




# *“Status and Potential of Biologicals for Invasive Species Management”*

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Invasive Species Corporation***

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# All Three Categories of Biologicals are Rapidly Growing

**\$3.5B (+17% CAGR)**

**Biopesticides**  
**Biocontrol**  
**Bioprotection**



**Regulated by the EPA**

**\$2.5B (+13% CAGR)**

**Biostimulants**  
*Crop Enhancement*  
*Stress Reduction*



**Regulated state by state; National biostimulant standards pending**

**\$1.6B (+13% CAGR)**

**Biofertilizers**  
**Bionutrients**

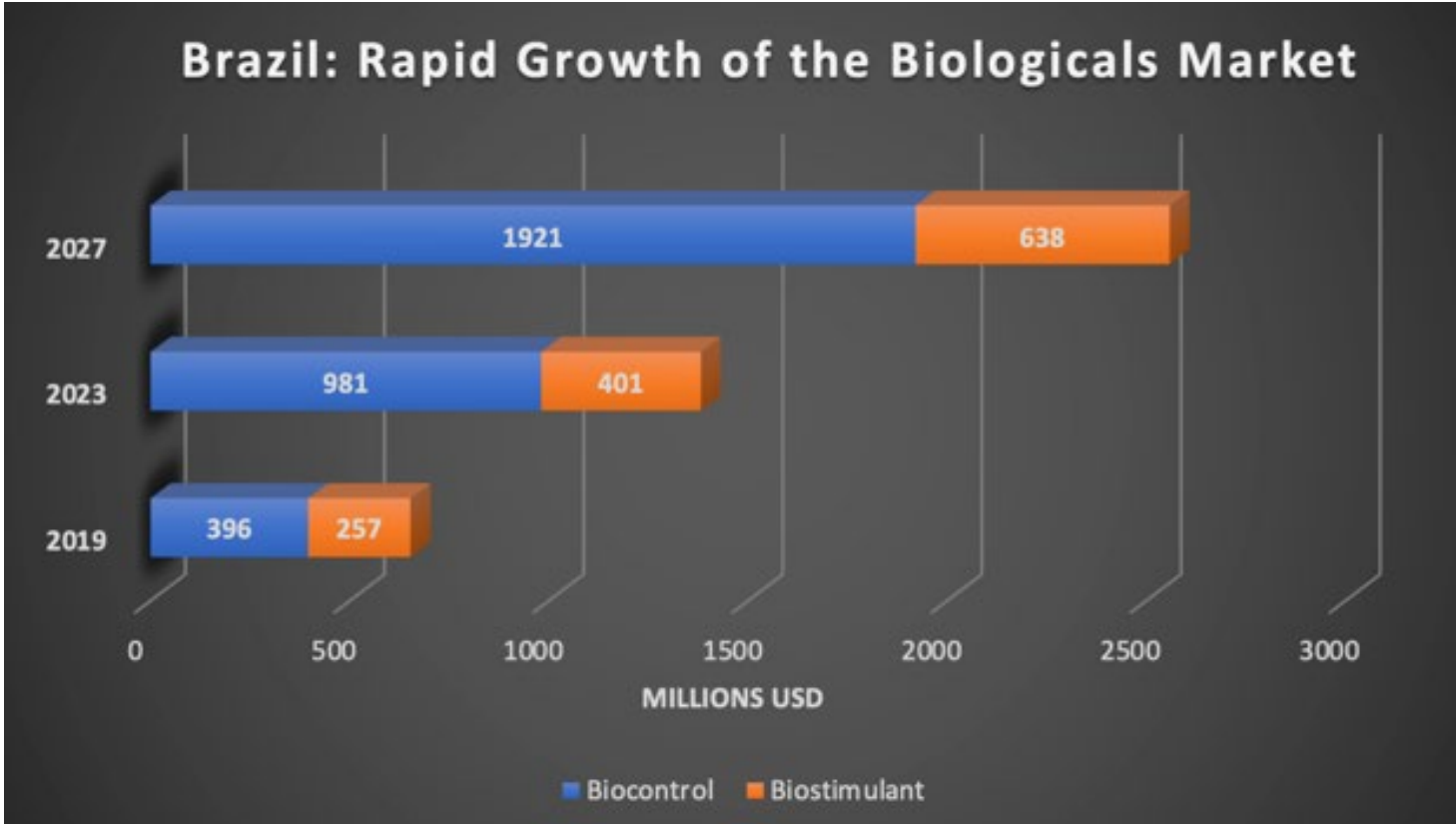


- Microorganisms, some plant extracts, pheromones, other natural materials and substances
- **Sulfur, copper, pyrethrum, spinosad are NOT biopesticides**

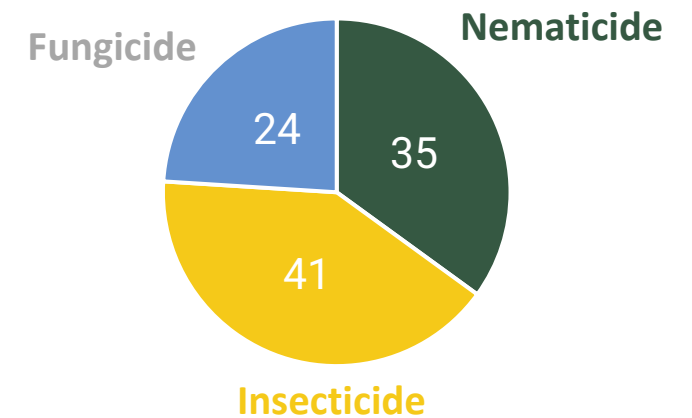
# Brazil has Become the Largest Biologicals Market Doubling Every Two Years



