MATINAS BIOPHARMA

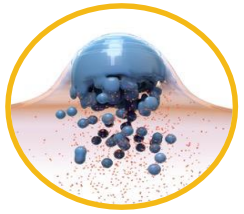
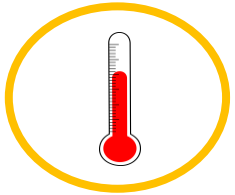
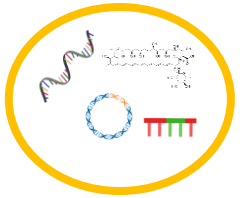
# Corporate Presentation

May 2022

# Forward-Looking Statement

This presentation contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including those relating to the Company's product development, clinical and regulatory timelines, market opportunity, cash flow and other statements that are predictive in nature, that depend upon or refer to future events or conditions. All statements other than statements of historical fact are statements that could be forward-looking statements. Forward-looking statements include words such as "expects," "anticipates," "intends," "plans," "could," "believes," "estimates" and similar expressions. These statements involve known and unknown risks, uncertainties and other factors which may cause actual results to be materially different from any future results expressed or implied by the forward-looking statements. Forward-looking statements are subject to a number of risks and uncertainties, including, but not limited to, our ability to obtain additional capital to meet our liquidity needs on acceptable terms, or at all, including the additional capital which will be necessary to complete the clinical trials of our product candidates; our ability to successfully complete research and further development and commercialization of our product candidates; the uncertainties inherent in clinical testing; the timing, cost and uncertainty of obtaining regulatory approvals; our ability to protect the Company's intellectual property; the loss of any executive officers or key personnel or consultants; competition; changes in the regulatory landscape or the imposition of regulations that affect the Company's products; and the other factors listed under "Risk Factors" in our filings with the SEC, including Forms 10-K, 10-Q and 8-K. Investors are cautioned not to place undue reliance on such forward-looking statements, which speak only as of the date of this release. Except as may be required by law, the Company does not undertake any obligation to release publicly any revisions to such forward-looking statements to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events. Matinas BioPharma's product candidates are all in a development stage and are not available for sale or use.

# Lipid Nanocrystals (LNCs) Simplify Intracellular Delivery of Nucleic Acids

| | Description | Benefit |
|---|---|---|
|  **INNATELY TARGET "ACTIVATED" CELLS** | ▪ Macrophages/monocytes, neutrophils, dendritic cells<br>▪ Infected/injured cells, tumor cells | ▪ Wide variety of extrahepatic targets |
|  **IMPROVED SAFETY** | ▪ Non-immunogenic platform<br>▪ Enter cells through non-destructive membrane fusion | ▪ Enables repeat administration |
|  **IMPROVED STABILITY** | ▪ Crystal structure protects nucleic acids | ▪ Avoid cold chain<br>▪ Flexible Administration (orally, IV, IM or via inhalation) |
|  **PAYLOAD VERSATILITY** | ▪ Nucleic acids (DNA, mRNA, siRNA, etc..)<br>▪ Proteins, peptides & small molecules | ▪ Choose best therapeutic cargo regardless of size |

***LNCs validated* in multiple clinical and pre-clinical studies**



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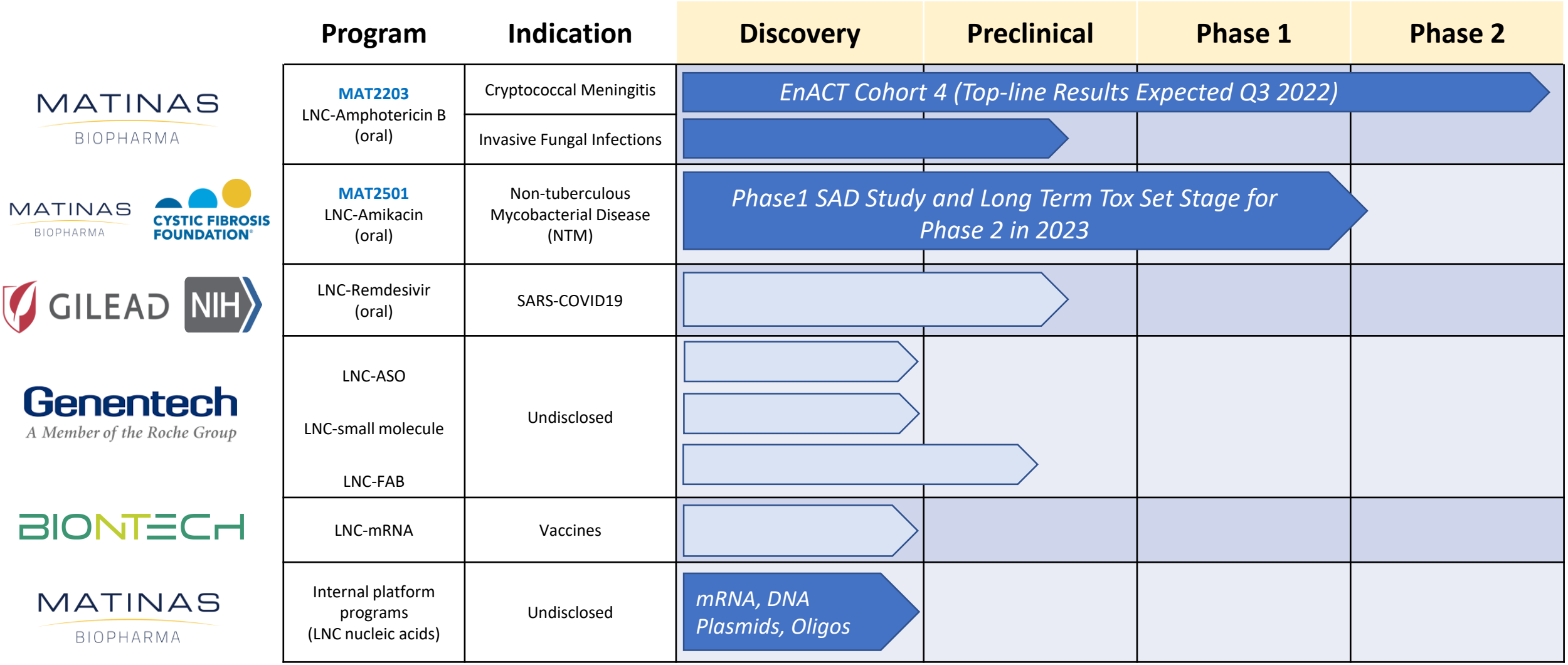
# Matinas Pipeline and Discovery Programs: Internal Clinical Stage Assets and External Collaborations




