Canaccord Genuity Capital Markets

Initiation of Coverage

Oramed Pharmaceuticals

Biotechnology

US Equity Research
20 April 2021

Rating	Price Target
BUY	**US$27.00**
ORMP-NASDAQ	Price **US$8.46**

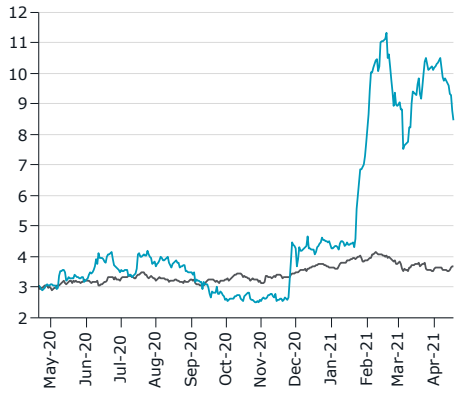
Market Data

52-Week Range (US$) :	2.40 - 12.73
Market Cap (US$M) :	255.7
Shares Out., Basic (M) :	30.2
Enterprise Value (US$M) :	199
Cash (US$M) :	56.8

FYE Aug	2020A	2021E	2022E
Revenue (US$M)	2.7	3.7	2.5
EPS GAAP (US$)	(0.56)	(1.56)	(1.41)

Quarterly Revenue	Q1	Q2	Q3	Q4
2020A	0.7	0.7	0.7	0.7
2021E	0.7A	0.7A	1.8	0.6
2022E	-	-	-	-

Quarterly EPS GAAP	Q1	Q2	Q3	Q4
2020A	(0.15)	(0.21)	(0.10)	(0.13)
2021E	(0.23)A	(0.17)A	(0.39)	(0.67)
2022E	-	-	-	-



Source: FactSet

Priced as of close of business 19 April 2021

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Making insulin an easy pill to swallow; initiating with a BUY and $27 PT

Looking to make oral insulin a near-term reality

ORMD-0801 is Oramed's lead clinical program in Phase III for the treatment of Type 2 diabetes (T2D). Oramed has broken new clinical ground, with ORMD-0801 the first oral insulin to enter Phase III clinical development. While large pharma and biotech have tried for decades to develop an oral insulin for T2D, all have failed to date clinically. ORMD-0801 has been tested extensively in multiple Phase I and Phase II trials in over 900 subjects and 10,000 doses with no serious adverse events, specifically no hypo- or hyperglycemia. Two Phase III trials began enrolling patients in 1Q21, one in patients on multiple T2D medications and still not successfully controlling blood glucose and one in patients controlling blood glucose through diet and metformin only. We expect both to report top-line data in 1H23, followed by a BLA filing and approval and launch in 2H24.

ORMD-0801 would be a major paradigm shift in T2D

Oramed looks to specifically target patients early in the treatment cycle. By doing so the hope is to better regulate blood glucose levels in a manner similar to how the body regulates glucose naturally in non-T2D patients. Insulin is currently only available as an injectable that when administered is delivered systemically throughout the body rather than focused solely in the liver where it is needed. An oral insulin would allow for gut absorption and delivery into the liver through the portal vein. Oramed is able to achieve a more directed oral delivery of insulin by leveraging the company's proprietary Protein Oral Delivery (POD) platform. POD coats the insulin molecule thereby protecting it from degradation in the stomach and gut and includes enhancers that assist in transporting the insulin across the gut lining.

Significant clinical data supports ORMD-0801's efficacy

While there are multiple markers used to determine the efficacy of a drug for T2D, HbA1c remains the key serologic test that determines the real efficacy of a T2D drug. The turning point for us in the ORMD-0801 story was the 12-week Phase IIb data announced last year that showed a statistically significant effect over a meaningful time period in the reduction of HbA1c vs placebo. It was the results from this study that propelled Oramed to consult with regulatory agencies and quickly move into the international Phase III program for ORMD-0801 in T2D.

A commercially tested market with significant upside

The use of insulin for the treatment of T2D is well understood, and an oral option has always been viewed by physicians and patients as highly desirable as a clinical option. We believe, if clinically successful and approved for T2D, ORMD-0801 would have fast adoption. Our model is purposely designed to be conservative to further highlight the value potential of ORMD-0801 as well as shares of ORMP. While the Phase III program is being conducted internationally, we only consider the U.S. market for T2D and include no other indications currently being developed, considering them solely as additional upside to our projections. We price ORMD-0801 at the low end of current injectable insulins and assume in the out-years a conservative peak penetration of 15%. This results in a peak market potential in the out-year of our model, 2036, of ~$3.5B for the U.S. T2D market alone for ORMD-0801.

POD is an agnostic platform technology

Oramed's POD technology has the ability to delivery proteins of all types, which creates multiple partnering and proprietary pipeline development options. The company is currently in Phase II development with ORMD-0801 for the treatment of NASH, with top-line data expected in 2H21. Additionally, the company has done initial work in T1D and has a GLP-1 molecule, ORMD-0901, for the potential treatment of T2D.

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Exhibits

Our investment thesis for ORMP

ORMD-0801 has the potential to be a gamechanger in the treatment of T2D

Oramed's lead oral insulin program ORMD-0801 leverages the company's proprietary Protein Oral Delivery (POD) platform. It is the first oral insulin program to successfully reach Phase III clinical development. Oramed looks to position ORMD-0801 as an early stage treatment option for pre-type 2 diabetics. By targeting patients before the need to be on other oral or injectable agents, ORMD-0801 offers the potential to stave off other undesirable therapies for a longer period. By delivering insulin orally, ORMD-0801 is absorbed by the body in the same way a healthy non-diabetic's insulin is absorbed. This differentiation is key as it allows for a natural control of blood glucose levels and avoids the glucose highs and lows associated with other molecules.

The American Diabetes Association estimates the prevalence of type 2 diabetes (T2D) to be approximately 10.1% in the U.S., accounting for roughly 34M people. Additionally, approximately 80% of diabetics in the U.S. are clinically diagnosed and 16% of those use injectable insulin. We project that T2D could generate net sales of up to $3.5B in 2036, the out-year of our model. The T2D indication along with the reported cash on the balance sheet contribute to 100% of our $27 12-month price target.

T2D is currently the sole value driver for Oramed, but NASH is next

While Oramed's lead indication is for T2D, the company is also conducting a Phase II blinded study in T2D patients that also have non-alcoholic steatohepatitis. This trial is currently enrolling, and data is expected in 2H21. We believe an oral insulin for this indication makes sense as most T2D patients also have NASH. The FDA has long been focused on the risk-to-benefit profile of any drug approved for both T2D as well as NASH. We believe ORMD-0801 has a significant chance of demonstrating a strong benefit to risk profile. Over 10,000 doses have been administered to >900 subjects in clinical trials to date, with no serious adverse events having been reported.

As an investment, we believe ORMP offers exposure to the T2D space with the following compelling attributes:

- A mechanism of action that is well understood and supported by a significant amount of scientific and clinical research with a mode of delivery (oral) yet to be achieved in the space.
- A compelling valuation given the upside potential of an oral insulin option
- Expertise in the oral delivery of peptides that allows for pipeline expansion and partnering options for currently approved peptides as well as for those in clinical development.
- Recent Phase IIb data from ORMD-0801 in T2D, we believe, has been a significant gamechanger. By demonstrating a robust effect on HbA1c through 12 weeks of dosing, we believe ORMD-0801 has delivered the proof-of-concept that many investors and potential partners have been waiting to see.

ORMD-0801 in T2D hits on 5 of our 5

Safety: No clinically meaningful incidence of hyperglycemia or hypoglycemia observed

Efficacy: Strong effect on fasting glucose levels as well as during nighttime and daytime

Market size: Assessing the U.S. market alone with a 15% market penetration translates into a $3.5B opportunity

Probability of approval: While we have muted the approval probability in our model to remain conservative, the data produced to date is extremely encouraging for a Phase III success

Competition: The insulin market is dominated by injectable insulins with no oral options currently available

Estimated 2024 launch of ORMD-0801 for T2D

We believe Oramed has the potential to launch ORMD-0801 as early as 2H24. Our projections assume the initiation of two-Phase III trials which are both now enrolling. As of March 16, 2021, the first Phase III has achieved 25% randomization. We expect top-line data from the Phase III trials in 1H23 followed by a BLA filing. We assume a market launch of ORMD-0801 for T2D in 2H24 targeting patients both on current anti-diabetic drug regimens as well as those using diet for glycemic control. Our peak sales estimate for the T2D indication in the U.S. is ~ $3.6B in 2036 with a peak market penetration of 15% in the U.S.

Figure 1: Type 2 diabetes revenue build

Oramed Pharmaceuticals, Inc. (ORMP) NASH Revenue Build	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E
Type 2 Diabetes (T2D) - U.S.													
U.S. population (MM)	337.6	340.0	342.4	344.9	347.3	349.8	352.3	354.8	357.3	359.8	362.4	364.9	367.5
T2D prevalence rate	*10.1%*	*10.3%*	*10.5%*	*10.7%*	*10.9%*	*11.1%*	*11.3%*	*11.6%*	*11.8%*	*12.0%*	*12.3%*	*12.5%*	*12.8%*
T2D prevalence, U.S.	33,986,982	34,912,855	35,863,951	36,840,957	37,844,578	38,875,540	39,934,587	41,022,486	42,140,020	43,287,998	44,467,250	45,678,627	46,923,004
T2D diagnosis rate	*79.0%*	*79.0%*	*79.0%*	*79.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*81.0%*	*81.0%*	*81.0%*	*81.0%*	*82.0%*
Diagnosed T2D patients, U.S.	26,849,716	27,581,155	28,332,521	29,104,356	30,275,662	31,100,432	31,947,670	32,817,989	34,133,416	35,063,278	36,018,473	36,999,688	38,476,863
Percentage of T2D patients taking injectible insulin	16%	16%	16%	16%	16%	16%	16%	16%	16%	16%	16%	16%	16%
T2D patients that use injectible insulin	4,295,955	4,412,985	4,533,203	4,656,697	4,844,106	4,976,069	5,111,627	5,250,878	5,461,347	5,610,124	5,762,956	5,919,950	6,156,298
ORMD-0801 market penetration	*0.1%*	*0.2%*	*0.6%*	*1.5%*	*3.3%*	*7.0%*	*9.0%*	*11.0%*	*13.0%*	*15.0%*	*15.0%*	*15.0%*	*15.0%*
Patients adopting ORMD-0801	4,296	8,826	27,199	69,850	159,855	348,325	460,046	577,597	709,975	841,519	864,443	887,993	923,445
WAC per patient per year	$3,174.4	$3,269.7	$3,367.8	$3,468.8	$3,572.9	$3,680.0	$3,790.4	$3,904.2	$4,021.3	$4,141.9	$4,266.2	$4,394.2	$4,526.0
Gross to net rate	85.0%	85.0%	85.0%	85.0%	85.0%	85.0%	85.0%	85.0%	85.0%	85.0%	85.0%	85.0%	85.0%
Net realized price per patient per year	$2,698.3	$2,779.2	$2,862.6	$2,948.5	$3,036.9	$3,128.0	$3,221.9	$3,318.5	$3,418.1	$3,520.6	$3,626.3	$3,735.0	$3,847.1
U.S. Product Sales - ORMD-0801 for T2D ($MM)	**$11.6**	**$24.5**	**$77.9**	**$206.0**	**$485.5**	**$1,089.6**	**$1,482.2**	**$1,916.8**	**$2,426.8**	**$2,962.7**	**$3,134.7**	**$3,316.7**	**$3,552.6**