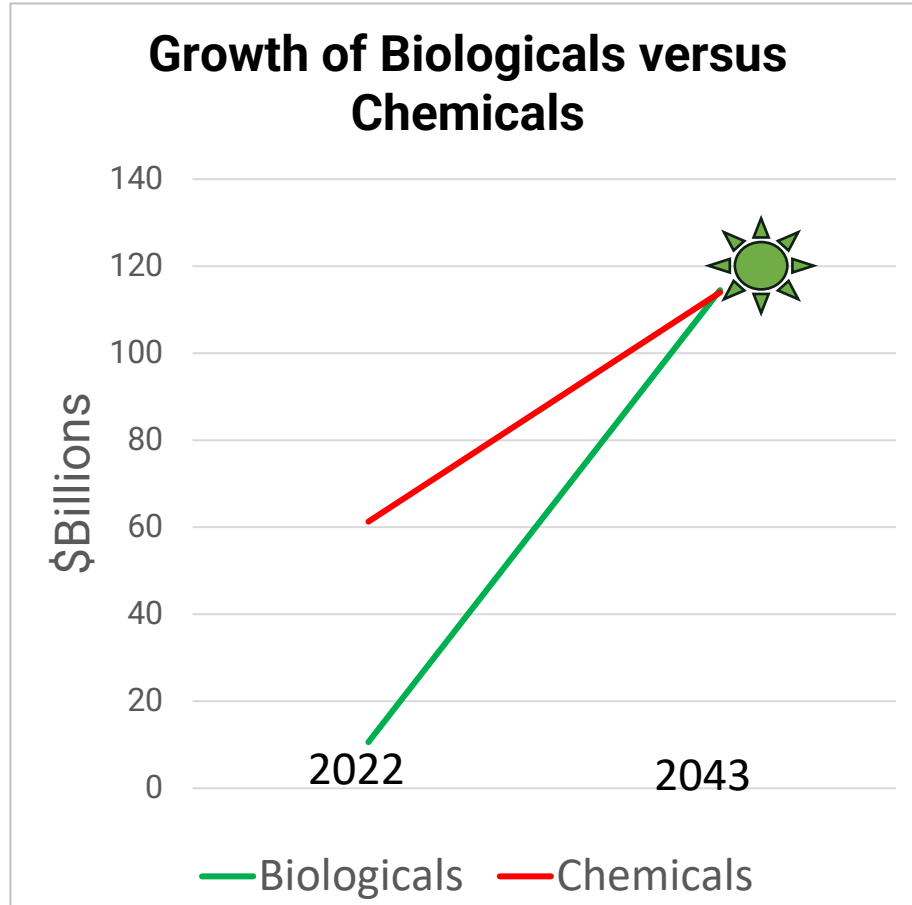
8-12 months for a new registration  
Registered ~500 biopesticides in 9 years!



Sales Percent



# Biologicals Market Could Equal Chemicals in ~20 Years!

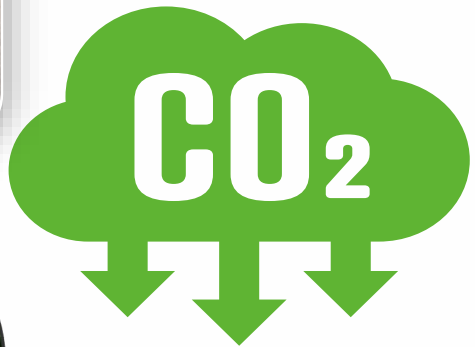


Growth rate (CAGR)		12 %
Number of periods	<b>Biologicals</b>	21
Initial value		10,600,000,000 \$
Final value		114,520,791,603.36 \$

Growth rate (CAGR)		3 %
Number of periods	<b>Synthetics</b>	21
Initial value		61,300,000,000 \$
Final value		114,036,057,245.79 \$

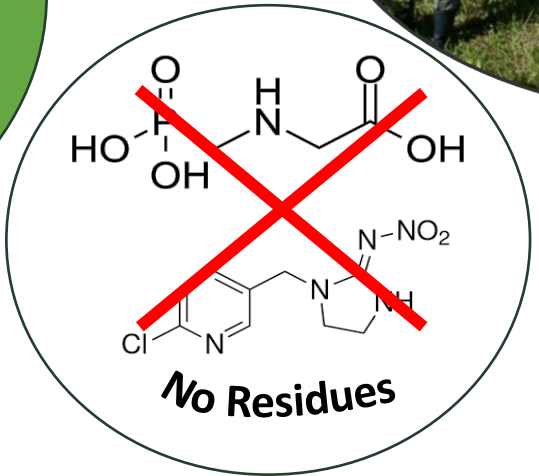
Source: Shane Thomas, Upstream Insights

# Why Biologicals are Growing Quickly



<\$5 million  
<5 years to  
develop

New Technologies





# Medium & Large Companies Continue to Acquire Biologicals

The image displays a collection of logos for major agricultural and biological companies, along with their recent acquisition values. The logos are arranged in a grid-like fashion, with some grouped together to show multiple acquisitions by a single company.

- Syngenta**: \$523 mil (deVGen), \$123 mil (PASTEURIA bioscience), \$596+ mil (Valagro)
- BASF**: \$1 billion (BECKER UNDERWOOD)
- UPL**: Arysta LifeScience, GOEMAR
- Bayer CropScience**: \$475 mil (AGRAQUEST), \$100 mil (JOYN JV), \$83 mil (GINKGO BIOWORKS, Sold back)
- Gowan**: ecoflora Aglo
- Novozymes**: TJ TECHNOLOGIES, NATURAL INDUSTRIES
- Mosaic**: PLANT RESPONSE
- AMVAC**: TYRATECH, Agrinos
- FMC**: \$200 mil (BioPhero), CHR HANSEN JV
- Valent BioSciences Corporation**: Mycorrhizal Applications, Inc., fbsciences
- Corteva Agriscience**: \$10 mil inv. (lavie bio), \$1.2 bil (Symborg, Stoller)
- Bioceres Crop Solutions**: \$260 mil (Marrone Bio Innovations)
- Biobest**: \$570 mil (BioWorks, BIOTROP)
- Rovensa Next**: AGRO-K

