ORBIS
Overview

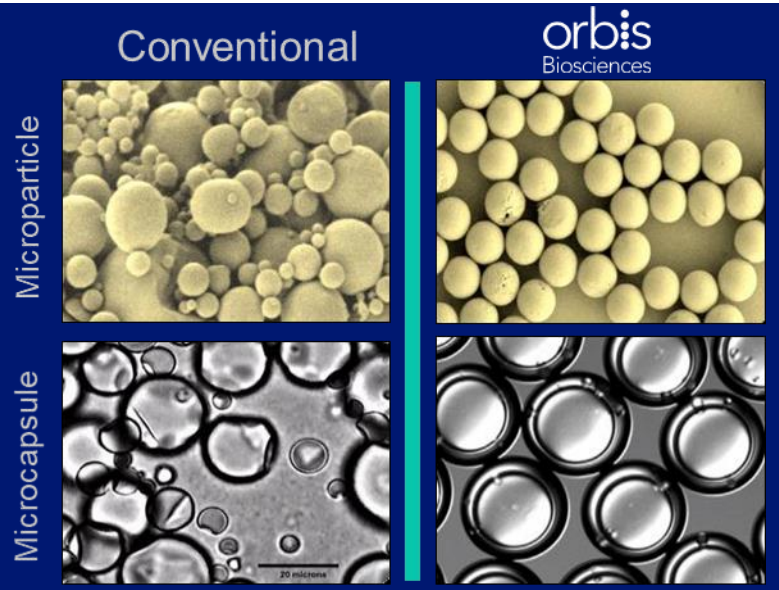
First name Last name
Title
5-28-20

Who is Orbis?

Orbis provides innovative taste-masking and controlled release solutions for oral and injectable pharmaceutical products

Multiparticulates are able to deliver:

- Uniformity
- Format Flexibility
- Dose Flexibility
- Taste Masking
- Variable Release Kinetics
- Single-step Microcapsules



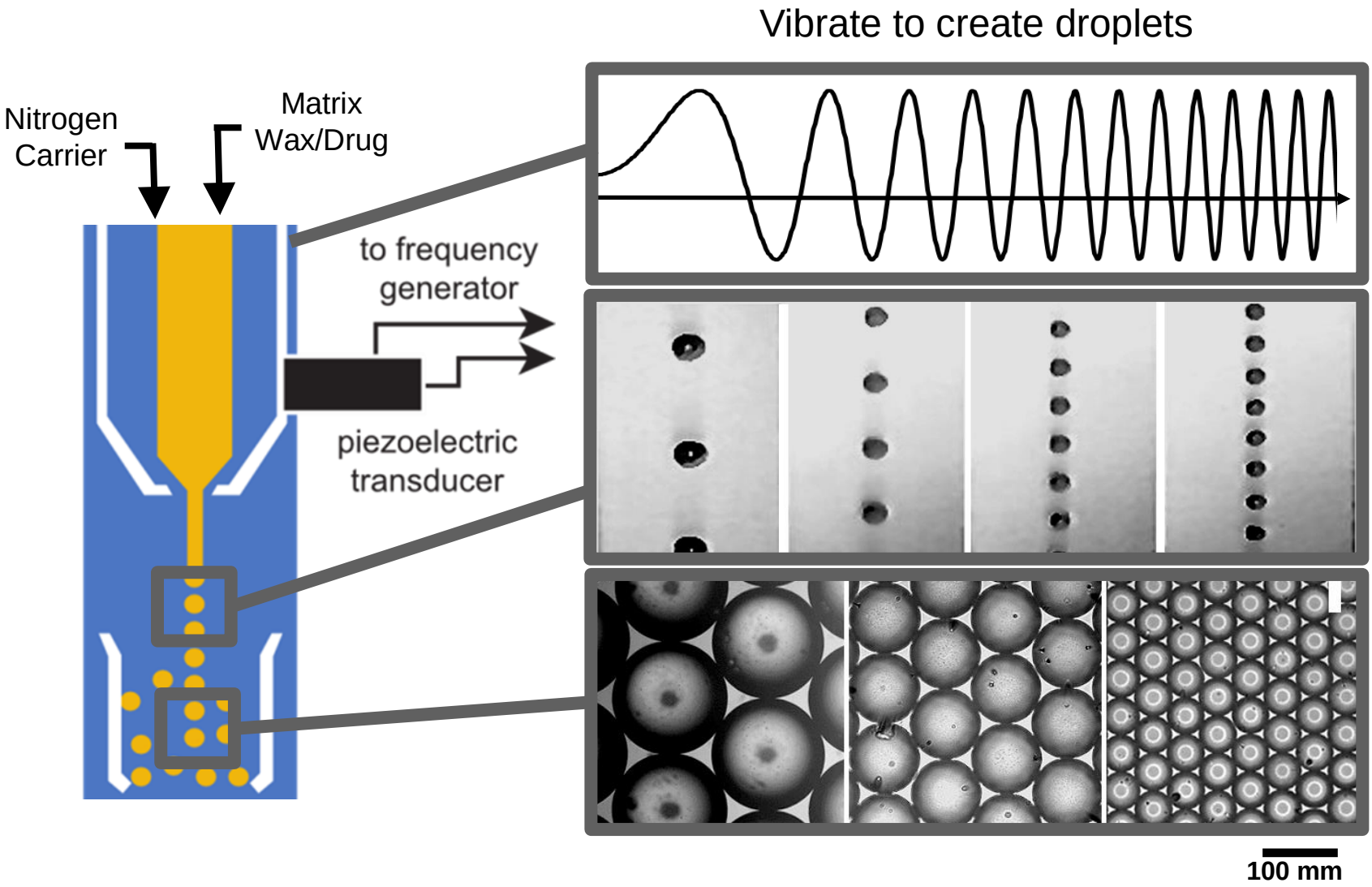
Adare is building commercial manufacturing capabilities of Orbis technology in Vandalia, OH

