



## Tolimidone

A novel Phase 2b clinical stage drug candidate to treat Type 2 Diabetes

*Melior Pharmaceuticals is pioneering work in the area of lyn kinase activation. Tolimidone is the most advance lyn kinase activator from Melior's pipeline, currently in development for Type 2 Diabetes Mellitus (T2DM) and nonalcoholic steatohepatitis (NASH).*

### Strong emerging profile in T2DM

- Novel mechanism: Lyn kinase activator that improves insulin sensitivity and lipid regulation
- Positive Phase 2a clinical data demonstrating:
  - Robust pre- and post-prandial glucose lowering
  - Once daily oral dosing
  - Favorable impact on lipid profile
  - Evidence of weight loss
  - Good safety and tolerability
- Predicted  $\beta$ -cell preservation based on in vivo data
- Phase 2b enrollment completed; results expected Q1 2019
- 300 clinical exposures to date and over 700 total clinical exposures expected by Q1 2019

## Overview

Melior Pharmaceuticals Inc. is developing tolimidone, a Phase 2 clinical stage candidate for treatment of type 2 diabetes and metabolic disorders. Tolimidone is a “next-generation” insulin sensitizer and lipid regulator that exerts its activity independently of the PPAR mechanism.

Tolimidone improves glycemic control by directly and selectively activating the enzyme Lyn kinase, which has been shown to modulate the insulin-signaling pathway<sup>1</sup>. MLR-1023 is the first described specific and direct activator of Lyn kinase that elicits glycemic control by potentiating insulin activity<sup>2,3</sup>. The mechanism has been validated clinically in a recently completed Phase 2 POC study<sup>4</sup>.

### Emerging Tolimidone Profile in Type 2 Diabetes

#### Dosing

- Once daily oral administration

#### Efficacy

- Glucose: Clinically significant glucose lowering as a monotherapy
- Lipids: Reduction in triglycerides
- Weight: Early evidence of weight reduction

#### Safety

- No meaningful risk of hypoglycemia

#### Tolerability

- Well-tolerated, with few drug-related discontinuations

#### Disease Modification

- Potential beta-cell sparing effect
- Potential improvement in beta-cell function

#### Combination Therapy

- Efficacy and safety profile create optionality for multiple drug combinations, including, metformin, DPP-IV inhibitors, SGLT-2 inhibitors and GLP-1s

## Background

Tolimidone was previously developed by Pfizer up to Phase 2 for gastric ulcers and demonstrated safety and tolerability in several clinical studies. Post-hoc analysis of blood glucose measures from the Pfizer trials provided an early indication that the drug had therapeutic potential in diabetes.

Melior Pharmaceuticals has since been studying tolimidone in type 2 diabetes.

Melior recently completed a successful 130-patient, Phase 2a proof of concept study in diabetes. Top line analysis revealed statistically and clinically significant improvements in both MMTT (mixed meal tolerance test) and FPG (fasting plasma glucose).

Improvements were also observed in all lipid parameters and there was evidence of weight loss, consistent with animal data<sup>4</sup>.

Tolimidone has the potential to become an important new therapeutic option for treating type 2 diabetes, based on results of the Phase 2a proof of concept study, as well as evidence from a breadth of *in vivo* preclinical models, as well as preclinical and clinical safety data up to 9 months in duration.

### **Partnering Thesis**

Melior has partnered MLR-1023 with Bukwang Pharmaceutical Co (Seoul, Korea) for Asia rights, excluding Japan. Bukwang and Melior have funded the development program up to Phase 2b.

Melior is now seeking Phase 3 co-development who have an interest commercial rights for North America, Europe, Japan and “rest of world” territories (excluding Asia).

