August 2018

MATINAS BIOPHARMA

Enabling the Delivery of Life Changing Medicines

Development of Non-Traditional Therapies for Bacterial Infections

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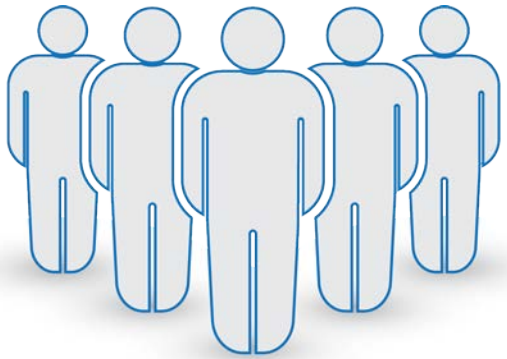
Treatment of Intracellular Pathogens Represents Significant Unmet Need

Sequestered Within a Cell, Pathogens are Protected by the Cell Membrane Barrier

~2 million*

people in the US become infected with antibiotic resistant bacteria annually[1]

~23,000*



people die each year as a direct result of these infections[1]

Example Pathogens

Salmonella, Neisseria, Brucella Mycobacterium, Listeria, Francisella, Legionella, Yersinia pestis

1: https://www.cdc.gov/drugresistance/threat-report-2013/index.html

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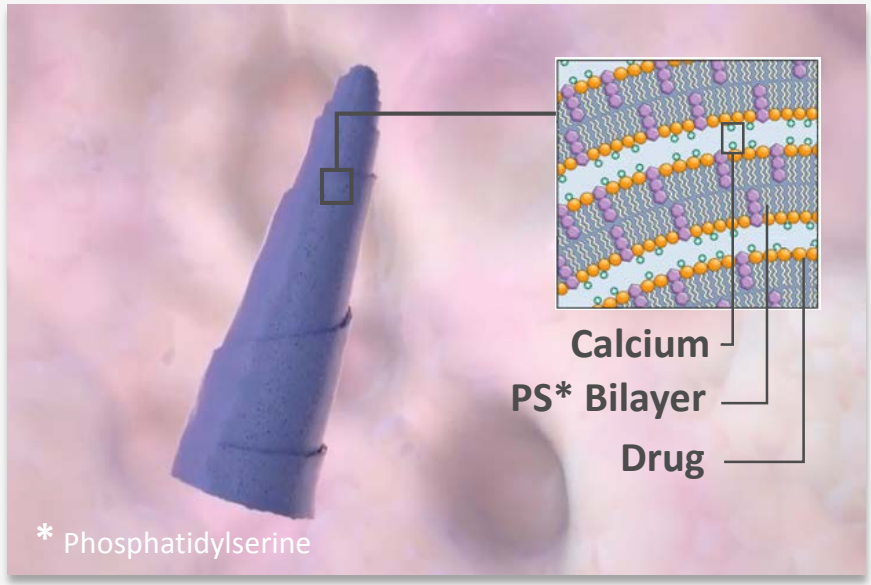
Matinas' Lipid Nano-Crystal (LNC) Platform Technology Enables Safe, Targeted and Intracellular Delivery of Potent Medicines

- Highly stable lipid nano-crystal particles
- Sheets roll up and capture drug molecules between the sheets
- Validated in multiple clinical and preclinical studies



LNC Platform Benefits

- Multiple routes of administration
- Rigid, solid multilayered membrane
- Non-aqueous interior
- Resists environmental attack
- Non-toxic

