

### **Safe Harbor**

This presentation contains forward-looking statements. For example, we are using forward-looking statements when we discuss clinical trials, including the timing thereof and potential approvals of products, catalysts and milestones, pipeline and the potential benefits of products, including in each case those of Oravax. These forward-looking statements are based on the current expectations of the management of Oramed only, and are subject to a number of factors and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements, including the risks and uncertainties related to the progress, timing, cost, and results of clinical trials and product development programs; difficulties or delays in obtaining regulatory approval or patent protection for our product candidates; competition from other pharmaceutical or biotechnology companies; and our ability to obtain additional funding required to conduct our research, development and commercialization activities. In addition, the following factors, among others, could cause actual results to differ materially from those described in the forward-looking statements: changes in technology and market requirements; delays or obstacles in launching our clinical trials; changes in legislation; inability to timely develop and introduce new technologies, products and applications; lack of validation of our technology as we progress further and lack of acceptance of our methods by the scientific community; inability to retain or attract key employees whose knowledge is essential to the development of our products; unforeseen scientific difficulties that may develop with our process; greater cost of final product than anticipated; loss of market share and pressure on pricing resulting from competition; laboratory results that do not translate to equally good results in real settings; our patents may not be sufficient; and finally that products may harm recipients, all of which could cause the actual results or performance of Oramed to differ materially from those contemplated in such forward-looking statements. Except as otherwise required by law, Oramed undertakes no obligation to publicly release any revisions to these forward-looking statements to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events. For a more detailed description of the risks and uncertainties affecting Oramed, reference is made to Oramed's reports filed from time to time with the Securities and Exchange Commission.

## **Oramed Snapshot**



#### **COMPANY OVERVIEW**

- Proprietary oral protein delivery platform
- Diabetes first initially targeting the lucrative insulin market
- NASDAQ/TASE: ORMP



#### SIGNIFICANT PIPELINE, IP, AND CATALYSTS

- Robust pipeline leveraging IP portfolio for additional significant market opportunities
- 88 granted patents, 35 pending patent applications, worldwide
- Multiple value-creation events for 2023



#### **KEY FINANCIAL METRICS**

- Strong financial position
- ~\$160M1 in cash and investments
- No debt



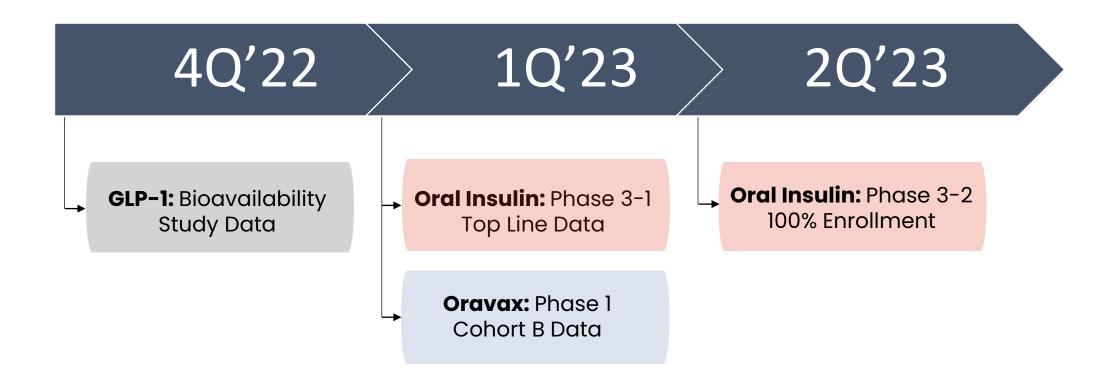
#### **COMPANY MANAGEMENT**

Experienced management team backed by worldclass scientific experts

As of September 30, 2022 (unaudited)



## **Upcoming Catalysts**



## **Proprietary Technology for Oral Drug Delivery**

Proteins and Peptides do Not Survive the Digestive System



#### Harsh pH

Stomach acidity cleaves and shreds protein



Oramed Technology Protects Drug Integrity and Increases Absorption

#### pH shield

Sensitive enteric coating protects capsule contents before entering small intestine





#### **Protease attack**

Proteases attack and break down proteins



#### **Protease protection**

Protease inhibitors protect the active agent





#### **Absorption barrier**

Therapeutic proteins fail to be absorbed via the intestinal wall (barrier)



Assists the permeation of proteins/ peptides across intestinal membrane and into bloodstream



## Multiple Clinical-Stage Programs

PHASE 1 PHASE 2 PHASE 3

ORMD-0801 (Oral Insulin) Diabetes

ORMD-0801 (Oral Insulin) NASH

ORMD-0901 (Oral GLP-1)

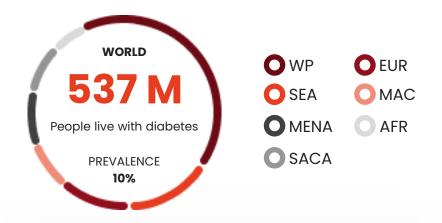
Oravax's Oral Covid-19 Vaccine
Phase 1 Trials Ongoing