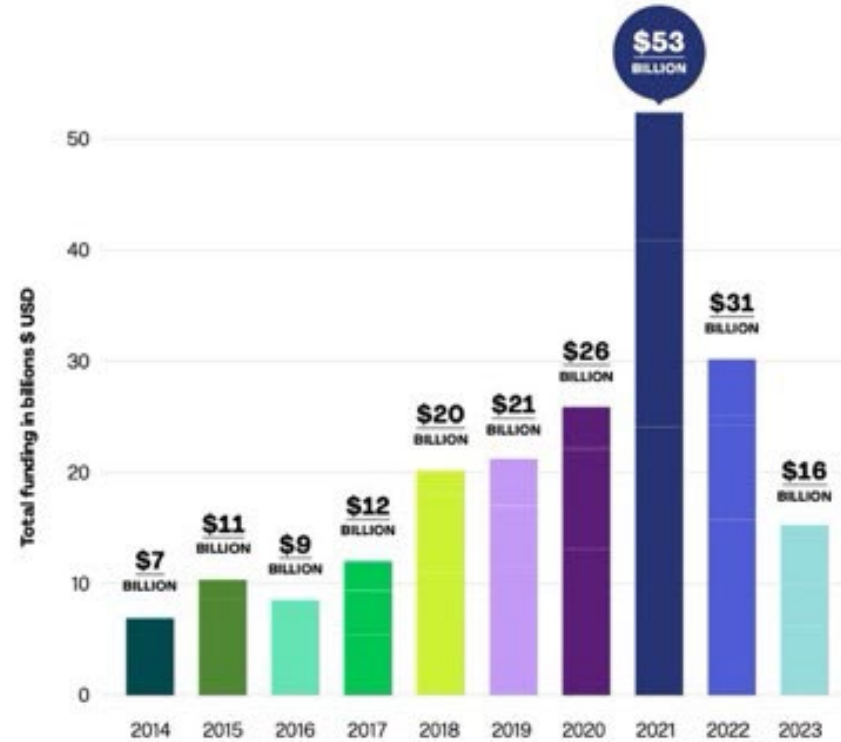
# Robust Investment in Agrifoodtech

10 years of agrifoodtech  
Global

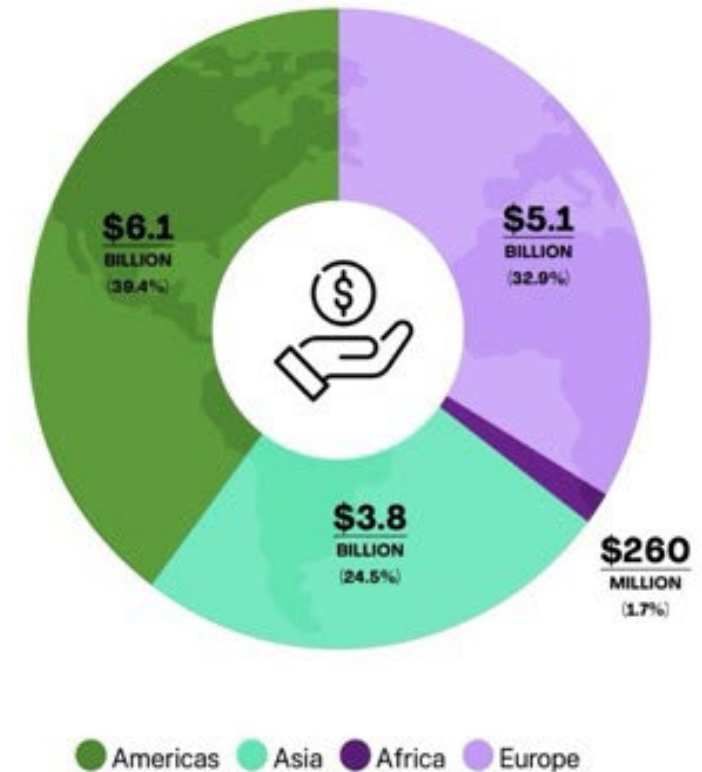
**\$15.6 billion**  
raised globally in 2023

