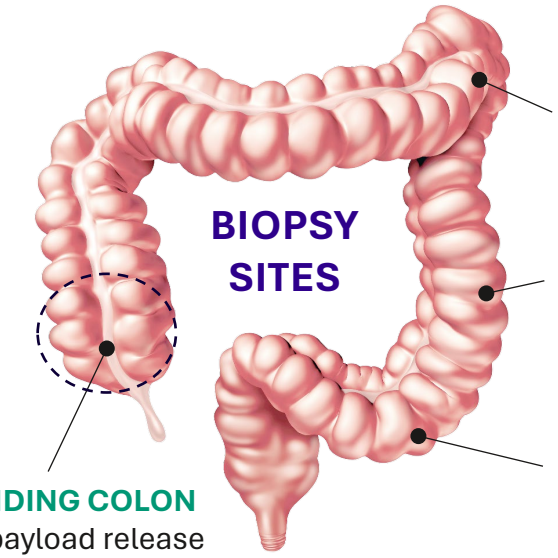
Biora successfully developed NaviCap through four human device function studies and a Phase 1 clinical trial

Q4 2022 – PM 601	Q4 2022 – PM 602	Q1 2023 – PM 611	Q2 2023 – PM 603	Q3 2024 – BT-600
DEVICE FUNCTION STUDY **Healthy Participants Fasted State**	DEVICE FUNCTION STUDY **Active UC Patients**	DEVICE FUNCTION STUDY **Healthy Participants Fasted & Fed**	DEVICE FUNCTION STUDY **Healthy Participants Fasted State**	PHASE 1 SAD/MAD CLINICAL TRIAL **Healthy Participants Fasted State**
• *n*=12 • Achieved distribution of payload across the entire colon[1]	• *n*=7 • 100% of devices performed as intended[1]	• *n*=39 • 97.4% of devices activated payload release function[1]	• *n*=16 • 94% of devices performed as intended[1]	• *n*=48 • PoC of topical delivery and uptake by colonic tissue[2]
HEALTHY PARTICIPANTS ✓	**ACTIVE UC PATIENTS** ✓	**FUNCTION w/wo FOOD** ✓	**PHASE 1-READY DEVICE** ✓	**PHASE 1 SAD/MAD** ✓

1. Lee SN, Razag G, Kelly C, et al. Results of human device function studies for the NaviCap™ Targeted Oral Delivery Platform in healthy volunteers and patients with UC. Poster presented at: *Digestive Disease Week*, May 18 – 21, 2024, Washington DC.
2. Feagan B, Razag, G, Lee SN, et al. Single ascending dose results from a Phase 1 clinical trial of BT-600, a combination product of the NaviCap targeted oral delivery platform and tofacitinib. Poster presented at *American College of Gastroenterology Annual Scientific Meeting*, October 25 – 30, 2024, Philadelphia, Pennsylvania.

NAVIcap™

Successful NaviCap Phase 1 study confirmed better, more consistent localized delivery and uptake



SPLENIC FLEXURE
tofacitinib present in **15/18 biopsies**

DESCENDING COLON
tofacitinib present in **15/18 biopsies**

SIGMOID COLON
tofacitinib present in **14/18 biopsies**

ASCENDING COLON
area of payload release

NAVICAP-DELIVERED BT-600 5MG QD AND 10 MG QD

Hours Post Last Dose	Plasma Concentration ng/mL	Colon Tissue Concentration (mean, 95% CI)		
		Splenic Flexure ng/g	Descending Colon ng/g	Sigmoid Colon ng/g
24 hours measured† (*n*=15)	3.0	**338** (28, 649)	**159** (96, 223)	**161** (72, 251)
16 hours projected‡	10	Range **3,000 – 10,000** ng/g		

- Measured tofacitinib levels **above IC50 at 24 hours** post dose
- Projected levels **above IC90 through at least 16 hours** post dose

† Tissue concentration measured at 22–26 hours post dose; plasma concentration measured at 20 hours post dose;
‡ Predicted tissue levels geometric means based on plasma drug level at 16 hours after device ingestion

KEY TAKEAWAYS

- Submitted IND for BT-600 in Q3 2023
- FDA approval to proceed in Q4 2023
- Initiated Phase 1 trial in Q1 2024
- Phase 1 readout Q3 2024

PRESIDENTIAL POSTER AWARD

American College of Gastroenterology
Annual Scientific Meeting
Oct 25–30, 2024

Feagan B, Razag, G, Lee SN, et al. Single ascending dose results from a Phase 1 clinical trial of BT-600, a combination product of the NaviCap targeted oral delivery platform and tofacitinib. Poster presented at *American College of Gastroenterology Annual Scientific Meeting*, October 25 – 30, 2024, Philadelphia, Pennsylvania.

