



MATINAS

BIOPHARMA

Corporate Presentation
April/May 2021

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.

LNC PLATFORM

Lipid Nanocrystal (LNC) Delivery Technology



- Proprietary and potentially disruptive platform technology focused on improving intracellular delivery of critical therapeutics
- **MAT2203 (oral amphotericin B):** Cohort 2 update of EnACT study in cryptococcal meningitis expected Q3 2021. Enrollment >50% and on schedule.
- **MAT2501 (oral amikacin):** Recent \$3.75M funding from CFF accelerates development of potential first oral aminoglycoside for treatment of nontuberculous mycobacterial disease and acute bacterial infections (i.e., gram negative)
- **Collaborations:** with NIH (oral formulation of Gilead's remdesivir), Genentech and others exploring LNC formulations of innovative compounds



LYPDISO™ (MAT9001)
Next Generation
Prescription Omega-3

- ENHANCE-IT data reported in Q1 2021 demonstrated robust plasma EPA levels vs. Vascepa®, supporting pursuit of a cardiovascular outcomes indication
- Clear differentiation from currently approved prescription omega-3 products, supported by strong barriers to entry
- Process underway to identify a partner for further development and commercialization

Lipid Nanocrystal (LNC) Platform

Targeted, Well-Tolerated
Intracellular Delivery

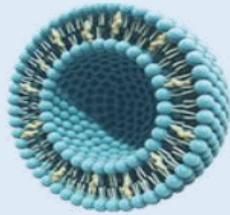
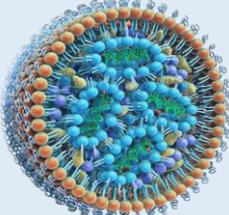
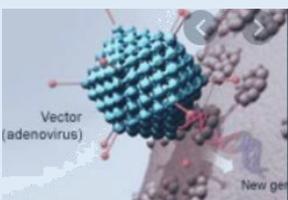
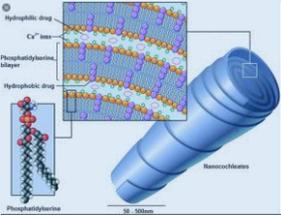
The Current Landscape of Intracellular Drug Delivery

Contents to be delivered	Target cells	Therapeutic areas	Delivery technology options
<p><u>Small molecules:</u></p> <ul style="list-style-type: none"> Antibiotic Antifungal Antiviral Anti-tumor Anti-inflammatory <p><u>Gene therapy:</u></p> <ul style="list-style-type: none"> Oligonucleotides DNA mRNA CRISPR/CAS-9 	<ul style="list-style-type: none"> Infected cells Macrophages Injured cells Tumor cells Bone marrow cells Monocytes Dendritic cells 	<ul style="list-style-type: none"> Anti-inflammatory Rx Infectious disease Oncology Vaccines Gene therapy 	<ul style="list-style-type: none"> Liposome LNP Viral vector LNC

The future of intracellular delivery

- Emerging importance of cell-mediated immunity (vaccines, immune enhancers)
- Growing needs for inhaled therapies (direct delivery to sites of infection)
- Need for more stable formulations (AAV/LNP -80°C storage)
- Need for improved delivery efficiency (LNP 1-2% endosomal escape)
- Opportunities to improve safety profile of AAV and LNPs: toxicity and immunogenicity
- Formulations of larger molecules: mRNA-protein complexes

How Are LNCs Differentiated from Liposomes, LNPs and Viral Vectors?

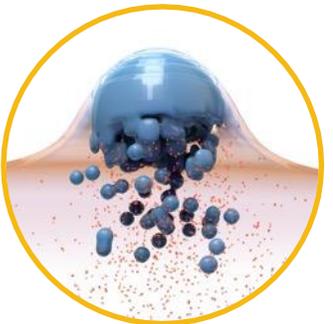
	Liposome	LNP	AAV (Viral Vector)	LNC
				
Structure	<ul style="list-style-type: none"> Aqueous interior surrounded by bilayer Drug can be encapsulated in aqueous core or bilayer 	<ul style="list-style-type: none"> Ionizable lipid complexing with mRNA Non-aqueous interior 	<ul style="list-style-type: none"> 26 nM Capsid housing <5 kb genome 	<ul style="list-style-type: none"> Natural components Non-aqueous bilayer Highly stable Much longer shelf life
Formulation goal	<ul style="list-style-type: none"> Reduce Toxicity Improve Bioavailability Prolong half-life 	<ul style="list-style-type: none"> Intracellular delivery (ASOs, siRNAs, mRNA) 	<ul style="list-style-type: none"> Mostly target liver Minimize empty vectors 	<ul style="list-style-type: none"> Encapsulate water-soluble drugs Control particle size Further expand gene delivery Significantly extend stability, shelf-life
Potential applications	<ul style="list-style-type: none"> Hydrophilic and Lipophilic drugs 	<ul style="list-style-type: none"> mRNA, ASOs, siRNAs 	<ul style="list-style-type: none"> Gene therapy 	<ul style="list-style-type: none"> Large and small molecules ASOs, mRNAs, siRNAs Large nucleotides (up to 11 kb)
Challenges	<ul style="list-style-type: none"> Leakage of encapsulated drug Fusion Limited shelf life 	<ul style="list-style-type: none"> Cationic lipid toxicity not suitable for chronic use Anti-PEG allergic response Very limited shelf stability Cold-chain requirements 	<ul style="list-style-type: none"> Very high production cost Viral genome integration Package size < 4k BP Re-treatment problematic Immunogenicity 	<ul style="list-style-type: none"> Limited clinical experience to date

Matinas' LNC Platform comprises highly efficient, fusogenic and non-toxic drug formulations