## 1 in 10 Adults Globally Have Diabetes



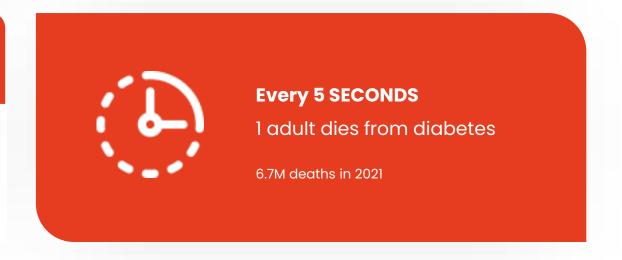


#246 Million
Expected increase

2021

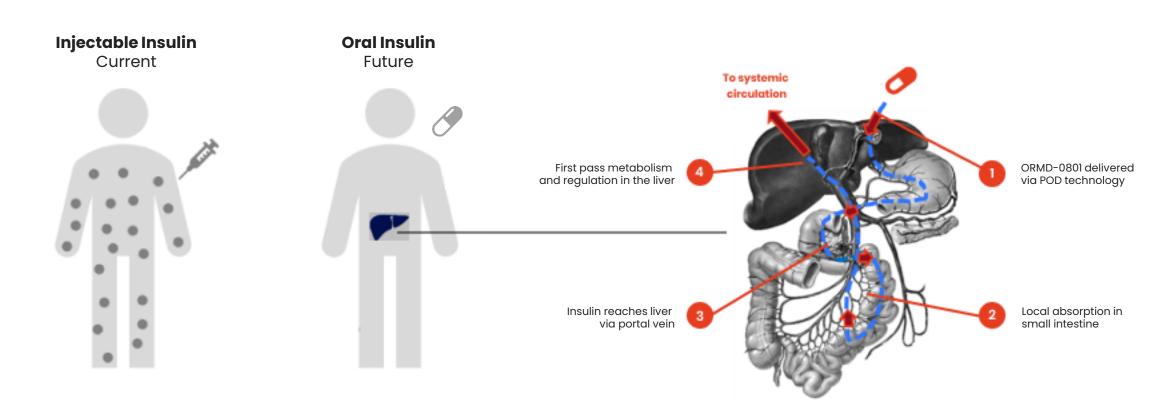
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2045





## Oral Insulin Mimics the Delivery of Endogenous Insulin



Injectable insulin is introduced directly to the bloodstream, with only a small fraction reaching the liver, where endogenous insulin is regulated

ORMD-0801 is delivered orally with first pass metabolism occurring in the liver, mimicking endogenous insulin regulation before reaching the bloodstream, thus reducing risks and complications associated with injectable insulin and enabling earlier patient engagement

# Oral Insulin: Significant Advantages Over Injectable Insulins



#### IMPROVED BLOOD GLUCOSE CONTROL

Insulin is regulated endogenously in the liver, limiting the amount of excess systemic insulin that can lead to hypo/hyper-glycemic events.



#### **NO WEIGHT GAIN**

Better insulin control prevents cells from absorbing excess glucose that can be converted to fat and lead to weight gain



#### **EASE OF ADMINISTRATION**

Oral delivery benefits diabetic patients with a fear of needles and should improve patient administration and compliance

## ORMD-0801 for Type 1 & Type 2 Diabetes

Diabetes inhibits the production of sufficient insulin and causes elevated levels of glucose in the blood

#### **TYPE 1 DIABETES**

- TID is autoimmune: The body destroys its own insulinproducing (beta) cells, leaving patients completely dependent on external insulin sources
- 10% of diabetics have T1D: Up to 54 million people worldwide have T1D
- Projected Market: \$24 billion by 2029

#### **TYPE 2 DIABETES**

- T2D is metabolic: The body becomes insulin resistant. Injections
  may be used to make up for the pancreas's inability to create
  sufficient insulin to keep blood sugar at normal levels
- 483 million people worldwide need treatment
- Projected Market: \$92 billion by 2029



## ORMD-0801 for Type 1 Diabetes (T1D)

## TID PATIENTS ARE TREATED WITH VARIOUS TYPES OF INSULIN REPLACEMENT THERAPY

- Long-acting insulin (basal) helps maintain stable insulin levels during fasting periods
- Rapid-acting insulin (bolus) prior to each meal to stabilize blood sugar
- Administration is via injection or pump

#### **ORAMED ORAL INSULIN**

- Easier use and reduced systemic exposure
- Potentially reducing multiple daily injections
- Tighter regulation and control of blood sugar levels by directly targeting liver glucose (TiR), due to portal administration

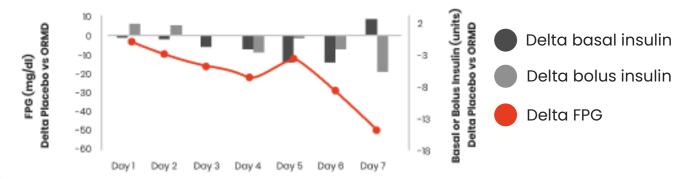


## Phase 2a Trial in T1D Completed

By directly targeting liver glucose, ORMD-0801 may provide tighter blood sugar regulation and control for the ~1.6M¹ Type 1 diabetes patients in the US – potentially reducing the need for multiple daily injections, including mealtime insulin.