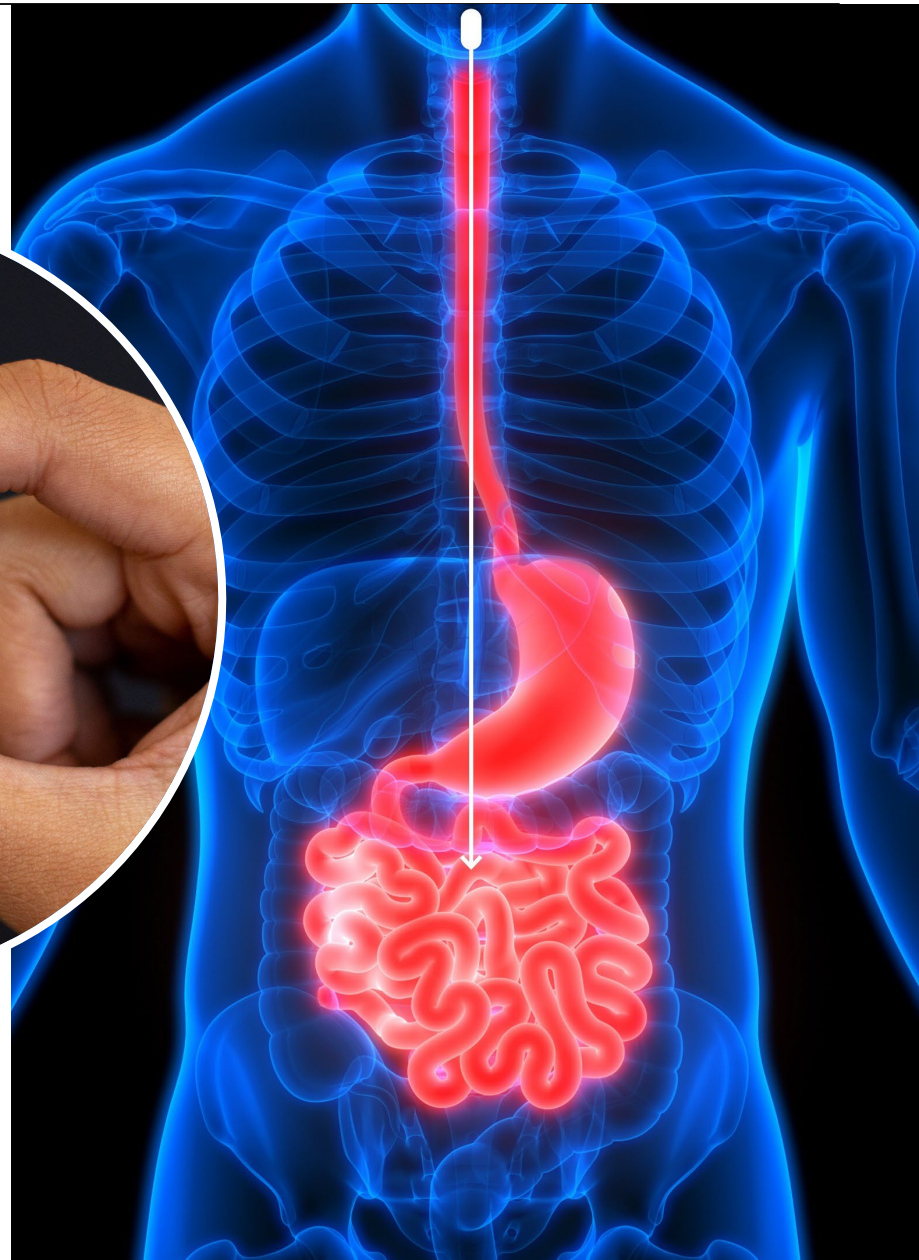
BIORA Therapeutics

BIO*jet*™

SYSTEMIC ORAL DELIVERY

Needle-free, oral delivery of biomolecules to small intestine

- Uses existing liquid formulations; no complex reformulation required
- Delivers a wide range of biomolecules from peptides and antibodies to oligonucleotides
- Payloads of over 300 µl and 50 mg have been dosed successfully with bioavailability >30%
- 00-size clinical candidate device