**\$204.7 billion**  
raised globally since 2014

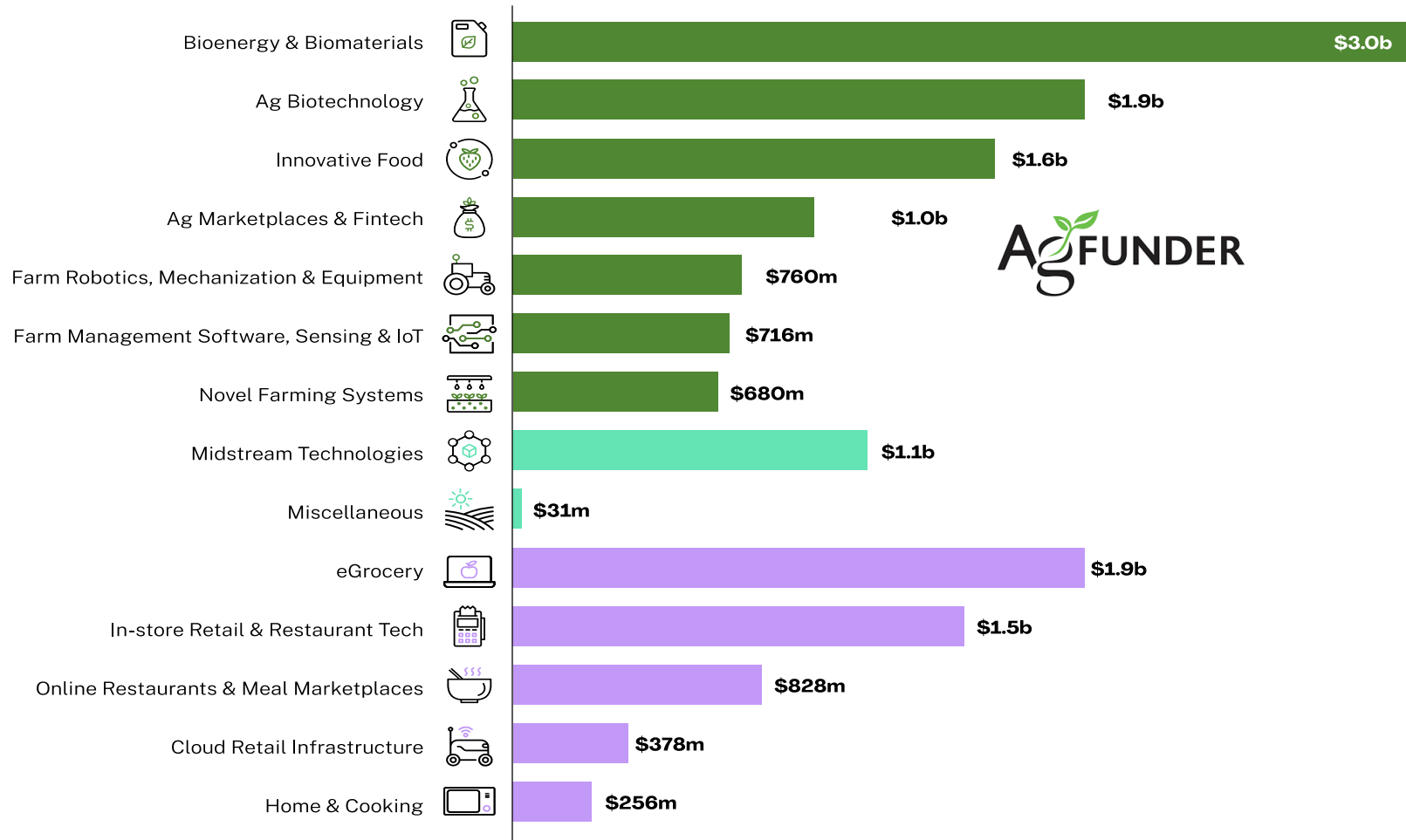
Global agrifoodtech investment by year



2023 agrifoodtech funding by region



# But Not Much of this Funding has Gone Directly Into Control of Invasive Species



**invaio sciences**  
A FLAGSHIP PIONEERING COMPANY

Peptides for citrus greening



RNAi engineered into algal capsules for aquatic invasive species

**INVERSA™**

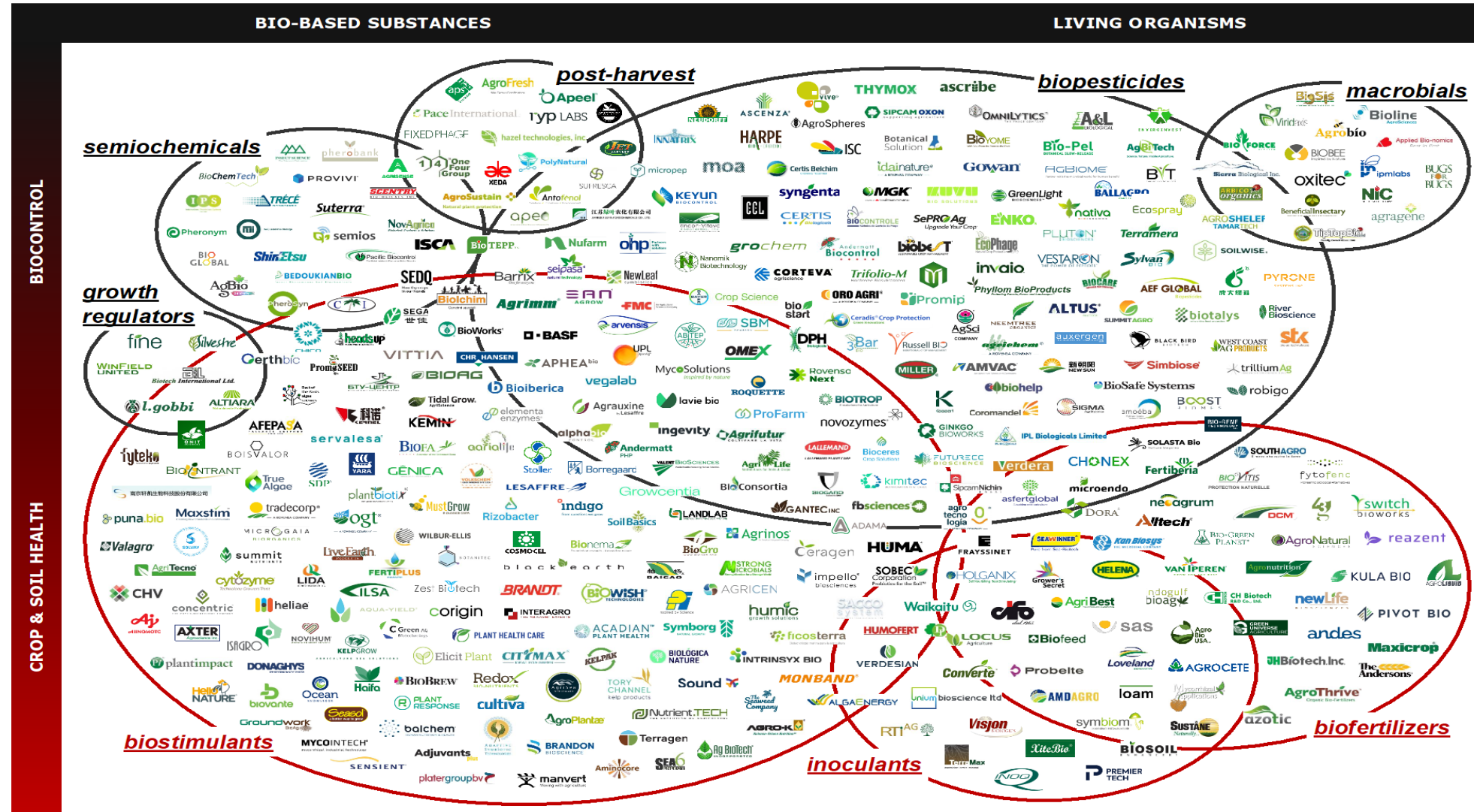
Leather from lionfish



Natural products for invasive species control



# 2023 AG BIOLOGICALS LANDSCAPE



Chris Taylor  
chris@mixingbowlhub.com

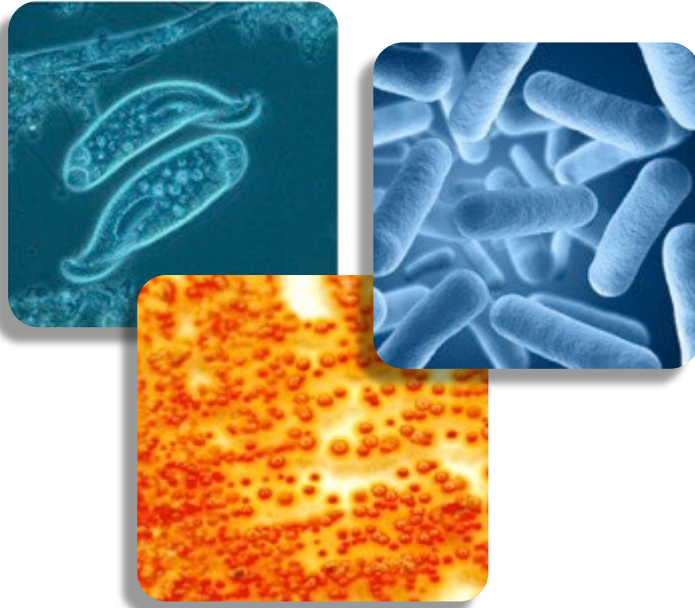
www.MixingBowlhub.com  
© Chris Taylor & THE MIXING BOWL



Companies appear on the landscape only once, although some may offer products in multiple segments. Overlapping areas are meant to imply this, however, logo positions are not necessarily indicative of any specific or limited product offerings.