### **Team and Track Record**

Melior Pharmaceuticals is a mid-staged biopharmaceutical company developing a pipeline of de-risked, molecules in therapeutic areas of significant unmet need. Our management team has had a track record of success identifying and developing de-risked drug targets that have potential for accelerated clinical development in therapeutic areas with significant unmet needs. <sup>Note 1</sup>

### **For Further Information Please Contact:**

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1. Müller, G. (2000) *The molecular mechanism of the insulin-mimetic/sensitizing activity of the antidiabetic sulfonylurea drug Amaryl. Mol. Med. 6(11): 907-933.*
2. Saporito, S., et al (2012) MLR-1023 is a potent and selective allosteric activator of lyn kinase in vitro that improves glucose tolerance in vivo. *J Pharmacol. Exp. Ther. 342: 15-22.*
3. Ochman, A.R. et al (2012) *The lyn kinase activator MLR-1023 is a novel insulin receptor potentiator that elicits a rapid-onset and durable improvement in glucose homeostasis in animal models of type 2 diabetes. J Pharmacol. Exp Ther. 342: 23-32.*
4. Greenway, F, et al. *Clinical POC for an Anti-Diabetic Agent with a Novel Mechanism for Reducing Insulin Resistance. Poster presentation at Am. Diabetes Assoc. 76<sup>th</sup> Scientific Session, New Orleans, LA, 2016*

## Note 1

### **Management Team**

#### **Andrew Reaume, PhD, President & CEO**

Dr. Reaume founded Melior Discovery Inc fourteen years ago and built it into a robust self-sustaining drug discovery organization. He subsequently spun off two sister companies with proprietary clinical stage candidates (Melior Pharmaceuticals I, Inc., Melior Pharmaceuticals II, LLC). As he has grown, first Melior Discovery, and then launched and grown the Melior Pharmaceutical companies he has been responsible for raising over \$15 MM of investment capital and completed over \$40MM in partnering deals including research partnerships with global pharmaceutical companies. He was responsible for spearheading and continues to oversee a complex global development partnership with an Asian pharmaceutical partner. Dr. Reaume's previous experience includes leadership roles in drug discovery and business analytics at Pfizer and Cephalon with more than twenty-five years of experience in the pharmaceutical industry.

#### **Mahen Gundecha, BSc, MBA, Chief Business Officer**

Mahen Gundecha is a seasoned health sciences leader with extensive business development, alliance management, new product commercialization and franchise P&L leadership experience across a range of companies, including Juno Therapeutics (Celgene), Novartis Group, Novo Nordisk, Endo Pharmaceuticals and GSK. Mahen has had hands on experience building business development strategies in multiple therapeutic areas and has executed foundational deals. Mahen's most recent experience has involved managing complex global oncology and gene editing partnerships, spanning R&D, manufacturing and commercialization. Mahen brings a broad base of therapeutic experience to Melior, including Neurosciences, Endocrinology, Hematology, Oncology, Rare Diseases, Cell Therapeutics and Gene Editing. Mahen will be leading investment and business development activities at Melior.

#### **Ramana Kuchibhatla, PhD, Senior VP of Clinical Development & Biostatistics**

Over the span of his career, Dr. Kuchibhatla has built deep experience in Clinical Development, Biostatistics and Data Management within large and small pharmaceutical companies. He has led filing of multiple INDs and sNDAs, including Zyban® and Lamictal® and has helped to bring several NCEs into clinical development. He was closely involved in several successful in-licensing and out-licensing deals. He is leading development of accelerated clinical development and registration strategies to shorten time to pivotal data read outs. Dr. Kuchibhatla's previous experience includes leadership roles at GSK, Targacept and QED Pharma.

#### **Vivian Cong, PhD, Head of Cardiovascular and Metabolic Disease**

Dr. Cong has 12 years of research experience in metabolic diseases including diabetes, obesity, fatty liver disease and NASH. She was a pioneer in the field of NASH having established one of the first comprehensive and predictive animal models to assess development of fatty liver disease and NASH and has authored or co-authored over 20 peer-reviewed articles in metabolic diseases and NASH. She has also had extensive experience in metabolic alterations in neurodegenerative diseases including Alzheimer's disease and Parkinson's disease. Dr. Cong conducted her postdoctoral training at the Hospital for Sick Children in Canada and was a research fellow at the US National Institute on Aging where she worked closely with Dr. Josephine Egan, the investigator responsible for first describing the GLP-1 receptor as a promising therapeutic target.