Source: Canaccord Genuity estimates

ORMD-0801 for T2D in U.S. drives value

We value shares of Oramed by employing a sum-of-the-parts analysis that includes programs where we believe clinical data is available to fairly determine the overall probability of success, as well as net cash on hand. Our estimates solely for the T2D program in the U.S. are used to generate our $27 12-month price target, and we view any additional programs such as T1D, NASH and T2D ex-U.S. as potential upside to our estimates.

Assumptions underlying our valuation of ORMP

- We estimate that ORMD-0801 sales for T2D in the U.S. start in late 2024. This launch projection assumes the company follows through on the current timeline with the two ongoing Phase III trials.
- We believe pricing of ORMD-0801 in T2D would be approximately $3,174 per patient per year at the time of launch. This is approximate in-line pricing with current insulin administered by vial. We assume an average T2D patient weight of 77Kg and 0.4 units of insulin per day. The range for T2D diabetics is typically 0.2 to 0.8 units per day. Finally, we apply a per unit cost of $0.25. We believe these estimates are highly conservative. If the efficacy and safety profile of ORMD-0801 continue to mirror what has been observed in the Phase IIb three-month HbA1c study, we believe this figure represents a reasonable estimate that would garner strong usage from prescribers and no pushback from payers. Our pricing strategy follows the same inputs we consider reasonable and that are employed for injectable insulins currently on the market. Importantly, if ORMD-0801 delivers on providing the first orally available insulin to the market with a meaningful reduction in HbA1c, a premium pricing strategy would be warranted.
- We believe ORMD-0801 offers the potential to be a true clinical option for T2D patients. Given the safety profile observed to date in combination with strong efficacy, we believe ORMD-0801 can be significantly differentiated from the current insulin market through oral delivery alone. The key for Oramed is to demonstrate that the oral dosing of insulin using its proprietary technology is just as safe and effective as injectable insulin.

ORMD-0801 pricing assumptions
We assume pricing for T2D on a per annum basis to start at $3,174 to gain the greatest market share through patient numbers rather than premium pricing. We believe penetration into the T2D population could be high if efficacy and safety are replicated in the ongoing Phase III trials.

Figure 2: Select factors influencing our pricing assumptions

Type	Pricing Factor	Importance Rank	ORMD-0801
Convenience	Oral delivery with equivalent safety and efficacy to injectable insulin	10	High
Efficacy	Significant impact in lowering HbA1c	10	High
Side Effect	Hypoglycemic events in line with placebo	8	High
Commercial	Premium Pricing Achievable	5	Likely
Commercial	Usage	8	Moderate

Importance Rank: 10=high

Source: Canaccord Genuity estimates

- Our current projections assume a peak market penetration for ORMD-0801 in T2D of 15% in the U.S., and we do not currently include any estimates for RoW to be conservative.
- T1D, NASH and ex-U.S. for T2D are not included in our current valuation and will only be included in our assumptions once clinical proof-of-concept is achieved for T1D and NASH and Phase III data is announced for T2D.

Figure 3: Probability adjusted sum-of-the-parts analysis

Drug	Status	Indication	Territory	Estimated Launch	Peak Sales ($MM)	Probability of Success	Prob. Wtd. NPV ($MM)	Per Share
ORMD-0801	Phase III	T2D	U.S.	2024	$3,552.6	40%	$1,474.4	$26.26
						Asset value	$1,474.4	$26.26
						Cash 2/28/21	$56.8	$1.01
						Equity value	$1,531.2	$27.27
						Shares 2036E	56.1	
						Per share		**$27.27**

Source: Company reports, Canaccord Genuity estimates

Stock-driving catalysts

The catalyst sensitivity analysis is our estimation of how ORMP shares could be affected based on future key clinical milestones. We also note our probability of a successful outcome for each catalyst (if applicable). The valuation assumptions we used are not static and will most likely evolve over time. While only the T2D indication is included in our current financial projections, we have also included the NASH indication in our catalyst probability and effect sensitivity analysis as these milestones could have a direct impact on stock performance regardless of whether included in our current valuation analysis.

Key catalysts to drive shares
Oramed's clinical read-outs for ORMD-0801 in T2D and NASH allow for multiple inflection points that we believe could drive shares.

Figure 4: Catalyst probability and effect sensitivity analysis

Drug: Event	Indication	Timing	Probability of Success	Impact on ORMP shares If Positive	If Negative
ORMD-0801: Phase II trial completion and top-line data read-out	T2D w/ NASH	2H21	60%	▲ ~15	▼ 5-10%
ORMD-0901: GLP-1 bioequivalence study	T2D	2021	75%	▲ ~5	▼ 6%
ORMD-0801: Phase III top-line data read-out	T2D	1H23	40%	▲ ~75%+	▼ ~80%%

Source: Company reports, Canaccord Genuity estimates

T1D vs T2D

Diabetes is characterized by elevated levels of glucose in the blood. There are two types of diabetes. Individuals diagnosed with Type 1 diabetes (T1D) have a pancreas that is unable to produce any insulin naturally. In Type 2 diabetes (T2D) either the pancreas does not produce sufficient insulin or cells have developed insulin resistance. If left untreated, patients with diabetes can suffer from several types of complications and morbidities such as eye disease (diabetic retinopathy), chronic kidney disease (diabetic nephropathy), cardiovascular disease (e.g. heart attack), central nerve system disease (diabetic neuropathy), and immune system dysfunction. Clinical research has proven that blood sugar management can reduce the risk of eye disease, kidney disease, and nerve disease by as much as 40%.

According to the Diabetes Atlas (9th Edition) published by the International Diabetes Federation (IDF), the worldwide prevalence of diabetes is estimated to be 463M, which represents 9.3% of adults 20 to 79 years of age. IDF estimates that by 2045, the global prevalence of diabetes will be ~700M.

Centers for Disease Control and Prevention (CDC) estimates show that as of 2018, there were ~34.2M diabetics in the U.S. Over 34M are adults, and 21.4% of diabetic adults in the U.S. (26.9M) are undiagnosed. Approximately 210,000 children and adolescents <20 years of age, or 25 per 10,000 U.S. youths, had a confirmed diagnosis of diabetes. This includes 187,000 specifically with T1D.

T1D, which accounts for ~5% of all diabetics, differs from T2D as it is an autoimmune disease whereby antibodies attack the insulin producing beta cells of the pancreas, resulting in the body's eventual inability to produce endogenous insulin. The destructive autoimmune process can take from months to years before any symptoms appear. T1D is also associated with mutations in certain genes that cause the individual to be more likely to develop T1D, though many with genetic mutations will not develop T1D. Exposure to environmental triggers, such as a virus, is also thought to play a part in the development of T1D. Poor diet and nutrition is not a causal factor of T1D.

T1D and T2D: Where does insulin fit in?

Human insulin

Insulin is a 51 amino acid peptide hormone that is secreted by the β-cells of the pancreatic islets, also called islets of Langerhans or Langerhans cells, that maintains normal blood glucose levels by facilitating glucose uptake, regulating protein/lipid/carbohydrate metabolism, and promoting cell division and growth.

There are two interrelated issues in T2D. One is when an individual becomes insulin resistant. In this case the cells in muscle, fat, and liver do not respond to insulin, resulting in a decreased ability to take up glucose from the bloodstream. The second issue is the inability of the pancreas to produce enough insulin to keep up with the rising levels of glucose in the bloodstream.

While insulin used to be one of the last options to use in treating T2D, it is now one of the treatments prescribed early in disease onset for patients unable to control blood glucose levels. This is not surprising given that recombinant human insulin is in fact replacing what the body normally produces to control blood sugar levels. There are currently eight different classes of drugs, including insulin, used in the treatment of T2D. While insulin is heavily used in treating T2D, the downside is that only injectable versions are commercially available and injecting insulin does not replicate biologically how insulin is normally secreted endogenously.

Figure 5: Select types of drugs used to treat T2D

Type	Generic	Brand	Mechanism
Biguanide	metformin	Glucophage	Decreases hepatic gluconeogenesis
Sulfonylureas & Glinides	glipizide	Glucotrol	Increases insulin secretion
Thiazolidinediones	pioglitazone	Actos	Increases insulin sensitivity
α-Glucosidase Inhibitors	acarbose	Precose	Decreases absorption of carbohydrates
DPP-4 Inhibitors	sitagliptin	Januvia	Increases insulin secretion
SGLT2 Inhibitors	empagliflozin	Jardiance	Blocks glucose reabsorption in the kidney
GLP-1 Receptor Agonists	exenatide	Byetta	Increases insulin secretion
Insulin	insulin	Lispro	Increases glucose uptake

Source: Company reports, Canaccord Genuity

No oral insulin options currently exist. Many attempts have been made to develop an oral insulin option, but none had success beyond Phase II. ORMD-0801 is the first oral insulin to reach Phase III.

According to the American Diabetes Association, approximately 7.4 million diabetics in the U.S. currently use at least one formulation of insulin. Based on CDC data, there are ~2.1M to 4.3M adult diagnosed T1D patients (≥20 years of age) in the U.S. Approximately 1.4M adult patients reported both having T1D and using insulin. An estimated 2.9M adult patients, having either T1D or T2D, started using insulin within a year of diagnosis. Many T2D patients also need insulin therapy at some point in the treatment course as the disease progresses. It is common for an individual with T1D to use both a short-acting insulin (meal-time insulin or bolus insulin) and an intermediate- or long-acting insulin (basal insulin). Individuals with T2D tend to be on

a basal insulin therapy. Approximately 50% of diabetics are not within their HbA1c target. It is estimated that insulin therapy is delayed by approximately eight years in people with diabetes.