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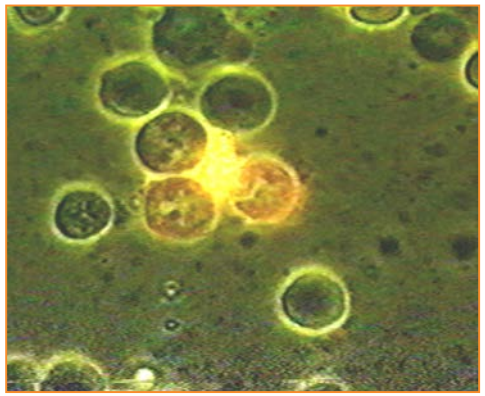
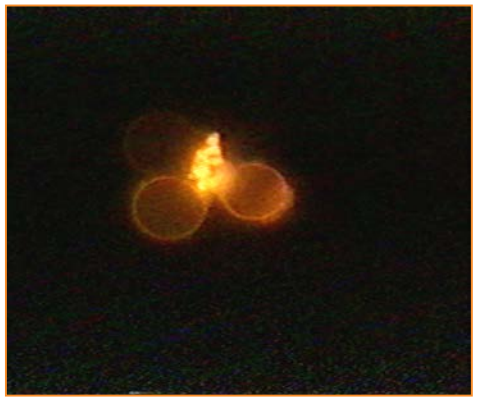
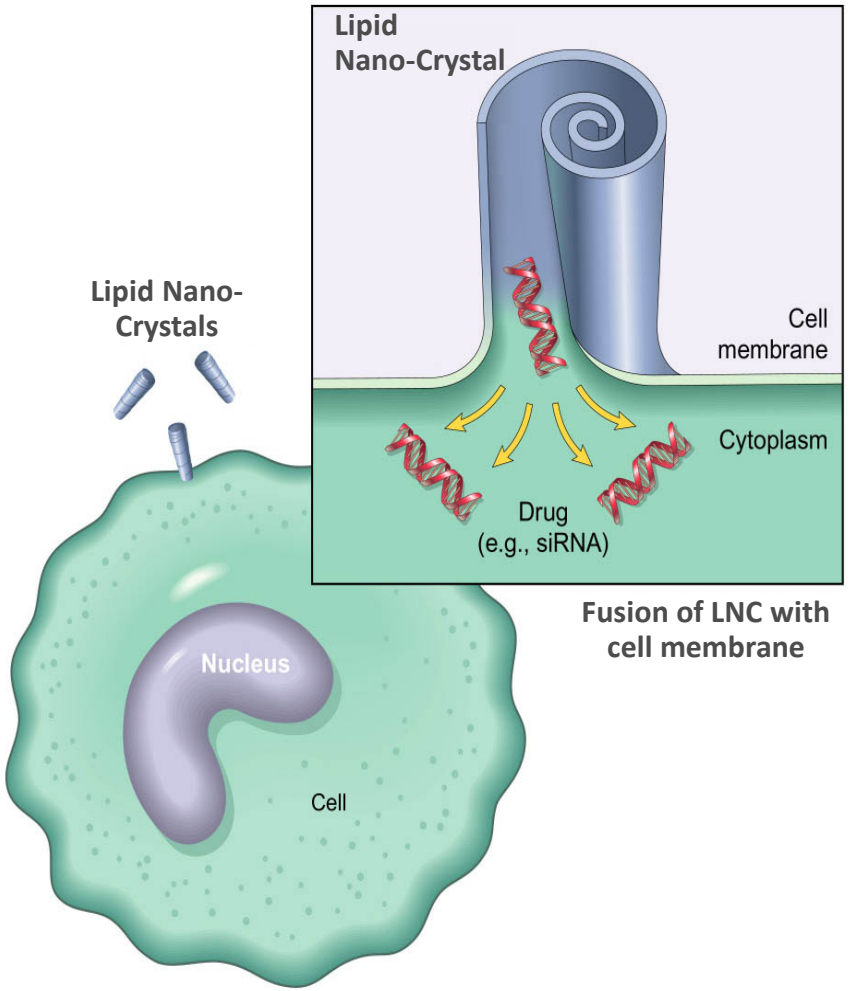
Naturally Targeted Intracellular Drug Delivery

- Naturally targeted to activated cells including cells of the immune system (e.g. macrophage, dendritic cells, neutrophils) or virally infected cells
- Enter cells through non-destructive, natural membrane fusion process
- Naturally unwind (low calcium environment) releasing drug payload

Fluorescent Labeled LNC
Incubated with Mouse Spleenocytes







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Preclinical and Clinical Development Experience of Matinas' LNC Delivery Programs

Drug	Organism	*In Vitro* Studies	Animal Model Studies	Human Studies
MAT2203 (Amphotericin B-LNC)	Candida	X	X	Phase 2 Efficacy
	Aspergillus	X	X	
	Cryptococcus		X	
	Leishmaniasis	X		
MAT2501 (Amikacin-LNC)	Mycobacteria	X	X	Phase 1 Toxicity
	Francisella	X		
Atovaquone-LNC	Pneumocystis		X	