BioJet 000 testing proved internal jet injection technology

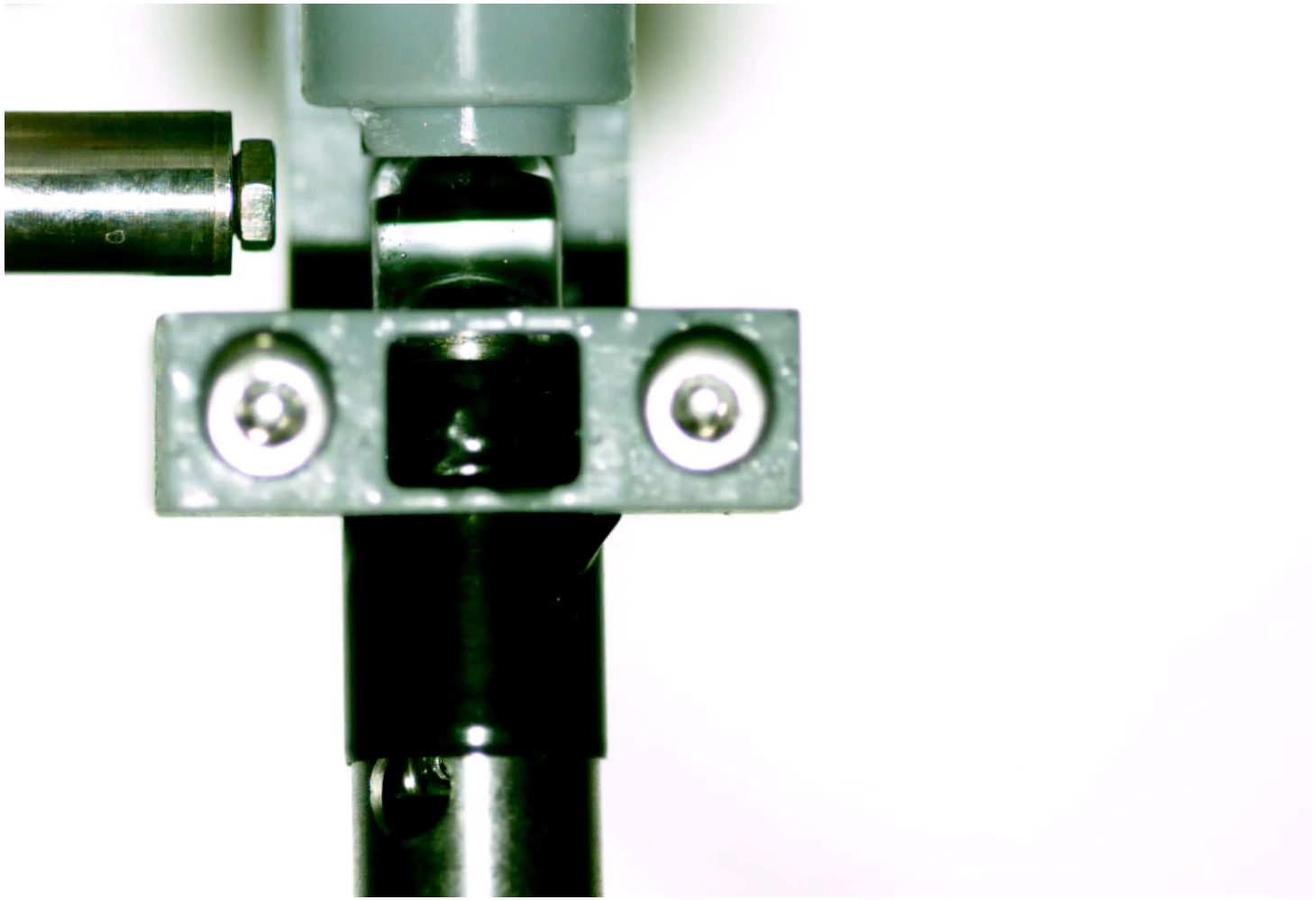
30+ *in vivo* studies carried out with internal and collaborator molecules

- Biora has conducted numerous internal studies with peptides and antibodies
- Five pharma collaborators tested peptides, antibodies and ASOs with 000-size device
- Bioavailability of >30% achieved for all molecule types compared to IV (equates to 60–80% of SC)
- Liver bioavailability of ~50% vs. IV