# ~30-40 new Biological Active Ingredients/Year @EPA

## Microbials



*Fungi, Bacteria, Viruses, and Protozoa*

## Biochemicals



*Plant Extracts (some), Pheromones,  
Soaps, and Fatty Acids*

***A 70-year history of safe use of biopesticides;  
Invasives: Bt for spongy moth, mosquitoes***

# US EPA Biopesticide Registration

***Cost is ~\$1 million for these toxicology studies for a microbial; ~\$400,000 for a biochemical***

## Biopesticide Pollution Prevention Division (BPPD)

Tiered Data requirements; Start with Tier I:

- Rat Acute Studies - Oral, Inhalation, Intravenous, Dermal; Rabbit Eye; Guinea pig skin sensitization
- Product chemistry, 5-batch analysis
- Microbiology/QC: no human pathogens
- Ecological effects (non-target birds, fish, *Daphnia*, honeybees, lacewings, ladybeetles, parasitic wasps) (30-day feeding studies)
- Endangered species review
- Exemption from tolerance petition (for food use)



# Chemicals & Biologicals: Very Different Business Models

## Average Chemical Pesticide

Discovery *~12 Years & ~\$300 Million Development Time & Cost* Launch

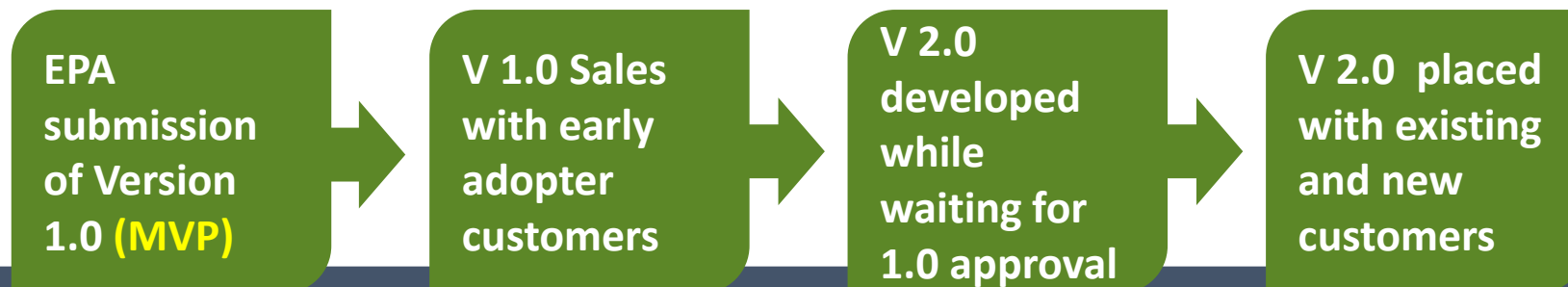
- Massive upfront capital
- Thousands of global field trials on many crops and pests
- Global launch with large marketing spend; Peak sales in 3 years

## Biopesticide

Discovery Launch

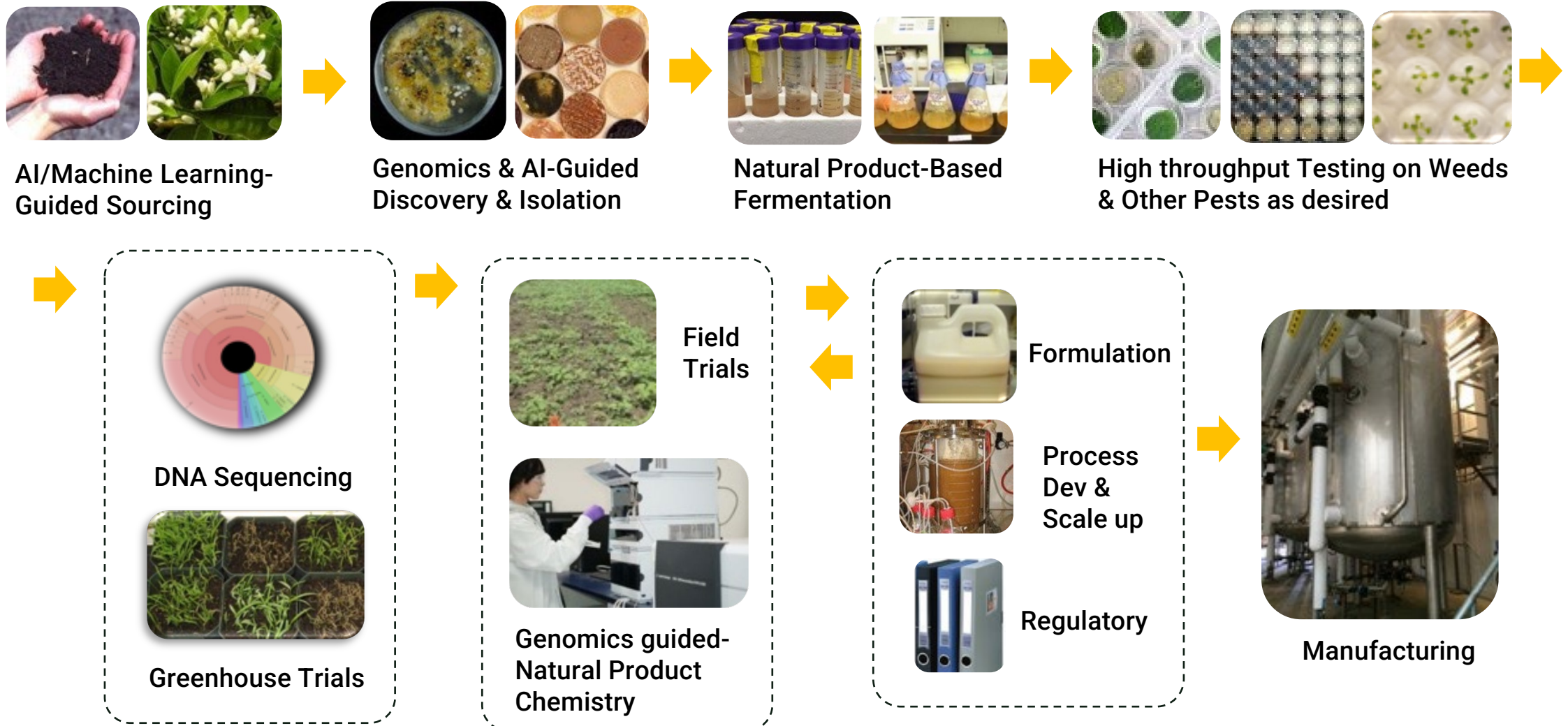
*3-5 Years & <\$5 Million*

- Capital efficient but peak sales take longer
- EPA registration granted with small number of pests & crops on label
- Commercial development continues while selling