#### Oral Insulin Reduces Exogenous Insulin Requirements

- Oral insulin met primary endpoint of reducing exogenous insulin requirements in Phase 2a T1D study
- Oral insulin decreased use of rapid-acting insulin, level of post-meal glucose, and levels of daytime glucose
- Additionally, day and night blood glucose levels were lower compared to control group



### T1D Phase 2a Highlights <sup>2</sup>

- 25 TID patients
- 7 Days of treatment
- Times a day (at mealtime)

## Phase 2 – Completed 180 Patient Trial for T2D



**US Sites** 



Patients



Day Treatment



Dose Groups 28 Day Treatment <sup>1</sup>

#### **Design**

Double-blind, randomized, placebo-controlled, 4 week, once daily (3 capsules) treatment

### Study Population

Enrolled patients with T2D who (1) are being treated by diet and exercise, (2) are untreated with antidiabetic medications, or (3) are treated with metformin as a monotherapy or in combination with one other antidiabetic drug (excluding insulin)

#### **Endpoints**

- **Primary:** mean nighttime glucose levels <sup>2</sup>
- **Secondary:** mean 24-hour glucose <sup>1</sup>, percent change in CGM mean fasting glucose between treatment and run-in; change from baseline to Week 4 of morning fasting c-peptide; percent change in AIC from Baseline to Week 4

#### **Dose Cohorts**

- Placebo: 3x placebo capsules
- Active: 16mg (1 dose/capsule) and 24mg (1.5 dose/capsule)

<sup>&#</sup>x27;Trial only had I dose level, but patients were given either a full dose, or 1.5 doses.

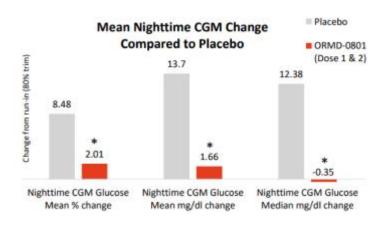
<sup>&</sup>lt;sup>2</sup> Based on 2 nights of CGM data by comparison of the mean percent change between Baseline and Week 4 of ORMD-0801 and placebo groups

# Phase 2 Trial Demonstrated No Drug Related Serious Adverse Events and Promising Efficacy on CGM Parameters

#### 1st

#### **Primary Endpoint**

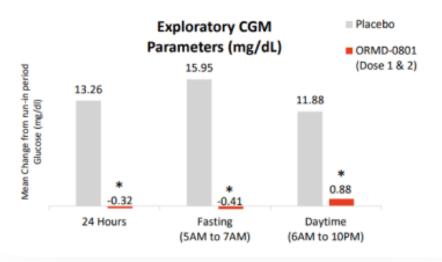
- Achieved primary endpoint and showed significant positive effects
- Safe/well-tolerated with no drug related serious adverse events
- Dose groups 1 & 2 are pooled on weighted mean nighttime glucose levels
- All ORMD-0801 values statistically significant versus the placebo (p-Value<0.05)



#### 2nd

#### **Exploratory Endpoints**

- ORMD-0801 showed promising reductions in mean 24-hour, fasting, and daytime glucose levels
- All ORMD-0801 values statistically significant versus the placebo (p-Value<0.05)</li>



<sup>(\*)</sup> Indicates statistically significant difference versus placebo (p-Value < 0.05)

## Phase 2b – Completed 298 Patient Trial for T2D



US Sites 1



Patients <sup>1</sup>



Day Treatment



Dose Groups 28 Day Treatment

#### Design

Double-blind, randomized, placebo-controlled, 12-week, once/twice/or three times daily treatment

#### Study Population

Patients with T2D who are taking metformin only (at least 1500 mg or maximally tolerated dose) or metformin in addition to no more than two of the following: Glibenclamide, Glipizide, Empagliflozin, Pioglitazone, Glimepiride, Dapagliflozin, Sitagliptin, Glibomet, Ertugliflozin

#### **Endpoints**

- Primary: mean change in A1C from Baseline to Week 12 of treatment period
- Secondary: safety (AES, hypoglycemic events); fasting plasma glucose (FPG) + CGM; weight

#### **Dose Cohorts**

Placebo comparator for each cohort

**8 mg/day** (8 mg, lx/day)

16 mg/day (8 mg, 2x/day or 16 mg, 1x/day) **32 mg/day** (32 mg, 1x/day or 16 mg, 2x/day)

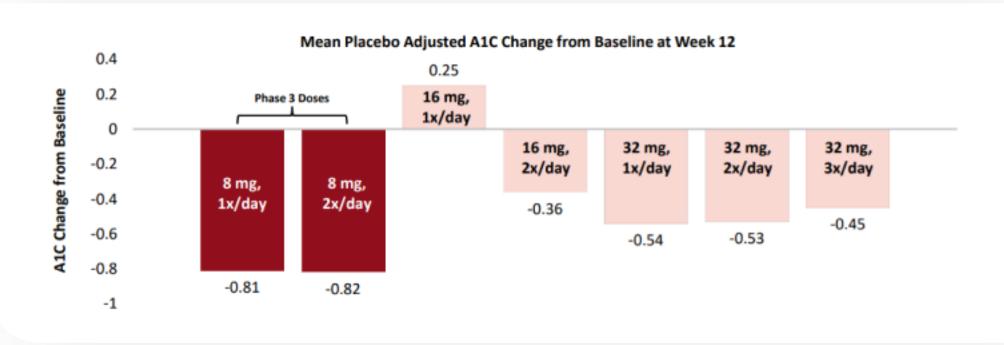
**64 mg/day** (32 mg, 2x/day)