Benchtop testing allows for rapid iteration and advancement

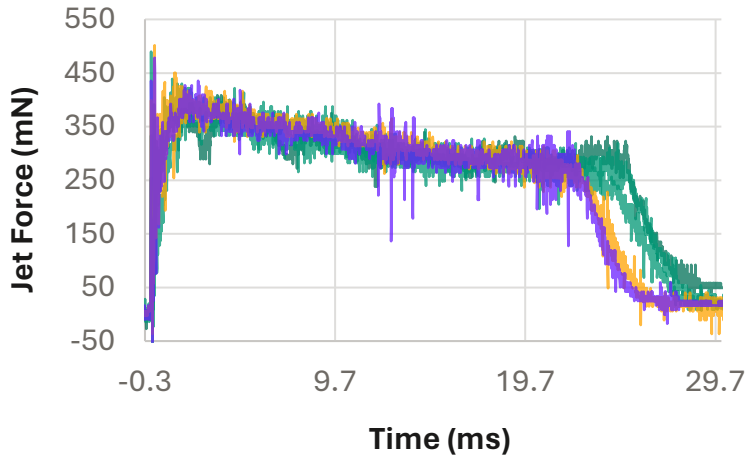
Biora has expanded current collaborations to include 00-clinical candidate device assessment and is in conversations with other parties

Jet force rig (JFR) developed to evaluate function and measure jet parameters



BioJet device mounted in JFR benchtop test fixture

- When trigger degrades, the device actuates, driving the piston into the drug reservoir, which drives payload out through nozzles as a liquid jet.
- A force sensor (left side) is used for jet assessment and characterization



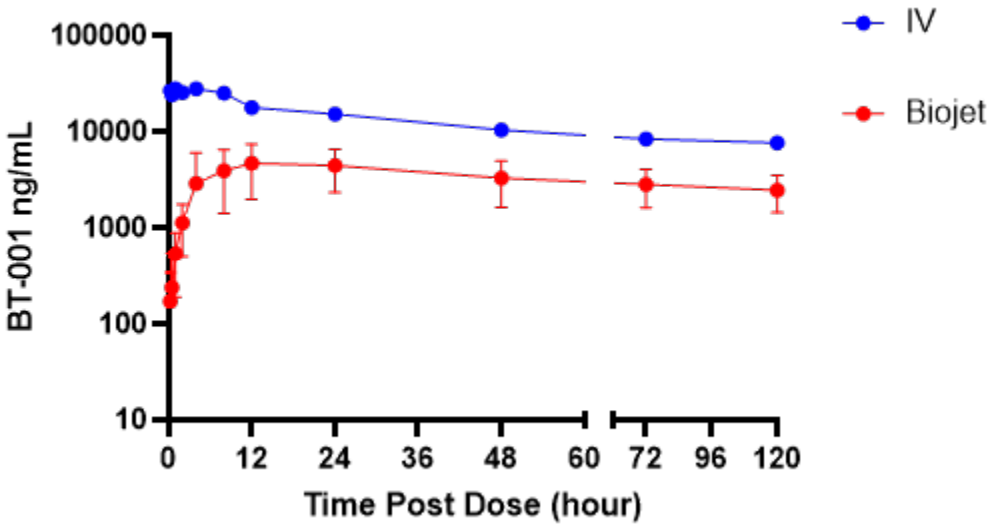
View video: https://biora.wistia.com/medias/48bbq4jvt4

Demonstrated bioavailability across multiple molecules

PRECLINICAL STUDIES IN SWINE MODEL WITH ENDOSCOPICALLY PLACED & AUTONOMOUSLY TRIGGERED BIOJET™ DEVICE

MOLECULE TYPE	DRUG	ORAL BIOAVAILABILITY[1]
ANTIBODY	adalimumab (monoclonal antibody)	**>30%** mean oral bioavailability **vs. IV control** (Equates to 60-80% of SC)
PEPTIDE	semaglutide (GLP-1 receptor agonist)	
OLIGONUCLEOTIDE	undisclosed antisense oligonucleotides	

SYSTEMIC EXPOSURE TO ADALIMUMAB BIOJET DELIVERY vs. IV CONTROLS



RESEARCH COLLABORATIONS

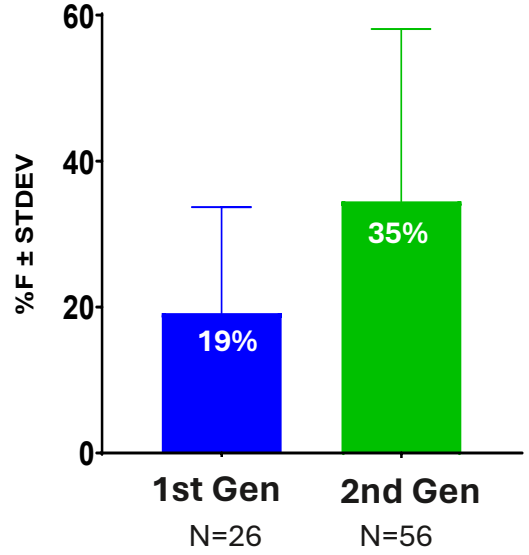
AstraZeneca IONIS ***Pharma 3**** ***Pharma 4**** ***Pharma 5****