Since the discovery and use of animal (bovine) insulin in 1921, many important breakthroughs have been made in insulin development. Genetic engineering made recombinant human insulin a reality in the 1980s. The introduction of rapid-acting and long-acting human insulin analogs in the 1990s drastically changed the way insulin was used in the treatment of diabetes. The prevalence of diabetes worldwide has increased over the past decades, but the U.S. has seen a slight decrease since 2008. The American Diabetes Association estimates the total direct and indirect estimated costs related to diabetes in the U.S. stands at an estimated $327B. Total direct estimated costs of diagnosed diabetes increased from $188B in 2012 to $237B in 2017; total indirect costs increased from $73B to $90B for the same period.

Currently the only way to administer insulin is by subcutaneous injection, resulting in less than ideal compliance among T2D patients. Subcutaneous administration of insulin can fail to provide continuous regulation of metabolism that occurs normally with insulin secreted from the pancreas directly into the liver via the portal vein.

The above two points continue to be the major driving force for the development of an oral insulin. Delivering insulin orally brings with it multiple advantages over subcutaneous administration:

- Increased patient compliance
- Dosing is pre-calculated and easier to modify
- No physical pain and injection site reactions
- Reduce systemic insulin exposure and excessive weight gain

However, the biotech and pharmaceutical industry to date has faced many challenges in developing an oral insulin. The nature of the GI tract is such that it does not readily absorb large molecules, like most peptides and proteins, without any pre-processing. The strong acidic environment in the stomach, as well as bile and enzymes in the intestine, denature peptides, which leads to the loss of bioactivity. Mechanical and enzymatic degradation, as well as the microbiome and associated metabolic products, also reduce the bioactivity of large peptides and proteins.

Protein-based drugs are poorly absorbable also owing to their high molecular weight and hydrophilicity, which causes low solubility in an aquatic environment. Insulin is constructed with 51 amino acids and the size of insulin is 5.8kDa, which makes it much harder, when compared to dipeptides and other small biologics, to be delivered orally.

For an oral drug to be transported into the blood stream from the gut, the drug needs to pass through a dense mucus barrier, then through the intestinal epithelium. The single layer of epithelial cells lining both the small intestine and the large intestine acts as a physical barrier, with tight junctions between adjacent cells limiting the passage of molecules and ions. Most materials must enter the cells by diffusion or active transport.

Previous research has demonstrated that protease inhibitors can serve as a protection against degradative threats along the GI tract, when incorporated in drug formulations. Research has also demonstrated that the absorption and stability of insulin in the GI tract can be improved by including absorption enhancers, or intestinal permeation enhancers (PE), in drug formulations. The main permeation enhancers are structured with medium chain fatty acid-based systems, bile salts, acyl carnitines, and EDTA. The mechanism of action of most PEs is to:

1. Fluidize the cell membrane, which increases the chances of the drug molecules of entering the cell membrane, and
2. Generate enzymatic and intracellular mediator changes that lead to alteration of tight junction protein expression and function.

The potential side effects of the long-term use of the PEs, introduced by increasing the "gap" between cells of the epithelium layer, is a concern that needs more clinical research to further elucidate.

Another difficulty in developing an oral insulin comes from location, or where the insulin has an effect, and this is tightly linked to the regulation of insulin secretion in the human body. In normal healthy people, the concentration of insulin in the liver is 2.5 to 3 times higher than it is in the brain, fat tissue, or other organs and tissues. Peripheral infusion of insulin would change the tissue accumulation and distribution of insulin, resulting in lower insulin levels in the liver than the arteries, thus reversing the normal gradient of insulin amongst the liver and peripheral tissues. The resulting excessive insulinization of non-hepatic tissues and insufficient liver insulinization could lead to metabolic dysfunction, including insulin resistance, weight gain, changes in body fat distribution and lipid metabolism, etc., as well as the risk of hypoglycemia.

The liver also has a self-regulating mechanism that controls the degradation of insulin – that is, changes in the metabolic rate of insulin along with fluctuations in insulin concentration. Hepatocytes mediate more than 90% of insulin degradation, mainly in cells and on cell membranes. The insulin degradation system on the cell membrane can regulate the ratio of bound insulin available for internalization. Therefore, by taking insulin orally to simulate the secretion process of insulin under physiological conditions, the peripheral insulin concentration can be better adjusted and the incidence of hypoglycemia can be reduced.

The reason why current injectable insulin therapies fail to restore normal physiology in people with diabetes is partially due to the inability to adequately deliver insulin in the manner by which pancreatic insulin is secreted in the body of a healthy non-diabetic: to the liver. To overcome this disadvantage, an insulin analog, which is about 10 times the cost of human insulin, is often required to regulate how fast insulin dissolves into the blood once injected.

Oramed is not the only company developing an oral insulin with a protease inhibitor and absorption enhancers. The trail to an approved oral insulin has been littered with many attempts and failures.

Biocon Limited conducted a Phase II study of its insulin product teregopil in 91 T2D patients to test the product's effect on reducing blood sugar level after 24 weeks of treatment. The study was completed in 2017. Results showed an increase of patients' HbA1c level, suggesting that the study missed its primary endpoint. Teregopil was formulated with a drug polymer conjugate technology. The goal was to increase the bioavailability of insulin by increasing its solubility. The formulation of the drug involved attaching short chain polyethylene glycol (PEG) with insulin derivatives coupled with caproic acid groups.

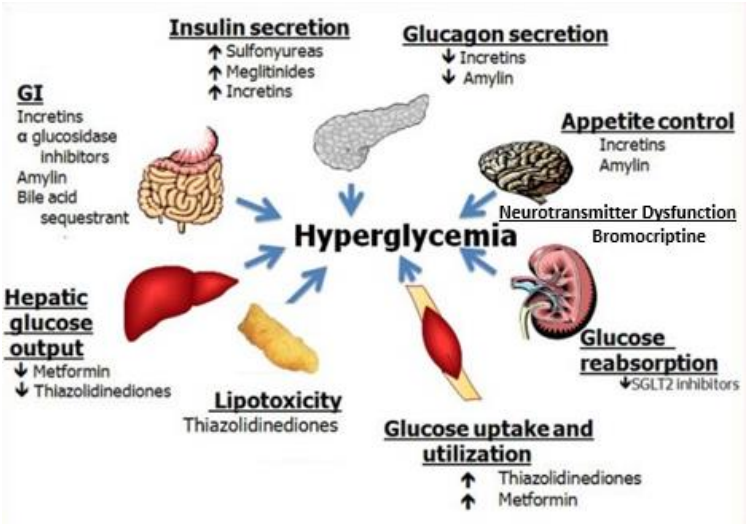
Pfizer completed a Phase III study of inhaled insulin (Exubera) in 2008 with 354 patients. The study results showed that 32% of patients in the inhaled insulin group achieved a decrease of HbA1c of < 7% after a 24-week treatment course. The company did not move further with the development of this product.

Novo Nordisk discontinued its oral insulin program in 2016 after announcing positive data from a Phase II head-to-head study compared to Sanofi's subcutaneous insulin glargine. Data from the study showed that a significant reduction of fasting glucose level was achieved by an average of 45mg/dL, similar to insulin glargine. Novo's

product used a permeation enhancer targeting the duodenum, the smallest section of the small intestine, which could be a limitation of the overall absorption of insulin due to the size of intestinal surface. The dose of insulin used in this trial was another possible reason for the discontinuation of the drug candidate. With a high dose needed to achieve clinically meaningful effect, the cost of miniaturing also become a challenge for the future commercialization of the product.

Oramed's lead product, ORMD-0801, instead of trying to affect a large decrease in blood glucose levels and trying to replace injectable insulin, is intended to keep glucose levels stable throughout the day. Oral delivery of insulin does not facilitate long-acting (basal) insulin administration; rather, it can potentially reduce the daily injection count and perhaps replace the bolus injection. Oral insulin could also delay the start point of injection. Oramed, with ORMD-0801, is working to add a middle stage option between oral blood glucose reducing medications and insulin injections to reduce insulin resistance and stimulate insulin secretion with the goal of delaying the onset of severity.

Figure 6: ORMD-0801 looks to delay the use of many T2D therapeutics



Source: National Institutes of Health

Oramed's oral drug delivery platform

With the challenges encountered historically in trying to develop a commercially viable oral insulin, we believe Oramed's oral insulin candidate, ORMD-0801, in leveraging the company's proprietary POD (Protein Oral Delivery) technology, has the best potential to become a clinical reality given the clinical results reported to date from multiple clinical trials in T2D patients.

Approved oral peptides
Only four have made it to the market, and two are not absorbed in the GI tract

There are currently four FDA approved oral peptide drugs:

- linaclotide (Linzess) from Allergan for IBS-C and CIC
- plecanatide (Trulance) from Salix for IBS-C and CIC
- octreotide (Mycapssa) from Chiasma for acromegaly
- semaglutide (Rybelsus) from Novo Nordisk for T2D

Linaclotide and plecanatide are used to treat constipation predominant irritable bowel syndrome (IBS-C) as well as chronic idiopathic constipation (CIC) and thus are not required to be absorbed by the body to function. Octreotide is used for the long-term maintenance treatment in acromegaly patients by reducing growth hormone levels.

Oramed's POD technology could be used for any protein where oral delivery is optimal. The active protein is encapsulated with a highly protective coating that remains intact in the most acidic segments of the GI tract; additionally, enzymatic support is provided by specialized protease inhibitors, thus reducing the proportion of proteolysis in the small intestine. Finally, absorption enhancers are added to further secure bioavailability by facilitating transport across the intestinal lining.

Once across the small intestine epithelial layer, insulin, in the case of ORMD-0801, is transported through the hepatic portal vein. The portal vein is the same transport route used by endogenously secreted insulin from the beta cells of the pancreas to the liver. Once delivered to the liver, insulin can be regulated in a manner like a healthy non-diabetic individual while also being released to peripheral sites of action as needed. Oral delivery of insulin is an important advantage as current intramuscular injected insulins need to be calculated and measured manually with a heightened risk of hypoglycemia (low blood glucose) or hyperglycemia (high blood glucose).