FLEXIBLE ADMINISTRATION

- Oral
- Intravenous
- Intramuscular
- Inhalation

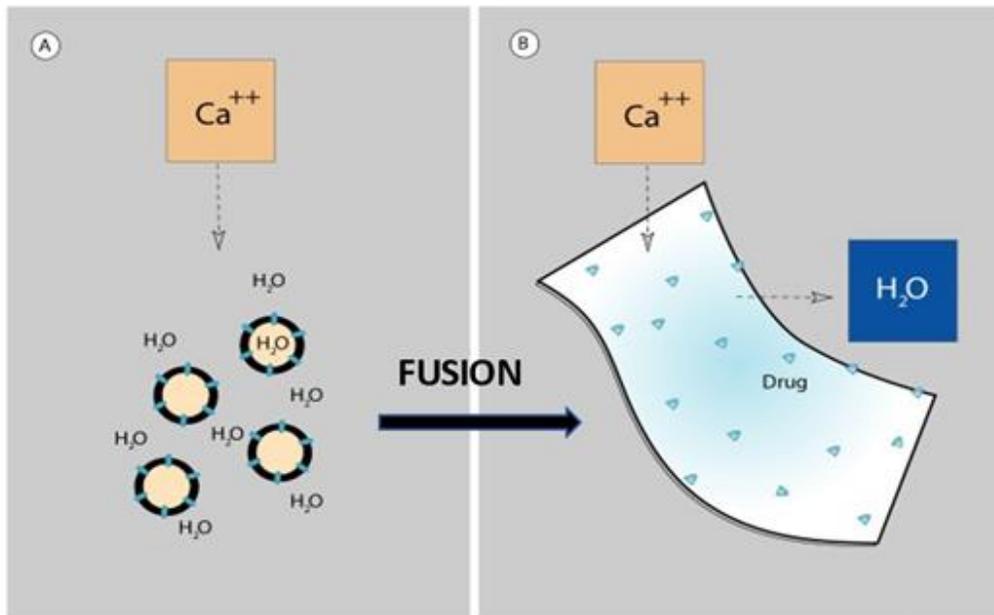


PHYSIOLOGICALLY TARGETS ACTIVATED CELLS

- Comprised of **phosphatidylserine and calcium** (critical components of natural cellular fusion)
- No evidence of adverse immune response
- Enter cells through non-destructive membrane fusion, phagocytosis or endocytosis
- Phosphatidylserine (PS) on LNC surface enables targeting of cells with exposed PS or PS receptors
- Reduced toxicity associated with delivery of drugs/molecules
- Ability to deliver a broad range of molecules (e.g., small molecules, nucleic acids, proteins) and vaccines
- Demonstrated ability to cross blood-brain barrier in animal models and in patients (EnACT study of MAT2203)
- Validated in multiple clinical and pre-clinical studies

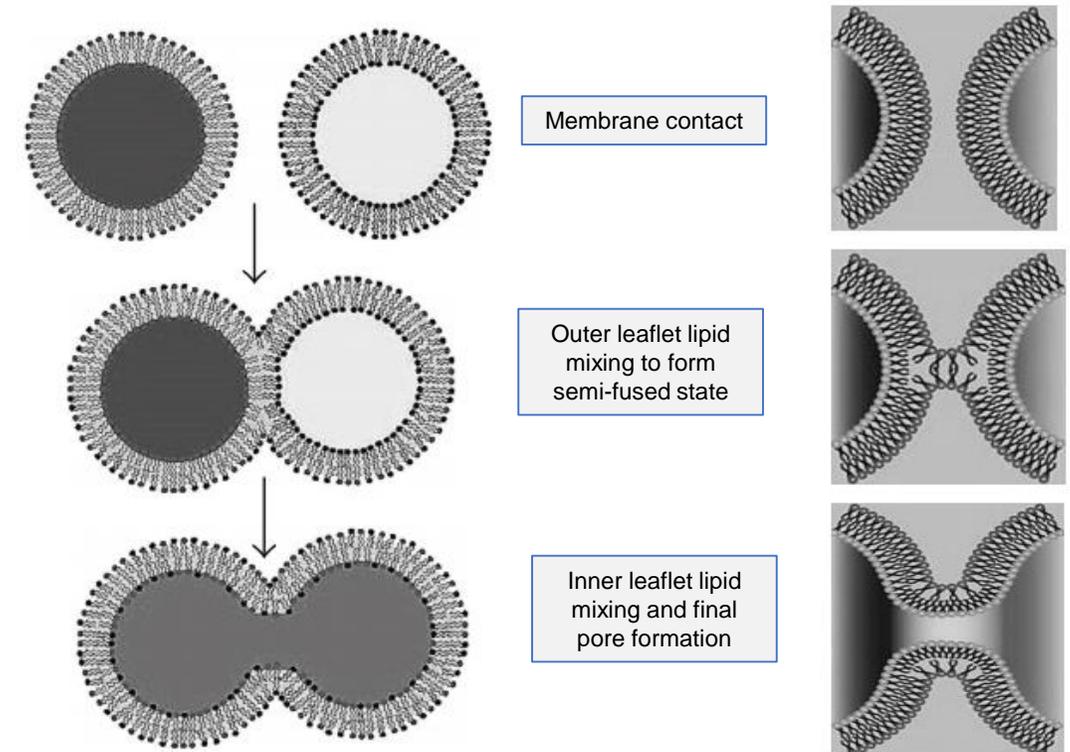
Importance of Phosphatidylserine (PS) in Membrane Fusion

LNCs are made by calcium-induced fusion of PS liposomes into lipid bilayer sheets and exposing them to Ca^{++}



LNCs are, in essence, intermediates in membrane fusion

Fusion of Cell Membranes (endosomes, exosomes, vesicles, viruses)



