BREAKTHROUGH TREATMENT FOR ASTHMA and LUNG TRANSPLANT

www.lignamed.com

Executive Summary

A biopharmaceutical company focused on development of breakthrough treatments for lung diseases and conditions

- **LGM2605, is a first in class, synthetic small molecule lignan with a unique mechanism of action proven to:**
  - Rehabilitate donor lungs prior to transplant
  - Mitigate radiation damage to lung tissue
  - Prevent pulmonary fibrosis with potential to "reverse" and/or treat symptoms of the disease

- **LGM1506, is a single isomer synthetic small molecule lignan with a unique mechanism of action proven to:**
  - Improve asthma

- **Company on track to achieve key inflection points:**
  - Device indication for human donor lungs – LGM2605 Market approval 2024
  - Asthma– LGM1506 Phase I studies in man 2024

- **LignaMed seeking partnerships and funding to support commercial indications**

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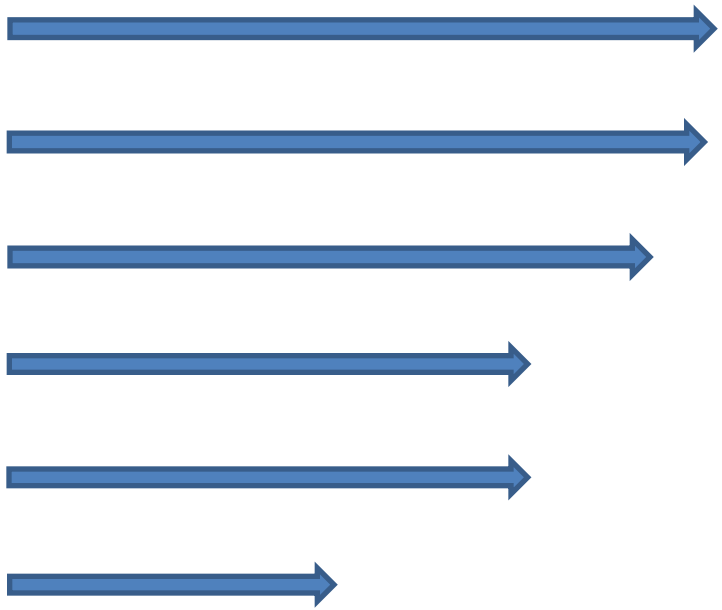
LignaMed Product Portfolio

Product	Indication	Regulatory Path	Discovery	PreClinical	Phase I
LGM2605	*Lung Transplant*	*Device*			
LGM2605	*Organ Preservation*	*Device*			
LGM1506	*Asthma*	*IND*			
LGM1506	*Fibrosis*	*IND*			
LGM2605	*Radiation*	*MCM*			
LGM1506	*Kidney transplant*	*IND*			



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Development Opportunities

Disease/ Condition	**Asthma**	**Idiopathic Pulmonary Fibrosis**	**Lung Transplant Donor Lungs**	**Lung Transplant Recipients**	**Radiation Oncology Side Effects**	**Radiation Poisoning from nuclear Accident/ Attack**
Indication	Mitigation of Th2-low Asthma	Mitigation of Fibrosis	Rehabilitate/ Improve Lung Function & Lung Preservation	Prevent Ischemia Reperfusion Injury	Prevent Lung Injury during Radiation Treatment	Mitigate lung damage from radiation exposure
US Market Opportunity	~$4 Billion	~$16 Billion	~$100 Million	~$500 Million	~$5 Billion	Gov't Stockpile Priority Review Voucher (4)($?)

Intellectual Property (select list)