In December 2019, Oramed presented data at the International Diabetes Federation Congress, demonstrating that formulation D, which utilizes 25mg rBBI along with 25mg KTI as protection from insulin degradation and digestion within the GI tract, achieved a greater glucose lowering effect in animal models. To establish a more cost-effective source of protease inhibitor, a recombinant Bowman-Birk inhibitor (rBBI), identical in sequence to its natural counterpart was cloned, expressed and purified. Soybean derived trypsin inhibitor (Kunitz trypsin inhibitor, or KTI) was also used.

In presented posters, results indicated that GMP rBBI preserves oral insulin bioavailability and exhibits a synergistic effect when mixed with KTI, reaching saturation at the tested PI:insulin ratio. Results suggest that the protective effect of rBBI on insulin exposed to the harsh conditions of the gastrointestinal tract would likely improve the clinical potential and value of orally delivered insulin. The poster also stated that GMP rBBI will soon be tested in a first-in-human clinical trial to confirm its effectiveness in patients with T1D.

The enteric-coated ORMD-0801 capsule has been shown to provide effective glucose control in both T1D and T2D patients. Clinical evidence further supported the development of ORMD-0801 for the treatment of T2D. As Oramed's lead oral program, ORMD-0801 has accumulated a significant amount of safety and efficacy data in over 900 study subjects to date.

Clinical results of ORMD-0801 in T2D

Phase IIa - NCT01889667

Lower fasting blood glucose achieved after dosing with ORMD-0801

In 2013, Oramed conducted a double-blind, placebo-controlled, Phase IIa study preceded by a five-day single-blind outpatient placebo run-in period to assess the safety, pharmacokinetics (PK), and pharmacodynamics (PD) of ORMD-0801 in adult patients with T2D who were inadequately controlled with diet and exercise or with diet, exercise, and metformin. The study enrolled 30 patients outfitted with a blinded continuous glucose monitor (CGM) and received a bedtime oral dose of either 460IU or 690IU of insulin, or placebo from Days 2 to 8 (n=10/cohort; Day 1 with placebo for

all participants). Plasma insulin, plasma glucose levels, and c-peptide levels were measured for five-hours post-dosing.

Results from the 460IU group showed that ORMD-0801 led to a stable, consistent, and short-lived rise in plasma insulin levels, as well as lower nighttime and daytime glucose levels. On Day 8, ORMD-0801-treated patients showed higher mean plasma insulin and c-peptide levels throughout the 180min post-dosing period, when compared to baseline levels at Day 1. C-peptide is a substance that is created naturally when insulin is produced and released into the body. The level of c-peptide is commonly used as a biomarker to reflect insulin levels. People with T2D, obesity, or insulin resistance may have a high c-peptide level. A normal range of blood c-peptide is between 0.5ng/mL to 2.0ng/mL.

In the first 60min post-dosing, plasma insulin exposure was 20.53mIU*h/mL greater among ORMD-0801-treated patients, compared to placebo. The results indicated an effective insulin uptake by oral delivery and a clinical impact on morning fasting blood glucose (FBG) levels.

The Phase IIa study demonstrated a reduction not only in fasting glucose levels but also in night-time mean glucose levels and daytime glucose levels, when compared to placebo. The drug was well tolerated, and no adverse events, including hypoglycemic events, were observed.

C-peptide and insulin
C-peptide correlates directly with insulin and is often used as a surrogate marker of insulin activity.

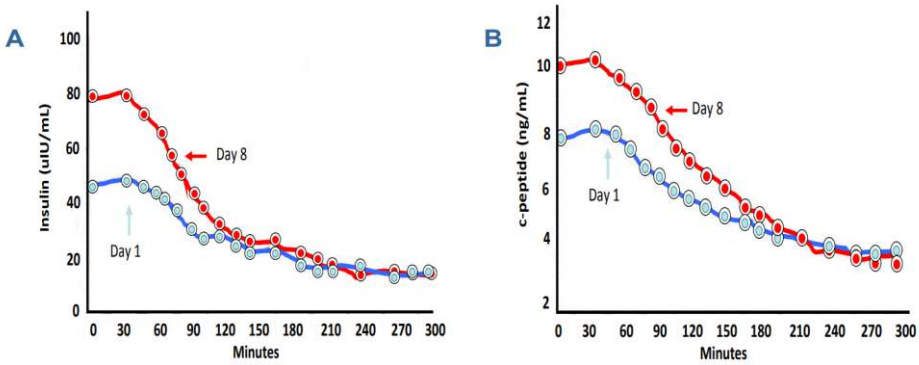
Figure 7: Average CGM glucose levels

Nighttime Mean (SD) mg/dL	Placebo n=10	ORMD-0801 460IU n=10	Δ (drug - placebo)
Last 2 days of data	167.95 (64.172)	135.64 (39.400)	-32.31
All 7 days	165.85 (60.760)	139.73 (38.861)	-26.12
Daytime Mean (SD) mg/dL			
Last 2 days of data	176.06 (63.698)	153.23 (40.160)	-22.83
All 7 days	175.99 (61.115)	152.55 (36.986)	-23.44
Fasted Mean (SD) mg/dL			
Last 2 days of data	156.26 (58.622)	126.02 (27.264)	-30.24
All 7 days	154.37 (57.993)	129.27 (27.426)	-25.1

Source: Adapted from company reports

Ubiquitous activity
ORMD-0801 showed strong mean glucose reduction at nighttime, daytime and in fasting glucose levels.

Figure 8: Plasma insulin and c-peptide levels on Day 8



Blood was drawn at set intervals during the five-hour postdosing period.
Insulin (A) and c-peptide (B) levels measured on Day 1 (placebo treatment) and Day 8 (following 7 days of ORMD-0801 treatment) are presented.

Source: Adapted from company reports

Phase IIb – ORA-D-007 – NCT02496000

Blood glucose lowering efficacy is demonstrated

In 2016, Oramed announced results from a randomized, double-blind, placebo-controlled Phase IIb study of ORMD-0801 in 188 adult patients with T2D. The treatment course of the study was four weeks, and the patients were inadequately controlled with diet, exercise, and/or metformin. The study met the primary endpoint and showed positive results on blood glucose control at night-time, daytime, on morning FBG levels, and on glycosylated hemoglobin A1c (HbA1c or A1c) levels.

HbA1c is an important indicator of long-term glycemic control with the ability to reflect the cumulative glycemic history of the preceding two to three months. HbA1c not only provides a reliable measure of chronic hyperglycemia but also correlates well with the risk of long-term diabetes complications. Elevated HbA1c has also been regarded as an independent risk factor for coronary heart disease and stroke in subjects with or without diabetes. The valuable information provided by a single HbA1c test has rendered it as a reliable biomarker for the diagnosis and prognosis of diabetes. An alternative test to the A1c is a fructosamine test. The fructosamine test reflects the average blood sugars only over a 2- to 3-week period and is not interchangeable with the A1c test. *Sherwani, Shariq I et al. "Significance of HbA1c Test in Diagnosis and Prognosis of Diabetic Patients." Biomarker insights vol. 11 95-104. 3 Jul. 2016.*

Figure 9: HbA1c levels vs. blood glucose

HbA1c level	Estimated average glucose (mg/dL)
5%	97
6%	126
7%	154
8%	183
9%	212
10%	240
11%	269
12%	298

Source: Sherwani, Shariq I et al. Biomarker Insights

An individual with an HbA1c measurement between 4% and 6% is clinically considered to be non-diabetic. The American Diabetes Association sets a clinical goal for individuals to have an HbA1c <7%. Research has shown that an HbA1c <7% lowers

the risk for clinical complications. The American College of Endocrinology goal is an HbA1c <6.5%.

The Phase IIb multi-centered study included patients with baseline HbA1c ≥7.5% if naïve to anti-diabetic therapy, or baseline HbA1c between 6.5% and 10% if on metformin (≥1,500mg daily for >two weeks) and/or one other anti-diabetic medication. Patients underwent a 14-day, single-blind placebo run-in period, during which they were monitored with the CGM for the previous seven days. Patients were then randomized to receive either placebo, 16mg ORMD-0801 or 24mg ORMD-0801 for 28 consecutive days and monitored with a CGM for the last seven days, followed by a 14-day follow up period. The primary objectives of the study were to evaluate the safety and PD effects on mean night glucose levels. Key secondary objectives included PD effects on FBG, morning blood insulin, HbA1c, c-peptide, and triglycerides.

Figure 10: Phase IIb study demographics and overview of adverse events

	Placebo	ORMD-0801 (16 mg)	ORMD-0801 (24 mg)
Patients randomized, n	64	61	63
Patients completed study, n	62*	56**	61***
Age, mean (SD)	58.6 (9.2)	57.9 (8.0)	57.3 (8.9)
Male, n (%)	29 (45.3)	39 (63.9)	34 (54)
White, n (%)	53 (82.8)	50 (82.0)	55 (87.3)
Black/African American, n (%)	7 (10.9)	8 (13.1)	4 (6.3)
Asian, n (%)	2 (3.1)	2 (3.3)	2 (3.2)
Native Hawaiian/Pacific Islander, n (%)	2 (3.1)	1 (1.6)	0 (0)

	Placebo	ORMD-0801 (16 mg)	ORMD-0801 (24 mg)
Patients randomized, n	64	61	63
Total Adverse Events*, n	34	34	42
TEAEs# , n	19	19	19
Severe TEAEs, n	0	1	0
Serious TEAEs, n	0	1	0
Related TEAEs, n	2	0	0
Hypo/Hyper-glycemia events, n	2	4	1

** Withdrawn consent (n=1), lost to follow-up (n=1)*
*** Withdrawn consent (n=2), noncompliance (n=2)*
**** Lost to follow-up (n=1), protocol violation (n=1)*

** Non-Hyper/hypoglycemic events*
 # TEAE: Treatment-emergent adverse event

Source: Adapted from company reports

Data from the last two days of monitoring that contained at least 80% of the readings were used for the comparative analysis between run-in and treatment phases for patients in both the placebo-treated cohort and ORMD-0801-treated cohort. Results from this study indicate a sustained and significant blood glucose reduction in every CGM parameter. A statistically significant decrease in HbA1c levels was observed after 28 days of treatment. No increase in peripheral insulin level was detected. The drug was well tolerated, with no significant hyperglycemic events observed.