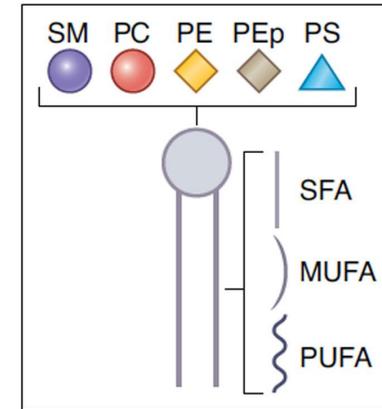
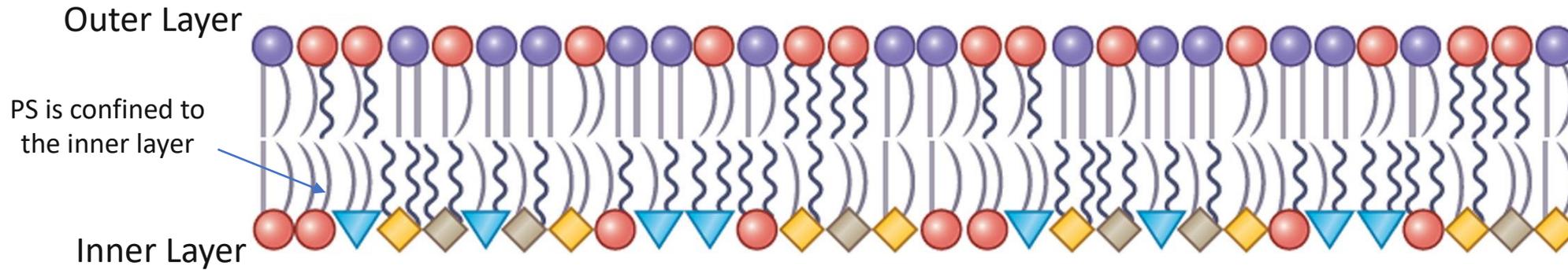
Roy SM et al. *Journal of Lipids* 2011
doi:10.1155/2011/528784

Bilayer lipid composition, tethering proteins and Ca^{++} are all important in initiating and propagating fusion

Asymmetry of the Phospholipid Membrane

Doktorova M et al. *Nat Chem Biol* 2020; 16: 1321-30
doi:10.1038/s41589-020-00688-0

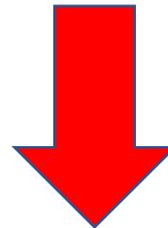
In the normal state, the inner and outer layers of the lipid membrane are very different



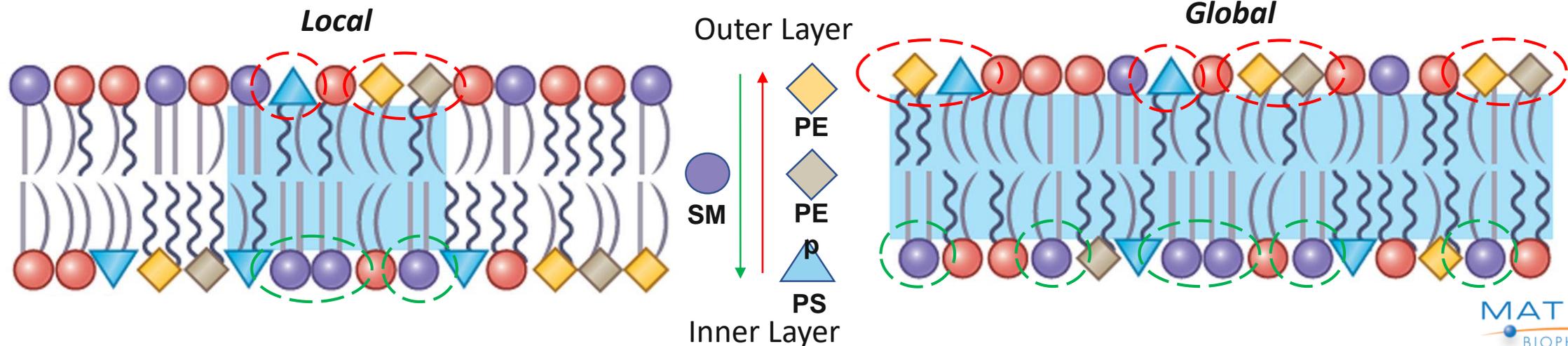
With cell "activation" (infection, injury, stimulation, death, etc.)

the lipid distribution across the membrane changes:

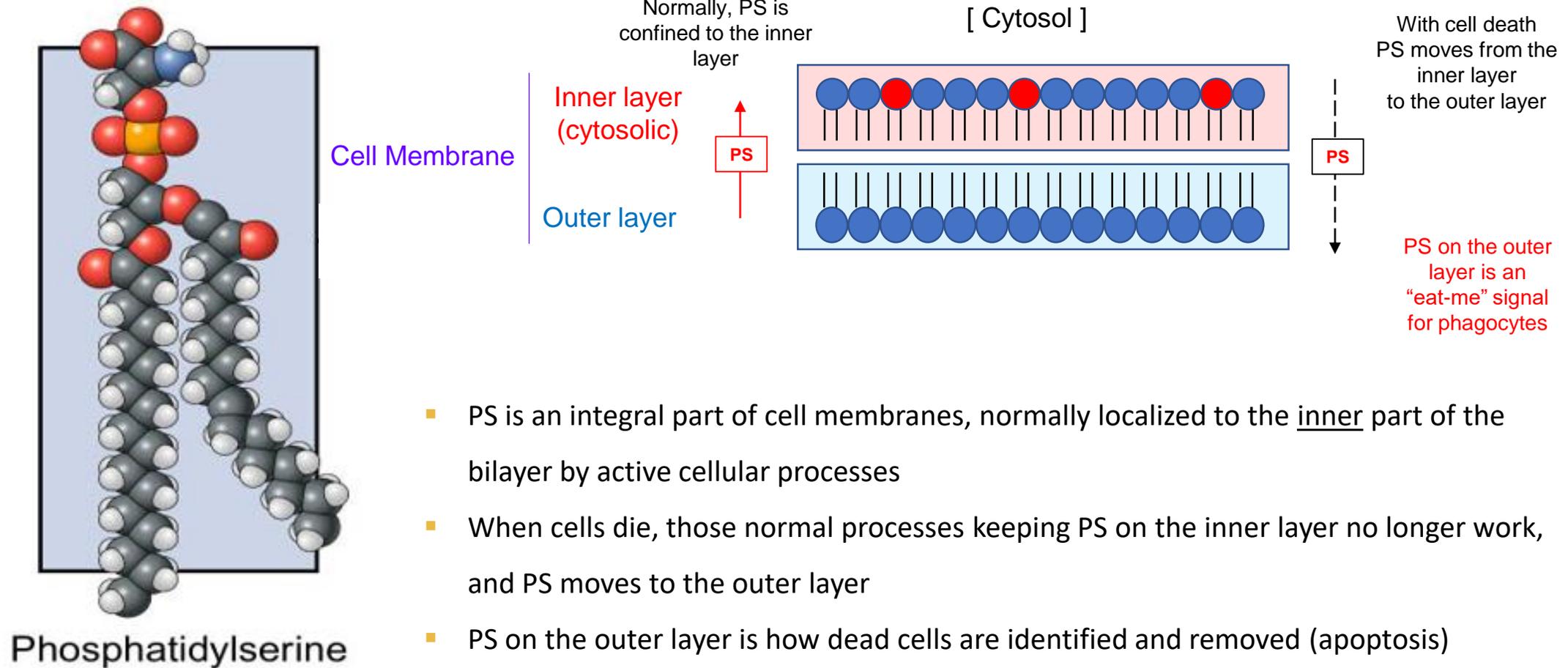
PS moves from the inner layer to the outer layer