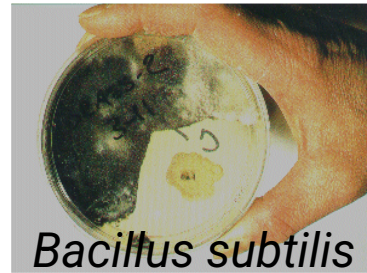
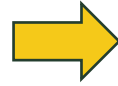


# It is Possible to Discover, Develop & Deploy A Natural Microbial Product to Control *Any* Invasive Species

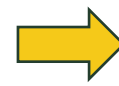
Our Optimized Process



# Examples of Rapid Discovery of Commercial Biopesticides



*Bacillus subtilis*  
QST #713



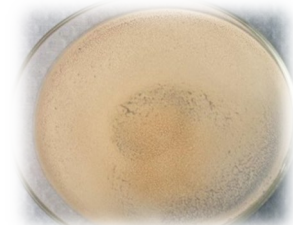
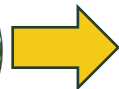
Version 1.0



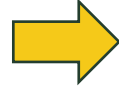
Version 2.0



Version 5.0



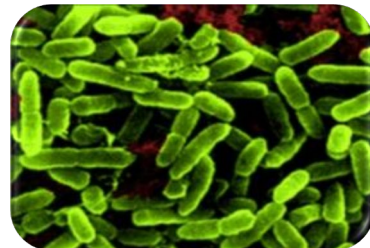
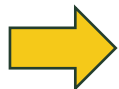
Microbe #396  
*Burkholderia rinojensis* sp. nov.



Version 2.0



Version 3.0  
Waiting EPA approval



Microbe #1000  
*Pseudomonas fluorescens* CL145A



Version 1.0



Version 2.0  
In development



# ZEQUANOX® for Zebra & Quagga Mussels

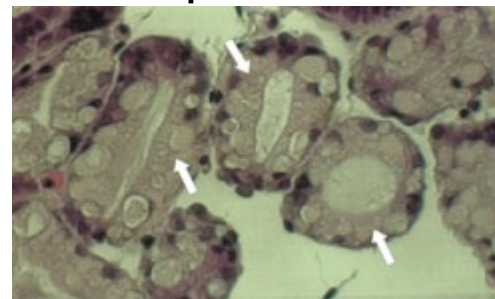
- Derived from soil bacterial microbe *Pseudomonas fluorescens*, (Pf CL145A), found from a zebra mussel-infested river in NY
- Extensive ecotox studies demonstrate that the application of Zequanox® has no impact on other aquatic species
- One 6-hour treatment controls all life stages; lower dose for veligers (larvae) (<25 ppm) vs adults (100 ppm)



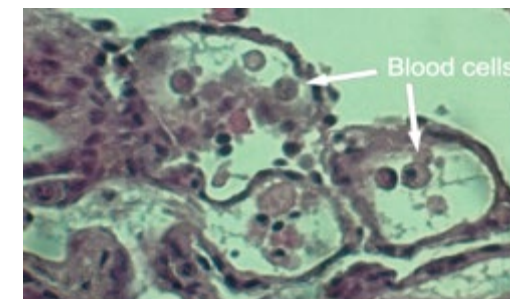
## How it Works:

- Mussels feed on Zequanox® by filtering treated water
- Ingestion results in stomach hemorrhaging
- Mortalities occur 3 – 28 days after one six-hour application (depending on water temp.)

## Protein produced in the Pf cells kills the mussels



In healthy mussels, epithelial cells (arrows) appear as a thick layer lining the tubules of the digestive gland.



Following treatment, epithelial cells are destroyed. Blood cells are abundant as the digestive gland hemorrhages.



# Extensive Ecotox Studies Show No Impact to Other Aquatic Species

## FISH

Bluegill sunfish (*Lepomis macrochirus*)  
Channel catfish (*Ictalurus punctatus*)  
Chinook Salmon (*Oncorhynchus tshawytscha*)  
Coaster brook trout (*Salvelinus fontinalis*)  
Common Carp (*Cyprinus carpio*)  
Fathead Minnow (*Pimephales promelas*) \*  
Klamath Suckers (*Catostomus sucker spp*)  
Lake sturgeon (*Acipenser fulvescens*)  
Largemouth bass (*Micropterus salmoides*)  
Rainbow Trout (*Oncorhynchus mykiss*) \*  
Sacramento Splittail (*Pogonichthys macrolepidotus*)  
Smallmouth bass (*Micropterus dolomieu*)  
Striped Bass (*Morone saxatilis*)  
Walleye (*Sander vitreus*)  
Yellow perch (*Perca flavescens*)



## OTHERS

Mallard Duck \*  
Midge (*Chironomidae*)  
Mayfly (*Baetis*)  
Amphipod (*Hyaella azteca*) \*  
European Freshwater Crayfish (*Austropotamobius pallipes*)  
Freshwater Crustacean (*Asellus aquaticus*)  
Freshwater Water Flea (*Daphnia magna*) \*



## MOLLUSCS

Blue Mussel (*Mytilus edulis*) \*  
Freshwater Mussel - Duck Mussel (*Anadonta anatina*)  
Freshwater Mussel - Black Sandshell (*Ligumia recta*)  
Freshwater Mussel - Fatmucket (*Lampsilis siliquoidea*)  
Freshwater Mussel - Pink mucket (*Lampsilis abrupta*)  
Freshwater Mussel - Hickorynut (*Obovaria olivaria*)  
Freshwater Mussel - Higgins Eye (*Lampsilis higginsii*)  
Freshwater Mussel - Mucket (*Actinonaias ligamentina*)  
Freshwater Mussel - Paper Pond Shell (*Utterbackia imbecillis*)  
Freshwater Mussel - Plain Pocketbook (*Lampsilis cardium*)  
Freshwater Mussel - Washboard (*Megalonaias nervosa*)  
Freshwater Snail (*Lymnaea peregra*)