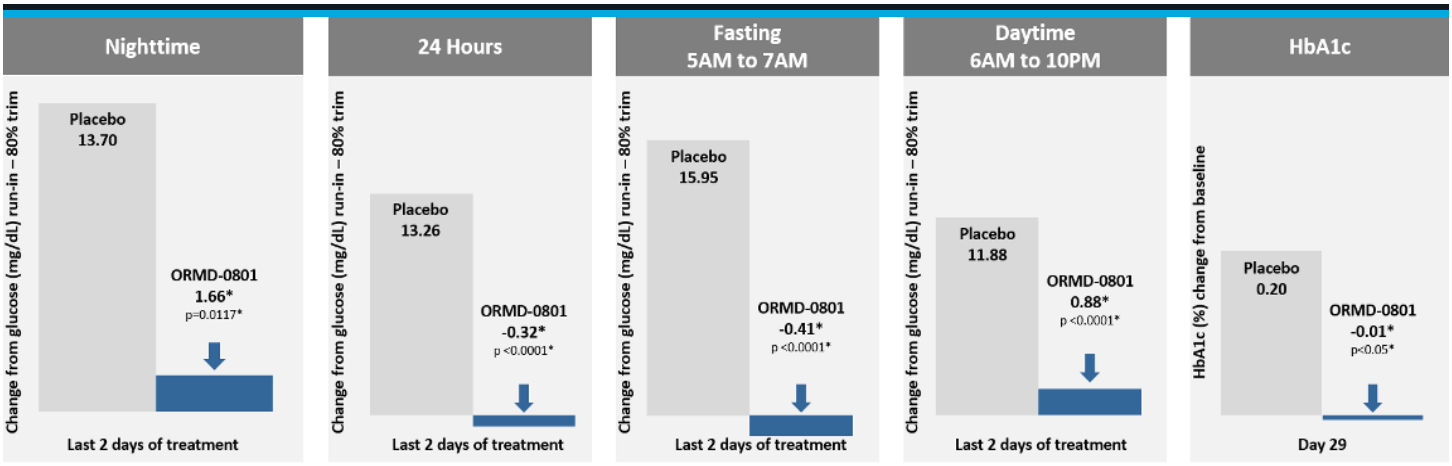
Figure 11: Phase IIb study results

	Placebo	ORMD-0801 (16 mg)	ORMD-0801 (24 mg)
Nighttime glucose*, mean (SD), mg/dL	13.70 (26.140)	-3.67 (18.983)	6.64 (26.361)
24-hour glucose*; mean (SD), % change	5.34 (13.881)	3.33 (21.499)	1.93 (19.795)
Fasting glucose*; mean (SD), % change	12.76 (23.245)	4.54 (24.153)	3.28 (27.331)
Fasting c-peptide**; mean (SD), % change	0.08 (0.252)	0.03 (0.476)	0.7 (0.300)
HbA1c***; mean (SD), % change	0.2 (0.497)	0.00 (0.544)	-.03 (0.554)

** Based on two nights of Continuous Glucose Monitor (CGM) by comparison of the mean change between baseline and Week 4 (two last nights unless specified) of ORMD-0801 treatment and placebo groups. ** Change in morning fasting c-peptide between baseline to end of the study. Time frame: Study Day 1 (±1 day) through Day 43 (± 1 day). *** Percent change from baseline to Week 4. Time frame: Study Day 1 (±1 day) through Day 29 (± 1 day).*

Source: Adapted from ClinicalTrials.gov

Figure 12: Blood glucose control effects of ORMD-0801 in Phase IIb study



Mean change in blood glucose concentrations: last two days of run-in vs. last two days of treatment period.
No significant difference in readings was observed between the two treatment groups and data are therefore presented as a pooled ORMD-0801 treatment cohort.
HbA1c is presented as the difference between Day 29 measures and baseline.

Source: Adapted from company reports

The results from the Phase IIb study support the potential mechanism of action of liver directed insulin deposition. This hypothesis was supported by evidence of observations, including prolonged anti-hyperglycemic effect despite an expected short half-life of human insulin once absorbed into the blood stream, as well as no observation of hypoglycemic events, increases in peripheral insulin or weight gain.

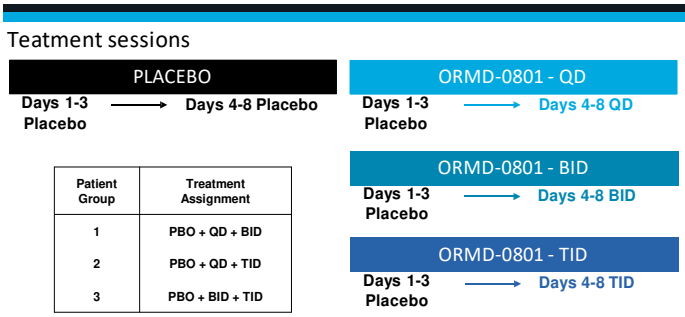
Phase IIa – NCT02954601

Crossover study comparing multiple dosing regimens

In 2018, Oramed conducted a crossover Phase IIa study to further assess the safety and efficacy of ORMD-0801 in patients with T2D, as well as to investigate an optimal dose for future clinical studies. This was a three-way crossover (non-parallel) study that included four treatment schedules: 460IU of ORMD-0801 once daily (QD), twice daily (BID), three times daily (TID), or placebo. Patients were randomized to receive three treatment sessions: one placebo session and two active treatment sessions. After each treatment session (Day 1 through Day 8), patients received a placebo washout on Day 9.

Post screening, eligible patients entered a three-day, single-blinded placebo run-in, and then randomized to a treatment sequence that include three treatment assignments for each of the three treatment periods. Patients received the randomized, double-blind treatment from Day 4 through Day 8, followed by single-blind placebo washout on Day 9. The dosing order (order of the treatment sessions) was random.

Figure 13: Phase IIa crossover study design



Patient Group	Treatment Assignment
1	PBO + QD + BID
2	PBO + QD + TID
3	PBO + BID + TID

Each patient is assigned to three treatment sessions with more than one week interval between sessions. The dosing order is random.

Source: Adapted from company report

During each treatment period, patients were confined to the unit for eight nights. Blood glucose levels were continuously monitored with a CGM. Insulin and c-peptide levels were measured from blood samples collected on Day 4 (pre-treatment) and Day 9 (post-treatment).

A decrease of mean 24-hour CGM glucose was observed in QD, BID, and TID groups, compared to placebo. Mean placebo-adjusted change from baseline in 24-hour glucose (mean of all run-in days vs. all treatment days) ranged from -7.65mg/dL for QD to -9.9mg/dL for TID, corresponding to a percent change from baseline ranging from -3.0% (BID) to -5.5% (QD). This effect was more dramatic among subjects with high glucose (>190mg/dL; n=17) at baseline (-12.4mg/dL for QD, -4.9mg/dL for BID, and -18.4mg/dL for TID), compared to those with low baseline glucose levels (10.6mg/dL for QD, 1.1mg/dL for BID, and -10.4mg/dL for TID).

Figure 14: Change in glucose between pre-treatment and end of treatment by mean 24-hour CGM

	Placebo	ORMD-0801 (460 IU, QD)	ORMD-0801 (460 IU, BID)	ORMD-0801 (460 IU, TID)
	n=31	n=20	n=21	n=20
Run-In, mean (SE), mg/dL	198.4 (6.2)	205.0 (4.9)	190.0 (6.0)	202.8 (9.7)
Treatment, mean (SE), mg/dL	191.9 (5.1)	185.0 (7.0)	188.4 (6.9)	181.3 (7.0)
Placebo-adjusted difference, mean (SE), mg/dL		-7.7 (6.3)	-4.0 (6.6)	-9.9 (7.3)
Placebo-adjusted % change, mean (SE)		-5.5 (3.2)	-3.0 (3.4)	-4.7 (3.6)

Source: Adapted from ClinicalTrials.gov, Company report

Figure 15: Key secondary outcomes

	Placebo	ORMD-0801 (460 IU, QD)	ORMD-0801 (460 IU, BID)	ORMD-0801 (460 IU, TID)
	n=31	n=20	n=21	n=20
c-pepetide ratio; post- : pre-	0.97 (0.034)	1.01 (0.056)	1.03 (0.047)	0.93 (0.051)
Daytime glucose, mean (SD), mg/dL	-4.11 (5.080)	-13.96 (7.775)	1.13 (7.772)	-16.78 (8.613
Hypoglycemic events	3	2	4	5

Source: Adapted from ClinicalTrials.gov

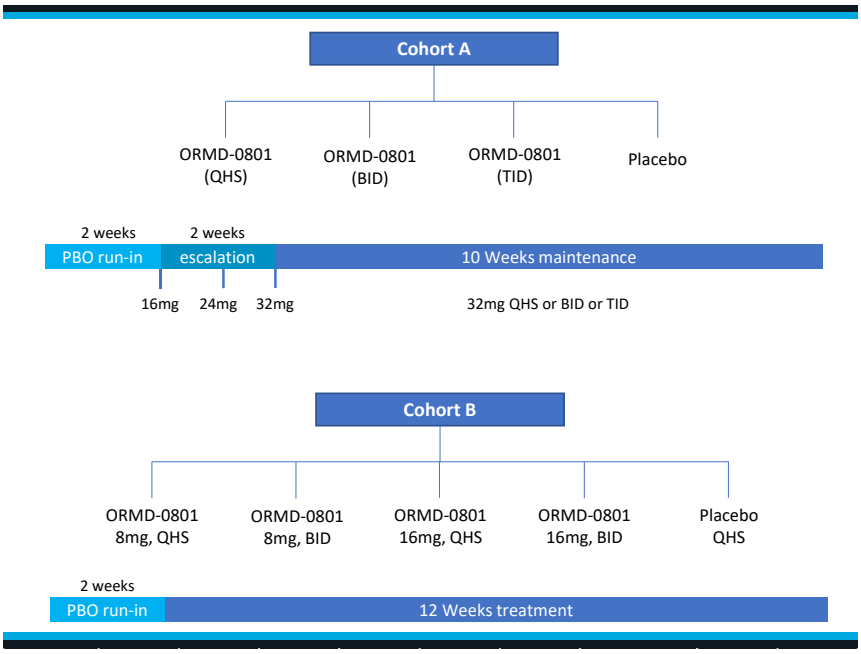
ORMD-0801 was well tolerated, and no serious adverse events were observed. The multiple-dose regimens safely provided improved glucose control, compared to placebo. Based on this outcome, Oramed decided to proceed to another Phase IIb study to focus on ORMD-0801's effect on HbA1c over a longer dosing period of 12 weeks.