This occurs either **locally** (local signaling) or **globally** (more intense signaling or cell injury/death)



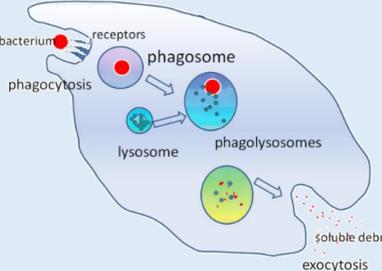
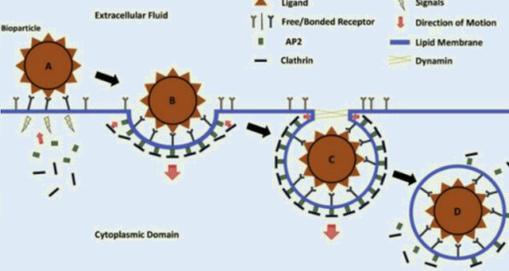
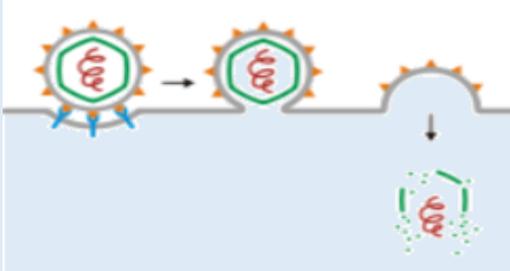
Central Role of Phosphatidylserine (PS) in Apoptosis / Virus Mimicry



Intracellular Uptake / Delivery Mechanisms: LNPs vs LNCs

Liposomes *not* very effective for intracellular delivery

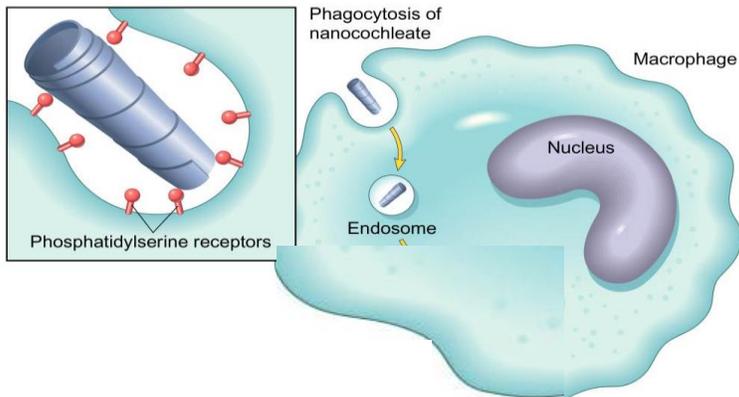
LNCs
LNPs

	Phagocytosis	Clathrin-mediated endocytosis	Membrane fusion
Mechanisms			
Uptake Conditions	<ul style="list-style-type: none"> ■ 0.5 -10 um particles ■ Presence of PS receptors 	<ul style="list-style-type: none"> ■ <100 nm optimal ■ Triggered by receptor binding (ApoE for LNP, glycoprotein for AAV) 	<ul style="list-style-type: none"> ■ Viral entry ■ Intracellular vesicles function ■ Ca⁺⁺ and phosphatidylserine
Characteristics	<ul style="list-style-type: none"> ■ Phagocyte with PS receptors ■ Killing, degradation, or antigen presenting ■ Trafficking via lymphatic circulation ■ Inflammatory response 	<ul style="list-style-type: none"> ■ Low pH endosome ■ Require large excess cationic lipid to disrupt endosomal membrane ■ 1-2% endosomal escape 	<ul style="list-style-type: none"> ■ Potentially high bioavailability ■ Less restrictions on particle size ■ Potential PS-to-PS bridging

Role of PS and PS Receptors in the Uptake of LNCs into Cells

Phagocytosis

Initiated by binding of PS to PS receptors



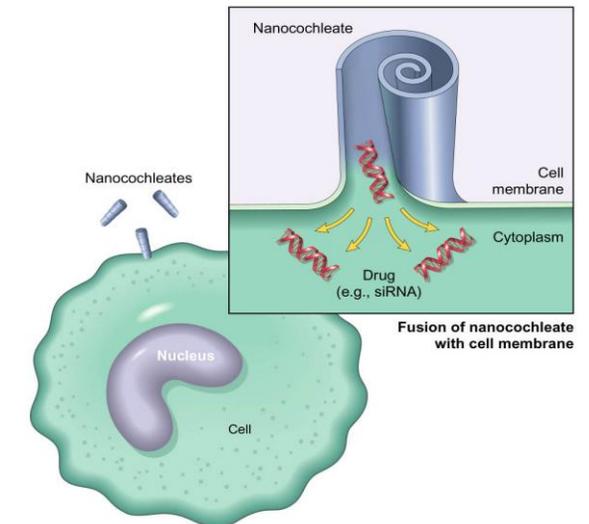
Macrophages readily engulf LNCs and their cargo into vesicles (endosomes).