## PLANTS AND ALGAE

Algae \*  
Bindweed (*Convolvulaceae*)  
Common Water Plantain (*Alisma subcordatum*)  
Curly Dock (*Rumex crispus*)  
Mallow (*Malvaceae*)  
Nightshade (*Solanaceae*)  
Smallflower Umbrella Sedge (*Cyperus difformis*)



\* EPA required

Studies conducted by Institute of Technology, Sligo, Ireland; New York State Museum and USGS; U.S. Bureau of Reclamation; Certified Good Laboratory Practices (GLP) Lab; Missouri State University; and MBI lab

# ZEQUANOX<sup>®</sup> is Proven Highly Effective for Power Plants



Oklahoma Gas &  
Electric Power Plant

- 1,138 MW coal-fired powerplant in OK
- Mussels colonized cooling water intake
- Static annual treatments 2012-15; 2018-23



NRG Power Plant

- 100 MW coal-fired power plant in IL
- Cooling water system application
- Low dose, periodic maintenance treatment 2017/19



Ontario Power  
Group Power Plant

- 144 MW hydropower facility in Ontario
- 1,940 gpm cooling water system
- Used as a replacement for chemical control



USBR Power Plant at  
Hoover Dam

- 2,080 MW hydropower Facility in Southwest
- 1,110 gpm cooling water system
- Low dose, periodic maintenance treatment



FirstLight Power  
Plants

- 28,900 & 42,600 KW hydro plants on Housatonic River, CT
- Low flow cooling water system
- Dose and hold strategy





# ZEQUANOX<sup>®</sup> is Highly Effective for Open Water Treatments



## Deep Quarry Lake

- Open water demonstration in Illinois
- Use of turbidity curtain for containment
- Adult mortality as high as 99%
- Veliger (larvae) mortality as high as 94%



## Christmas Lake

- Open water rapid response treatment in MN
- Use of turbidity curtain for containment
- 100% mortality in all monitoring methods at 11 days post-treatment



## Lake Michigan

Lake Michigan (Sleeping Bear Dunes) (2019)

<https://www.mlive.com/news/2020/12/experimental-project-successfully-removes-invasive-mussels-near-sleeping-bear-dunes.html>

- Benthic containment held concentration at bottom one meter
- 99% mortality based on substrate surveys
- Valuable in removing toxic algae and restoring reef



.....Also several golf courses

# Natural Product for Invasive Carp Control

## What is Piscamycin™?



Looking for  
someone to test  
lionfish

- Fermentation product from *Streptomyces* sp., Antimycin A, is applied directly to water to manage fish populations and restore native fish habitats in lakes, ponds, reservoirs, rivers, streams, and in aquaculture.
- Antimycin A is absorbed into the gills of fish; kills by interfering with respiration. Irreversible, once a fish has had brief exposure. Can achieve selectivity to species based on dose.
- In studies conducted by EPA, Antimycin A degraded relatively rapidly under static conditions. Treatment concentrations of 25 ppb would exceed acute risk levels of concern to aquatic nontarget organisms.
- More effective and lower risk than the only other fish toxicant, Rotenone.
  - **Status:** ISC & USGS working on re-registering current Gen 1.0 product with the EPA
  - Product 1.0 emergency use as soon as some is made
  - Gen 2.0 in development, CRADA with USGS for testing and development and bait specific formulations



# PRODUCT PIPELINE • **Advanced licenses & in-house development**

Program	Products	Market	TAM (B)	Launch Yr	Discovery	Develop	Regulatory	Commercial
Zequanox Gen 1	1	Aquatic	\$0.2	2023	→			
Zequanox Gen 2	2	Aquatic/Ag	\$1.5	2026	→			
Piscamycin Gen 1	1	Aquatic	\$0.4	2025	→			
Piscamycin Gen 2	1	Aquatic	\$2.0	2027	→			
Herbicide	2	Ag/Aquatic/ Forestry	\$30.5	2028	→			
Algaecide	1	Aquatic	\$2.5	2029	→			
Bioinsecticide	2	Forestry	\$0.5	2026	→			

TOTAL IN 2030

8

EXISTING LEVEL OF DEVELOPMENT



# Collecting Samples Where Burrowing Shrimp *Neotrypaea californiensis* Live and Have Died Out (Washington State)





# On-site Isolation





# From Sample Collecting to Killing Shrimp (Surrogate) in 4 Mos.



**Idea: shrimp contain chitin, so look for chitinolytic bacteria**

**Grow microorganisms isolated from the two collecting trips in media amended with chitin**

**Get 16S RNA identification to prioritize isolates for testing**

Thanks to WSDA, Shoalwater Bay Indian Tribe; David Beugli, Executive Director, Willapa-Grays Harbor Oyster Growers Assoc., Marilyn, Brian and Jeb Sheldon, Northern Oyster Co.; Kathleen Nisbet-Moncy, Nisbet Oyster Co. & Kim Patten, WSU



# Many Companies with Biological Innovations for Disease Control



Bees to deliver microbial fungicides (Vectorite® based on *Chlonostachys*)



Lysed cells of the amoeba *Willaertia magna* C2c Maky, had strong fungicidal properties.



Biofungicide based on the microbe *Kosakonia cowanii*, Biotrinsic X19 to fortify plant growth



Cerevisane, a purified extract of the yeast, *Saccharomyces cerevisiae* Strain LAS117 biofungicide



Natural & gene-edited microbes as fungicides and nematicides, biostimulants



Plant culture to supply key botanical products for disease control (esp *Botrytis*)



Bio-encapsulation from *Bacillus* micelles; 1<sup>st</sup> product: FunThyme™ from Thyme oil



Peptides and enzymes to boost plant immunity against citrus greening and other diseases



Microbe signaling compounds to control fungal & bacterial diseases



Novel microbial screening discovery & development platform



Strigalactone to signal for selection of soil microbes as biofungicides

# Some Biological Innovations for Insect/Nematode IPM



Pink-pigmented methylotrophs for plant/soil health/Biocontrol (corn rootworm & nematodes) (EPA approved)



Biotrinsic microbe combines microbially enhanced plant defenses to help protect plants against nematodes.