Phase IIb study – ORA-D-015 – NCT03467932

The key 12-week HbA1c study

In 2019, Oramed conducted a placebo-controlled, randomized Phase IIb study in T2D patients with inadequate glycemic control with medication to further evaluate the efficacy and safety of ORMD-0801, as well as to find an optimal dosing regimen. The primary endpoint was mean change in HbA1c from baseline to Week 12. Key secondary endpoints include safety, change in HbA1c over time, change in glucose by CGM, and change in body weight. The study enrolled 347 patients, and 266 patients were included in the primary data analysis for week 12 HbA1c results.

Figure 16: Phase IIb study design



Source: Adapted from ClinicalTrials.gov and company reports

Results from this Phase IIb study was reported at multiple international conferences. The study met the primary endpoint and showed a clinically meaningful reduction in HbA1c levels. The reduction of HbA1c observed in the 8mg QHS (at bedtime) group (-0.81%, placebo adjusted), 8mg BID group (-0.82%, placebo adjusted), 32mg QHS group (-0.54%, placebo adjusted), and 32mg BID group (-0.53%, placebo adjusted) were statistically significant. The decrease of HbA1c achieved in patients with higher baseline HbA1c (>9%) was greater than the pooled patient population.

Figure 17: Significant HbA1c (%) changes observed in Phase IIb study

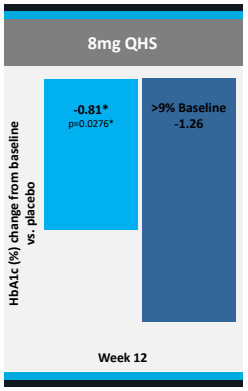
	HbA1c (%) change	p-value
8mg QHS	-0.81*	0.028
8mg BID	-0.82*	0.029
16mg QHS	0.25	
16mg BID	-0.36	
32mg QHS	-0.54*	0.036
32mg BID	-0.53*	0.042
32mg TID	-0.45	

All Patients were on Metformin.

Glucose lowering agents taken in addition to Metformin included: Glibenclamide,Glipizide, Empagliflozin, Pioglitazone, Glimepiride, Dapagliflozin, Sitagliptin, Glibomet, Ertugliflozin

Source: Adapted from company reports

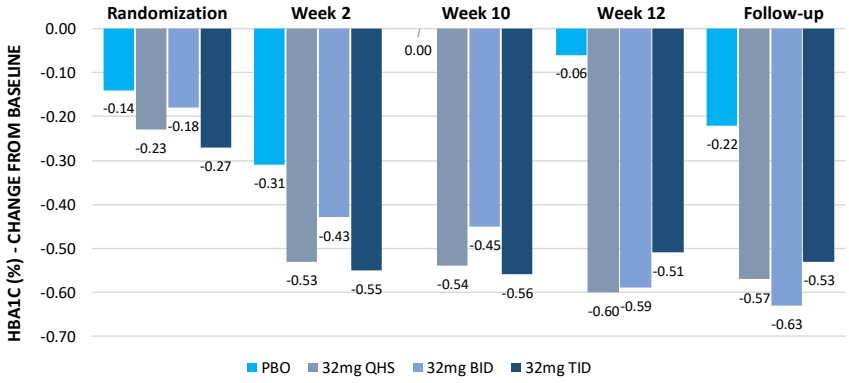
Figure 18: HbA1c (%) showed > reduction in patients with >9% at baseline



Source: Adapted from company reports

More results on the reduction of HbA1c and glycemic control in both Cohort A and Cohort B are shown in the exhibits below.

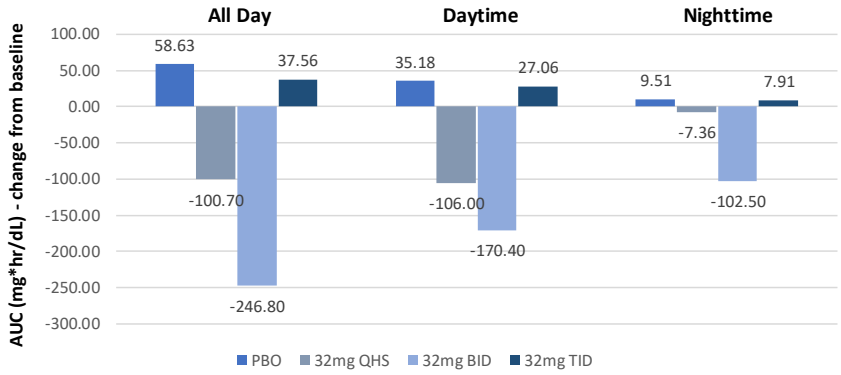
Figure 19: Cohort A HbA1c (%) change from baseline (Least Square Means)



Data presented as primary analysis from intention to treat (ITT) population.

Source: Adapted from company reports

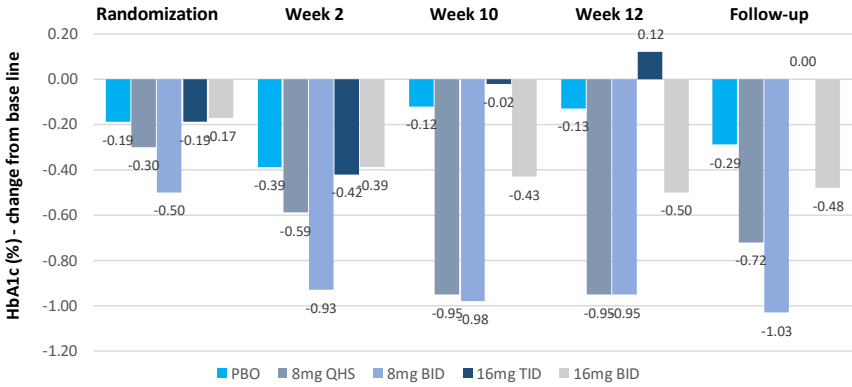
Figure 20: Cohort A glucose (CGM) change in ITT population



AUC: Area Under the Cursve. CGM: Continuous Glucose Monitoring. Data presented as primary analysis from intent-to-treat (ITT) population.

Source: Adapted from company reports

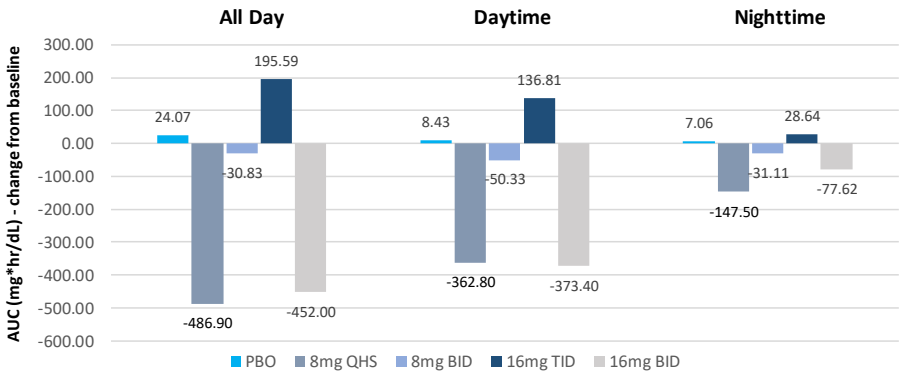
Figure 21: Cohort B HbA1c (%) change from baseline (Least Square Means)



Data presented as primary analysis from intention to treat (ITT) population.

Source: Adapted from company reports

Figure 22: Cohort B glucose (CGM) change in ITT population



AUC: Area Under the Cursve. CGM: Continuous Glucose Monitoring. Data presented as primary analysis from intent-to=treat (ITT) population.

Source: Adapted from company report

The study reported no increase in adverse events, no increase in hypoglycemic events, and no weight gain, compared to placebo.

Figure 23: Adverse events and hypoglycemic events observed in the Phase IIb study

Hypoglycemia	Placebo	8mg QHS	8mg BID	16mg QHS	16mg BID	32mg QHS	32mg BID	32mg TID
# events	25	0	16	20	0	16	4	32
# patients	5		4	1		6	3	6
# mild	25		15	20		15	4	32
# moderate	--		1	--		1	--	--
DRAEs								
# patients	3	2	0	0	1	6	3	9
conditions	Hypoglycemia, papules on fingers and toes, dry throat	Abdominal cramping, nausea, constipation, loose stools			Headache, abdominal bleeding	Diarrhea, headache, loss of appetite, dry mouth, anxiety, nausea, epigastric pain	Intermittent diarrhea, gastroesophageal reflux, pruritis, weight gain	Diarrhea, intermittent abdominal pain, loose stools, increased stool frequency, vomiting, soft stools

Source: Adapted from company reports

Based on these Phase IIb and prior clinical study results, Oramed has initiated a pivotal Phase III program for ORMD-0801 in the treatment of T2D.

ORMD-0801 enters Phase III for T2D

Phase III - ORA-D-013-1 & ORA-D-013-2 – NCT04606576 & NCT04754334

ORMD-0801 becomes first oral insulin to successfully reach Phase III

In November 2020, Oramed announced the initiation of its first Phase III study of ORMD-0801 for the treatment of T2D. In line with the FDA expectations and recommendations, two Phase III studies are being conducted concurrently in patients with T2D:

- ORA-D-013-1: a double-blinded, randomized, placebo-controlled, double dummy study to evaluate the efficacy and safety of ORMD-0801 in T2D patients with inadequate glycemic control on two or three oral glucose-lowing agents.
- ORA-D-013-2: a double-blinded, randomized, placebo-controlled study to evaluate the efficacy and safety of ORMD-0801 in T2D patients with inadequate glycemic control on diet control alone or on diet control and metformin monotherapy.

The studies combined will enroll approximately 1,125 patients to provide evidence of ORMD-0801's safety and efficacy in T2D patients over a treatment period of six to 12 months. A geographically diverse patient population will be recruited from multiple sites throughout the U.S., European Union countries, and Israel. Efficacy data from the studies will become available after all patients have completed the first six-month treatment period. Both trials are 90% powered to demonstrate a statistically significant difference in HbA1c vs. placebo.