ADARE PHARMACEUTICALS

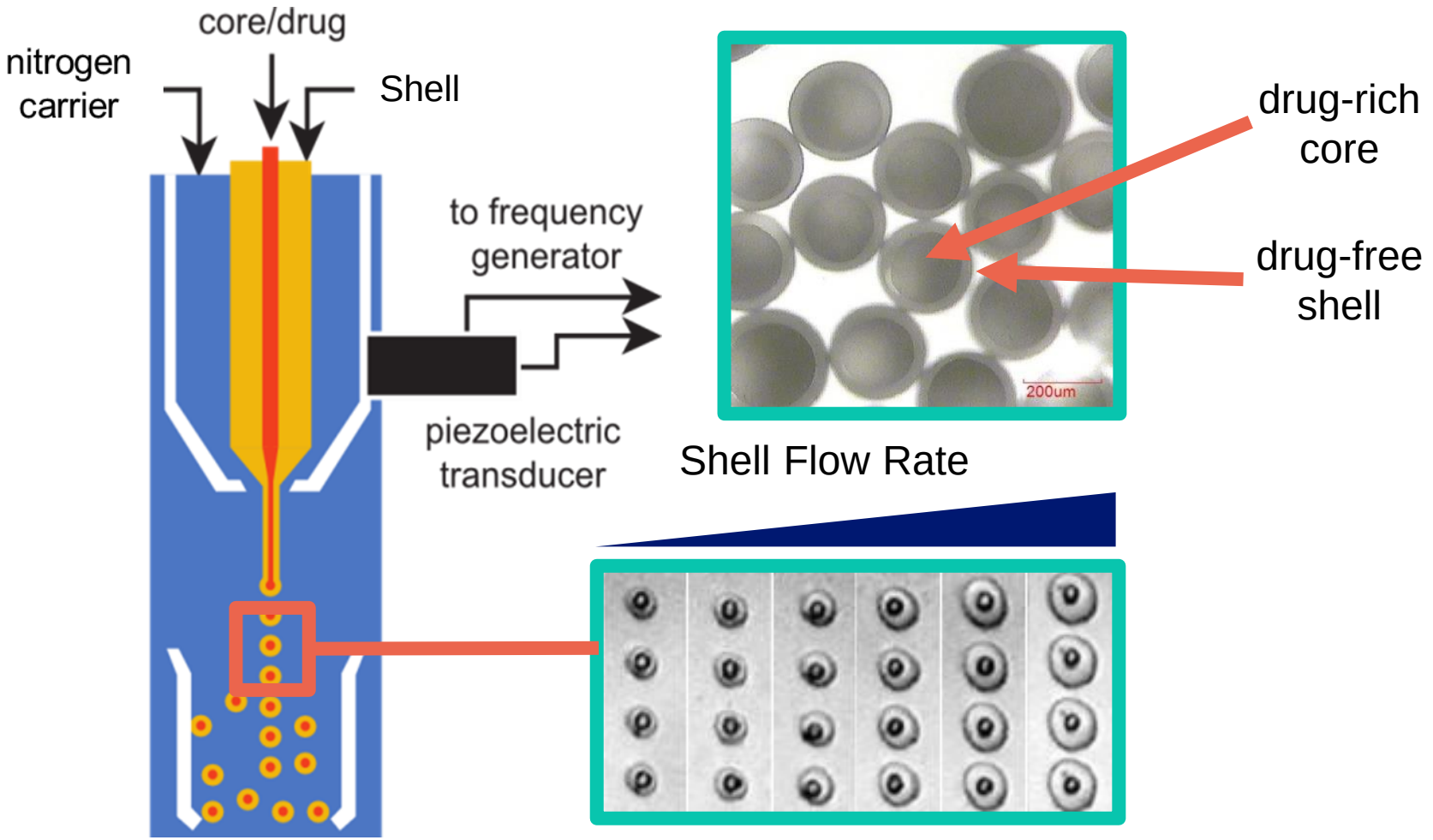
Orbis' Technology Provides Controlled Release Powders for Format and Dose Flexibility