1. Biora Therapeutics data on file

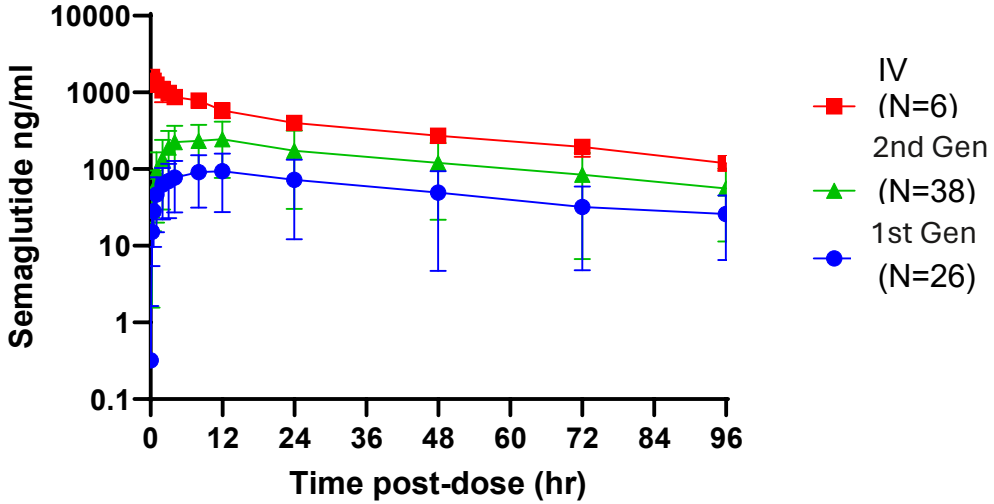
*undisclosed pharma collaborators

35% mean bioavailability of peptides achieved

BIOJET-DELIVERED PEPTIDES
Mean F% vs. IV*



BIOJET-DELIVERED SEMAGLUTIDE
Plasma PK vs. IV*



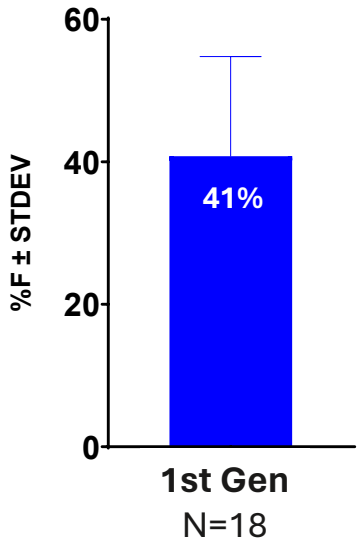
ACROSS 10 STUDIES OF INTRADUODENALLY PLACED DEVICES IN PORCINE MODEL:

- 35% mean bioavailability (compared to IV; 60-80% Vs SC) was achieved with 2nd generation devices (*n*=56, CV=69%)
- Combined internal and collaborator study data for 3 peptides of similar sizes

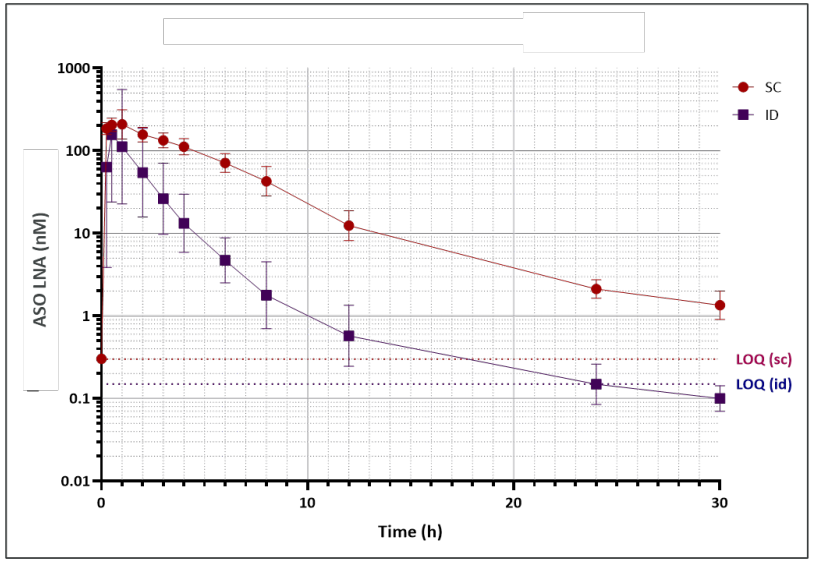
(*) Data from animals with detected drug in blood. Biora Therapeutics data on file