Intracellular delivery via phagocytosis, fusion, or BOTH

- Bone marrow-derived hematopoietic cells
(Macrophages, dendritic cells, natural killer (NK) cells)
- Infected Cells
- Injured Cells
- Tumor Cells
- Astrocytes and microglial cells (CNS macrophages)
- Specialized epithelial cells that participate in efferocytosis
 - Retinal epithelial cells
 - Alveolar lung epithelial cells
 - Mammary epithelial cells
- Actively dividing cells

Fusion

Initiated by expression of PS on the surface of cells



LNCs can fuse with cell membranes and deliver cargo molecules directly to the cytoplasm

LNCs achieve effective intracellular delivery through **BOTH** phagocytosis and fusion.

LNCs are designed to mimic enveloped viruses

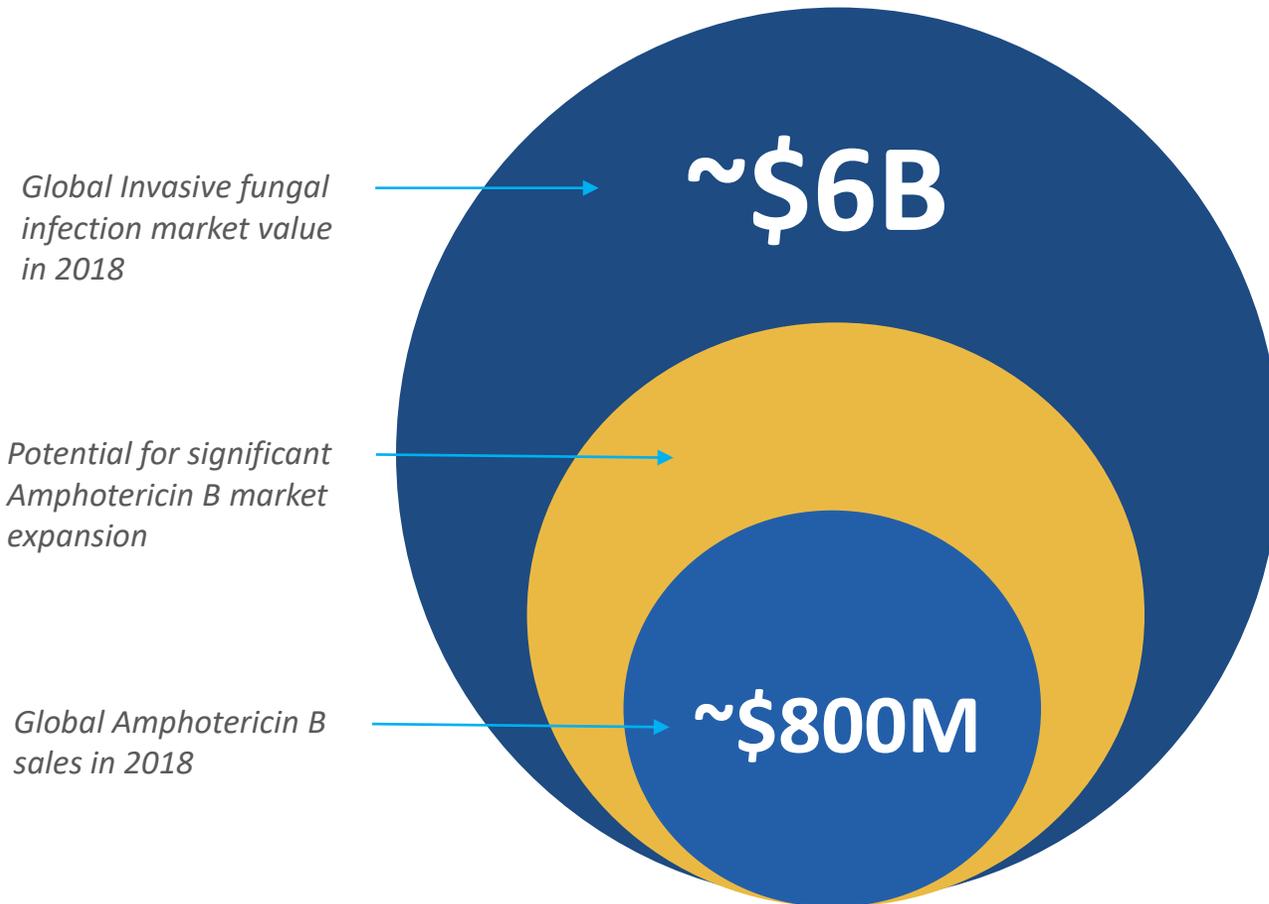
They exponentially increase the chances for cellular uptake, without adverse immune responses



MAT2203

Oral Amphotericin B

Invasive Fungal Infections Represent an Urgent Growing Global Need



- Invasive fungal infections are an urgent and largely overlooked global problem due to increasing use of immunosuppressive therapies, and growing resistance to current anti-fungal therapies due to lack of recent innovation.
- Amphotericin B is the gold standard broad spectrum antifungal treatment but has inconvenient IV administration and significant toxicity that limit its use in prophylaxis and maintenance settings.
- Amphotericin B sales ~\$800M globally despite toxicity and management of associated AE's accounting for up to 85% of cost of hospital stay.
- ***A safer and more convenient amphotericin B would be a game-changer in the fight against invasive fungal infections.***