PRECISION PARTICLE FABRICATION® TECHNOLOGY ENABLES PARTICLE UNIFORMITY WITH PRECISION ENGINEERING, ALLOWING FOR TIGHTER CONTROL OF RELEASE KINETICS

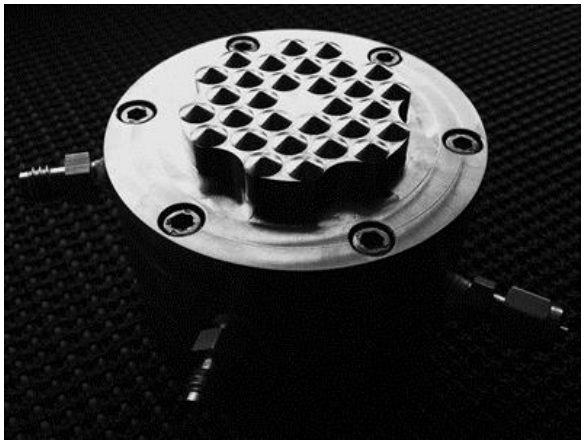
Technology Offers Significant Improvement over Traditional Technologies

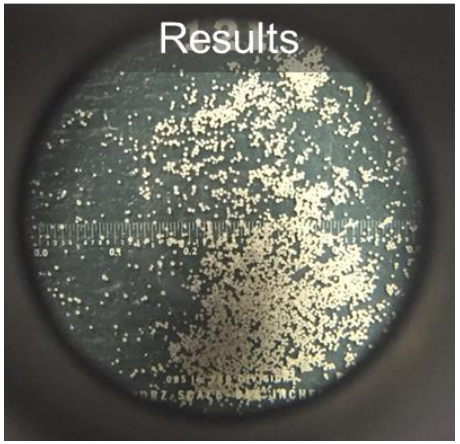


Single-Step Core Shell Option Adds Capabilities and Eliminates Downstream Coating Steps



Demonstrated Manufacturing Scale Up and Broad Intellectual Property Portfolio

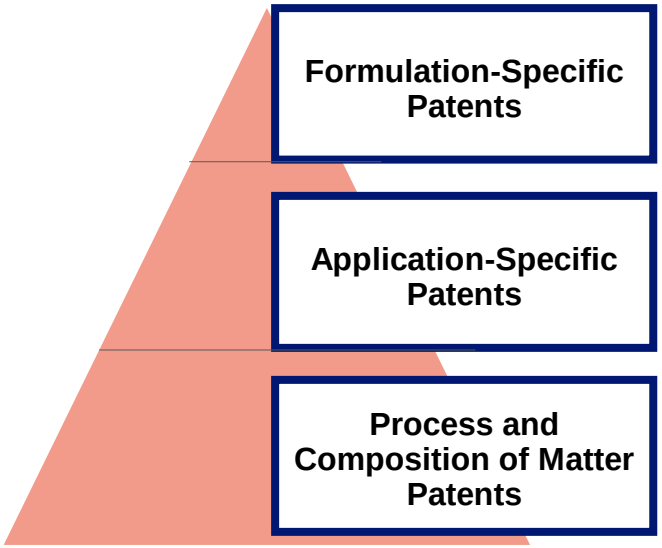




- 5 issued patents on base technology
- 5 pending patents on applications
- Specific formulation patents underway