LALLEMAND ANIMAL NUTRITION

*Cordyceps javanica* registered against *Bemisia tabaci* whitefly in Brazil



METARHIZIUM ANISOPLIAE) Strain F52  
Thrip pupae and weevils



Fermentation-enhanced MBI-306 *Burkholderia rinojensis* A396 (insects, mites & nematodes) (waiting EPA approval)



Bacteria for plant health and disease/nematode control; nematicide (waiting EPA approval)



Biological insecticide based on Lolines from the endophyte fungus *Epichloë uncinata*, active against important insect sucking & chewing pests

# Bioherbicide Innovations



Screening marine microbes for herbicidal natural products



Specific strains of the fungus *Fusarium oxysporum* as bioherbicides



Two microbes and one plant extract with novel modes of action



Mint plant extracts as bioherbicides



Microbial natural product discovery platform for controlling algae, aquatic and terrestrial weeds



Platform for new pesticidal natural products



Short natural peptide molecules as fungicides & for resistant weeds



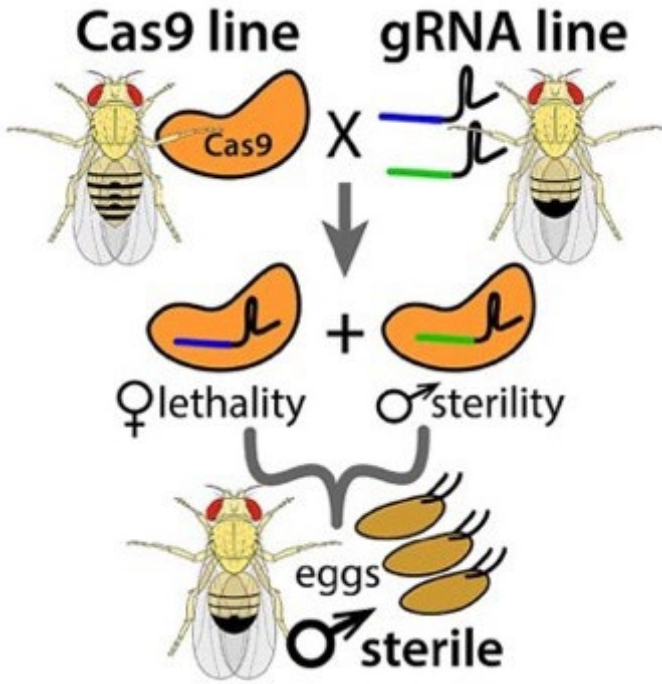
Exploiting sterility to win the battle against resistant weeds



Natural herbicidal compound from onion rot pathogen



# Sterile Male/Gene Editing Solutions



NC STATE UNIVERSITY

UC San Diego



AGRAGENE

Oxitec's Friendly™ products for mosquitoes & fall armyworm carry two introduced genes that produce proteins, tTAV (the self-limiting gene) and DSRed2 (the fluorescent marker)



Our first two (non-GMO) solutions are approved for sale in England & four USA states (WA, OR, CA and FL) for control of spotted wing *Drosophila* (SWD) and codling moth.

Navel orangeworm

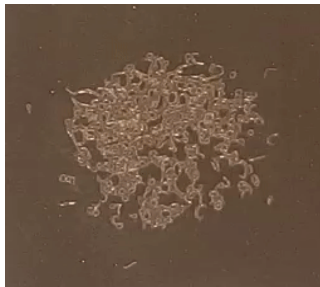


# Pheromone Innovations



**Pheronym**

Developing Nematode pheromones for better pest control of both insect and nematode pests



We produce our pheromones using renewable raw materials in a single fermentation step using yeasts



- Innovative synthesis
- Controlled release formulations
- Weevils, vine mealybug, caterpillars, fruit flies, red scale, others



Proprietary (bio)catalysts and low-cost raw materials to reduce the steps needed to synthesize pheromones and increase yields.



Tech enabled pheromone traps and application for orchards and vineyards

# Peptide Innovations for Insect, Nematode & Plant Pathogen Control



Spider venom peptides for insect control



Based on insect neuropeptides that disturb pest physiological processes that kill the pest.



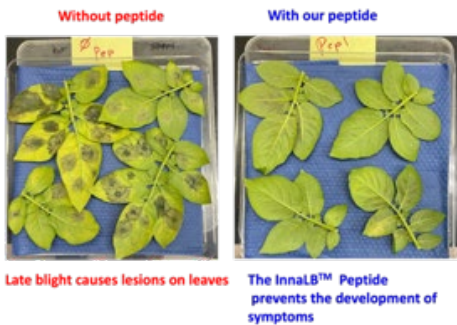
Peptides for citrus greening



AGROBODY Foundry™ for rapid generation of biocontrol solutions to tackle a wide range of crop pests and diseases. **Evoca™** is the first product, for disease control (*Botrytis*)



Antifungal peptide platform



computational biology & AI to rapidly browse genomes to ID micropeptides sequence candidates.



Antimicrobial peptide (AMP) technology



Harpin $\alpha\beta$  and PREtec (Plant Response Elicitor Technology)



# RNAi for Insect, Nematode and Plant Disease Control



**“Agrisome” RNAi platform provides new ways to deliver a range of biopesticides with far greater precision and efficacy**



**Our delivery platform enables, for the first time ever, an effective and practical way to insert RNA into plant cells**



**RNAi for soybean cyst nematode control**



**Sprayable, double-stranded RNA for control of Varroa mite, Colorado Potato Beetle, Powdery mildew, Botrytis, Downy mildew**



**Naturally occurring microbes from crops to deliver the power of RNA for solutions for pests and disease control**



**Our RNAi designs have dramatically improved the efficacy of RNAi-based pesticides for Lepidoptera, including diamondback moth**

**NOT IF**  
**They Work,**  
**but HOW to**  
**Make Them**  
**Work**

# Concluding Points

- **Innovation** in biologicals is happening rapidly and outpaces synthetic chemicals. 80 new biological active ingredients at the EPA; only 9 new synthetic chemicals.
- **New tools and science** are resulting in better and better products
- **More education & training needed** on how the products work based on their unique modes of action for both testing and deployment.
- For management, a **holistic systems-based approach** in combination with other tools leads to enhanced outcomes (e.g., less damage, better control, biodiversity preservation/enhancement).
- Some biopesticides can be used for **eradication** of invasive species.



ISC

- Based on their pace of innovation, efficacy, specificity, lower cost and time to develop than chemical pesticides, microbial natural products should be considered for frontline invasive species management

CONTACT



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