Application/Patent number	Application title	Status
10,045,951 US	USE OF FLAXSEED, FLAXSEED LIGNANS TO TREAT RADIATION INDUCED LUNG DISEASES AND LUNG CANCER. (Expiry 2028)	Granted US
10,449,224 US	USE OF FLAXSEED, FLAXSEED LIGNANS TO TREAT ACUTE LUNG INFLAMMATION, OXIDATIVE LUNG TISSUE INJURY OR CHRONIC LUNG FIBROSIS. (Expiry 2028)	Granted US
10,030,040 US **ZL201480041131.2 China** **6321788 Japan** PCT/US14/041636	SYNTHESIS OF (S,S)-SECOISOLARICIRESINOL DIGLUCOSIDE AND (R,R)-SECOISOLARICIRESINOL DIGLUCOSIDE (Expiry ~2034)	Granted US, China, Japan Australia
10,966,995 US App 16/678,734 PCT/US2015/033501	GRANTED CLAIMS INCLUDE: USE OF SDG TO TREAT ASTHMA (Expiry ~2035)	Granted US
PCT/US16/049780	NOVEL SYNTHETIC (S,S) AND (R,R)-SECOISOLARICIRESINOL DIGLUCOSIDES (SDGS) PROTECT NAKED PLASMID AND GENOMIC DNA FROM GAMMA RADIATION DAMAGE/RADIOPROTECTIVE AGENTS. (Expiry ~2036)	Pending
PCT/US17/035960	METHOD OF PROTECTING , PREPARING OR PRESERVING A LUNG FOR TRANSPLANTATION (Expiry ~2037)	Pending
9,987,321 US	USE OF FLAXSEED AND FLAXSEED DERIVATIVES FOR TREATMENT OF NEUROLOGICAL DISORDERS AND VIRAL DISEASES (Expiry ~2033)	Granted US

LGM2605 Is Efficacious in Multiple Mechanistically Related Models**

- Demonstrated Efficacy in irradiated cell model:
  - Cosmic Radiation exposure model of flow-adapted endothelial cells (UPenn/NASA)

- Demonstrated Efficacy in rodent models:
  - **Radiation lung damage - fibrosis(UPenn/NIAID)**
  - **Idiopathic Pulmonary Fibrosis (MDBiosciences/LignaMed)**

- Demonstrated Efficacy in NHP models:
  - **Radiation lung damage - fibrosis (SNBL/NIAID)**
  - **Ozone inhalation asthma (UC Davis/NIAID)**

- Demonstrated Efficacy in ex vivo human models (EVLP, for transplant):
  - **ex vivo human lung (UPenn)**

***data from these models shared upon request*

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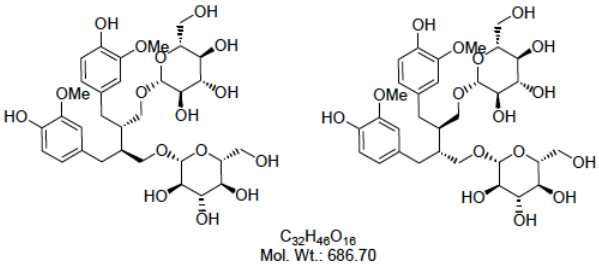
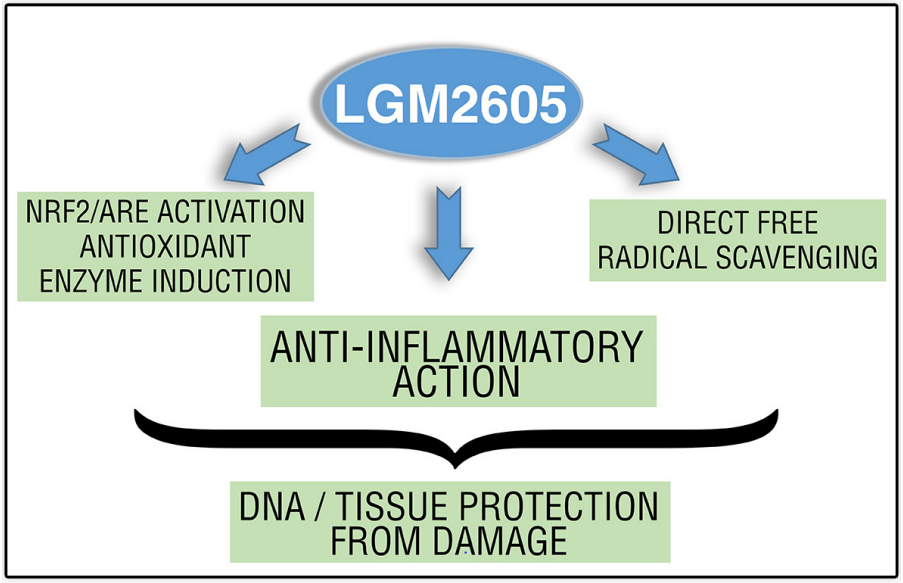
LGM2605