Patent Strategy is a Multi-Layered Approach
Focus on Patent Life Optimization

Proprietary Technology with Multi-Layered Patent Strategy



Trade Secret Program to Extend Patent Life

Trade Secret Program:

- Leverages Orbis' experience using and scaling the technology
- Documented with claims for future patent application filings that will provide patent life beyond issued base patents

Current Patent Landscape

PENDING

- US Patent Application No. 15/785,342, titled "Sustained Release Particle Formulations" (Corresponding Foreign Patent Applications in Canada (Allowed) and Europe)
- US Patent Application No. 15/244,455, titled "Taste Masking Drug Formulations" (Corresponding Foreign Applications in Europe and Japan)
- US Patent Application No. 14/738,174, titled "Extended-Release Drug Delivery Compositions" (Corresponding Foreign Applications in Canada and Europe)
- US Patent Application No. 15/643,857 titled "Extended-Release Drug Delivery Compositions" (Allowed)
- US Patent Application No. 16/172,134, titled "Biodegradable Polymer Composition for Parenteral Administration (Corresponding Foreign Applications in Canada, China, Europe, and Japan)

ISSUED

- US Patent No. 6,669,961, titled "Microparticles" (Corresponding Patents in Canada, Switzerland, Europe, France, Germany, Ireland, Great Britain, and Korea)
- US Patent No. 7,309,500, titled "Microparticles"
- US Patent No. 7,368,130, titled "Microparticles"
- US Patent No. 8,409,621, titled "Microparticles"
- US Patent No. 9,814,678, titled "Sustained Release Particle Formulations"

Proven Product Capabilities Demonstrate Broad Applicability of the Technology

ORAL PRODUCT SOLUTIONS

Optimμm® ORAL DOSE MICRO ENCAPSULATION

Taste Masking	Extended Release	Enteric Coating
ORB-101 Prednisone	ORB-103 Guaifenesin	ORB-113 Ibuprofen
ORB-102 Ritonavir	ORB-107 Quetiapine	
ORB-111 Riluzole	ORB-108 Ibuprofen	
ORB-112 Ibuprofen	ORB-110 Combination product	
ORB-116 Cetirizine		

INJECTABLE PRODUCT SOLUTIONS

Stratμm® INJECTABLE MICRO ENCAPSULATION

Unisun® OTIC INJECTABLE TECHNOLOGY

Pulsatile Release	Extended Release	Extended Release
ORB-203 Exenatide	ORB-201 Tramadol	ORB-202 Betamethasone
ORB-208 H1N1 Antigen	ORB-204 Etonogestrel (6-mo)	ORB-211 Ganciclovir
ORB-217 VLP	ORB-207 Elvitegravir	
	ORB-210 Meloxicam	
	ORB-212 Octreotide	
	ORB-214 Etonogestrel (12-mo)	
	ORB-215 Risperidone	
	ORB-216 Moxidectin	

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Orbis Technologies

Proven Taste Masking Capabilities
Single-Step Core Shell for Taste Masking (Pulsatile Release)

Target Product Profile

A taste masked solution that offers the opportunity to **improve medication compliance for ritonavir**

Current pediatric formulations are difficult to administer:

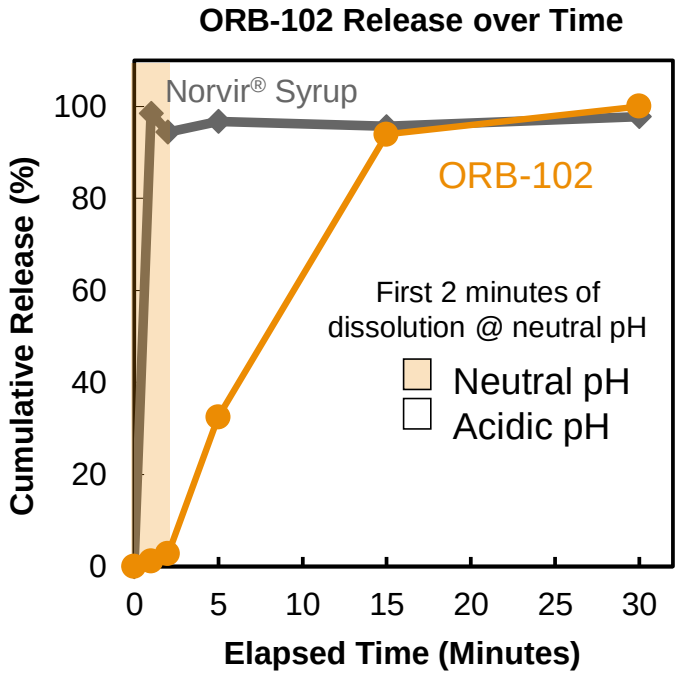
- Syrups have to be taken in large amounts
- Contain too much alcohol
- Have a foul taste