*LYPDISO™* *Partnering efforts ongoing*

# Exclusive Research Collaboration with BioNTech

- Exclusive collaboration between Matinas and BioNTech focused on mRNA and certain other nucleic acids
- BioNTech's mRNA vaccine development expertise combined with Matinas' LNC delivery platform
- Builds on Matinas' extensive prior preclinical *in-vitro* vaccine work with LNC formulations of proteins, peptides and DNA plasmids
  - Oral bioavailability
  - Non-immunogenic transfection
  - Focus on eliciting strong humoral and cellular immunity
- $2.75 million upfront exclusive access fee plus research funding
- Initiated license agreement discussions

# Exclusive Research Collaboration with BioNTech Builds on Previous Vaccine Results

## Efficacy previously demonstrated w/LNCs (*in-vivo*)

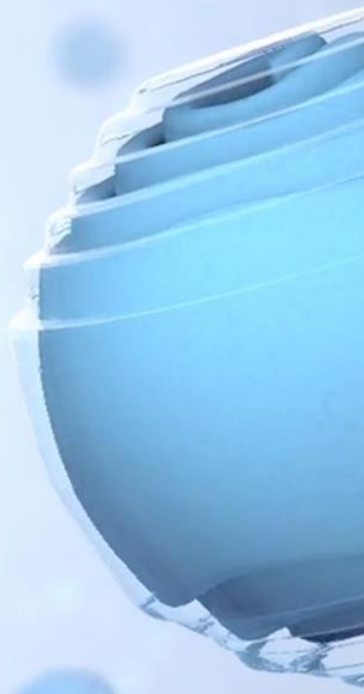
- ✓ Successful oral immunization
- ✓ Substantial increases in antibody titers
  - Out to 5 months after a single oral immunization
  - Boosted with repeat administration
  - Can be even further increased with adjuvants
- ✓ Enhanced cell-mediated response (lymphocyte proliferation, cytolytic T-cell response)
- ✓ High degree of protection against viral replication
- ✓ Protective against lethal challenge
- ✓ Enhancement of a commercial vaccine

## LNCs Provide Differentiation

- ✓ Can be administered SQ, IM, via inhalation, and **orally**
- ✓ Enhanced mucosal and systemic responses, humoral and cellular immunity
- ✓ High efficiency of delivery (proteins, peptides and DNA plasmids)
- ✓ Delivery mechanism itself not immunogenic
- ✓ Potential for much more stable formulations

# Lipid Nanocrystal (LNC) Platform

## Targeted, Well-Tolerated Intracellular Delivery



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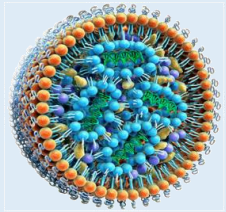
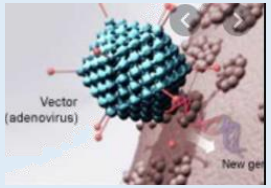
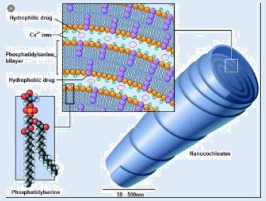
# LNCs Provide A Strong Alternative to LNP and AAV Delivery

| | LNP | AAV Viral Vector | LNC |
|---|---|---|---|
| |  |  |  |
| **Structure** | • Ionizable lipid complexing with mRNA<br>• Non-aqueous interior | 26 nM Capsid housing | • Natural components<br>• Non-aqueous bilayer |
| **Targeting** | • Avid uptake by RES, liver, spleen limits availability | • Limited set of targeted tissues<br>• Local delivery to CNS, eye | • **Targeted to phagocytes and activated cells** ( e.g. infected, inflamed or cancerous cells) |
| **Payload** | • Few practical limitations on size<br>• Only 1-2% endosomal escape substantially lowers delivery efficiency | • <5 kb genome | • Demonstrated incorporation of nucleic acids (ASOs, DNA plasmids, mRNA), proteins and small molecules<br>• Up to ***at least*** **11 kb capacity** (gene therapy, CRISPR, etc.) |
| **Safety** | • Cationic lipid toxicity not suitable for chronic use<br>• Anti-PEG allergic response limits retreatment | • Viral genome integration concerns<br>• Immunogenicity limits retreatment | • **Non-immunogenic platform**<br>• No cellular toxicity due to natural PS |
| **Stability** | • Very limited shelf stability<br>• Cold-chain requirements | • Cold chain requirements | • Solid structure allows **prolonged storage**<br>• mRNA formulations have demonstrated 4 month stability at room temperature<br>• Enables **oral** dosing as well as IV, inhaled & SC |

***LNCs can delivery large payloads in a stable delivery vehicle with no immunogenicity, novel targeting and oral delivery***