MAT2203: A Novel Approach with a Proven Therapeutic



- Oral amphotericin B formulation utilizing LNCs
- Being developed with support from the NIH
- Proprietary formulation with robust intellectual property protection
- Potential to expand use into larger prophylaxis and maintenance settings



- LNC formulation enables oral administration, bioavailability and improved toxicity
- Preclinical and early clinical evidence of ability to cross the blood-brain barrier with an oral therapy
- Following efficient intracellular delivery to immune cells, delivers drug right to infected tissues

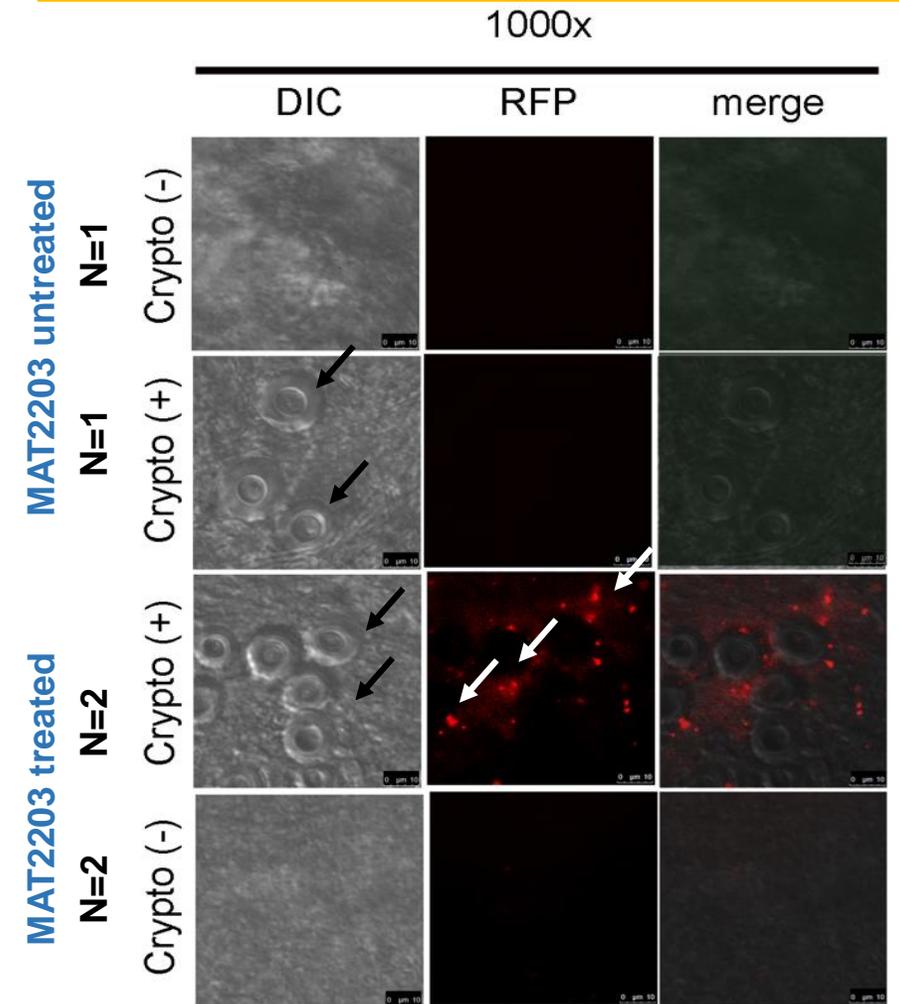


- Potential to become the preferred antifungal agent for treatment of cryptococcal meningitis and other invasive fungal infections
- Potential to cross the blood-brain barrier with an oral therapy
- Orphan Drug Designation + 4 QIDP and Fast Track Designations
- Up to 12 years marketing exclusivity, if approved

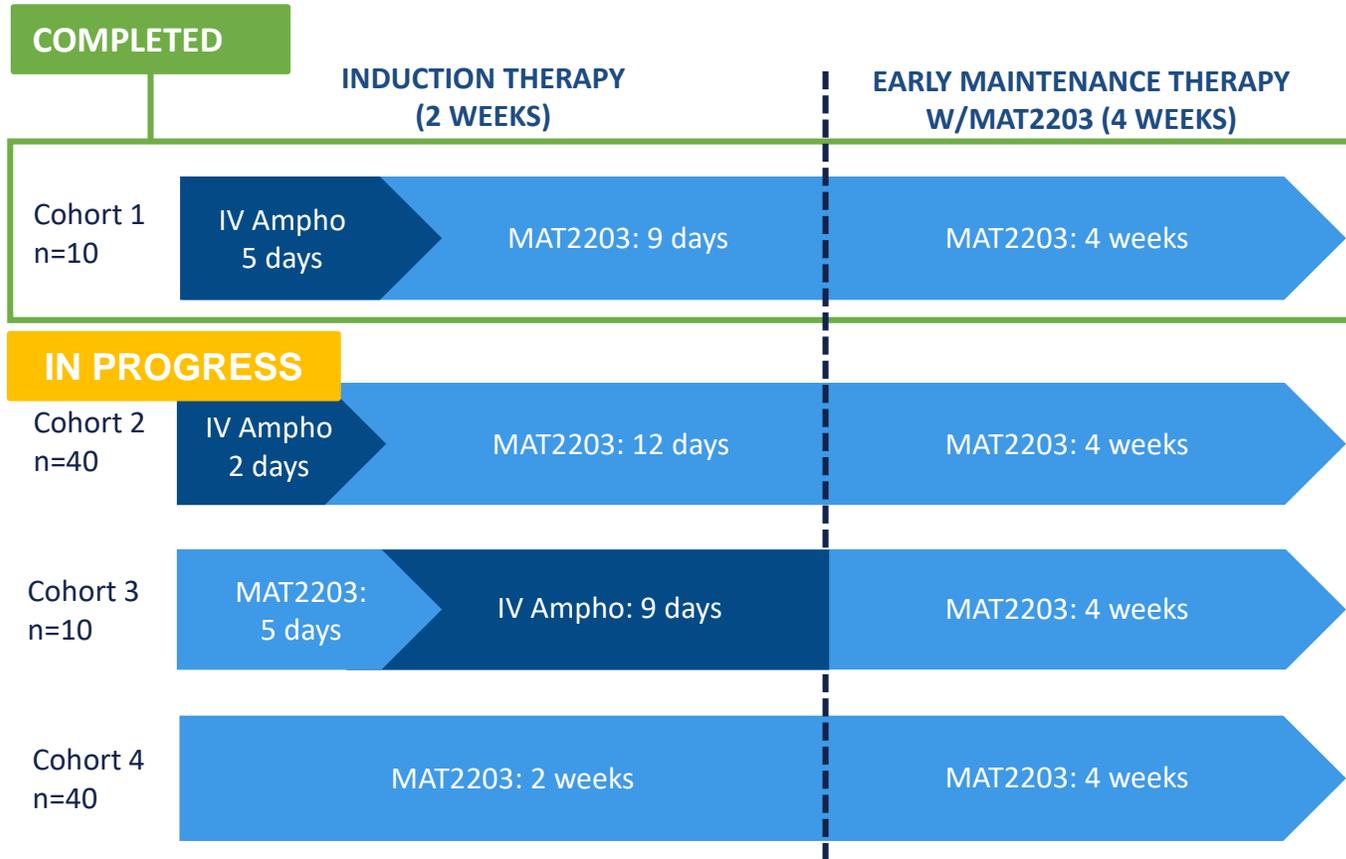
Brain localization of fluorescent LNCs after oral dosing