	ORB-102 Ritonavir	Norvir® Oral Solution
Indication	HIV	HIV
Delivery route	Oral	Oral
Dosage form	Microcapsules for Resuspension	Liquid Solution
Dose	80mg / 1mL	80mg / 1mL
★ Free Ritonavir*	1.1%	100%

* Greater amounts of free ritonavir in liquid = worse taste

NOVEL SINGLE-STEP MICROCAPSULE CREATES BARRIER TO FOUL TASTING APIS

Results



Microcapsules are 200µm with a 50µm shell

Proven Controlled Release Capabilities
Product Line Extension – Extended Release Format Switch

Target Product Profile

An extended release formulation of guaifenesin in liquid suspension **that improves compliance for those unable to swallow large bi-layer tablets**

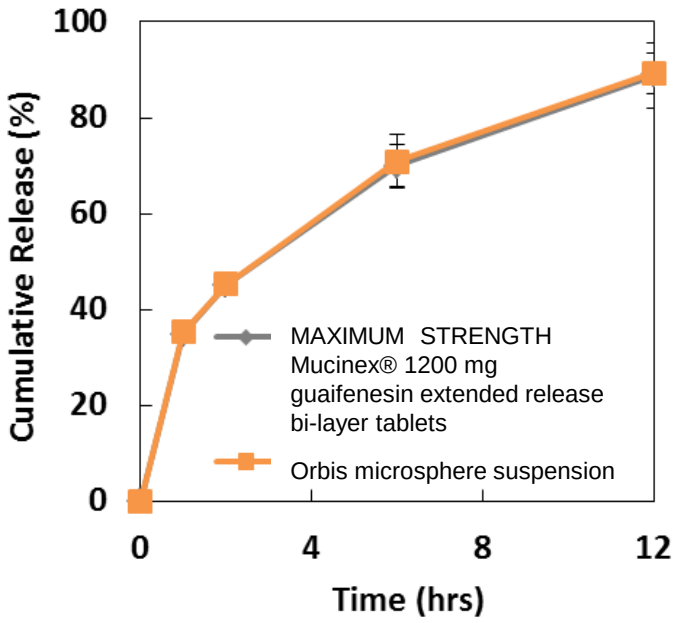
	ORB-103 Guaifenesin	Mucinex® Maximum Strength
Indication	Chest Congestion	Chest Congestion
Delivery route	Oral	Oral
★ Dosage form	Microsphere Suspension	Bilayer Tablet
Dose	1200mg / day	1200mg / day
Duration of Release	12 hours	12 hours

CONTROLLED RELEASE FORMULATION IS RATED AS ONE OF THE MOST EFFECTIVE METHODS FOR EXTENDING PRODUCT LIFE; LEVERAGES 505(B)(2) PATHWAYS

(1) An F2 value between 50 and 100 denotes that two release profiles are statistically similar (100 being exactly alike). The FDA relies heavily on the F2 value when comparing dissolution profiles between brand name drugs and generic drugs that are attempting to get approval.

Results

ORB-103 Release Over Time



Stable Orbis microsphere suspension matches release of Mucinex® bi-layer tablet

Novel Enteric Release Capabilities Format Flexibility with Modified Release ("Enteric-Coated Particle")

Target Product Profile

A modified release version of ibuprofen offering an **enteric delivery in a single manufacturing step**