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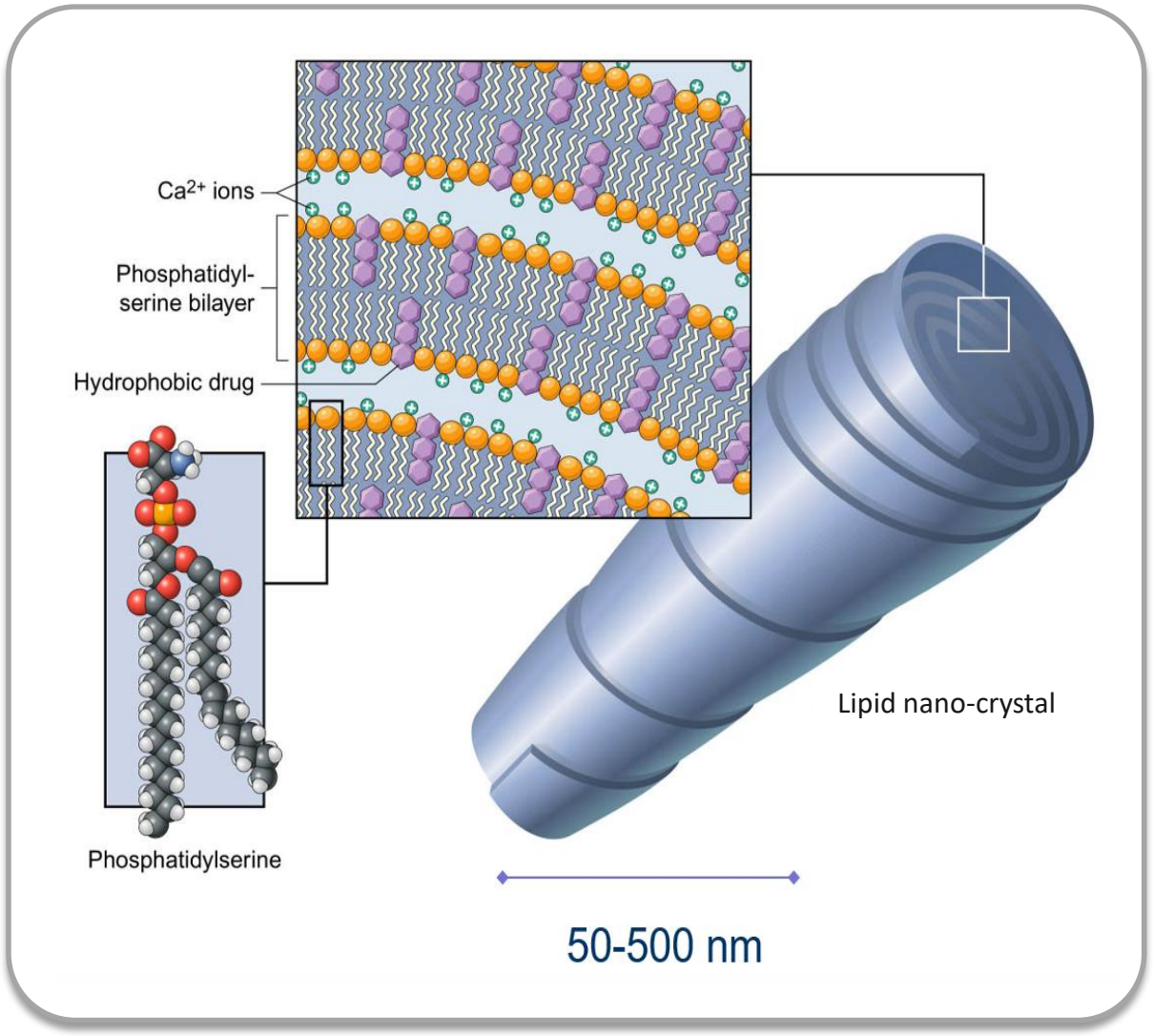
# Lipid Nanocrystals (LNCs) Consist of Phosphatidylserine, Calcium and Cargo and Deliver Cargo Intracellularly

- Stable, phospholipid-calcium crystalline nanoparticles
- Calcium ($Ca^{++}$) – Phosphatidylserine (PS) crystalline shell
- Engineered to self-assemble into nano-crystals in the presence of $Ca^{++}$
- Multilayered structure with little or no internal aqueous space
- Payload can be incorporated into the layers
  - ***Hydrophobic*** molecules packaged in the <u>interior</u> of the bilayer
  - ***Hydrophilic*** molecules packaged <u>between</u> the wrapped layers
- Two routes for drug delivery
  - LNCs can fuse with target cell membranes (delivering drugs directly inside the cell)
  - LNCs can also be taken up (via phagocytosis) by target cells and deliver their contents from within endosomes to the cell interior



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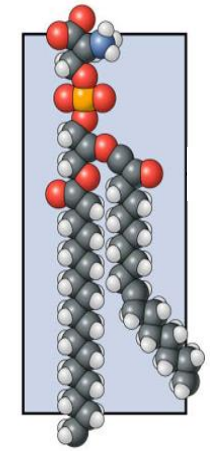
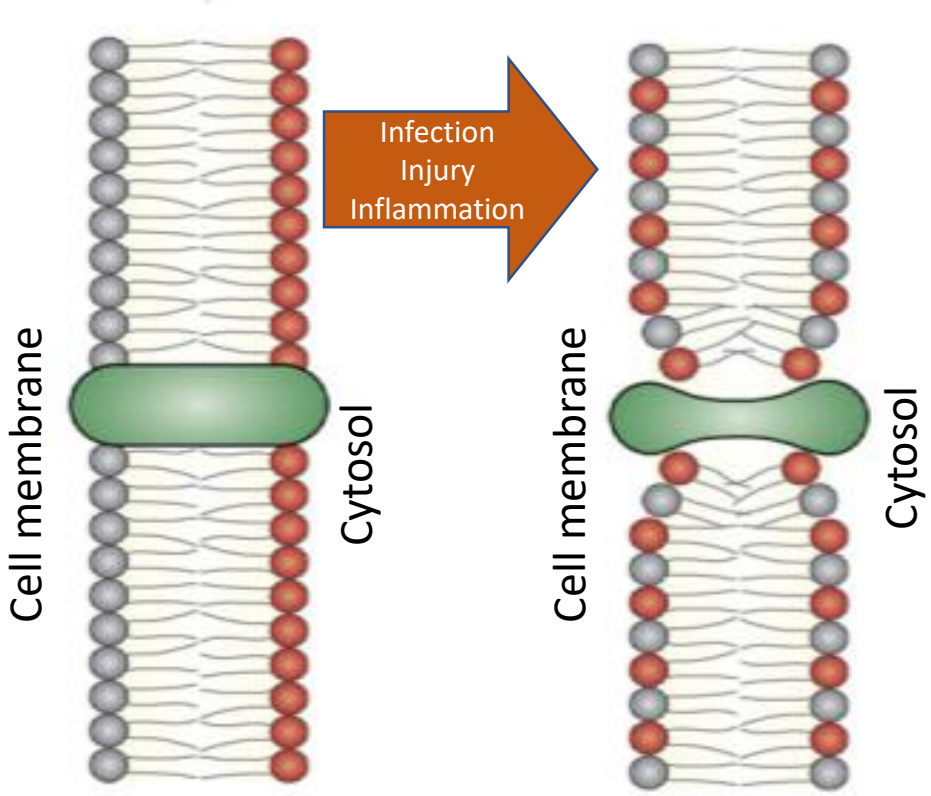
# LNCs Work Because of PS, Which Enables Intracellular Delivery Via Two Biological Pathways