- *Secoisolariciresinol diglucoside*
- *Synthetically generated >97% purity*
- *48/52 isomeric mixture*
- *Amorphous white powder*
- *Stored at <10°C (RT possible)*



LGM2605 Has a Unique Mechanism of Action



A. Boosts endogenous antioxidant tissue defenses: *– upregulates the antioxidant/cell protective gene response via activation of the NRF2/ARE pathway.*

B. Anti-inflammatory activity *– inhibits inflammasome activation, proinflammatory cytokine secretion, immune cell activation and recruitment.*

C. Free radical scavenger: *protects against radiation damage through Reactive Oxygen Species (ROS) removal via direct free radical scavenging.*

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Prelim Safety/Tox Studies Show Excellent Safety Profile

- No signs of acute toxicity in mice(decreased activity, squinting eyes, hunching, labored breathing or injection site swelling).
- No signs of chronic toxicity (weight loss, decreased activity, hunched posture, labored breathing or any other abnormal clinical signs of toxicity)
- No gross changes observed in drug group when compared to naïve or PBS groups at necropsy.

LGM-2605 dosed s.c. 400mg/kg (4X typical dose s.c.) and oral 100mg/KG

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LGM2605 Can Be Dosed Orally, Subcutaneously or Inhaled

- Oral PK/PD completed in black-6 mice
- Oral PK/PD completed in LJ mice
- Subcutaneous PK completed in black-6 mice
- Oral PK/PD completed in non-human primates
- All oral PK studies suggest once or twice a day dosing
- Aerosolized in ex vivo human lung completed

LGM1506 in Th2-Low Asthma

LGM1506

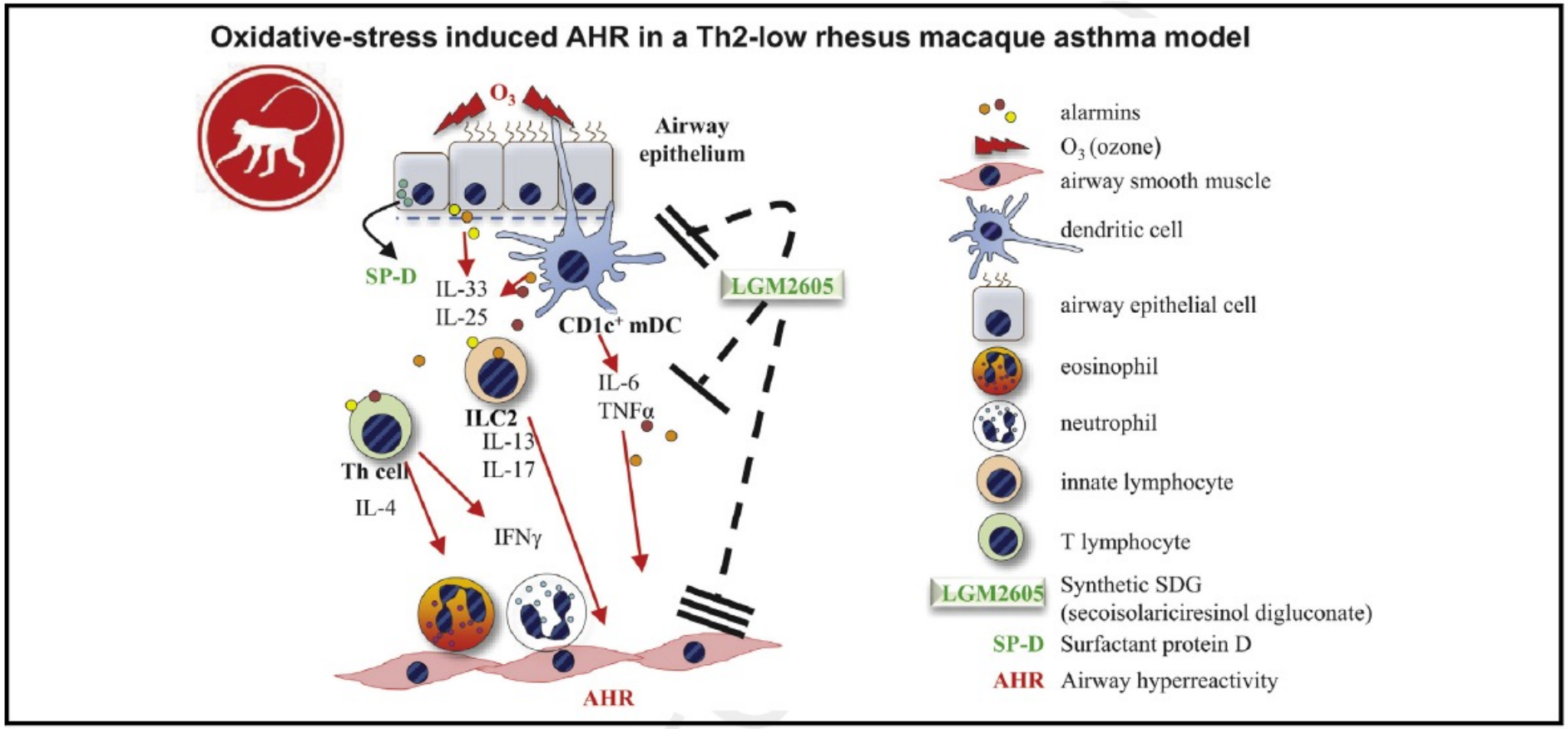
- LGM1506 is the single isomer of LGM2605
- Identical physical properties
- Equal in vitro/in vivo potency between isomers
- For chronic (years of dosing) LignaMed feels it is prudent to proceed with a single isomer
- All preliminary asthma and IPF work was done with the racemic LGM2605
- Current NHP PK and efficacy study was completed with LGM1506 (single isomer)