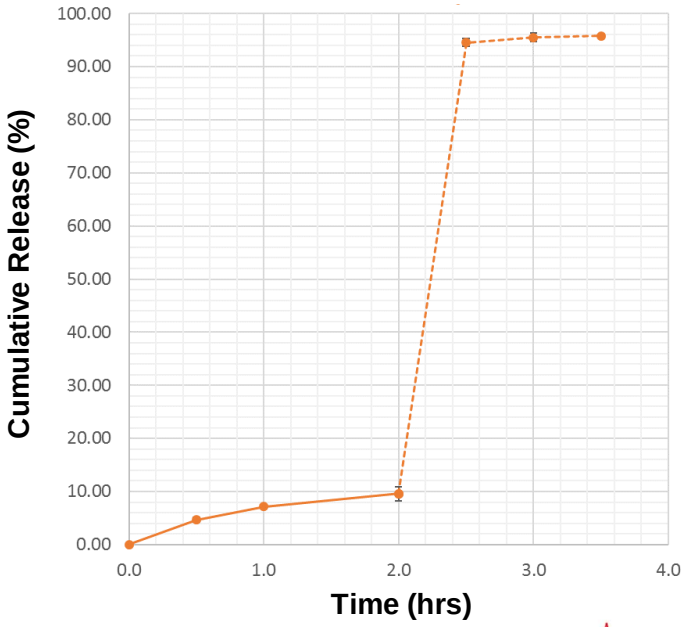
	ORB-108 Ibuprofen	Ibuprofen
Indication	Anti-Inflammatory	Anti-Inflammatory
Delivery route	Oral	Oral
★ Dosage form	Enteric Coated Microcapsules	Tablet
Dose	400mg	400mg
★ Release Profile	Delayed Release	Immediate Release

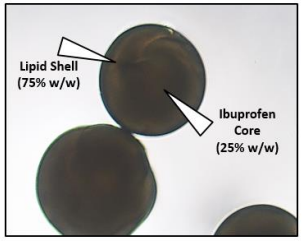
Enteric and reverse-enteric excipients can be titrated in until the desired dissolution behavior is reached

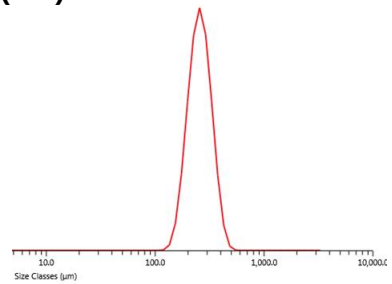
ENTERIC COATING OFFERS A SOLUTION FOR LOCAL DELIVERY AND IMPROVED SYSTEMIC AVAILABILITY

Results

ORB-108 – Enteric Release
Acidic vs Neutral pH







Proven Pulse Release Capabilities Pulsatile Release to Reduce the Number of Administrations

Target Product Profile

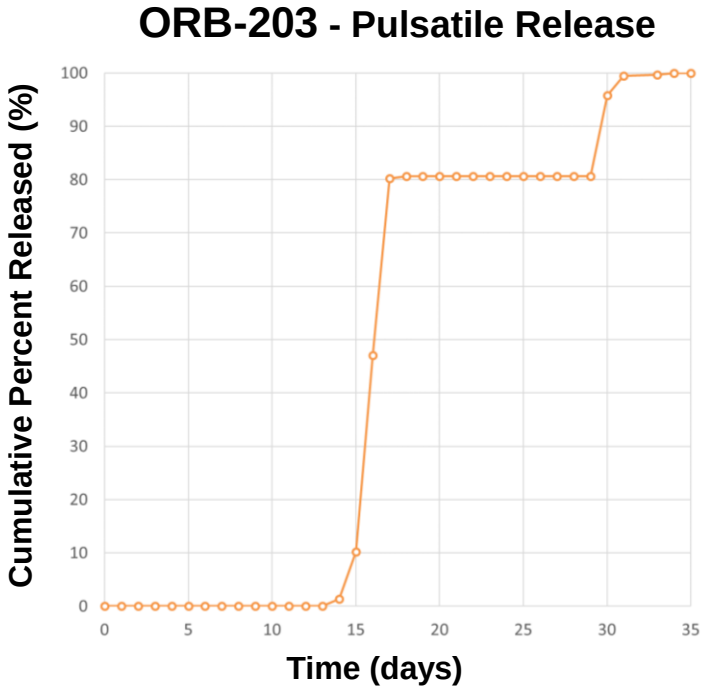
A pulse release enables multiple doses to be **administered in one injection, improving compliance**

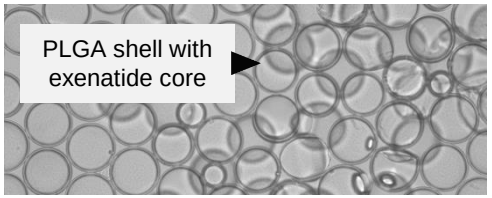
	ORB-203 Exenatide	Bydureon®
Indication	Diabetes	Diabetes
Delivery route	Injectable	Injectable
★ Dosage form	Microcapsule Suspension	Microsphere Suspension
★ Dose	8mg	2mg
★ Duration of Release	1 month	1 week