Phosphatidylserine

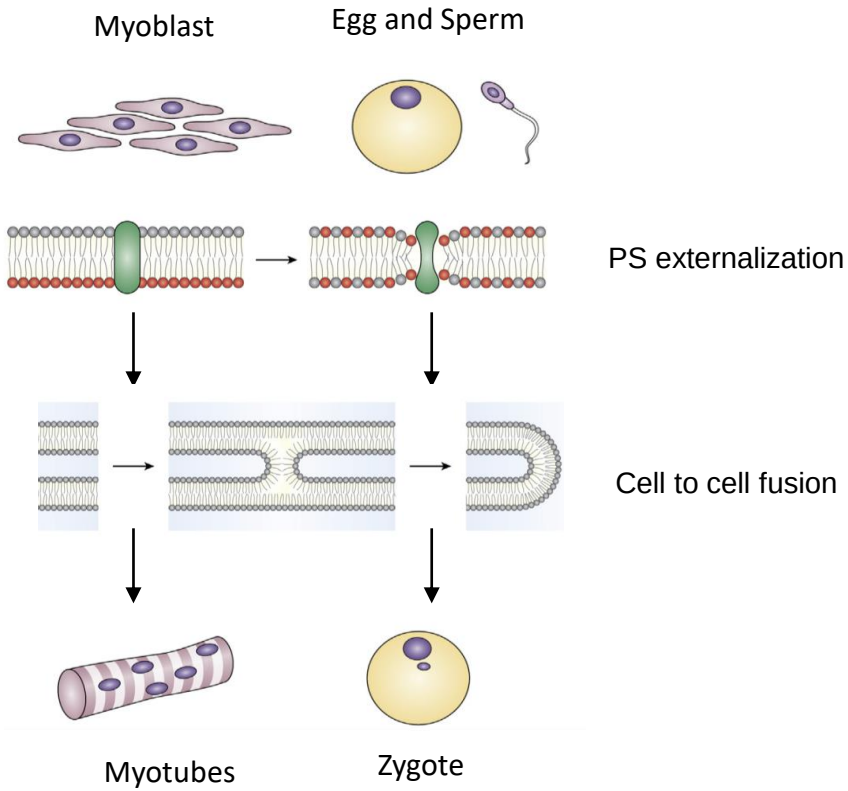
PS on the outer layer is an “eat-me” signal enabling **phagocytosis**




Normally, **PS** is confined to the inner layer ( facing cytosol)

With “activation” **PS** moves from the inner layer to the outer layer (cell membrane)

PS on the outer cell membrane is also a precursor for cell-to-cell **fusion**




Whitlock JM *et al.* ***J Biol Chem*** 2021; 296: 1-16
https://doi.org/10.1016/j.jbc.2021.100411



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# LNCs Have the Potential to Target a Wide Array of Cells & Tissues

| | Cells with PS Receptors or Expressing High PS Levels | Demonstrated uptake |
|---|---|---|
| Cells Capable of Phagocytosis | **Bone marrow-derived hematopoietic cells** | |
| | ▪ **Macrophages** | ✓ |
| | ▪ **Dendritic cells** | |
| | ▪ **Natural killer (NK) cells** | |
| | **Astrocytes and microglial cells (CNS macrophages)** | |
| | **Specialized epithelial cells that participate in efferocytosis** | |
| | ▪ **Retinal epithelial cells** | |
| | ▪ **Alveolar lung epithelial cells** | |
| | ▪ **Mammary epithelial cells** | |
| "Activated Cells" (context dependent) | **Actively dividing cells** | |
| | ▪ **Fibroblasts** | ✓ |
| | ▪ **Tumor Cells** | ✓ |
| | **Infected Cells** | ✓ |
| | **Injured / Inflamed Cells** | ✓ |

***LNCs are Designed to Mimic Enveloped Viruses***



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# Multiple Potential Future Directions For LNC Platform

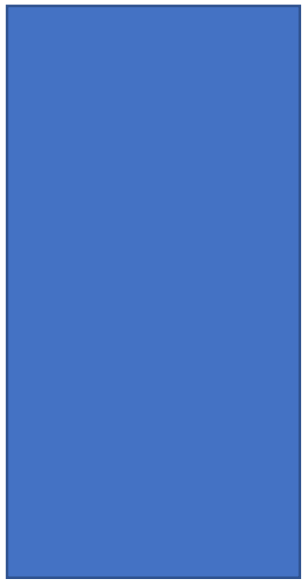
**Past** | **Current** | **Future**

Oral formulations of anti-infectives

MAT2203

MAT2501

Intracellular delivery of nucleic acids



| | |
|---|---|
| Infection | Antivirals<br>Anti-infectives |
| Immune system | Vaccines<br>Immune tolerance |
| Inflammation | Autoimmune diseases<br>Acute/chronic inflammation |
| Oncology | Direct tumor cell targeting<br>Tumor associated macrophages |
| Diseases of phagocytes | Monogenetic rare diseases |
| Fibrosis | Organ fibrosis<br>Wound healing |