NHP Study Published JACI

Ozone-induced enhancement of airway hyperreactivity in rhesus macaques: Effects of antioxidant treatment

Cameron H. Flayer, BS,[a] Erik D. Larson, BS,[a] Anjali Joseph,[a] Sean Kao, BS,[a] Wenxiu Qu, MD,[a,b] Austin Van Haren, BS,[a] Christopher M. Royer, DVM, PhD,[a] Lisa A. Miller, PhD,[a] John P. Capitanio, PhD,[a] Thais Sielecki, PhD,[c] Melpo Christofidou-Solomidou, PhD,[d] and Angela Haczku, MD, PhD[a] *Davis, Calif, Shenyang, China, and Philadelphia, Pa*

Low Th2 Asthma Model



Asthma NHP Phase I STTR Study Results: LGM2605 Abolished Ozone Induced Airway Hyperreactivity (AHR)

- O3 induced significant BAL fluid neutrophilia and eosinophilia and increased AHR and expression of IL6 and IL25 mRNA in the airway epithelium together with increased BAL fluid group 2 innate lymphoid cell (ILC2s), CD1c1 myeloid dendritic cell, and CD41 T-cell counts and diminished surfactant protein D expression.

- LGM2605 …… ***completely abolished O3-induced AHR.***

2nd Proof of Concept in NHP Using LGM1506 (study protocol mimics Phase I STTR study)

Preliminary Conclusions Supported by Statistical Analysis

1. LGM1506 (50 mg/kg b.i.d.) prevents ozone-induced eosinophilia involved in asthma exacerbation in bronchoalveolar lavage fluid.
2. Bronchoalveolar lavage fluid neutrophil influx observed with ozone-induced asthma exacerbation was significantly ameliorated by LGM1506.
3. LGM1506 significantly increased expression of the antioxidant enzyme NQO1 in cells derived from bronchial brush biopsies.
4. Significant treatment effects with LGM1506 were irrespective of animal sex, age, and weight.

