



BIONDD™ for Oral Delivery of Biologics – The Future Delivery of Pharmaceuticals

INNOVATION IN THE FORMULATION AND DELIVERY OF BIOTHERAPEUTICS

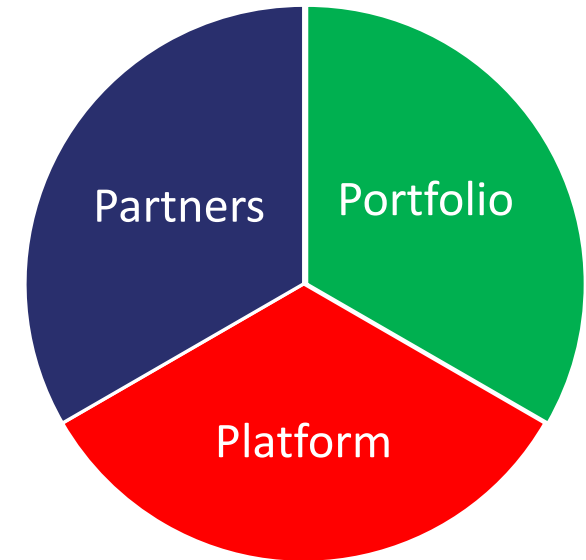
CASSS, WASHINGTON DC, 2023 JANUARY 23RD

BIO▶GRAIL®

Biograil Highlights

*Patients prefer oral v. injections
and is not associated with risk of
local pain and tissue necrosis*

- BIONDD™ - Best in class technology
 - Replacing Injections by proprietary BIONDD™ capsules
- Multiple Clinical Opportunities within 2 years
 - Addressing 400 Billion Dollar Market in 2025
 - Partner/Portfolio/Platform flexible strategy
- Outstanding Investment Opportunity
 - Experienced Management, Board and Advisors
 - Collaborations with large Pharmaceutical companies already established
 - Excellent Investors, Technical Suppliers, and Partner Funding
 - Near term Public Listing Potential



BIO▶GRAIL®

Collaboration Agreement

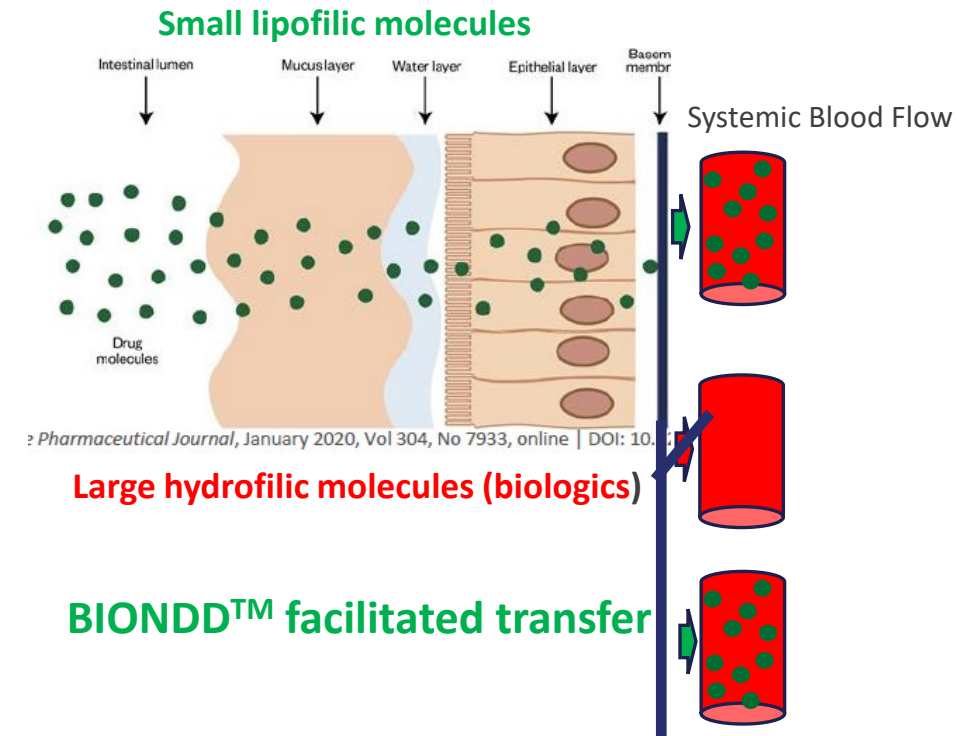
- October 4th Biograil announced a collaboration with Lilly
- “Biograil ApS, a Copenhagen based biotech company developing a unique oral device for delivery of therapeutics that would otherwise be administered by injection, has signed a Collaboration and License Agreement with Eli Lilly and Company. The agreement includes an upfront payment, research funding, development milestones, royalties, and an equity investment by Lilly in Biograil.”
- *“Our Lilly colleagues have been enthusiastic and supportive in the promises of the BIONDD™ platform technology, and we look forward to working with Lilly experts in progressing the technology. This commitment from Lilly is an important next step for Biograil in our vision of making the BIONDD™ platform the preferred technology for oral delivery of biologics. We look forward to advancing the BIONDD™ technology and the potential for Lilly to utilize such technology with key Lilly compounds. Providing patients with additional oral delivery options has been a strong goal for our Company and for the pharmaceutical industry for many years.”.*

Biograil CEO Karsten Lindhardt

BIO▶GRAIL®

Intrawall– “Holy Grail of Drug Delivery”

- Biologics (Ab, RNA/DNA, peptides and proteins)
 - Currently injected
 - Billions \$ spent to find oral alternative
 - Barriers such as enzymatic, size exclusion, lipofilic and physical prevent efficient oral absorption
- BIONND™ facilitates oral absorption
 - Intrawall Insertion
 - Typically 50-200% rel. BA to SC injection