- Single initial pulse observed by increasing polymer molecular weight and decreasing peptide content
- "Agonal"-type release seen when entirety of PLGA shell breaks down

Potential to improve therapies in multiple large markets like diabetes and vaccines

Results





Proven Extended Release Capabilities Extended Release Reduces the Number of Administrations

Target Product Profile

An extended release contraceptive product that allows multiple doses to be **administered in one injection, improving compliance**

	ORB-204 Etonogestrel	Depo-Provera®
Indication	Contraception	Contraception
Delivery route	Injectable	Injectable
Dosage form	Microsphere Suspension	Microsphere Suspension
★ Dose	11.3mg or 22.7mg	150mg
★ Duration of Release	6,12 months	3 months

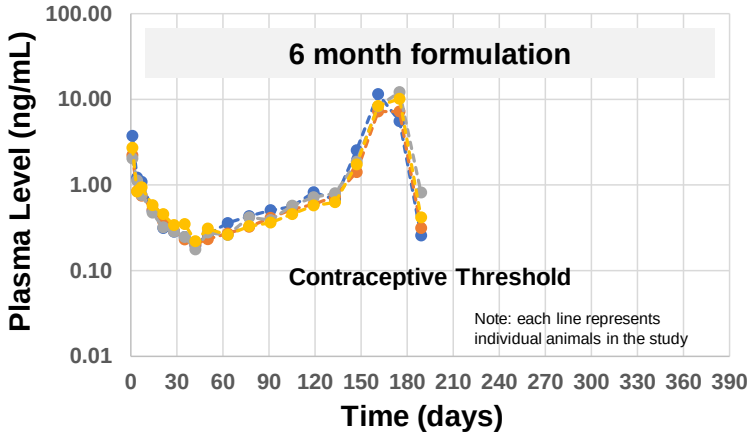
- No initial burst
- Established *in vitro-in vivo* correlations provide R&D efficiencies

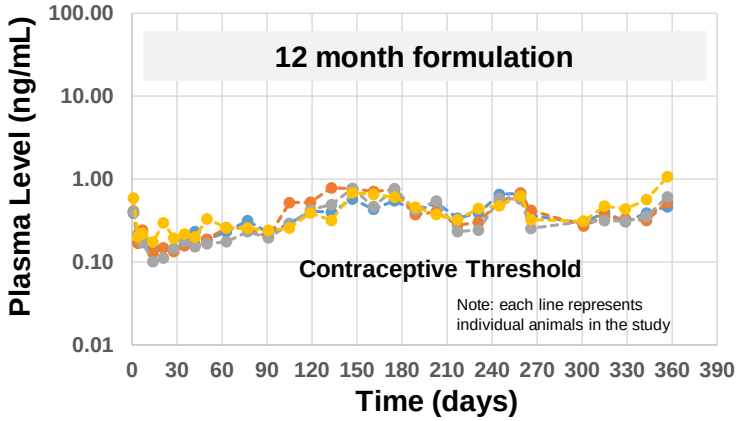
Single injection provides for a duration of release 2-4x current therapies

Results

ORB-204 Blood Concentration

***In vivo* – rat model**





Proven Extended Release for Local Delivery
Extended Release to Reduce Number of Injections

Target Product Profile

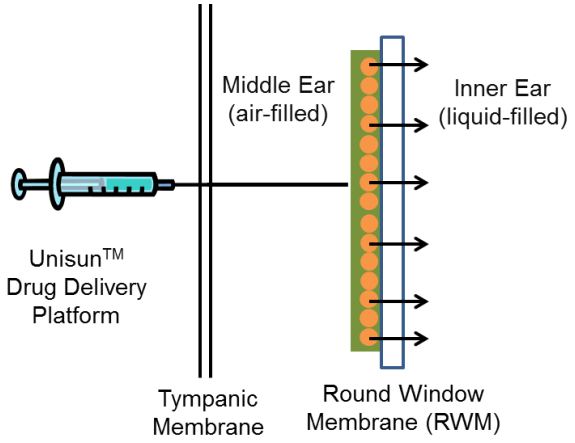
Unisun®
OTIC INJECTABLE TECHNOLOGY

Betamethasone microparticles paired with Orbis' proprietary film forming agent are administered directly to the round window membrane, **eliminating the need for weekly injections**