MAT2203: Efficacy Results – NIH and VVC Phase 2 Studies

NIH Study – Dr. Alexandra Freeman, Principal Investigator

- 100% (4 out of 4) patients met the primary endpoint in achieving ≥ 50% clinical response
- Study met predetermined endpoint for success, which was 3/16 patients demonstrating clinical response
- All patients reported improved quality of life
- There have been no signs of nephrotoxicity, hypokalemia or hepatoxicity after oral dosing:
  - Patient 1 – 545 days (800 mg/day)
  - Patient 2 – 554 days (400 mg/day)
  - Patient 3 – 205 days (800 mg/day)
  - Patient 4 – 169 days (800 mg/day)
- All patients have elected to enroll in the long-term extension study

VVC Study

- In the composite clinical cure score of signs and symptoms at Day 12, MAT2203 demonstrated an 81% improvement in clinical symptoms at 200 mg/day, 80% improvement at 400 mg/day, compared to 94% improvement in clinical symptoms for the patients on fluconazole

MAT2203: Delivery Across the Blood Brain Barrier

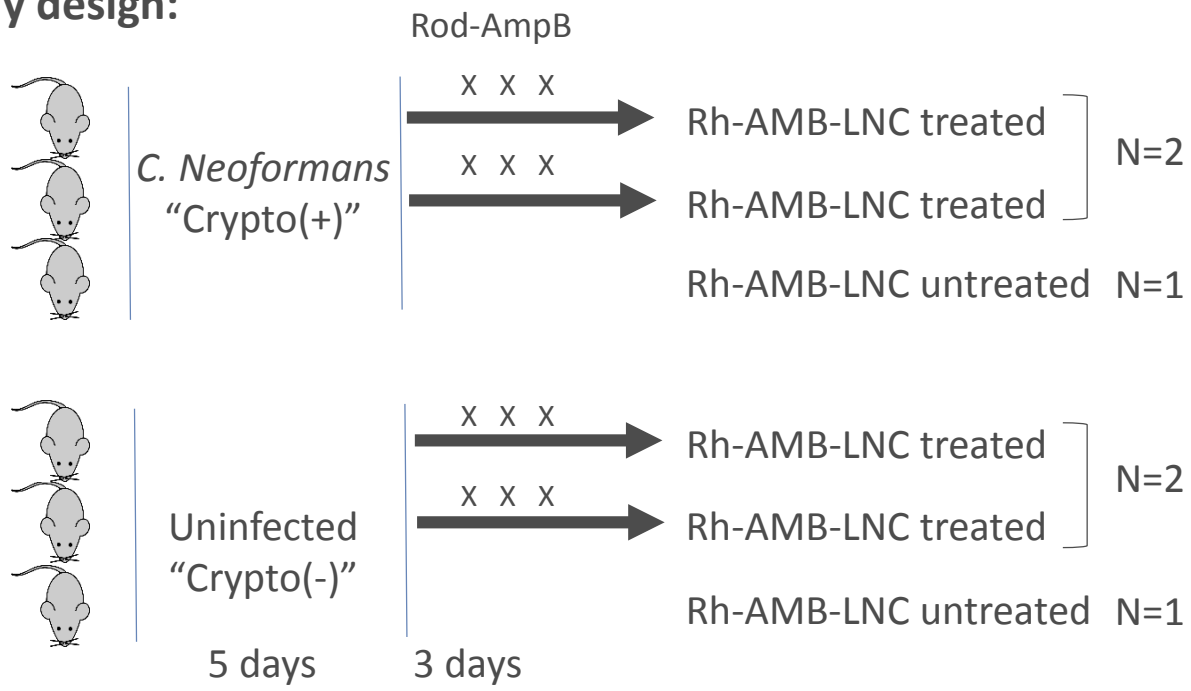
Preclinical studies in a mouse model of cryptococcal *meningoencephalitis*