**96 mg/day** (32 mg, 3x/day)

(1) 36 Sites: 2 sites (49 subjects) were excluded due to significant treatment by center interaction; 347 subjects received primary treatment and had baseline Alc (included in ITT); 298 subjects included in primary analysis; 266 included in final analysis (Week 12 AlC results)

# ORMD-0801 Phase 2b Achieved Safety and Primary Endpoints

- Achieved primary efficacy endpoint in reduction in A1C at Week 12
- The 8 mg once-daily and twice-daily arms achieved statistically significant values at Week 12 vs. Placebo (p-value 0.028 and 0.029, respectively)

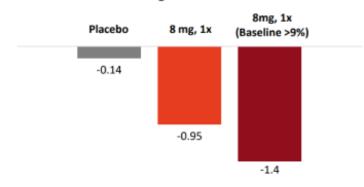


# ORMD-0801 Phase 2b Exhibited Strong A1C Lowering Activity at 8 mg 1x/Day Dose

#### Significant AIC lowering with 8 mg, 1x/day dose

- 8 mg 1x/day showed 0.95 (0.81 placebo adjusted) reduction in A1C (p=0.028)
- 8 mg 1x/day for patients with baseline A1C >9% showed 1.40 (1.26 placebo adjusted) reduction in A1C

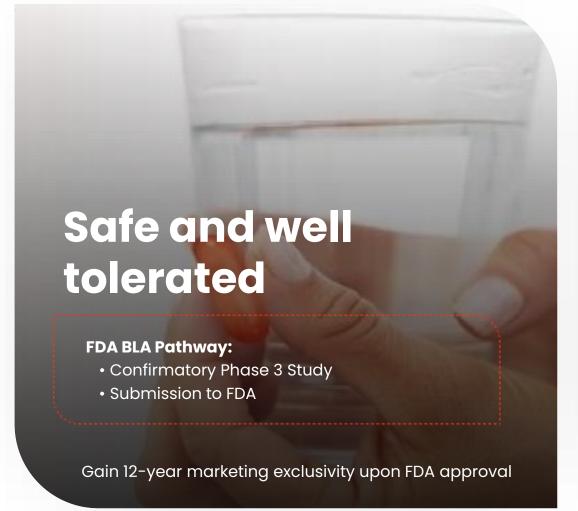
#### Mean A1C Change from Baseline at Week 12



## ORMD-0801 upheld safety profile previously exhibited in first Phase 2 study

- No increase in Serious Adverse Events compared to Placebo
- No increase in Hypoglycemic Events compared to Placebo
  - 6.1% (5/82) of subjects in placebo group compared to 0% (0/15) of subjects in 8mg 1x/day had at least 1 hypoglycemic event
- On weight gain compared to Placebo at Week 12

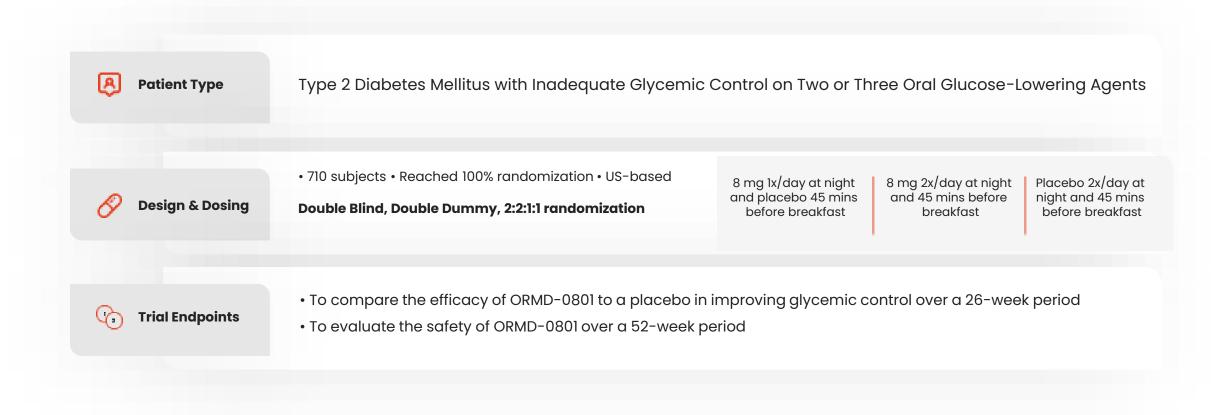
# FDA Phase 2b Trial Results Primary Endpoint Successfully Met