	ORB-202 Betamethasone	Steroid Injection Dexamethasone
Indication	Steroid-responsive Inner Ear Conditions	Steroid-responsive Inner Ear Conditions
Delivery route	Transtympanic Injection	Transtympanic Injection
★ Dosage form	Microparticles in Film Forming Agent	Free Drug in Solution
★ Dose	11mg	Varies, Off-label Treatments
★ Duration of Release	> 1 month	≤ 1 week

Provides 1 month of release compared to < 1 week with current therapies

Delivery Platform



Functional Components of Unisun® Drug Delivery Platform

LABEL	UNISUN COMPONENT	FUNCTION
●	Microparticles	• Precisely control drug release
■	Fast Film Forming Agent (FFA)	• Injection vehicle • Localize microparticles to RWM

Source: Comparison of intermittent intratympanic steroid injection and near-continual transtympanic steroid perfusion as salvage treatments for sudden sensorineural hearing loss. Laryngoscope. 2013 Sep;123(9):2264-9. doi: 10.1002/lary.23909. Epub 2013 Jun 26.

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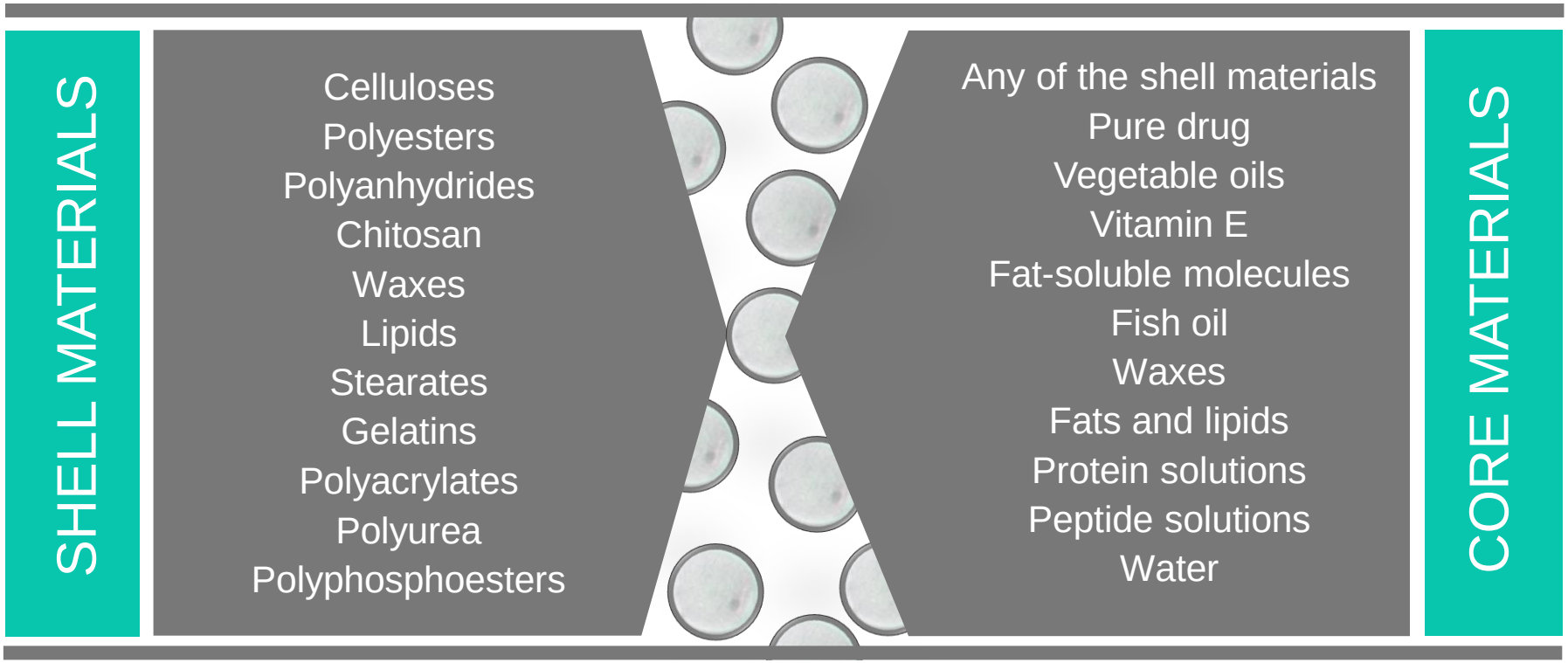
Material Independent Capability



APPENDIX


ADARE™
PHARMACEUTICALS