MAT2203: Preclinical Studies in a Mouse Model of Cryptococcal Meningoencephalitis

- MAT2203 LNCs tagged with rhodamine and dosed orally
- Crypto-positive, MAT2203 treated mice show fluorescence of LNCs at site of crypto infection
- Crypto-negative, MAT2203 treated mice show no fluorescence
- No fluorescence in either crypto-positive and or crypto-negative mice not treated with MAT2203
- **Supports immune-mediated delivery hypothesis that LNCs are preferentially taken up by activated cells and delivered to sites of infection/inflammation**



EnACT: Phase 2 in HIV Patients with Cryptococcal Meningitis



Each Cohort will have a control arm of patients of varying size receiving SOC:

IV AMB + 5-FC during induction and fluconazole during maintenance therapy

PROTOCOL DETAILS

- Open-label, sequential-cohort study assessing safety, tolerability and efficacy of MAT2203
- Assess MAT2203 as both induction and maintenance therapy
- Primary endpoint: Rate of CSF fungal clearance as measured over induction period of 2 weeks
- N=100 patients receiving MAT2203 + flucytosine (5-FC) in 4 stages of escalating durations of MAT2203 and decreasing duration of IV Amphotericin B (AMB)
- Safety and efficacy monitored throughout study by an independent DSMB
- All arms to receive 5-FC during induction therapy and fluconazole during maintenance therapy
- **Currently enrolling Cohort 2 following DSMB review of Cohort 1 safety and efficacy data and unanimous recommendation to proceed**



MAT2501

Oral Amikacin



- Oral, LNC formulation of the broad-spectrum antibiotic Amikacin
- Initial indication in treatment of non-tuberculosis mycobacterium (NTM) infections
- Proprietary formulation with robust intellectual property protection
- Development to be accelerated with recent \$3.75M Cystic Fibrosis Foundation grant



- 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)



- 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) ~ \$3.4B valuation

Non Tuberculosis Mycobacterium

- 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

- **2021** – Preclinical PK and Tox studies
- **Q4 2021** – Single Ascending Dose Phase 1
- **2022** – Begin Phase 2 Program in CF patients with NTM infections

Driving Opportunities for Value-Added Partnerships



Working with multiple strategic and research partners to expand potential successful applications of our LNC technology.

In January 2019, we collaborated with a top global pharmaceutical company to execute our first LNC platform research evaluation of oligonucleotides. Later in 2019, we entered collaborations with ViiV Healthcare and Genentech/Roche, to evaluate various molecules.



In November 2020, announced \$3.75 million award from the Cystic Fibrosis Foundation to support preclinical development of MAT2501, focused on treatment of nontuberculous mycobacterial (NTM) lung disease, including infections in patients with CF.



In December 2020, we announced a collaboration with the National Institute of Allergy & Infectious Disease (NIAID) to evaluate oral formulations of Gilead's antiviral drug remdesivir, used in the fight against COVID-19. Gilead will provide remdesivir and work with Matinas to evaluate the data from a series of planned preclinical studies with NIAID.



LYPDISO™ (MAT9001) Overview



OMEGA-3 BENEFITS

- Prescription Omega-3s offer a rare combination of potency, safety, and affordability
- Substantial benefits for both patients AND the US healthcare system
- Potential multi-billion-dollar market in the US (approval of Vascepa to treat patients at CV risk with TGs > 150 mg/dL)
- Well defined pathway to approval

LYPDISO™ BENEFITS

- Specifically designed to optimize treatment of dyslipidemia and severe hypertriglyceridemia
- EPA + DPA drive enhanced lipid lowering potency without raising LDL.
- EPA associated with cardio-protective benefits showing improved outcomes in a large clinical trial
- DPA has unique effects and combines superior TG-lowering with synergistic positive impact on PCSK9, Apo-CIII and HMG-coA reductase
- Enhanced bioavailability may lead to higher EPA blood levels – linked to improved outcomes
- Free fatty-acid formulation drives superior absorption with minimal food-effect