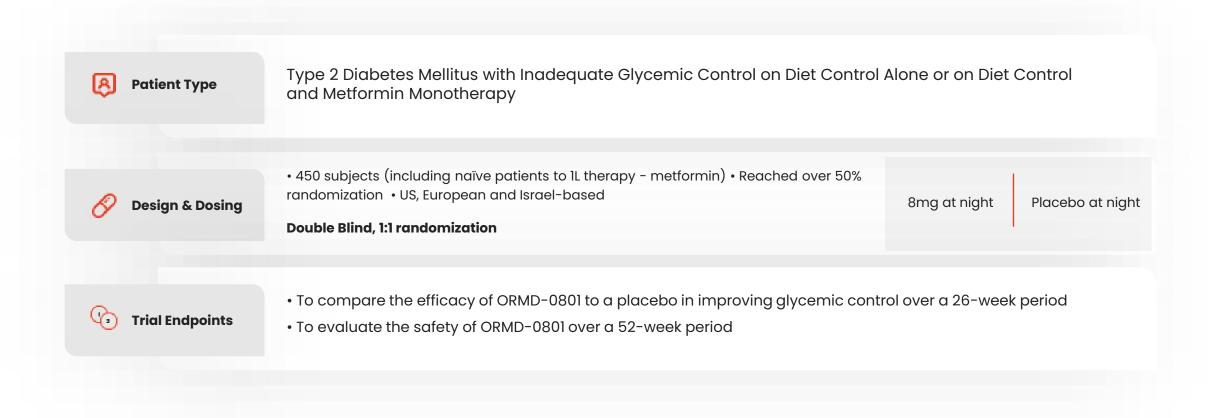




# Two Pivotal Phase 3 Trials will Maximize ORMD-0801's Success in the Market: ORA-D-013-1



# Two Pivotal Phase 3 Trials will Maximize ORMD-0801's Success in the Market: ORA-D-013-2





# Oramed Commissioned IQVIA to Perform Market Research in the US, UK and EU

Country	Endos	PCPs	Total
	19	21	40
1 b 1 b	13	12	25
	14	12	26
	13	12	25
	14	12	26
	15	13	28
Total	88	82	170



Note: Sample size selected to ensure appropriate N size to support PMR data analytics



# HCPs Were Receptive to Prescribing Oral Insulins and ORMD-0801, If Approved

Most of the prescribers (85%+) were willing to prescribe oral insulins or ORMD-0801, if approved

## Future Willingness to Prescribe (n=170)

	Willingness to prescribe oral insulin (A)	Willingness to prescribe ORMD- 0801 (B)
Definitely would NOT prescribe	0%	0%
Probably would NOT prescribe	2%	1%
Might or might not prescribe	20%	22%
Probably WOULD prescribe	53%	57%
Definitely WOULD prescribe	23%	20%

No HCPs listed that they would definitely not prescribe the product, indicating high interest

ORMD-0801 appears to meet physician expectations for an oral insulin given minimal change in their response after seeing the ORMD-0801

profile



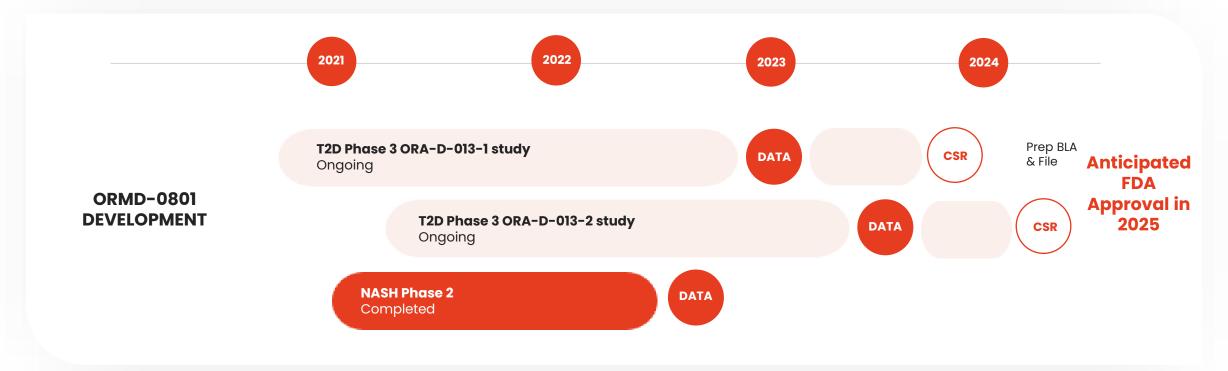
Q: What is your willingness to prescribe oral insulins for T2D patients, if oral insulins were launched in the market?

Q: What is your willingness to prescribe Product X (ORMD-0801) for T2D patients, if it was launched in the market?

Source: IQVIA market research of treating physicians (n=170 Endos and PCPs) in the US and Europe (UK/EU4), December 2021



## ORMD-0801's Robust Clinical Development Program has Paved the way Towards Anticipated Approval











### **Strong Efficacy**

(1) Includes all clinical studies across all indications, including formulation studies

#### **DEVELOPMENT HIGHLIGHTS:**

- First T2D Phase 3 trial 100% randomization
- Second T2D Phase 3 trial 50% randomization
- Phase 2 in NASH and potential future TID

studies support additional upside

## China License Deal: 500M patient potential





#### **DIABETIC**

(10.9% of adult population)



#### **PREDIABETIC**

(35.7% of adult population)

#### LICENSEE: HEFEI TIANHUI ("HTIT")

Owns with Sinopharm a state-of-the-art GMP API insulin manufacturing facility

HTIT clinical trials of ORMD-0801 underway

#### \$50M PAYMENTS + ROYALTIES:

- \$12M in restricted stock (at premium)
- \$38M milestone payments
  - \$33M received to date
- Up to 10% royalties on net sales