BIOGRAIL®

BIONDD™ – Simple Efficient Biologics Delivery

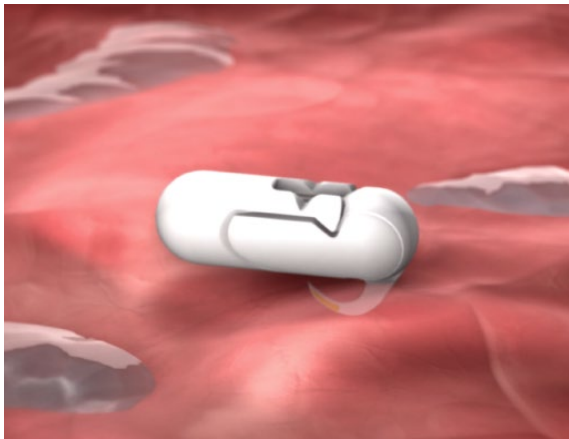
The logo features the text "BIO▶GRAIL" in a bold, sans-serif font. The "BIO" and "GRAIL" are in a dark blue color, while the "▶" symbol is a lighter blue. The text is centered within a rectangular area that has a blue background with soft, wavy, layered patterns.

BIO▶GRAIL

BIO▶GRAIL®

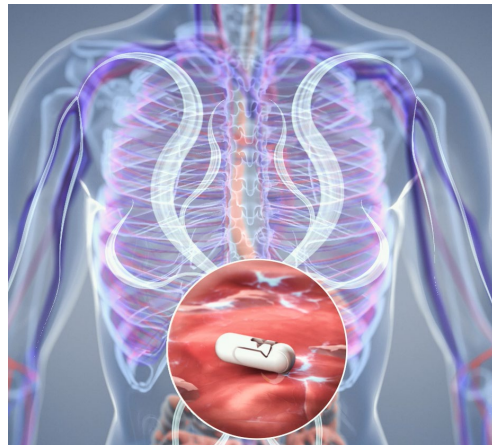
Key Steps

Attachment



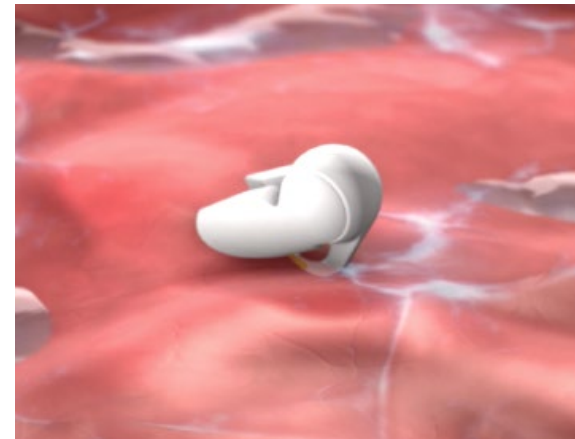
- Capsule dissolves
- Spring mechanism released
- Tissue clamps under device body

Drug Delivery



- Active substance inserted in wall
- Distributed passively to blood vessels
- Effective systemic delivery

Detachment



- Device body released
- Tissue clamp removed
- Device wiggles free by peristalsis

Elimination



- Insertion part folded in device
- Pass through GI tract
- Biocompostable material