Strong evidence | Initial evidence | Theoretical basis



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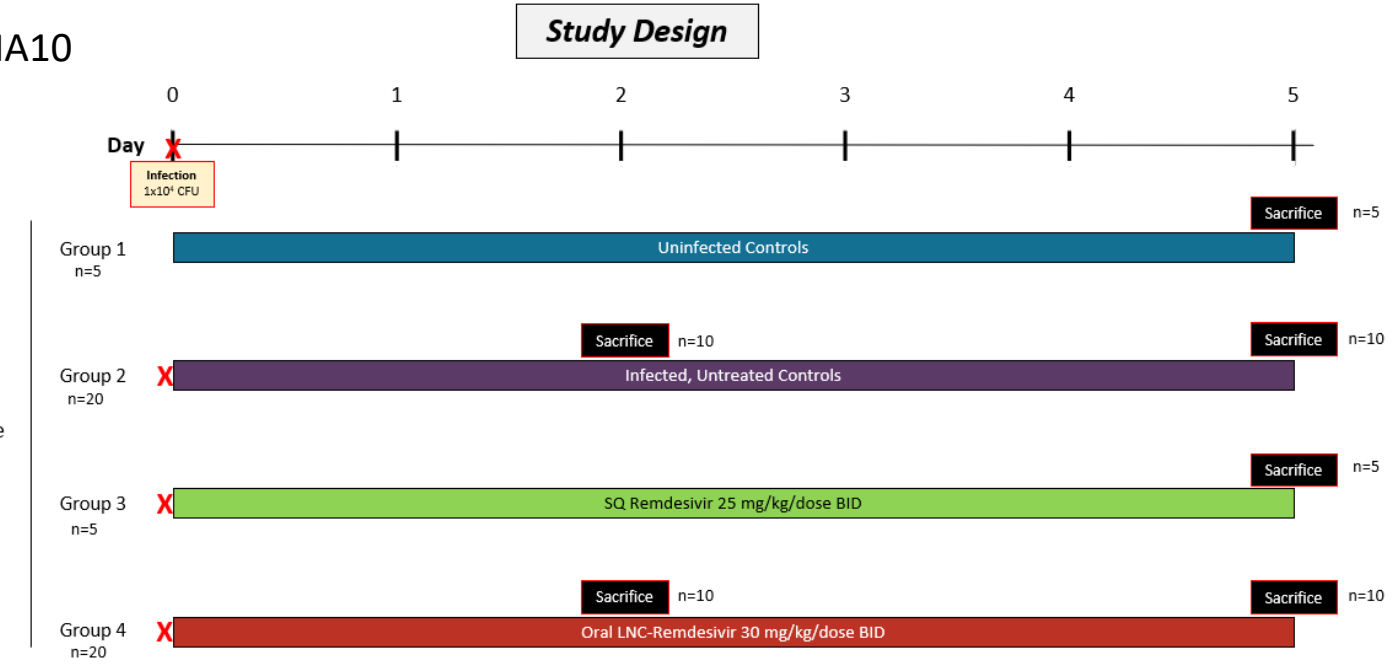
# *In vivo* Assessment of the Efficacy of LNC-remdesivir in SARS-CoV-2 Infection

**Goal:** Evaluate the capacity of an orally bioavailable remdesivir formulation to block viral replication and prevent severe disease in a mouse model of SARS-CoV-2*

* Leist and Dinnon et al., ***Cell*** 2020.

- 10-week-old female BALB/c mice
- Intranasal inoculation of $10^4$ PFU of SARS-CoV-2-MA10
- 4 Groups - Rx beginning 12 hours after infection
  - Uninfected controls
  - Infected, untreated controls
  - SQ RDV 25 mg/kg BID
  - Oral LNC-RDV 30 mg/kg BID
- Daily body weight
- Sacrifice at Day 2 and day 5
  - Lung titers, gross pathological congestion score (0-5) and histology.