## South Korea Commercial Distribution Agreement

### **Agreement:**

Exclusive distribution rights to ORMD-0801 in South Korea



#### South Korean Partner: Medicox Co., Ltd.

- Medicox (Kosdaq: 054180) is an emerging pharmaceutical R&D company
- Has built an excellent consortium of partnerships across established leaders in South Korea
- Responsible for local regulatory approval
- 10 year license to commercialize oral insulin in South Korea

# 1 in 7 South Korean adults have diabetes

#### **MILESTONE PAYMENTS + ROYALTIES:**

- \$18M in potential milestone payments
  - \$2M received to date
- Up to 15% royalties on gross sales
- Medicox to purchase ORMD-0801 from Oramed at fixed transfer price



## Phase 2 Trials for T2D with NASH Completed

With direct action on the liver, ORMD-0801 has the potential to address diabetics suffering from NASH, a population with increased mortality.

#### Positive clinical results in completed pilot study of NASH\*

- Open label, 90-day treatment, N = 9 T2D patients with NASH, 8mg x2/x1 morning
  - Efficacy: 30% relative reduction measured by MRI-PDFF; 6.9±6.8% mean reduction in liver fat content (p value: 0.035)
  - Safety: No drug-related serious adverse events

**Patients** 

**Day Treatment** 

### Positive Phase 2 trial results reported: Safety & Efficacy of ORMD-0801

#### Design

- Double-blind, randomized, placebocontrolled, multi-center study
- 90-day treatment

- 32 T2D patients with NASH
- 8mg x1/x1 morning & 8mg x1/x1 night
- US and Israel

### Study **Population**

32 Patients with T2D, fat concentration in the liver of moderate steatosis (>8% liver with steatosis)

#### **Endpoints** Reached

Primary endpoint met: ORMD-0801 was safe and well tolerated with no treatment-related adverse events Secondary endpoint met: Showed clinically meaningful reduction of liver fat from baseline at 12 weeks

# Positive Phase 2 NASH trial results reported: Achieved Safety and Primary Endpoints

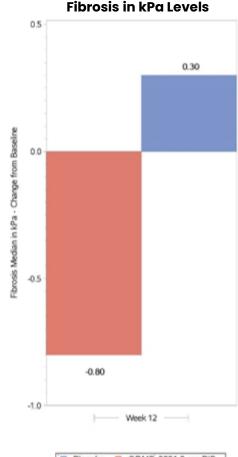
### **Safety Data Summary**

 Primary objective of safety met with no serious adverse events and no difference in the incidence rate of adverse events between ORMD-0801 and placebo.

### **Efficacy Data Summary**

- Secondary objective of reducing liver fat content in patients with NASH and T2D Percent Change from Baseline to Week 12 in MR PDFF (%):
  - Liver Segment 3 (left lobe) showed placebo adjusted mean decrease of 1.8 with placebo adjusted median decrease of 5.7 for ORMD-0801
- Exploratory objective of median change from baseline in Fibroscan fibrosis levels:
  - Median Change from Baseline to Week 12 in Fibrosis Median (kPa) showed placebo adjusted median decrease of 1.1 for ORMD-0801.
  - Median change from Baseline to Week 12 in Steatosis Median (dB/m) showed placebo adjusted median decrease of 29 for ORMD-0801.

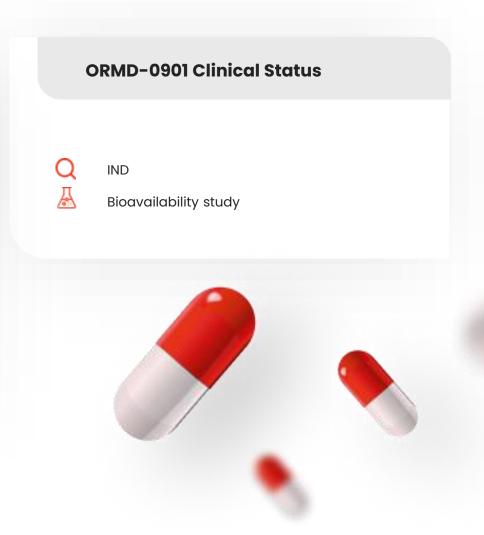




Median change in Fibroscan

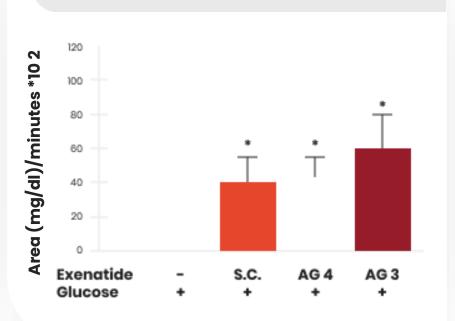
## GLP-1 Analog: ORMD-0901 for Oral GLP-1 (T2D)