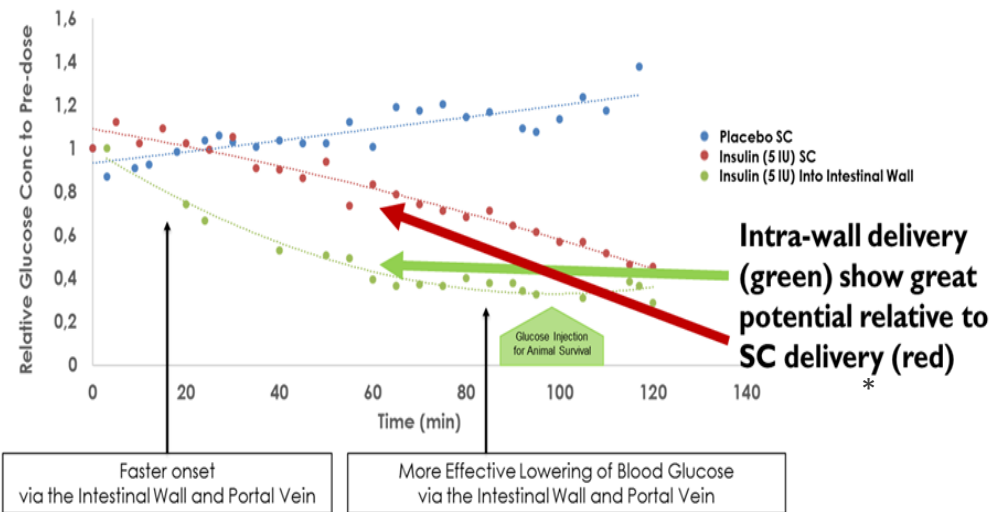
BIO▷**GRAIL**®

BIONDD™ Technology Maturation



BIONDD™ – In Vivo Proof of Principle

Absorption/distribution confirmed



*) Subcutaneous

Hooking Confirmed

> 95% hooking

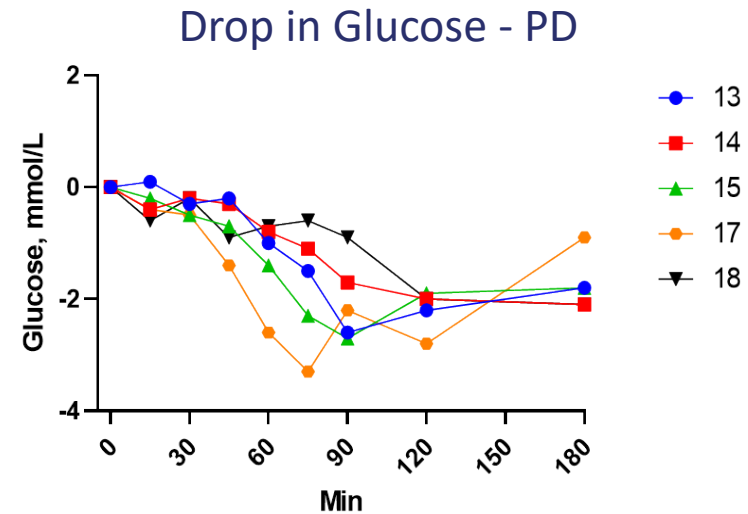
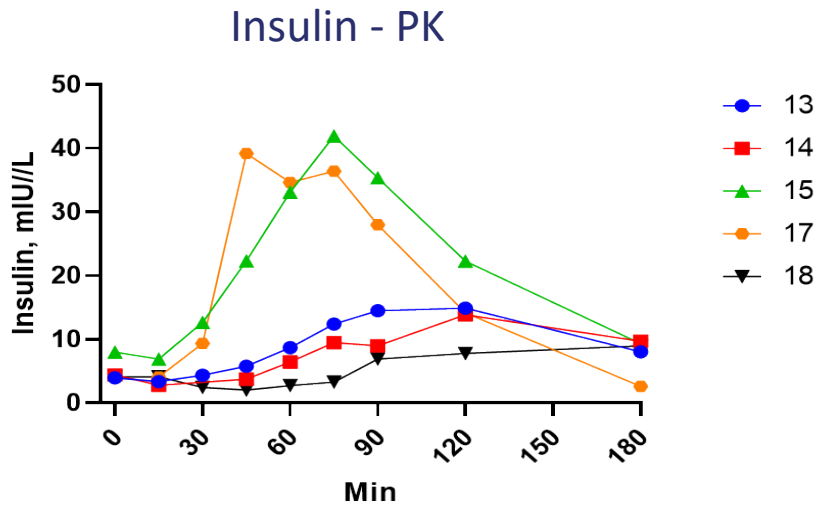
Hooking confirmed*	Yes	Yes	Yes	Yes
First fixed position (hooking)	15 min	15 min	15 min	15 min
Last fixed position (hooking)	>5½ h	>5½ h	>5½ h	>5½ h

* Hooking confirmed when fixation >4 h, which provides time window (>2-3 h) to deliver active substance

BIOGRAIL®

BIONDD™ – In Vivo Proof of Concept

BIONDD™ (00)



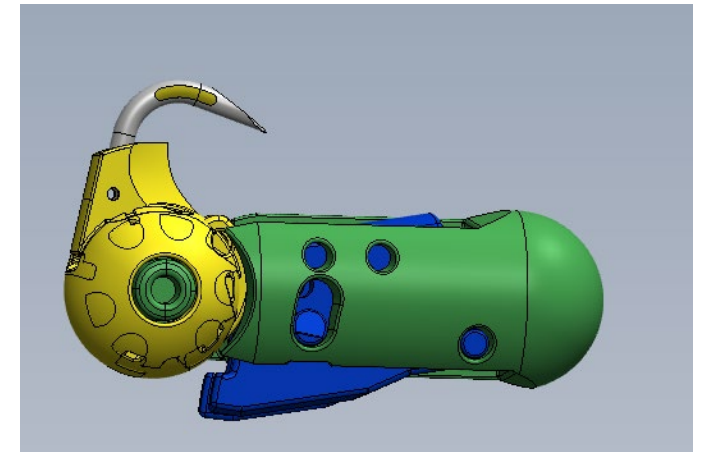
- Delivery from all animals
- Variation on profiles can be improved
- Bioavailability 50% of SC
- Insulin challenging molecule

- Effective drop in glucose >1.5 mM
- Consistent effect
- Fast Onset

BIOGRAIL®

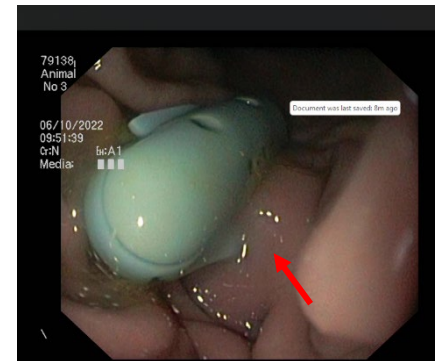
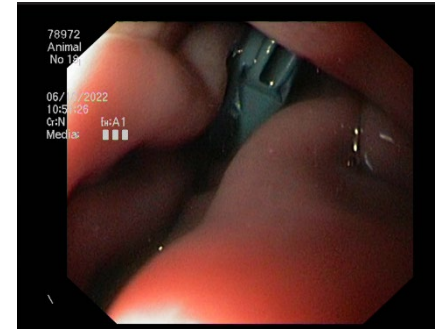
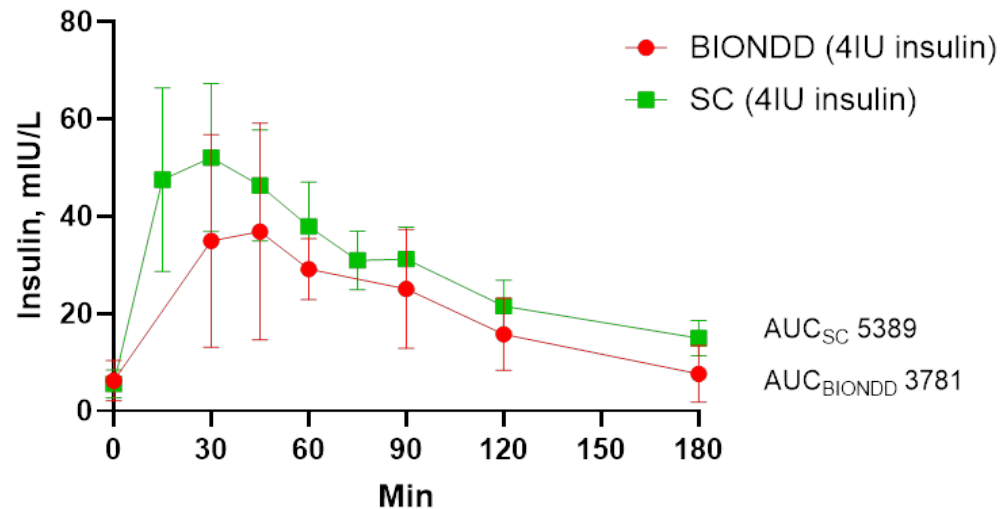
Clinical Design Focus Points