50 BALB/c mice (female)



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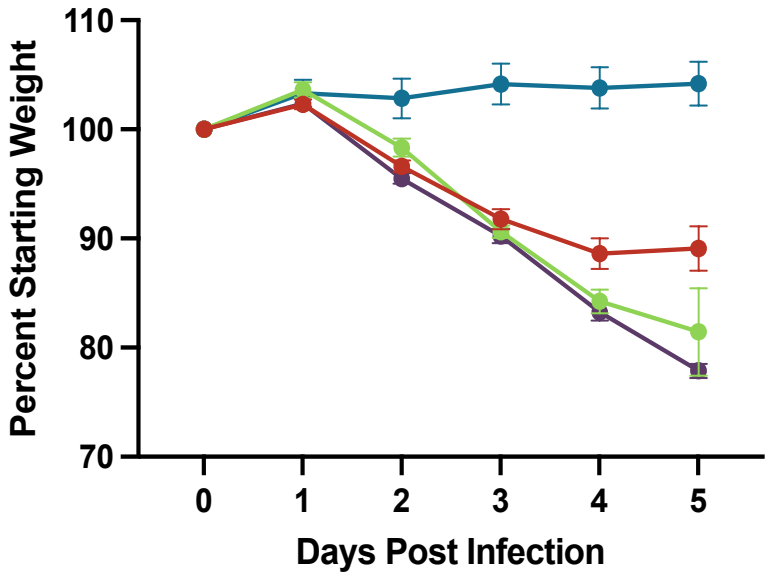
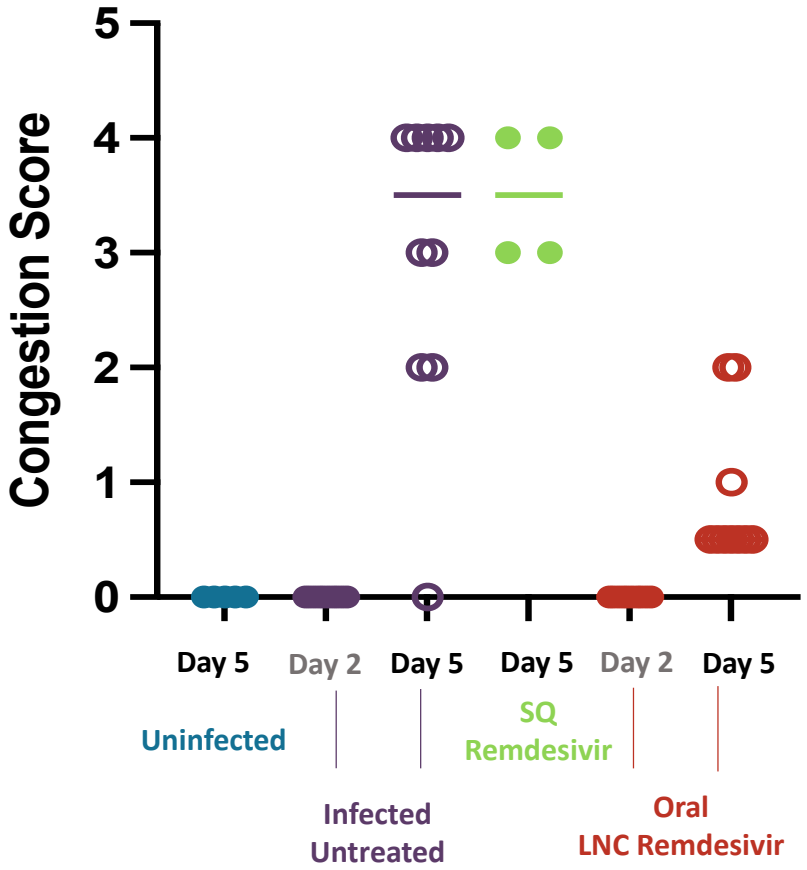
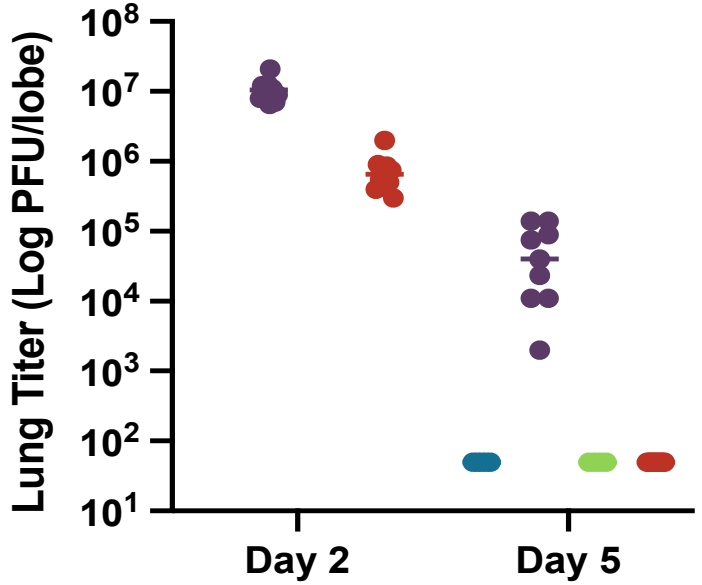
# *In vivo* Assessment of the Efficacy of LNC-remdesivir in SARS-CoV-2 Infection




Uninfected Control  Infected, Untreated Control  SQ Remdesivir 25 mg/kg BID  Oral LNC-Remdesivir 30 mg/kg BID

**In mice infected with SARS-CoV-2, oral LNC-Remdesivir reduced viral lung titers (beginning on Day 2), improved congestion scores, and mitigated weight loss**



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# MAT2203

## Oral Amphotericin B

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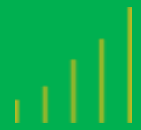
# MAT2203: A Novel Approach with a Proven Therapeutic Agent

**MAT2203**

- Oral amphotericin B formulation utilizing LNCs
- Proprietary formulation with robust intellectual property protection
- Potential to expand beyond treatment of CM to treatment of other invasive infections and prophylaxis
- Program supported by the National Institutes of Health (NIH)/NIAID

**IMPROVED PROFILE**

- LNC formulation enables oral administration, bioavailability and improved toxicity over IV amphotericin
- Efficient intracellular delivery to immune cells with delivery directly to infected tissues
- Demonstrated ability to cross the blood-brain barrier with an oral therapy



**POTENTIAL CLINICAL IMPACT**

- Potential to become the preferred antifungal agent for all invasive fungal infections ($8 billion+ market)
- Orphan Drug Designation + 4 Qualified Infectious Disease (QIDP) and Fast Track Designations
- Up to *12 years marketing exclusivity*, if approved