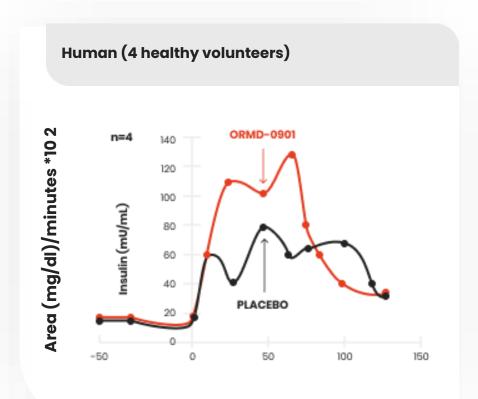
## **GLP-1** Analog T2D medication Mimics the natural hormone in the body Compelling safety profile Decreases blood glucose levels Preserves beta cell function Effectively reduces HbA1c Promotes weight loss



### **Oral GLP-1 - ORMD-0901**

Preclinical: Oral exenatide delivery amounted to a >50% reduction in mean glucose (similar to SC)





ORMD-0901 formulations

Preserved the biological activity of orally delivered exenatide. ORMD-0901 successfully curbed blood sugar excursions following glucose challenge

# Oravax | Novel Oral Vaccine Company





The Oravax technology integrates Premas Biotech's D-Crypt™ technology with an oral delivery platform from Oramed Pharmaceuticals based on their proprietary POD™ delivery technology.

#### **JOINT VENTURE**

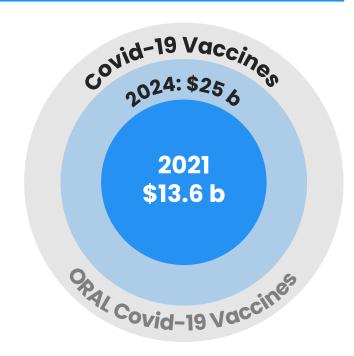
Oramed is the majority shareholder of Oravax (63%)

#### **LICENSE**

- Royalties: 7.5% of net sales

- Sublicensing: 15%

- Sales milestone: \$25M - \$100M



# Oravax | Advantages

Triple antigen vaccine expected to be effective against COVID variants

#### **Manufacturing Advantages**



Ease of scale up



Straight-forward tech transfer



Manufacturing and COGs optimization



Consistent process

#### **Oral Format**



No needles



Easy to administer at home (no need for professional administration)



No need for low temperature storage (freezer)



Potential for further reduction in side effects (greater safety)

#### Safe, non-toxic, and efficacious in preclinical and GLP Tox studies in animals:

- No temperature rise, no body weight loss/gain, no adverse events noted in any animal
- Significant antibody response, as well as cellular immune response
- Long term retention of the antibody response in animals, post 150 days



## Oravax | Highlighted Milestones

#### 50/50 Joint Venture with Genomma Lab



- Commercialize Oral COVID-19 Vaccine in Mexico
- Drive Business in LATAM
- Contribute to oral vaccine's clinical, regulatory,
   and commercial activities
- Participate in a future investment in Oravax

#### **Collaboration Agreement with Tan Tanh Holdings**



- Pre-purchase of 10 million oral COVID-19 vaccines
- TTH to commercialize Oral COVID-19 Vaccine in

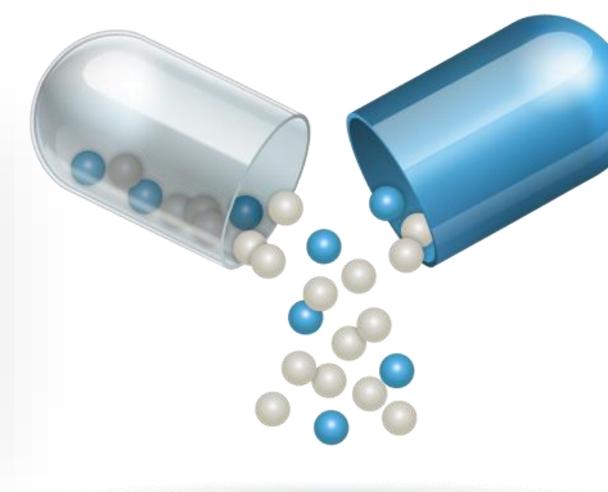
  ASEAN
- Oravax obtained approval from Vietnam MOH to run P2/3 in Vietnam
- TTH to contribute to funding of clinical trials