- Encapsulation needed for easy administration in First in Man study
- Improved trigger mechanisms tested
- Simplicity & robustness
- Scale manufacturing
- Clinical Design lock expected in March 2023



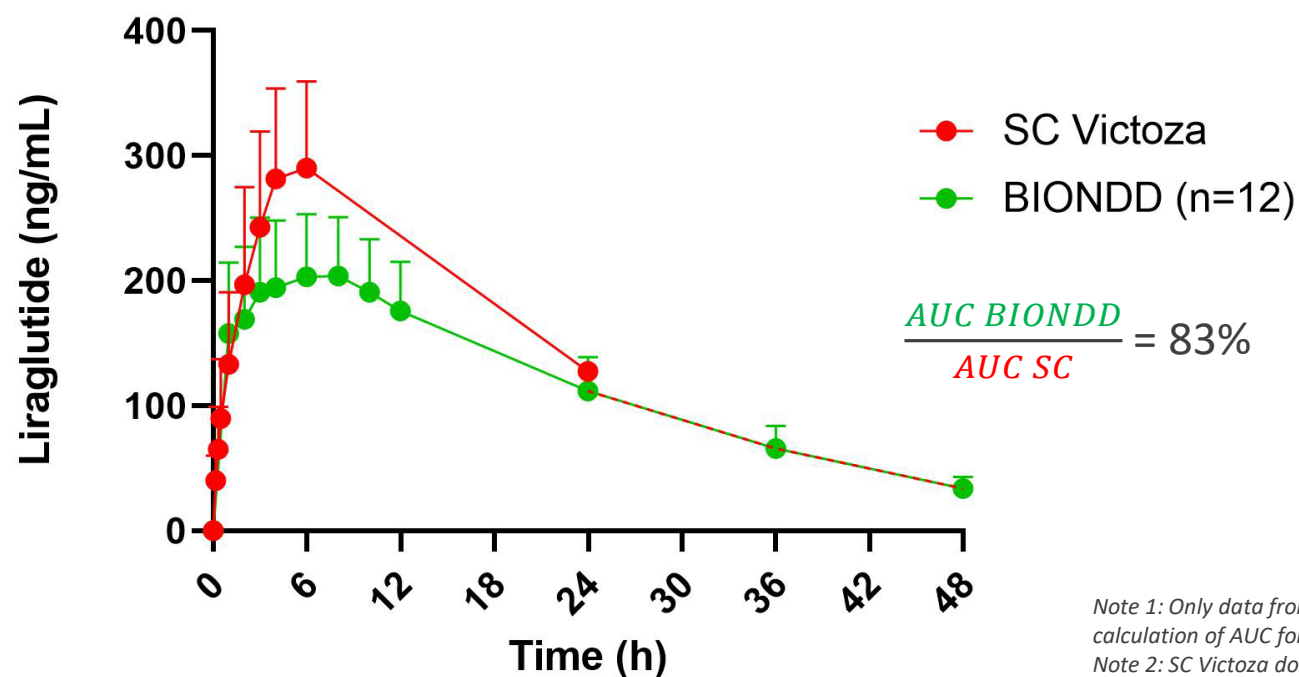
BIONDD™ Clinical Design (Insulin)

- Insertion Rate: 100% (12/12)
- Drug Delivery frequency: 100% (12/12)
- Drug delivery effectiveness: BA 70% of SC (6/6)



BIOGRAIL®

BIONDD™ Liraglutide - BA higher for BIONDD™



Plasma concentration shown as: Mean \pm SEM

Note 1: Only data from 1 subject available at 24 h for SC Victoza. This value is used for the calculation of AUC for all 3 subjects.

Note 2: SC Victoza dose of 0.5 mg/dog normalized to 0.4 mg/dog as administered by BIONDD™

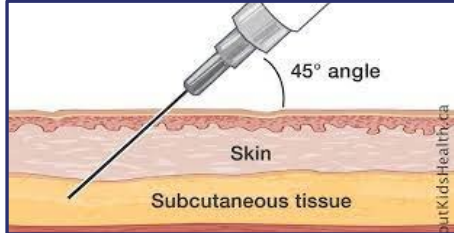
Note 3: SC Victoza AUC 0-48h = SC Victoza AUC 0-24h + BIONDD™ AUC 24-48h

BIOGRAIL®

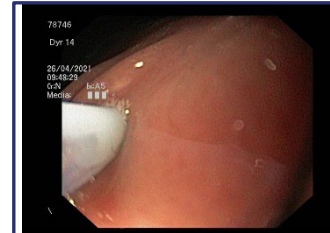
Effective Feasibility Model for Partnering