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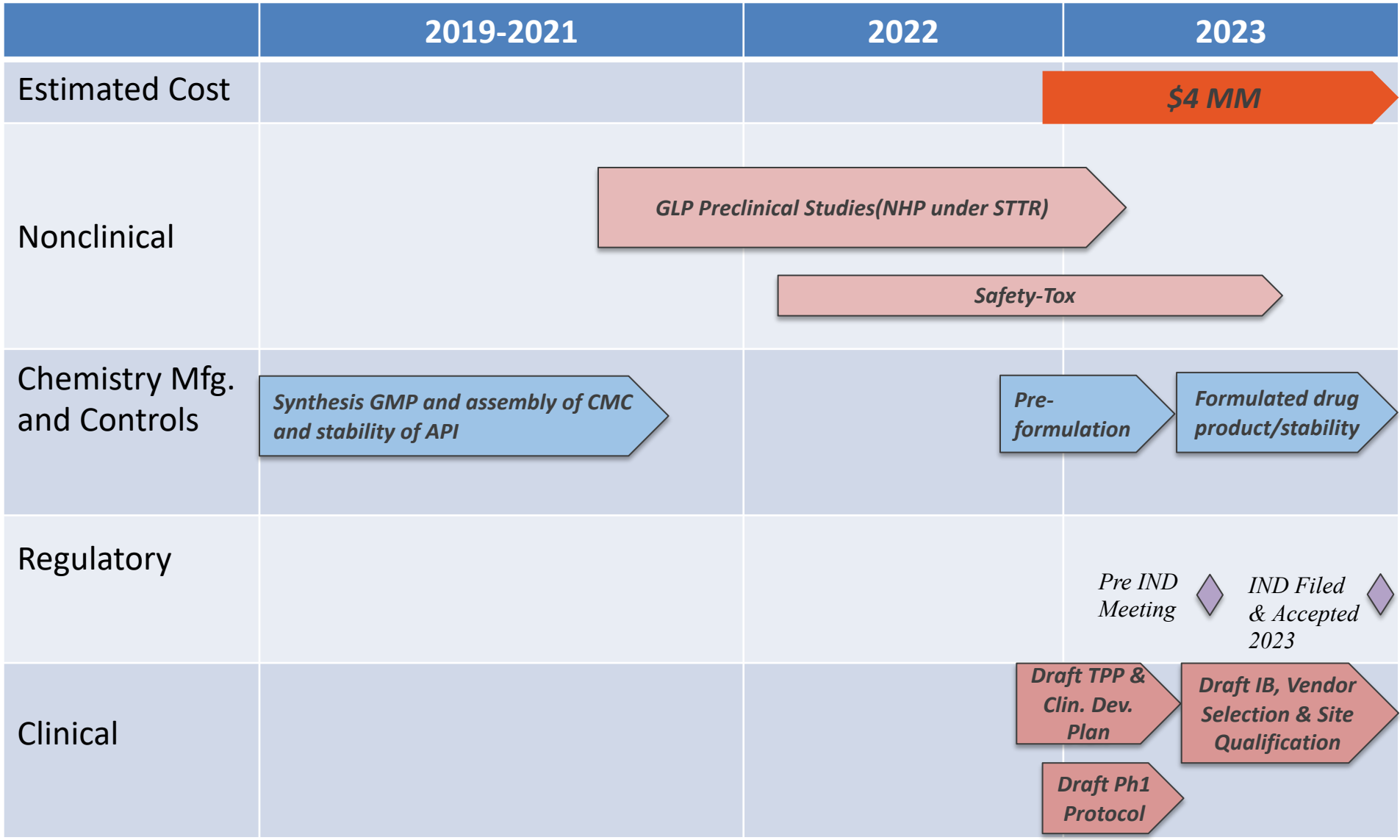
Development Timeline: LGM1506 ASTHMA