ENHANCE-IT Study: LYPDISO™ vs Vascepa®

OBJECTIVES

To assess pharmacodynamic (PD) effects of LYPDISO™, compared with Vascepa®, on TGs and other lipoprotein lipids, apolipoproteins, hs-CRP, and PCSK9 in men and women with elevated TGs

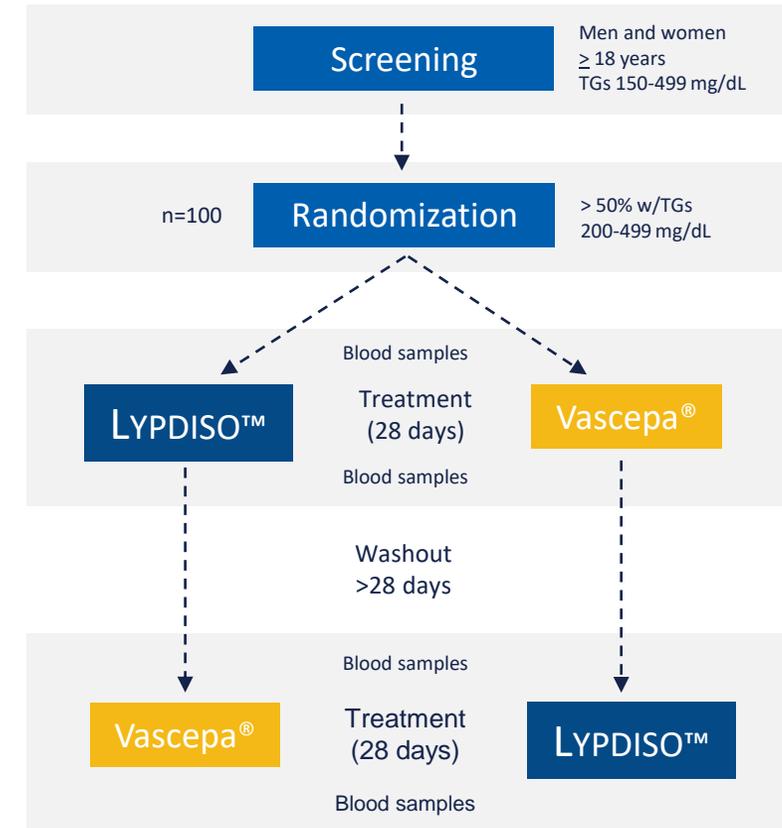
- Randomized, open-label, active-control crossover design (n=100)
- LYPDISO™ vs. Vascepa®, administered per Vascepa® label at 2g 2x/day with a meal each time; TLC diet
- Fasting TG 150-499 mg/dL (at least 50% with TGs \geq 200-499 mg/dL)
- No other lipid-lowering Rx (stable-dose statins allowed)
- Two 28-day treatment periods, \geq 28-day washout between treatments
- Measurement of PD parameters and omega-3 blood levels

PRIMARY ENDPOINT

- % change from baseline to end-of-treatment in plasma TG

SECONDARY ENDPOINTS

- Total-C, LDL-C, VLDL-C, HDL-C, non-HDL-C, Apo A1, Apo B, Apo C3, PCSK9, hs-CRP
- Omega-3 fatty acids (EPA, DHA, DPA, total) in plasma



Primary Endpoint: % Change from baseline in plasma TG

The pharmacodynamic (PD) population included all subjects for whom estimation of PD parameters was possible for both treatment periods.

The per protocol population (PP) included all subjects in the PD population for whom compliance for both treatment periods was \geq 80% with no clinically important protocol deviations.

ENHANCE-IT – Summary and Conclusions

- Plasma EPA concentrations were significantly higher with LYPDISO™, (46% relative percent increase change from baseline EPA level vs. Vascepa®)
- Levels of EPA have been directly correlated with improvements in cardiovascular outcomes (Vascepa® in REDUCE-IT)
- The ENHANCE-IT data indicate potential for superior cardioprotection with LYPDISO™ vs. Vascepa®
- The primary endpoint of percent change from baseline to end-of-treatment in triglycerides (TGs) did not meet statistical significance in the prespecified Pharmacodynamic (PD) Population
- Analysis of the Per Protocol (PP) Population demonstrated statistically significant improvement and superiority vs. Vascepa® in TGs, Total Cholesterol, and VLDL
- There were also significant reductions in hs-CRP with LYPDISO™ compared with Vascepa®, suggesting potential superior anti-inflammatory impact of LYPDISO™ (with additional potential cardiovascular and anti-inflammatory implications)
- The ENHANCE-IT data support the pursuit of a cardiovascular outcomes indication for LYPDISO™
- There were no serious adverse events reported and no dropouts related to study drug adverse events

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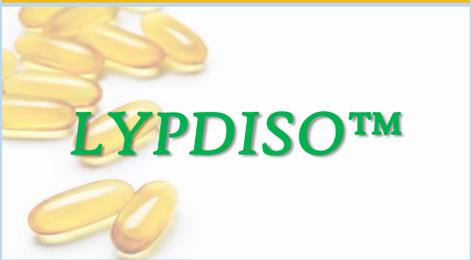
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Jerome D. Jabbour
Director



Key Catalysts Supporting Investment Thesis

	Q4 2020	Q1 2021	Q2 2021	Q3 2021	Q4 2021
 <p>LYPDISO™</p>		ENHANCE-IT - Top Line Data	Partnering Process Underway		
 <p>MAT2203</p>	EnACT- Cohort 1 Completed		EnACT - Cohort 2 DSMB Evaluation Q3 2021	EnACT- Enroll Cohort 3	
 <p>MAT2501</p>	\$3.75M Grant from CF Foundation for MAT2501 in NTM	Preclinical PK and Tox studies			Phase 1 – Single Ascending Dose
 <p>LNC Platform</p>	Collaboration with NIAID on Gilead's remdesivir	Collaboration Progress Updates Throughout 2021			



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