Liquid Formulation

STEP 1 SC injection

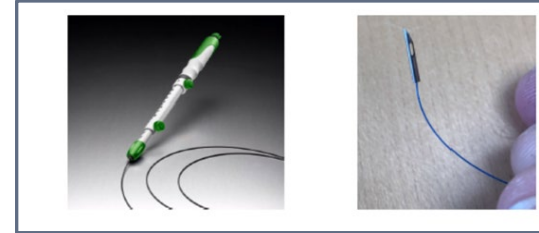


STEP 2 Intra-wall injection

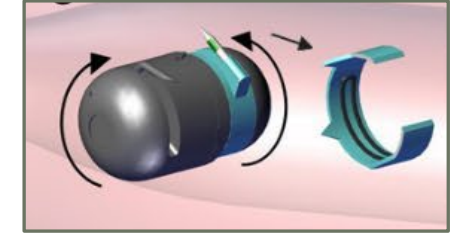


BIONDD™ Formulation

STEP 3 Intra-wall spike insertion



STEP 4 BIONDD dosing

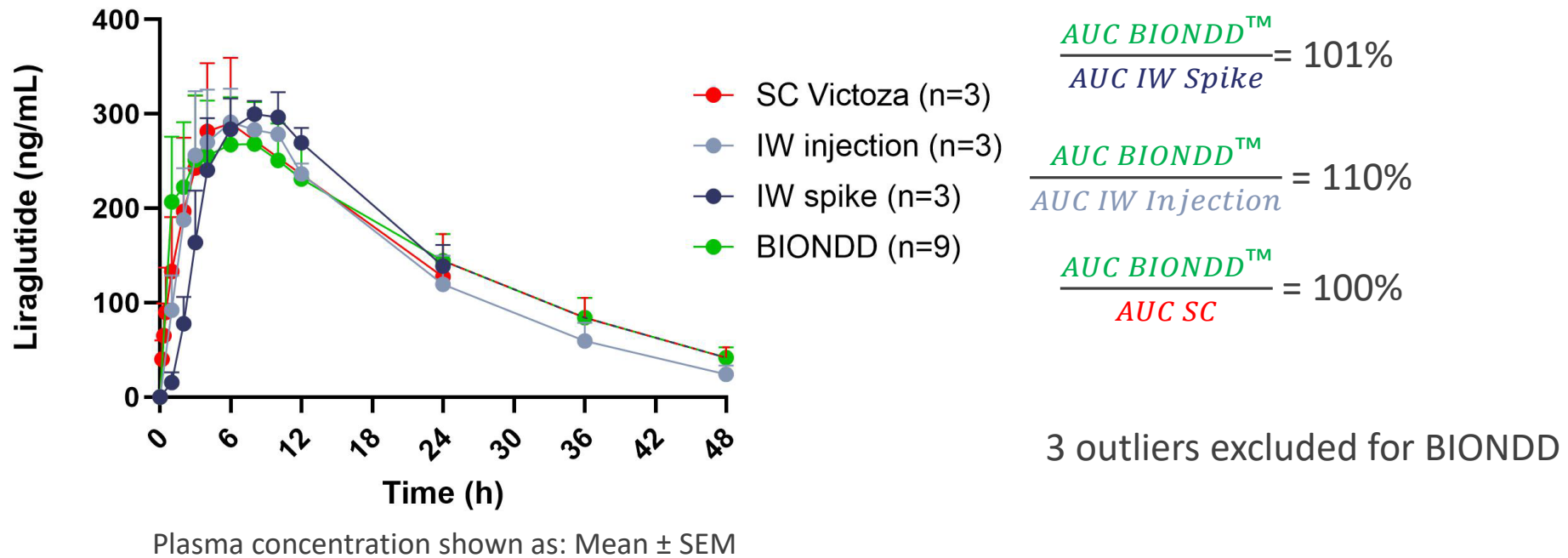


Parallel Formulation Development and in-use stability

BIONDD™ Pre-clinical Proof of Concept Established in Dog

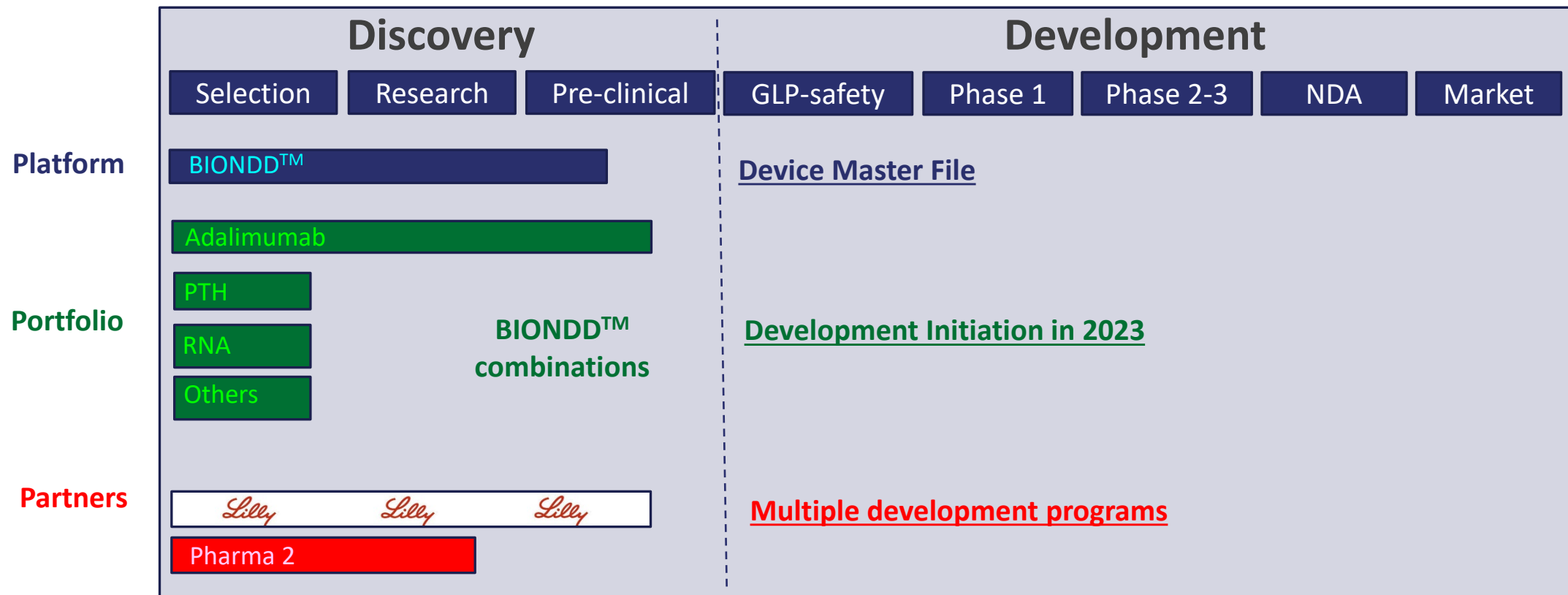
BIO ▶ **GRAIL**®

BIONDD™ – 4-step BA Liraglutide



Note 1: Spike insertion is the optimal benchmark and has similar BA when excluding a few outliers. 