Device Indication for EX VIVO Human Donor Lungs

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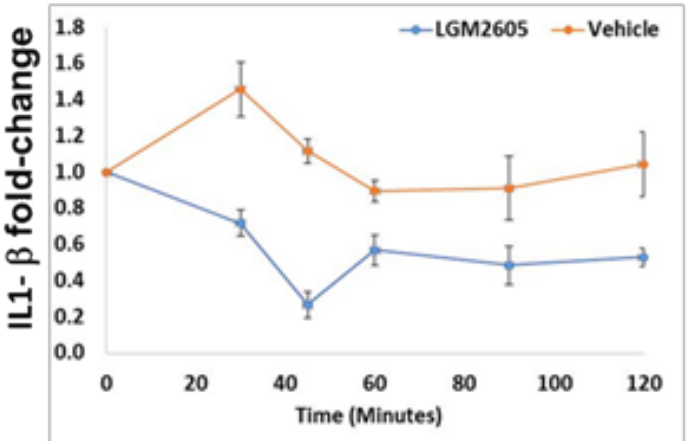
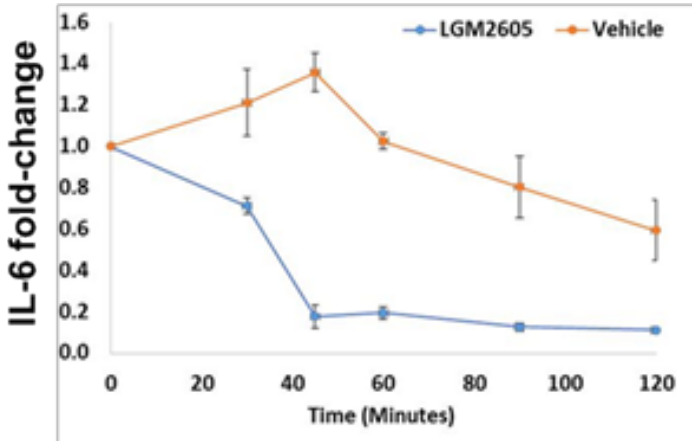
LignaMed Transplant Indications

- Device regulatory pathway for use in Ex Vivo Lung Perfusion (EVLP) to rehabilitate donor lungs
- Device regulatory pathway for organ preservation
- IND for administration to recipient post transplant – lung and kidney

Effects of LGM2605:
Cytokine gene expression levels decrease





**Gene expression levels determined in lung biopsies*

Summary – Lung Transplant Device

- LGM2605 prevents lung tissue senescence
- LGM2605 prevents lung ischemia/reperfusion induced damage
- Regulatory
  - FDA background package submitted July 2017, meeting with FDA held on November 8th, 2017.
  - FDA suggested several options for accelerating time to market

Lung Preservation

- Protocol follows established clinical practice for removal of lung and perfusing then submerging in **Perfadex supplemented with LGM2605.** Done at time of organ removal.

- Data completed in:
  - C57/Bl6 mouse (n=4)
  - human ex vivo lung (n=3)

LGM2605 Treatment of Ex-Vivo Human Donor Lungs Reduces:

- ICAM-1 Expression
- IL-6 Expression
- TGFb Expression
- TNF Expression
- IL-1b Expression
- NLRP3 Expression

(All data Statistically Significant-Statistical Analyses available)

TEAM

Melpo Christofidou-Solomidou, PhD
Founder

Key Opinion Leader in antioxidants in lung disease and pre-clinical models; Adjunct Professor of Medicine University of Pennsylvania

David Leach, MBA
Chief Executive Officer

Former Merck Executive Expertise in product marketing through the lifecycle; cross functional leadership with research and development, commercial functions and manufacturing

Thais Sielecki, PhD
Chief Scientific Officer

Drug development expert Expertise in research & development, regulatory, manufacturing and Intellectual Property Cytokine, Bristol-Myers Squibb, Dupont Merck

ADVISORS

Jim Harris, MBA
Board Chair

Jim is a former Merck Executive who led US Mature Brands Unit He has 30 years in Life Sciences and is a serial entrepreneur with expertise in business creation, commercialization, brand marketing

Edward Cantu III, MD
Scientific Advisory Board

Dr. Cantu is Associate Professor of Surgery, Associate Director of Lung Transplantation, Director of Ex Vivo Lung Perfusion Center, Hospital of the University of Pennsylvania

Angela Haczku, MD/PhD
Scientific Advisory Board

Professor of Medicine, Director of the UC Davis Lung Center and Associate Dean for Research at the UC Davis School of Medicine. She is a respiratory immunologist and a key opinion leader in asthma research.

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ADVISORS

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President at DJA Pharma, a regulatory and medical affairs consulting group with emphasis on FDA communications and strategic drug development

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George Moker, CPA
Accounting & Tax

Director, Ambrosi CPA an accounting firm that specializes in SBIR accounting, government contracting and Human Resources services

Summary

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