41% mean bioavailability of ASOs achieved

BIOJET-DELIVERED ASOs Mean F% vs. SC*



BIOJET-DELIVERED ASOs Plasma PK vs. SC*



Data shown as geometric mean with geometric SD; Values below LOQ are set as LOQ/2

ACROSS 2 STUDIES OF INTRADUODENALLY PLACED DEVICES IN PORCINE MODEL:

- 41% mean bioavailability (compared to **SC**) was achieved with baseline configured devices (*n*=18, CV=34%)
- Tissue bioavailability was assessed for an ASO with 44% in liver and 49% in kidney vs SC

(*) Data from animals with detected drug in blood. Biora Therapeutics data on file

BIOJET 00-SIZE DEVICE DEVELOPMENT

Clinical candidate device available by year-end

00-DESIGN IMPROVES UPON 000 DEVICE

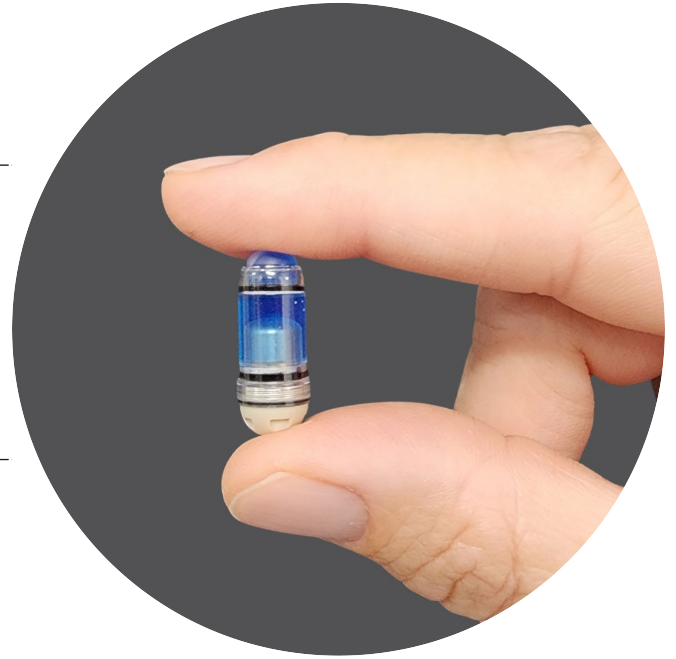
- Smaller 00-size desired by pharma and patients
- Enhanced and simplified triggering mechanism
- Designed for automated manufacture, fill, and sterilization

BENCHTOP TESTING ALLOWS FOR RAPID ADVANCEMENT

- Benchtop assessments have correlated with *in vivo* results
- Advanced engineering modeling helps inform iteration plan
- Rapid iteration enabled quick establishment of proof-of-concept device

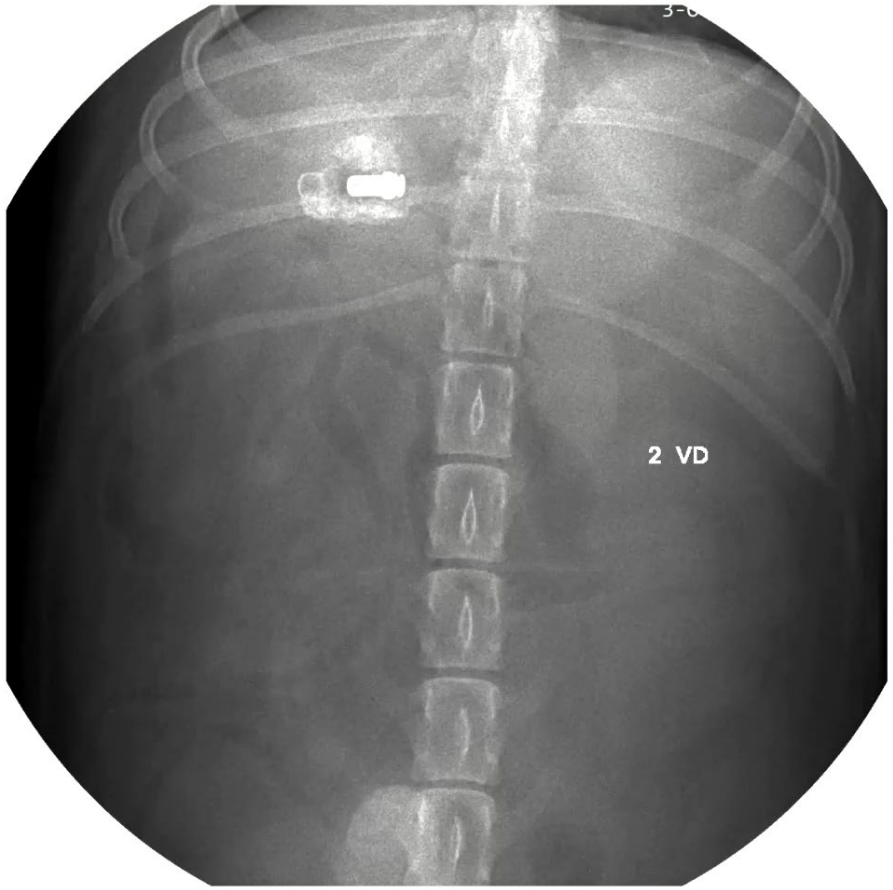
00-SIZE DEVICE UNDERGOING *IN VIVO* ASSESSMENT