9 out of 12 BIONDD™ devices with successful delivery included in BIONDD™ data. Significant reduction of outliers expected when moving from 3D printed devices to injection molding.

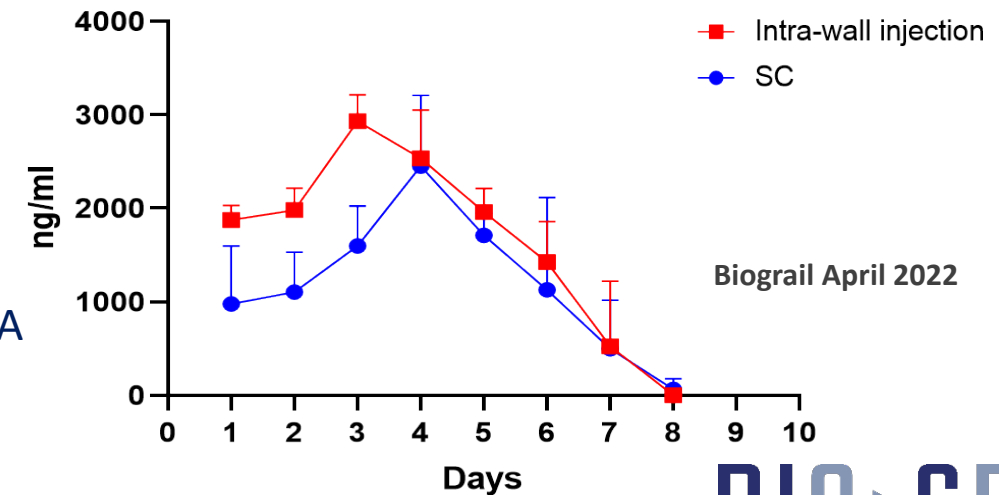
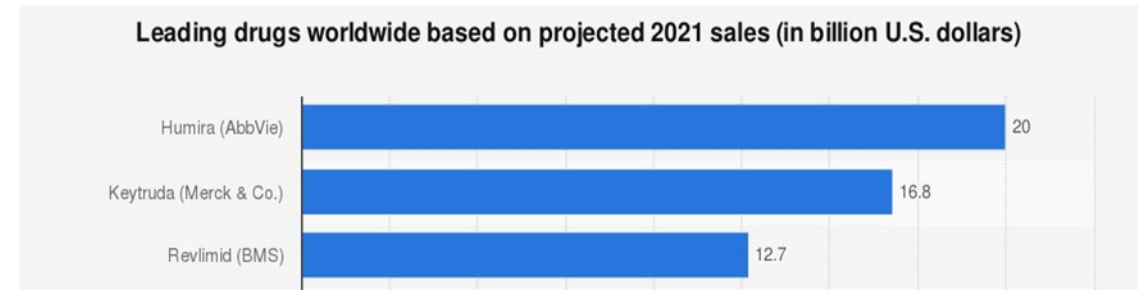
Biograil Oral Biologics Pipeline



BIOGRAIL®

Candidate 1 – BIONDD™ ADMAB

- Humira (Adalimumab)
 - Best selling drug 2021 (Abbvie)
 - Annual sales 20 bill USD
 - SC injection suboptimal for RA patients
- BIONDD™ ADMAB
 - Excellent absorption from stomach intra-wall
 - Relative Bioavailability 136% rel. To SC
 - More efficient and more convenient products for RA patients address an important medical need