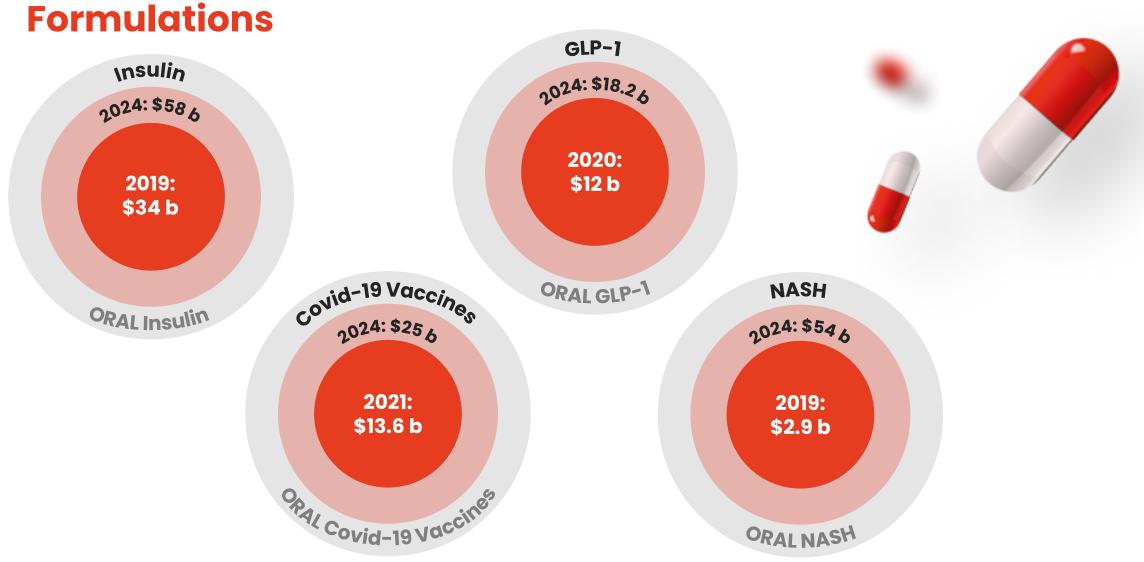
## Oravax | Phase 1 Trial Ongoing

#### **South Africa**

- Open-label
- N=24 naive participants (no prior COVID-19 vaccine or infection)
- Endpoints:
  - Safety & tolerability
  - Efficacy
- Cohort A (12 participants) **positive data received** Q3 2022
- Cohort B (12 participants) data expected Q1 2023



Funneling Huge Injectable Drug Markets to Novel Oral



## **Management Team**



Nadav Kidron, Esq, MBA
Chief Executive Officer & Director

Entrepreneur whose experience includes decades of senior executive roles in a wide range of industries including business, law and technology



**Josh Hexter**Chief Operating & Business Officer

More than 18 years of prominent leadership roles in biotech and pharma



Miriam Kidron, PhD
Chief Scientific Officer & Director

Senior Researcher at the Diabetes Unit of Hadassah Medical Center for more than 25 years



Netanel Derovan
Chief Legal Officer

Highly accomplished executive leader, having spent over 20 years in senior legal positions.



David Silberman, CPA
Chief Financial Officer

Extensive experience in corporate financial management



Michael Rabinowitz
Chief Commercial Officer

Over two decades of experience in launching and marketing new medications and treatments

### **Board of Directors**

#### NADAV KIDRON, ESQ, MBA

Chief Executive Officer, President & Chairman

Entrepreneur whose experience includes decades of senior executive roles in a wide range of industries including business, law and technology

#### **ARIE MAYER, PH.D**

**Independent Director** 

Managing Director and Chairman of the Board of Merck Life Science Israel

#### **LEONARD SANK**

**Independent Director** 

Entrepreneur and business leader; Director of Macsteel Service Centres SA (Pty) Ltd

#### **YADIN ROZOV**

**Independent Director** 

Investment professional with experience in capital markets, corporate finance, investment banking, and investment management. Founder and Managing Partner at Terrace Edge Ventures LLC.

#### **MIRIAM KIDRON, PH.D**

Chief Scientific Officer & Director

Senior Researcher at the Diabetes Unit of Hadassah Medical Center for more than 25 years



## **Scientific Advisory Board**

#### **ROY ELDOR, MD, PHD**

Director, Diabetes Unit, Institute of Endocrinology, Metabolism & Hypertension, Tel-Aviv Medical Center.

### AVRAM HERSKHO, MD, PHD; NOBEL LAUREATE

Distinguished professor in the biochemistry unit in the B. Rappaport Facility of Medicine, Technion, Haifa, Israel.

#### JAY SKYLER, MD, MCAP

Professor of Medicine, Division of Endocrinology, Diabetes & Metabolism, Department of Medicine, University of Miami.

#### **ELE FERRANNINI, MD, PHD**

Professor, Internal Medicine, University of Pisa School of Medicine. Past President of the EASD.

#### **HAROLD JACOB, MD**

Chief Medical Officer, NanoVibronix. Previously, Director, Medical Affairs at Given Imaging.

#### **ANNE PETERS, MD**

Professor of Medicine at Keck School of Medicine of USC and Director of the USC Clinical Diabetes Programs.

#### **Alexander Fleming, MD**

Recognized authority in the metabolic and endocrine fields with extensive FDA experience.

#### JULIO ROSENSTOCK, MD

Director, Dallas Diabetes Research Center, Professor, University of Texas Southwestern Medical Center; Associate Editor, Diabetes Care.



## Oramed (NASDAQ/TASE: ORMP)

### Addressing the Multibillion-Dollar Injectable Drug Markets with Oral Formulations

- Diabetes First: Initially targeting the lucrative insulin market; additional markets in the pipeline
- Strong financial position with ~\$160M¹ in cash and investments, no debt ~39M shares outstanding (~43M fully diluted)²
- Proprietary oral protein delivery platform
- Strong management team backed by world-class scientific experts
- Multiple near-term value-creation catalysts for this year
- Robust IP Portfolio
  - Methods and compositions for oral administration of proteins Methods and compositions for oral administration of exenatide
  - Methods and compositions (insulin + exenatide) Improved protease inhibitors

<sup>1</sup>As of September 30, 2022 (unaudited) <sup>2</sup>As of September 30, 2022