- Successfully completed test of enteric trigger and device actuation with orally dosed 00 in canines; time to deployment correlates with benchtop testing
- Canine studies with drug payload underway to further assess actuation
- PK studies in swine and/or non-human primate model in Q4
- Full assessment and feasibility with collaborator molecules in Q1/25



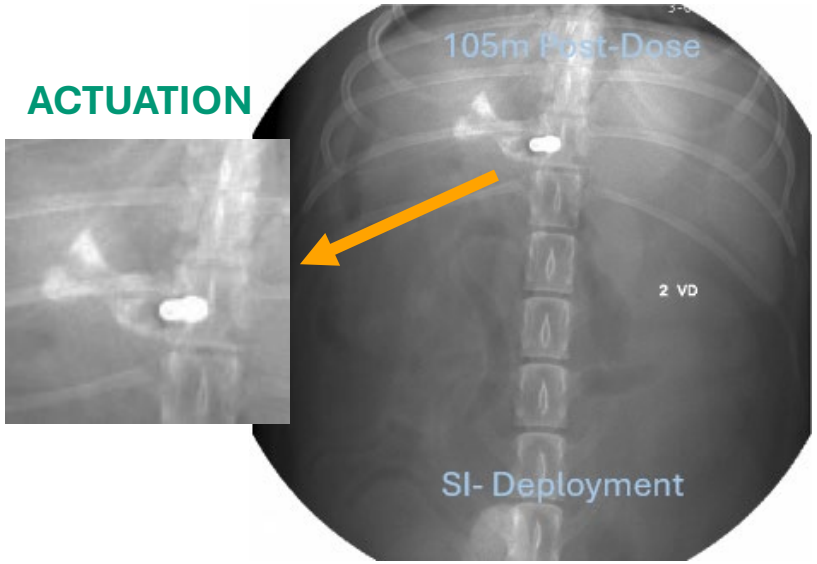
BIOJET 00-SIZE DEVICE DEVELOPMENT

Canine studies with contrast agent payload confirm fully autonomous actuation

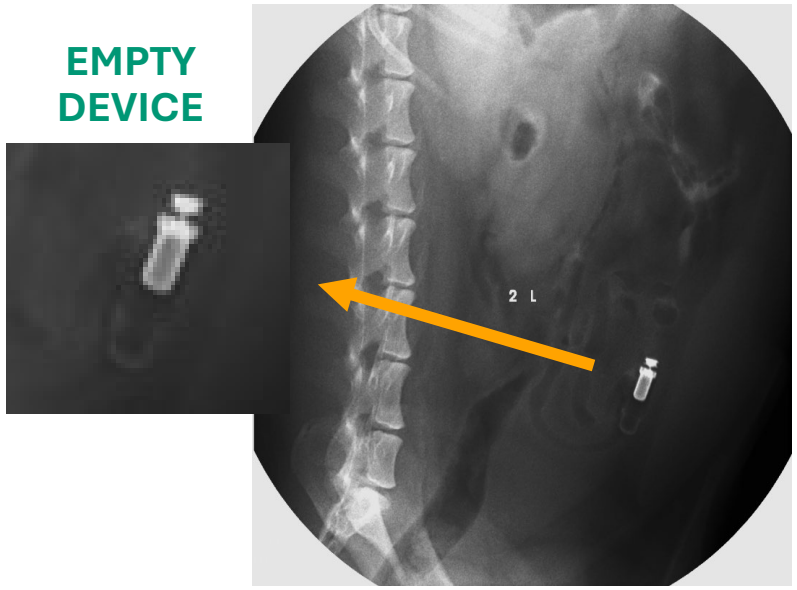


Using underpowered devices so as not to inject contrast agent

ACTUATION



EMPTY DEVICE

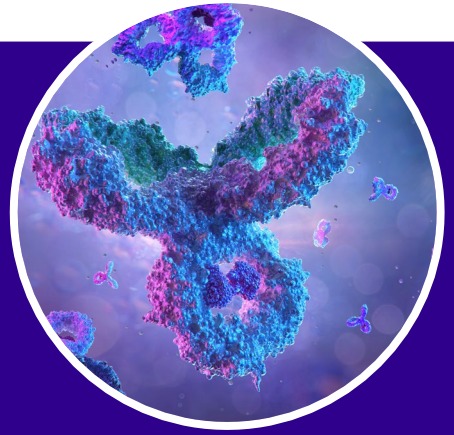


Working with current and future collaborators to assess 00-size device in Q1-25 as a prelude to licensing and development discussions