BIOGRAIL®

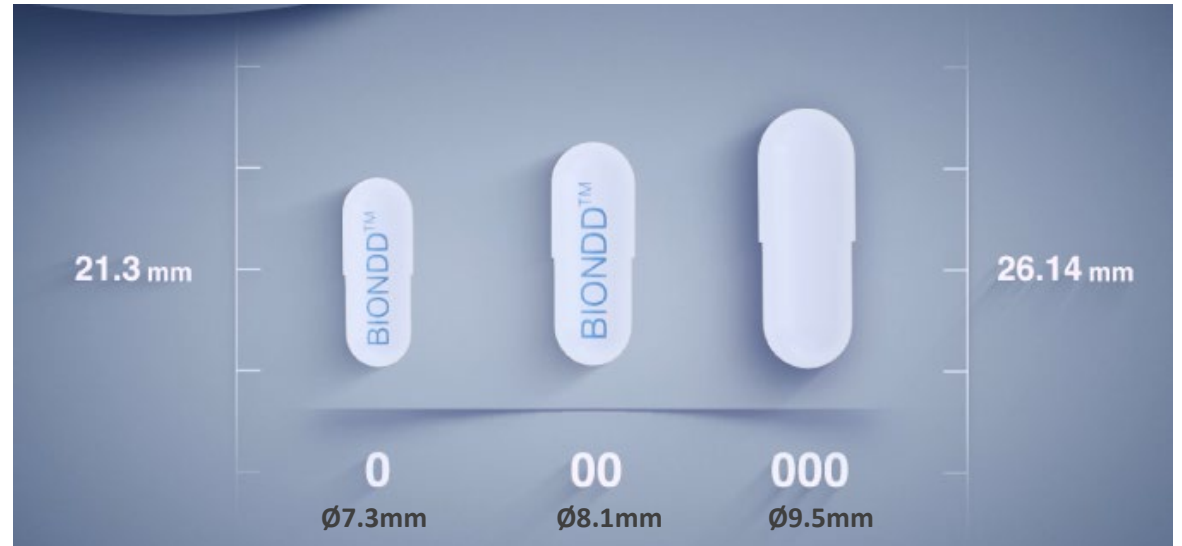
Candidates for Consideration

- PTH – Osteoporosis
 - ~2 bill USD market with frequent injections, need of fluctuating plasma levels
 - Low dose (30 µg), easy to formulate
 - FDA accepts bone density as validated biomarker
- RNAs
 - M-RNA - ONPATTRO, (hATTR amyloidosis)
 - Orphan Drug
 - Lipid nanoparticle formulation
 - Si-RNA
- EPO – Kidney impairment
 - 15 bill USD (2027) with frequent injections



Miniaturization to Size 0

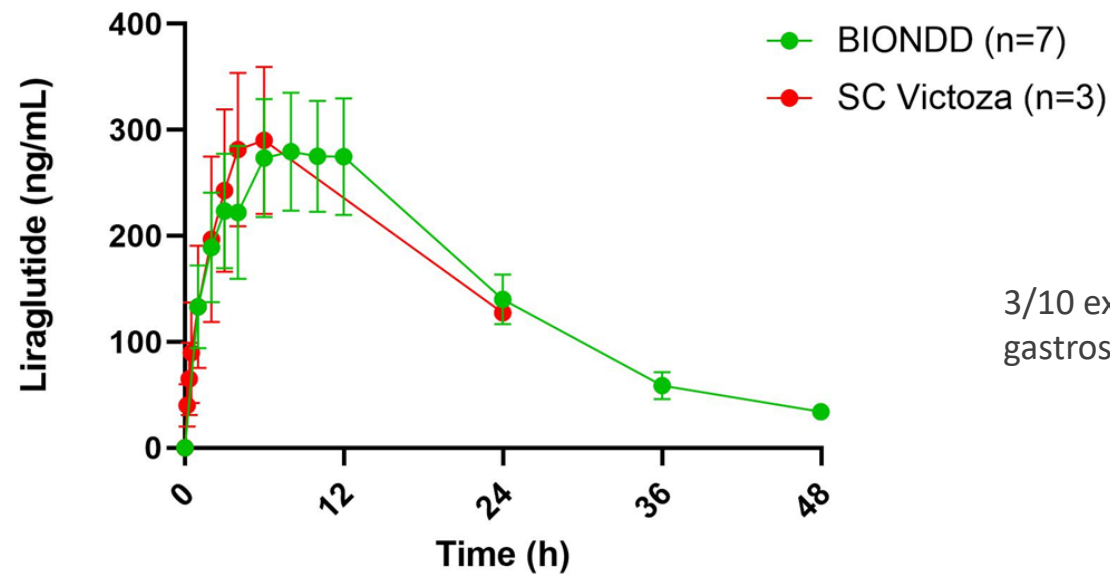
- Smaller size → More convenience to patients/children
- Similar success rate



BIO▷GRAIL®

Miniaturization to Size 0

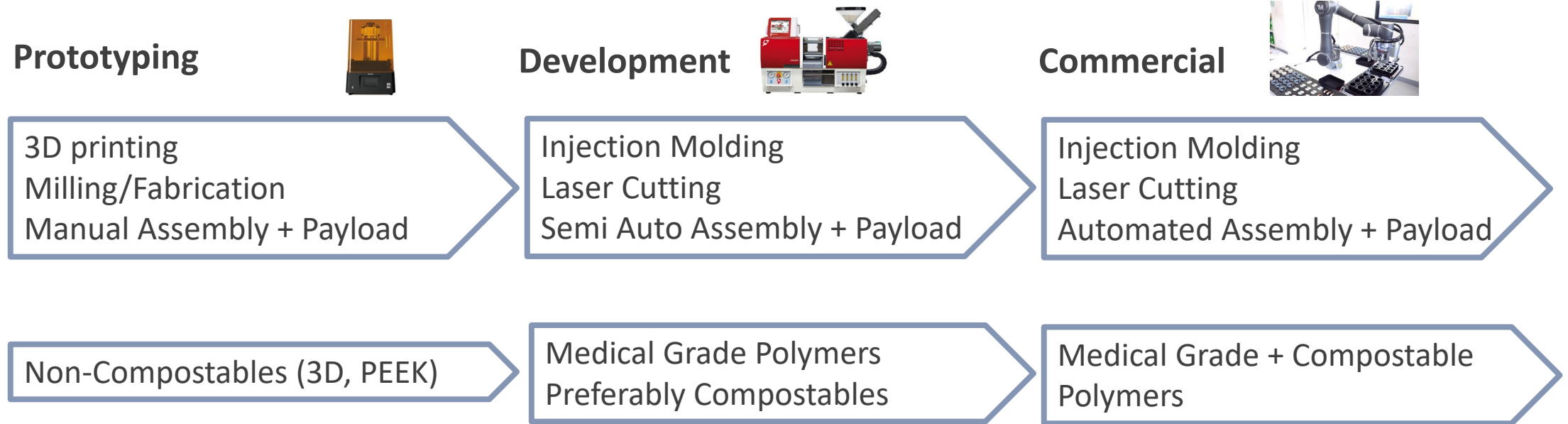
- Great performance also with size 0
- Gastroscopic imaging can be used to evaluate success to optimize device performance