Figure 24: Design of the Phase III studies for ORMD-0801 in T2D

ORA-D-013-1

1:1:1 randomization
675 adult patients
U.S.
75 U.S. sites

	night	45min before breakfast
Group 1:	✓ 8mg	placebo
Group 2:	✓ 8mg	✓ 8mg
Group 3:	placebo	placebo

Primary objective: efficacy in improving glycemic control by HbA1c (vs. placebo)

Secondary objective: safety of repeat administration

ORA-D-013-2

1:1 randomization
450 adult patients
U.S., EU, Isreal
28 U.S. sites, 25 ex-U.S. sites

	night
Group 1:	✓ 8mg
Group 2:	Placebo

Primary objective: efficacy in improving glycemic control by HbA1c over a 26-week treatment period (vs. placebo)

Secondary objective: efficacy in maintaining glycemic control over a 52-week treatment period

Source: Adapted from company report

The ORA-D-013-1 study has enrolled and randomized >25% of the 675 patients as of March 2021. Patients must have a HbA1c ≥7.5%, but ≤11.0% at screening. For a three-month period prior to screening, patients must be on a stable dose of two or three of the following glucose-lowering agents: metformin, DPP-4 inhibitor, SGLT-2 inhibitor, thiazolidinedione, and sulfonylurea.

The ORA-D-013-2 study began screening the first patients in March 2021. Patients must have a HbA1c ≥7.5%, but ≤11.0% at screening. For a three-month period prior to screening, patients must be on diet and exercise alone or diet and exercise with a stable dose of metformin only (≥1,500mg or MTD).

We project both Phase III studies to have top-line data read-outs in early 2023, followed by a BLA filing and subsequent FDA approval in 2024 under a normal review timeline of ten months.

Oramed licenses ORMD-0801 exclusively to Hefei Tianhui (HTIT) in China

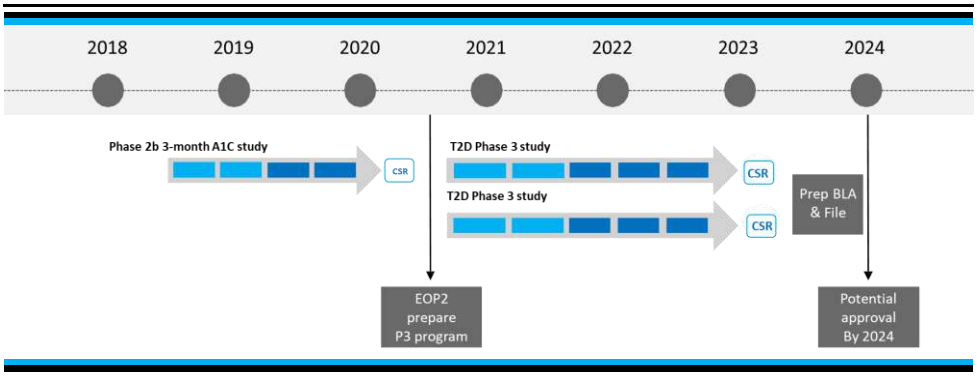
The first of what could be many territorial deals

HTIT is currently conducting T2D trials with ORMD-0801 in China. The deal includes $50M in upfront and milestone payments as well as up to 10% royalties on net sales. The $50M is comprised of $12M in restricted stock purchased at a premium and $38M in milestone payments. $33M has been received to date, and the additional $17M is expected to be realized over the next two to three years.

The diabetes market in China is significant. The World Health Organization estimates that approximately 11% of the Chinese population or 114M people have diabetes and ~388M of the total population are considered pre-diabetic.

We believe Oramed has a high potential of negotiating additional deals in varying territories worldwide.

Figure 25: Oramed's clinical development timeline



Source: Adapted from company reports

Oramed's pipeline potential

ORMD-0901: an oral GLP-1 for T2D

A growing medication class with limited oral options

Glucagon-like peptide -1 (GLP-1) is another hormone used in the treatment of diabetes. It plays important roles in regulating appetite and blood sugar levels. Endogenous GLP-1 decreases blood sugar levels in a glucose-dependent manner. Upon ingestion of food, the intestinal L-cells secrete GLP-1 into the hepatic portal system in a biphasic pattern (10-15min after meal ingestion and 30-60min after meal ingestion). GLP-1 then stimulates the release of insulin and inhibits the secretion of glucagon, which together leads to a net effect of lowering blood glucose levels. GLP-1 activity is preserved in patients with T2D, thus making it a target for drug development. Besides the peptide GLP-1 itself, GLP-1 receptor (GLP-1R) agonists injections are also commonly used post failure of oral blood sugar controlling drugs. Worldwide sales of GLP-1 analogues in 2020 were $12.8B, and Novo Nordisk estimates 2025 sales will reach $22B. Hot targets, such as GLP-1 peptide, GLP-1R agonists are under active clinical development or have already been approved by regulatory agencies. However, most are designed to be delivered by injection.

- Dulaglutide (Trulicity) SQ injection QW – Eli Lilly
- Exenatide ER (Bydureon) SQ injection QW - AstraZeneca
- Exenatide (Byetta) SQ injection BID - AstraZeneca
- Liraglutide (Victoza) SQ injection QD – Novo Nordisk
- Lixisenatide (Adlyxin) SQ injection QD - Sanofi
- Semaglutide (Ozempic) SQ injection QW – Novo Nordisk

- Semaglutide (Rybelsus) oral QD – Novo Nordisk

Oral semaglutide received FDA approval in 2019. Novo Nordisk uses the Eligen technology from Emisphere, which it acquired in December 2020 for $1.35B in cash.

ORMD-0901 is Oramed's GLP-1 capsule, an analog of exenatide, based on the company's POD technology. Glucagon-like peptide-1 (GLP-1) is an incretin hormone that stimulates the secretion of insulin from the pancreas.

In January 2019, Oramed initiated recruitment for a Phase I pharmacokinetic (PK) study for ORMD-0901. This was the first study of ORMD-0901 under Oramed's existing FDA Investigational New Drug (IND) application. The study was a randomized, single-blind, placebo-controlled, crossover study that evaluated the safety in addition to the pharmacokinetics of ORMD-0901 compared to placebo and to open label Byetta in 16 healthy subjects.

In June 2019, Oramed announced that it had completed the Phase I PK study and is assessing future study options.

ORMD-0801 as a potential first oral insulin option for NASH

Phase II – Proof of concept study – NCT02653300

The Phase pilot study of ORMD-0801 is being conducted in T2D patients with non-alcoholic steatohepatitis (NASH). In June 2020, data from the initial eight subjects was presented at the American Diabetes Association virtual annual meeting. ORMD-0801 was shown to be safe and well tolerated, with an encouraging lowering of fatty liver content, as seen by MRI- derived proton density fat fraction (MRI-PDFF). The pilot, open-label study of the first 8 patients of a planned 30-patient multi-center study aimed to assess the safety, tolerability, and early effects of 16mg ORMD-0801 (2×8mg capsules) on liver fat in T2D patients with NASH.

The 12-week, once-daily treatment had no serious adverse events and induced an observed mean 6.9±6.8% reduction in liver fat content (sign test p value: 0.035), and the relative reduction was 30% as measured by MRI-PDFF. In parallel, concentrations of gamma-glutamyltransferase (GGT), a key marker of chronic hepatitis, were significantly lower after 12 weeks of treatment as compared to baseline (-14.6±13.1 U/L; sign test p value: 0.008), as were fasting insulin levels (-96.5±206.0pmol/L; sign test p value: 0.035).

To date, ten additional patients in the EU have been enrolled in the study.

Phase II – NCT04618744

In additional to the pilot study, Oramed has initiated a 36-patient Phase IIa trial for ORMD-0801 in patients with T2D and NASH.

In December 2020 screening of the first patients in the U.S. began. The trial is being conducted in the U.S., EU and Israel. The trial will be comprised of eight clinical sites: three in the EU, three in the U.S. and two in Israel. The trial will measure efficacy endpoints via MRI-PDFF at 12 weeks of dosing. The trial is a double-blind, randomized, placebo-controlled, multi-center study using the oral ORMD-0801 insulin formulation in patients with NASH and confirmed T2D. The study will consist of a screening phase, placebo run-in phase, treatment phase and an end-of-study phase. Approximately 36 subjects will be randomized in a 2:1 ratio to receive either 8mg ORMD-0801, one capsule twice a day (once in the morning approximately 30 to 45 minutes prior to breakfast and no later than 10 AM, and once at night between 8 PM to midnight and no sooner than one hour after dinner) or matching placebo. The primary endpoint will be the number of treatment-related adverse events and the secondary endpoint will be liver fat content as measured by MRI-PDFF.

Reference product exclusivity – 12 years

While Oramed has filed and issued patents related to the company's oral delivery technology, we view the 12 years of exclusivity that ORMD-0801 would be granted upon BLA approval as the most significant barrier to competition. In 1997, Congress established the biologics license application (BLA), an application for biological product approval filed under section 351(a) of the Public Health Service (PHS) Act. Subsequent, substantial growth in biologic drug applications urged the development of the Biologics Price Competition and Innovation Act of 2009 (BPCIA).

Under BPCIA, sponsors of new, licensed biological products approved through a BLA receive 12 years of "reference product exclusivity." The FDA cannot license any 351(k) application for a biosimilar or interchangeable product that relies on the previously approved product as a reference for biosimilarity during this 12-year period. The Reference Product Exclusivity does not attach to molecules that are the "same" as a molecule previously approved for the same sponsor.

Investing in Oramed – the risks

Clinical risk: Although ORMD-0801 has demonstrated clinical proof-of-concept in patients with T2D, the molecule is now being dosed in larger Phase III trials, and as more patients are exposed to drug over time there is the chance that issues could appear relating to efficacy, safety or both. While there is a significant amount of literature speaking to insulin use in treating T2D, ORMD-0801 is a unique orally delivered version of insulin and only through additional clinical trials can the molecule be further de-risked.

Regulatory risk: Given that there are currently no oral-insulin options approved for the treatment of T2D, the FDA is in new territory regarding the review of this type of molecule administration. The FDA continues to be unpredictable even with the review pathways, designations and outside panel reviews that can be employed during the review process.

Commercial risk: Given that there are currently no oral insulin therapeutics approved for the treatment of T1D and T2D, grasping the true commercial opportunity post-launch is difficult. The outcome of the two-Phase III trials and final labeling will be key to understanding the true market potential for ORMD-0801.

Competitive risk: The competitive landscape for T2D drug development is crowded. The opportunity to tap into a mature multi-billion-dollar market opportunity will result in the space remaining competitive. In addition to the overall T2D clinical landscape being competitive, specific to Oramed there are multiple players attempting to develop an oral delivery option for insulin.