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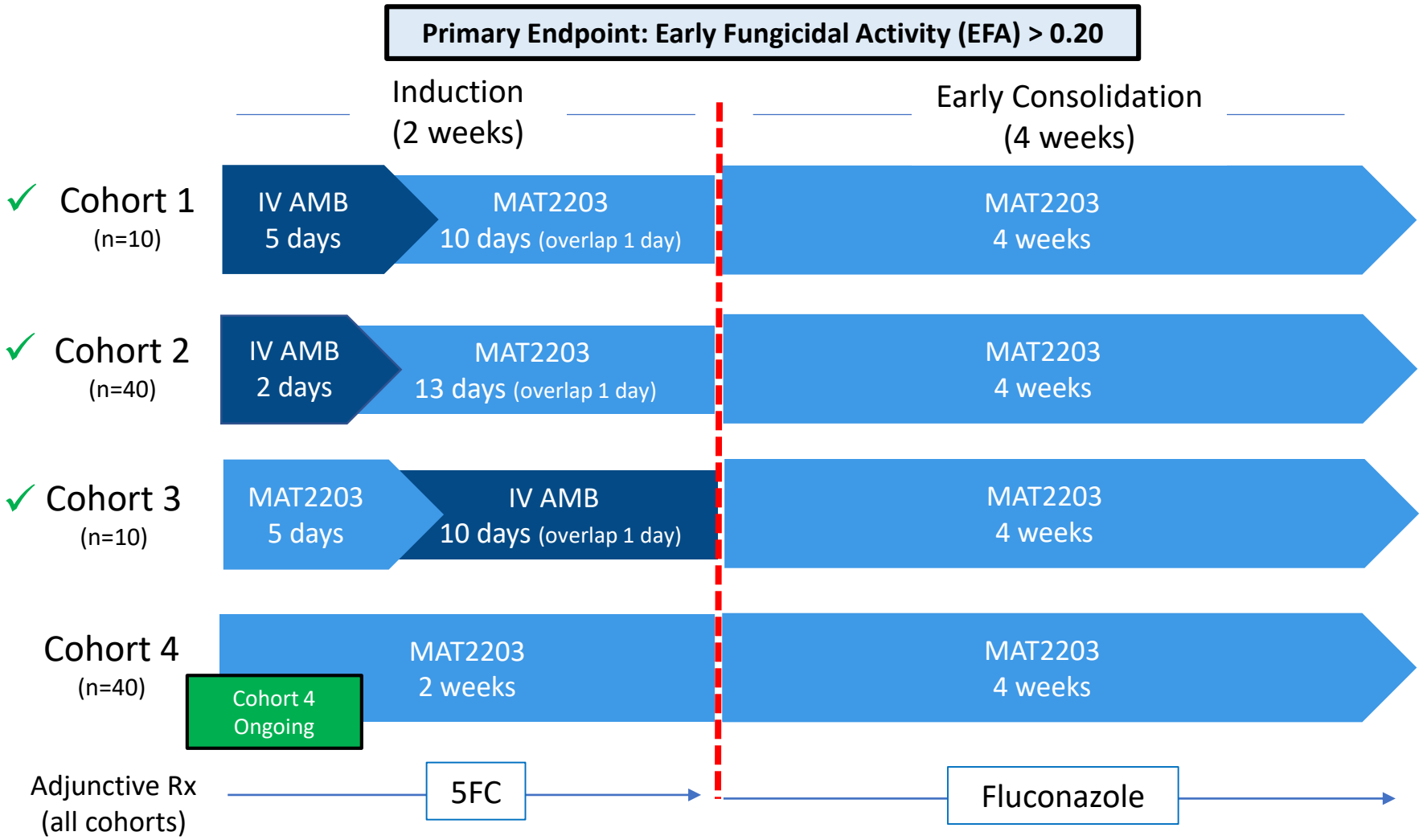
# EnACT Study Design




**MAT2203 TREATMENT REGIMENS:**

**Cohort 1**

- Induction: 2.0g/day
- Consolidation: 1.5g/day

**Cohort 2**

- Induction: 1.8g/day
- Consolidation: 1.2g/day

- *For each Cohort, a control group receives standard of care IV AMB +5FC (7 days), followed by 1200mg Fluconazole (7 days) for Induction and then only Fluconazole (800mg) for Early Consolidation*
- *Control arm present primarily to assess patient safety*
- *EnACT **not** powered to formally test comparisons with the control arm standard of care*

*IV AMB = intravenous amphotericin B



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# EnACT Cohort 2 Met Primary Endpoints – Effective at Delivering Drug ACROSS Blood Brain Barrier

## EnACT Cohort 2 Endpoints

- **Primary Endpoint**: Early Fungicidal Activity (**EFA**) $\log_{10}$ CFU/mL/day at Day 14 >0.20
  - EFA > 0.20 - associated with lower mortality and improved clinical outcomes[1]
- **Secondary Endpoints**
  - Sterilization of CSF cultures
  - Prevention of relapse (no breakthroughs)
  - Survival at 18 weeks
  - Demonstrated safety

## EnACT Cohort 2 Results

- ✓ EFA for MAT2203 was **0.42** (95% CI 0.29 to 0.55), exceeding the primary endpoint threshold
- ✓ All 39 MAT2203 patients completing induction achieved CSF sterility
  - (a) 97% for patients receiving MAT2203
  - (b) 76% for patients receiving SOC
- ✓ No breakthrough infections during MAT2203 treatment (10 weeks)
- ✓ "Early Survival" at Day 30
  - (a) 98% for patients receiving MAT2203
  - (b) 88% for patients receiving IV Ampho (SOC)
- ✓ MAT2203 was safe and well-tolerated over **6 weeks** of treatment
  - No renal toxicity or electrolyte abnormalities
  - No discontinuations due to AEs nor MAT2203-related SAEs

***EnACT Clinical Data Validate the Use of LNCs to Overcome Delivery Challenges***



1 ***Clin Infect Dis.*** 2020;71(5):e45-49 EFA is measure of antifungal activity in the CSF during induction treatment for CM

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# MAT2203 EnACT Update and Lifecycle Management for Label Expansion

## EnACT Cohort 4 Update

- All-oral regimen administered during induction (14 days) followed by consolidation treatment through Week 6
- Target: 40 patients on MAT2203 and 16 patients on SoC
- 50% enrolled (28 patients) through May 12th
- First DSMB review already conducted with recommendation to continue enrollment in the cohort without any changes to study design or dosing regimen
- Next DSMB review (50% enrollment) scheduled for end of May 2022
- Topline Interim Data expected Q3 2022

## Preclinical Update

- Preclinical studies in *C. Auris* and *Mucormycosis* initiated to support the label expansion of MAT2203
- Preliminary preclinical study conducted assessing effect of MAT2203 vs standard of care (SoC) liposomal amphotericin B (L-AMB) in an established murine model of *mucormycosis* caused by *Rhizopus delemar* infections
  - Data generated to date demonstrate that MAT2203 is as effective as L-AMB in protecting against *mucormycosis* due to *R. delemar*
  - Confirmatory studies in additional strains ongoing
- Preclinical evaluation of MAT2203 for *C. Auris* initiated April 2022; preliminary data expected Q3 2022.