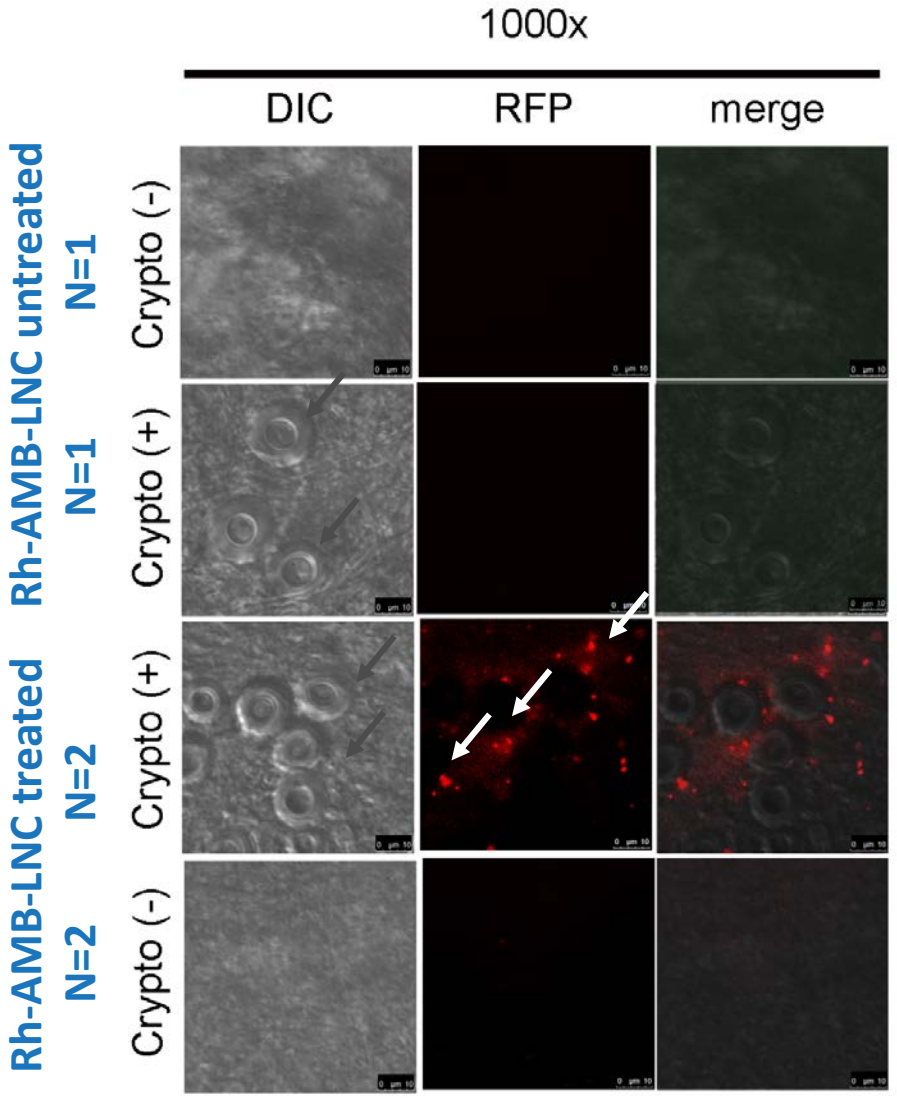
NIAID Clinical Center – Dr. Peter Williamson, Principal Investigator

Brain localization of fluorescent LNC after oral dosing

Three mice were infected by tail vein with 10^4 *Cn* and three remained uninfected. Five days later two from each group were treated daily for 3 days with fluorescent LNC preparations (Rh-AMB-LNC) by gavage and sacrificed. Brains were recovered and homogenized and subjected to microscopy using differential interference contrast (DIC), or red fluorescence (RFP) at the indicated magnifications. Black arrows indicate *C. neoformans* encapsulated organisms, white arrows indicate LNC fluorescence. Bar = 10 mm

Study design:





MAT2501: Cystic Fibrosis Mouse Model – Lung Target Mycobacteria

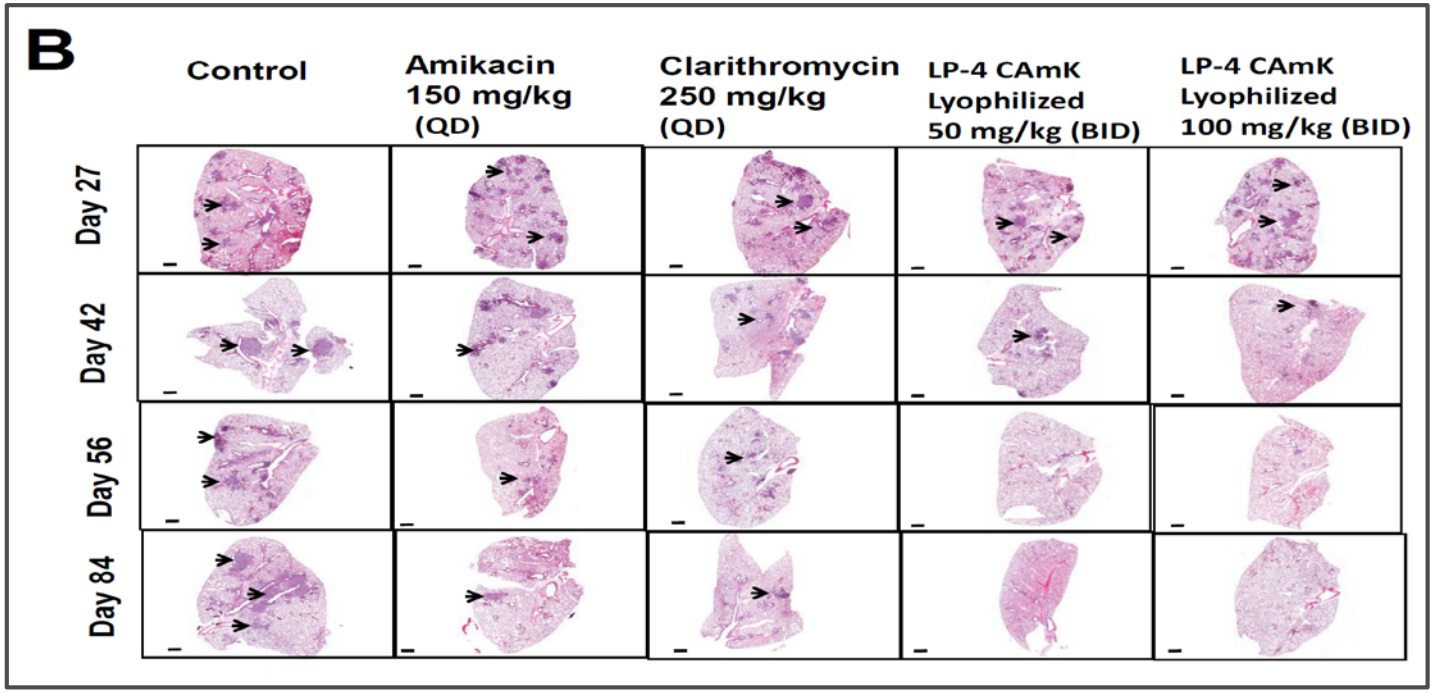
Colorado State University:
Dr. Diane Ordway, Principal Investigator

- In the cystic fibrosis lung, infections by intracellular pathogens, such as intracellular mycobacteria, are problematic to treat due to a thick buildup of mucous in the lung, as well as the difficulty of many anti-microbial agents, such as amikacin, to penetrate across the plasma membranes of infected cells
- Oral administration of amikacin-LNCs safely and effectively treat mycobacteria infections in a mouse model on cystic fibrosis

Bacterial Counts in the Lungs Spleen Liver

Day 84 Control (n=2)	7.21±0.03	6.14±0.05	5.99±0.03
Amikacin (AMI), 150 mg/kg QD (n=4)	**3.76±0.03**	**3.73±0.06**	**3.93±0.07**
Clarithromycin 250 mg/kg QD (n=5)	**5.11±0.05**	**4.13±0.02**	**4.13±0.07**
AmK-LNC 50 mg/kg BID (n=5)	**3.68±0.08**	**4.01±0.04**	**4.15±0.01**
AmK-LNC 100 mg/kg BID (n=4)	**2.97±0.10**	**3.23±0.08**	**3.48±0.06**

Lung Pathology



LNC Platform Technology Offers a New Paradigm for Drug Therapy with Broad Utility

- Proprietary LNC platform technology enables safe, targeted intracellular delivery of life-changing medicines
- Increase oral bioavailability of injectable drugs
- Cell targeting and intracellular delivery – sustained release activity
- Reduced toxicity of drugs – increased therapeutic index
- Inexpensive to manufacture and scale-up
- Stable as dry powders or in suspension
- Human clinical trials in progress
- Preclinical data supporting formulation and delivery of RNA and DNA polymers

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