3/10 excluded for BIONDD based on gastroscopy pictures

Plasma concentration shown as: Mean \pm SEM

Manufacturing Optimization



Excellent Technical Partners

- SPT Vilecon



- Medical device engineering and upscaling
 - Iterative 3D-drawing and prototyping BIONDD™
 - *Design for manufacturing* – expertise in scale up
 - Clean suites ISO-13485 qualified

- Meko



- World leaders in laser cutting technologies and scalable micro device engineering
 - Develop biodegradable metal alloy materials for stents

- Evonik



- World Leaders in pharmaceutical excipients
 - Core expertise in biodegradable polymers
 - One of the worlds targets polymer manufacturer






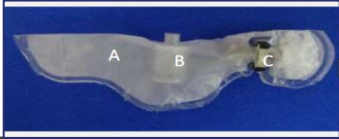
- Scantox



- Pre-clinical GLP-accredited CRO
 - Pharmacology
 - Regulatory toxicology

BIO▶GRAIL®

Biograil - Strong Competitive Technical Edge

	BIOGRAIL	 		
Technology	BIONDD™ 	SOMA 	RaniPill 	Rybelsus Co-formulation Semaglutide-SNAC
Drug delivery success	>75%	70%	50%	100%
Bioavailability v. SC	50-200%	50-200%	50-200%	0.4%
Capsules Size	(Size 0-00) Ø7.3-8.1mm	(Size 000+) Ø10-12mm	(Size 000) Ø9.5 mm	Tablet
Deal	Lilly, upfront, milestones, royalty and equity	Fully controlled by Novo Nordisk. All work internalized	Successful IPO July 2021 Market Cap >\$1B	Novo Nordisk bought Emisphere >\$1.8B
Investors	HTGF, Megatrend, Evonik, Verve Ventures, Sanner Investiere	Novo Nordisk full funded	Google Ventures, AstraZeneca, Novartis	Novo Nordisk full funded BIOGRAIL®

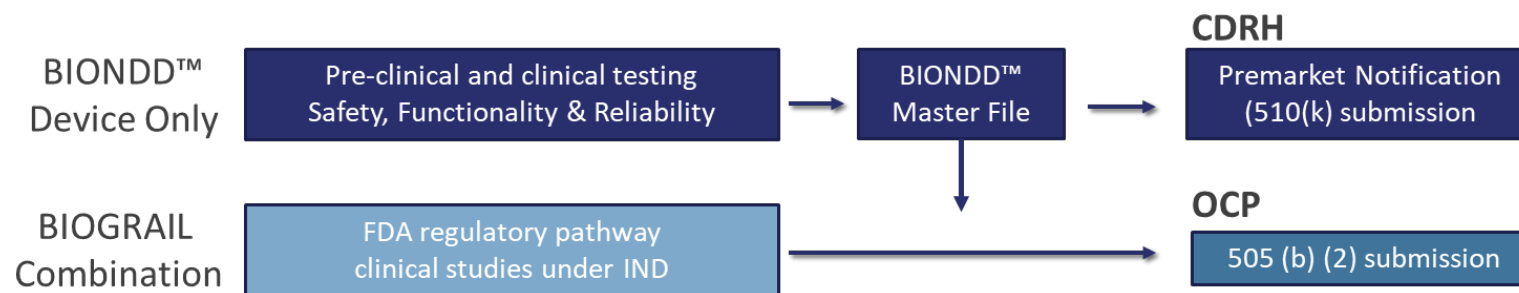
Regulatory Affairs - Considerations for RFI

- RFI - 513(g) to CDRH
 - Determining device classification, premarketing authorization path
 - Determining a proposed device's jurisdiction authority
 - BIONDD™ fall within the jurisdiction of CDRH
 - 510(k) application (facilitating 505b2s for combination products)
 - Prefilled syringe as predicate
 - Breakthrough Device Designation Application (New guideline from Nov 2022)
 - BIONDD™ fall within the jurisdiction of OCP (Office of Combinations Products)
 - INDs/combination
 - 505b2

Contains Nonbinding Recommendations

Draft – Not for Implementation

**Select Updates for the Breakthrough
Devices Program Guidance: Reducing
Disparities in Health and Health Care**



BIOGRAIL®

First in Man – Pathway

IDE (Device only)



IND (Combination)



Backed by Leading Scientific & Technical Advisors

Scientific Advisory Board

Ester Caffarel-Salvador, Former Associate Director Regenerative Medicine Leo Pharma, Research Lecturer at Massachusetts Institute of Technology

- Co-inventor of SOMA – Expert in Oral Delivery Devices



Claus Michael Lehr, Professor Helmholtz-Institute for Pharmaceutical Research Saarland (HIPS). Helmholtz Center for Infection Research (HZI)

- Expert in drug delivery and biological barriers



Phillip Just Larsen, SVP Global Head of Research, Bayer Pharmaceuticals, formerly research executive in Sanofi & Grünenthal

- Expert in pharma company research strategy



David Brayden, Professor of Advanced Drug Delivery, Veterinary Sciences Centre, University College Dublin, Ireland

- Expert in oral drug delivery and intestinal transport



BIOGRAIL®

Thank You for Your Attention!



Karsten Lindhardt
CEO & Founder



Nikolaj Skak
CTO & Founder



Nils Piwon
CDO



Martin Rex Olsen,
Dir. Manufact.



John Barberich
Chairman & Founder
Finance Advisor



Lene Havsteen
Assoc. Director
Regulatory Affairs



Raimo Urban
Butzbacker Sr.
Design Engineer



Kirsten Asser
Larsen
Project Director



Hanne Bruun
Rasmussen
Sr. Lab. Tech



Lisbeth Nordly
Lauritzen
PA & Admin. Assistant



Nina Mertz,
Industrial Post Doc

BIO►**GRAIL**®

Biograil – the Holy Grail of Biologics Delivery

KARSTEN LINDHARDT, CEO

KL@BIOGRAIL.COM



BIO▶GRAIL®