# MAT2203 Regulatory Updates: Pathway to NDA Approval and Phase 3 Registration Trial

**Follow-up Clinical Type C Meeting held April 2022**

- FDA is evaluating potential registration of MAT2203 for **both** step-down induction and consolidation indications based upon the conduct of a **single** Phase 3 Trial
  - Represents a further streamlined development program, compared with the traditional requirement of two separate, "adequate and well-controlled" Phase 3 trials per indication for registration
- Pivotal study design features a non-inferiority trial with an IV amphotericin B and flucytosine (5-FC) comparator arm
- FDA recommended the following for the planned Phase 3 pivotal study:
  - Primary endpoint for induction: All-Cause Mortality at 2 Weeks
  - Non-inferiority margin of 10% (N=~250 patients; 80% power)
  - Total safety database ~300 patients (patients treated at the to-be-recommended dose and duration of treatment)
  - Key secondary endpoint for consolidation indication: meningitis culture-positive relapse-free survival time through Week 18
  - FDA meeting planned for July 2022 to reach final agreement on study design; Phase 3 to potentially commence later in 2022
  - NIH continued financial support of Phase 3 program anticipated

# MAT2501

## Oral Amikacin

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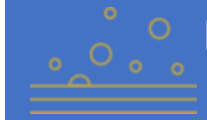
# MAT2501: A Better Amikacin

**MAT2501**

- Oral, LNC formulation of the broad-spectrum antibiotic Amikacin
- Initial indication in treatment of non-tuberculous mycobacterial (NTM) infections
- QIDP and Orphan Designations potentially provide 12+ years of exclusivity upon approval
- Proprietary formulation with robust intellectual property protection
- Development accelerated with $4.5M Cystic Fibrosis Foundation award



**IMPROVED PROFILE**

- LNC formulation enables oral administration and bioavailability
- Encouraging safety profile potentially eliminates oto- and nephro-toxicity
- Shown targeted delivery and efficacy in preclinical models of disseminated, pulmonary and biofilm NTM
- Activity against both Mycobacterium avium complex (MAC) and M. abscessus complex (MABC)

**SIGNIFICANT UNMET NEED**

- Potential to become the first oral aminoglycoside
- 80-90K US NTM patients; 40% refractory to treatment
- Potential use in acute, gram-negative infections
- Improvement over *INSM's Arikayce® (inhaled amikacin)

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# MAT2501: NTM Program Overview and SAD Topline Results

## Non-Tuberculous Mycobacterial Disease

- NTM organisms, widely present in the environment, are a frequent cause of challenging pulmonary infections, especially in patients with pre-existing inflammatory lung diseases such as cystic fibrosis
- Approximately 40-60% of patients have infections that are macrolide-resistant, and cure rates in these macrolide-resistant patients can be as low as 40-60%
- IV amikacin carries significant concomitant risk of both oto- and nephro-toxicity
- Inhaled amikacin (Arikayce®) has similar side effects and presents a challenge for absorption in CF patients with excessive pulmonary mucus

## Preliminary Development Timeline

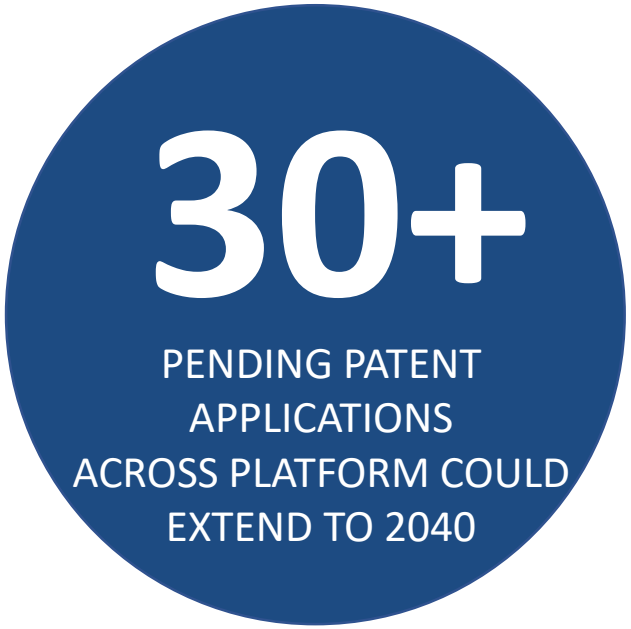
- **2022** – Long Term Tox and Positioning for Phase 2 in NTM (2023); planning for other indications

## Single Ascending Dose (SAD) PK Study Topline Results

- Results confirmed earlier findings with legacy formulation at the same doses (200, 400, 800) with an additional higher dose (1000 mg; fasted/fed) tested in this study
- No SAEs or study discontinuations (only dose-related adverse event was diarrhea (mild to moderate))
- No evidence of ototoxicity or renal toxicity
- Rapid absorption with oral administration ($T_{max}$ 2 hours)
- Dose-proportional increases in exposure
  - Exposure significantly lower compared with IV administered amikacin

# Expanding LNC Intellectual Property Portfolio


**20 Patents Issued Within Last 5 Years**




**Additional IP to be developed as clinical development plan progresses.**


**MAT2203 and MAT2501 both have QIDP and Orphan Designations Potentially Entitling Each Product to 12+ Years of Exclusivity**



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# Summary and 2022 Milestones & Catalysts

| | 1H 2022 Milestones & Catalysts | 2H 2022 Milestones & Catalysts |
|---|---|---|
| MAT2203 | ☑ FDA Feedback on Cohort 5 of EnACT<br>☑ Initiate preclinical studies of MAT2203 in *C. auris* and *mucormycosis* | ☑ Interim Topline Data from Cohort 4 of EnACT<br>☑ Data from MAT2203 preclinical studies in *C. auris* and *mucormycosis*<br>☑ Potential MAT2203 Partnership |
| MAT2501 | ☑ Data availability from MAT2501 Phase 1 SAD study in healthy volunteers | |
| LNC Platform and Collaborations | ☑ Initiate and receive data from 2nd *in vivo* study of oral LNC-RDV sponsored by NIAID/Gilead<br>☑ Conduct internal **in-vitro** and in-vivo studies with mRNA, DNA, oligonucleotides<br>☑ Potential research collaboration with large pharma in nucleic acids | |

MATINAS BIOPHARMA

# Corporate Presentation

May 2022