BIOjet™

CATEGORY-LEADING BIOAVAILABILITY

- Liquid jet delivery to the small intestine designed to **maximize systemic uptake**
- Enables **liver-targeted delivery** of large molecules



BROAD APPLICABILITY

- Proven to deliver multiple molecule types in a **300 µl capacity with the potential for >50 mg doses**
- Leverages **liquid formulation** without complex reformulation

NOVEL DRUG DELIVERY TECHNOLOGY

- Has **comprehensive patent protection**
- Provides opportunity to **extend drug exclusivity**

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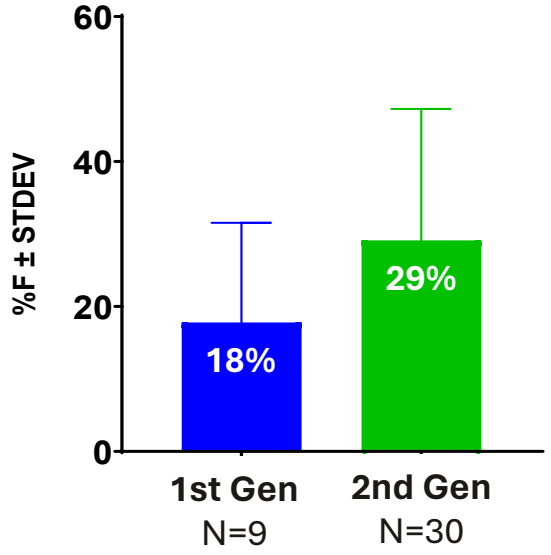
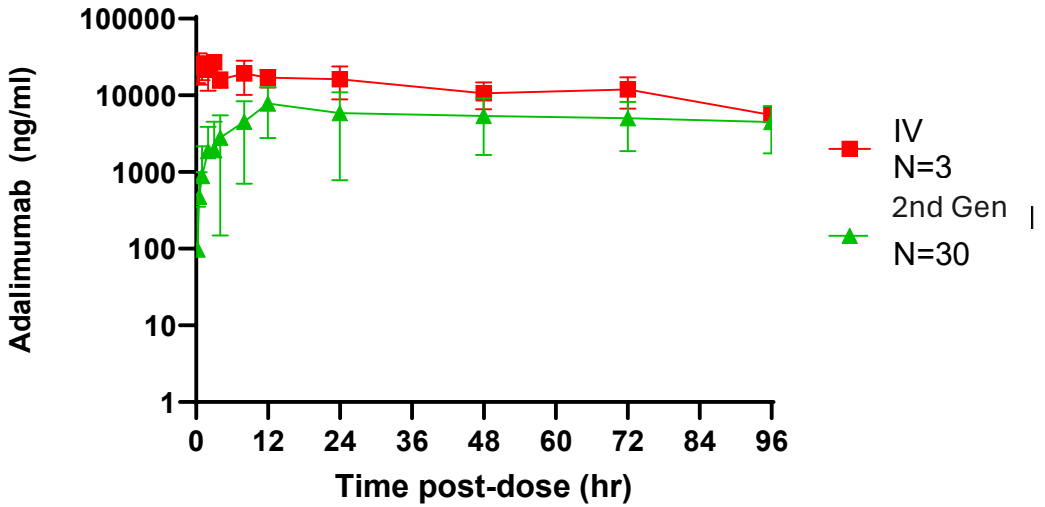
29% mean bioavailability of antibodies achieved

BIOJET-DELIVERED ANTIBODIES
Mean F% vs. IV*



BIOJET-DELIVERED ADALIMUMAB VARIANT
Plasma PK vs. IV*



ACROSS 4 STUDIES OF INTRADUODENALLY PLACED DEVICES IN PORCINE MODEL:

- 29% mean bioavailability (compared to IV; 60-80% of SC) was achieved with advanced configured devices (*n*=30, CV=62%)
- Using an adalimumab variant payload with doses >50mg

(*) Data from animals with detected drug in blood. Biora Therapeutics data on file