Management risk: For a clinical stage biotech, stability in the C-suite roles is key as it is with any company. Turnover, especially in regulatory agency-facing roles such as CEO and CSO, could negatively impact share performance.

An experienced management team

We believe Oramed has strong scientific leadership with focused experience in the biotechnology sector and a deep focus on diabetes. Both the CEO and COO have extensive experience in leading their respective efforts at multiple biotech companies in differing stages of life-cycle evolution. In addition to reviewing management's previous experience and making an assessment as to their "fit" in their current role, we also examine the overall compensation structure of the senior management team. We compare the compensation of the C-suite executives to other executives at biotech companies of the same size and stage of development. We view this exercise as important in making sure executive compensation is in line with the interests of shareholders. We believe the comp structure at Oramed is aligned with shareholder interests and falls in line with the comp of similar executives at biotech companies of comparable size and stage of development.

Nadav Kidron, Esq – President, Director and Chief Executive Officer

Mr. Kidron serves as Chief Executive Officer & Director of Oramed Pharmaceuticals, which he co-founded in 2006. He is an entrepreneur whose experience includes senior executive roles in a wide range of industries. He co-founded Entera Bio as a joint venture formed by Oramed and DNA Biomedical Solutions. He is a member of the IATI Board and an international lecturer on Israel's entrepreneurial culture and the country's roots as an oasis of innovative ideas. He holds a bachelor's degree in law and an international master's in business administration, both from Bar-Ilan University in Israel. Mr. Kidron is a fellow of the Merage Business Executive Leadership Program and a member of the Israeli Bar Association.

Miriam Kidron, Ph.D. – Chief Scientific Officer and Director

Dr. Kidron serves as Chief Scientific Officer and Director of Oramed Pharmaceuticals, which she co-founded in 2006. She is a pharmacologist and biochemist who earned her Ph.D. in biochemistry from the Hebrew University of Jerusalem. For close to 20 years, Dr. Kidron has been a senior researcher in the Diabetes Unit at Hadassah-Hebrew University Medical Center in Jerusalem, Israel, earning the Bern Schlanger Award for her work on diabetes research. She was formerly a visiting professor at the Medical School at the University of Toronto and is a member of the American, European and Israeli Diabetes Associations.

Josh Hexter – Chief Operating and Business Officer

Mr. Hexter serves as Chief Operating and Business Officer of Oramed Pharmaceuticals. Mr. Hexter has nearly two decades of prominent leadership, business development and operations know-how, entrepreneurialism and management experience in the life science sector. Prior to his current position, Mr. Hexter was Chief Business Officer of BrainsWay Ltd. Previously, he served as the Chief Operating Officer of Oramed. Mr. Hexter has also served as Executive Director of Corporate In-Licensing at BioLineRx and in the private equity and venture capital sector where he served as CEO of a VC-backed start-up. As founder and CEO of Biosensor Systems Design, Mr. Hexter was instrumental in shaping the company's strategic focus and in forging strategic agreements with Fortune 100 companies in the areas of food safety, medical diagnostics and homeland security. Mr. Hexter earned a bachelor's degree from the University of Wisconsin and a master's degree in management from Boston University.

Figure 26: Oramed Pharmaceuticals, Inc. (ORMP) - income statement ($MM)

	2019	2020					2021E					2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E
		1Q	2Q	3Q	4Q	Year	1Q	2Q	3QE	4QE	Year															
ORMD-0801 T2D product sales	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	11.6	24.5	77.9	206.0	485.5	1,089.6	1,482.2	1,916.8	2,426.8	2,962.7	3,134.7	3,316.7	3,552.6
Collaboration revenue	2.7	0.7	0.7	0.7	0.7	2.7	0.7	0.7	1.8	0.6	3.7	2.5	2.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total Revenue	**2.7**	**0.7**	**0.7**	**0.7**	**0.7**	**2.7**	**0.7**	**0.7**	**1.8**	**0.6**	**3.7**	**2.5**	**2.5**	**11.6**	**24.5**	**77.9**	**206.0**	**485.5**	**1089.6**	**1482.2**	**1916.8**	**2426.8**	**2962.7**	**3134.7**	**3316.7**	**3552.6**
Cost of U.S. product sales	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.2	2.5	7.8	20.6	48.5	109.0	148.2	191.7	242.7	296.3	313.5	331.7	355.3
Gross profit	2.6	0.7	0.7	0.7	0.7	2.7	0.7	0.7	1.8	0.6	3.7	2.5	2.5	10.4	22.1	70.1	185.4	436.9	980.6	1334.0	1725.1	2184.1	2666.4	2821.2	2985.0	3197.3
R&D	13.5	2.0	3.3	1.9	3.0	10.2	5.8	3.9	12.5	21.9	44.0	50.0	55.0	60.0	58.0	59.7	61.5	63.4	65.3	67.2	69.3	71.3	73.5	75.7	77.9	80.3
G&A	3.7	1.1	1.4	1.0	0.7	4.2	0.7	1.7	1.3	1.0	4.7	5.0	6.5	8.0	8.4	8.8	9.3	9.7	10.2	10.7	11.3	11.8	12.4	13.0	13.7	14.4
Sales expense	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	18.8	31.3	37.5	38.6	39.8	41.0	42.2	43.5	44.8	46.1	47.5	48.9	50.4
Operating expense	17.2	3.1	4.7	3.0	3.7	14.5	6.5	5.5	13.8	22.9	48.7	55.0	61.5	86.8	97.7	106.1	109.4	112.9	116.5	120.2	124.0	127.9	132.0	136.2	140.6	145.0
Operating Profit (Loss)	**(14.6)**	**(2.4)**	**(4.0)**	**(2.3)**	**(3.0)**	**(11.8)**	**(5.8)**	**(4.9)**	**(12.0)**	**(22.3)**	**(45.0)**	**(52.5)**	**(59.0)**	**(76.3)**	**(75.6)**	**(36.0)**	**75.9**	**324.0**	**864.1**	**1213.8**	**1601.1**	**2056.2**	**2534.4**	**2685.0**	**2844.5**	**3052.3**
Interest income	1.1	0.2	(0.2)	0.2	0.5	0.7	0.3	0.3	0.2	0.2	0.9	0.8	0.8	0.8	0.8	0.8	0.8	3.2	8.6	12.1	16.0	20.6	25.3	26.9	28.4	30.5
Interest expense	0.5	0.0	0.0	0.0	0.4	0.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Loss (gain) fair value of investments	0.0	(0.3)	(0.2)	0.2	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Pretax profit (loss)	(14.1)	(2.5)	(3.7)	(2.3)	(3.0)	(11.5)	(5.6)	(4.6)	(11.8)	(22.1)	(44.1)	(51.7)	(58.2)	(75.5)	(74.8)	(35.2)	76.7	327.3	872.8	1226.0	1617.1	2076.7	2559.8	2711.9	2872.9	3082.8
Income Tax	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	20.7	88.4	235.7	331.0	436.6	560.7	691.1	732.2	775.7	832.4
Tax rate	-2.1%	0.0%	0.0%	0.0%	0.0%	0.0	0.0%	0.0%	*0.0%*	*0.0%*	0.0%	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*27.0%*	*27.0%*	*0.3*	*0.3*	*0.3*	*0.3*	*0.3*	*0.3*	*0.3*	*0.3*
Net Income (Loss)	**(14.4)**	**(2.5)**	**(3.7)**	**(2.3)**	**(3.0)**	**(11.5)**	**(5.6)**	**(4.6)**	**(11.8)**	**(22.1)**	**(44.1)**	**(51.7)**	**(58.2)**	**(75.5)**	**(74.8)**	**(35.2)**	**56.0**	**238.9**	**637.1**	**895.0**	**1180.5**	**1516.0**	**1868.6**	**1979.7**	**2097.2**	**2250.4**
EPS - basic	**($0.82)**	**($0.15)**	**($0.21)**	**($0.10)**	**($0.13)**	**($0.56)**	**($0.23)**	**($0.17)**	**($0.39)**	**($0.67)**	**($1.56)**	**($1.41)**	**($1.30)**	**($1.45)**	**($1.36)**	**($0.64)**	**$1.01**	**$4.32**	**11.5**	**16.1**	**21.2**	**27.2**	**33.5**	**35.4**	**37.4**	**40.1**
EPS - diluted	**($0.82)**	**($0.15)**	**($0.21)**	**($0.10)**	**($0.13)**	**($0.56)**	**($0.23)**	**($0.17)**	**($0.39)**	**($0.67)**	**($1.56)**	**($1.41)**	**($1.30)**	**($1.45)**	**($1.36)**	**($0.64)**	**$1.01**	**$4.32**	**11.5**	**16.1**	**21.2**	**27.2**	**33.5**	**35.4**	**37.4**	**40.1**
Weighted average basic shares	17.5	17.5	17.8	23.2	23.7	20.5	23.7	27.0	30.5	32.8	28.3	36.7	44.7	51.9	55.0	55.1	55.2	55.3	55.4	55.5	55.6	55.7	55.8	55.9	56.0	56.1
Weighted average diluted shares	17.5	17.5	17.8	23.2	23.7	20.5	23.7	27.0	30.5	32.8	28.3	36.7	44.7	51.9	55.0	55.1	55.2	55.3	55.4	55.5	55.6	55.7	55.8	55.9	56.0	56.1

Source: Company reports, Canaccord Genuity estimates. A more detailed financial model, including balance sheet, income statement, and cash flow projections, if available, may be obtained by contacting your Canaccord Genuity Sales Person or the Authoring Analyst, whose contact information appears on the front page of this report.

Figure 27: Oramed Pharmaceuticals, Inc. (ORMP) - cash flow statement ($MM)

	2019	2020					2021E					2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E
		1Q	2Q	3Q	4Q	Year	1Q	2Q	3QE	4QE	Year															
EBIT	(14.6)	(2.4)	(4.0)	(2.3)	(3.0)	(11.8)	(5.8)	(4.9)	(12.0)	(22.3)	(45.0)	(52.5)	(59.0)	(76.3)	(75.6)	(36.0)	75.9	324.0	864.1	1,213.8	1,601.1	2,056.2	2,534.4	2,685.0	2,844.5	3,052.3
D&A	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Amortization of lease asset	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Stock compensation expense	0.8	0.3	0.6	0.9	(0.6)	1.2	0.3	0.7	1.0	1.1	3.1	3.0	4.0	15.0	15.5	15.9	16.4	16.9	17.4	17.9	18.4	19.0	19.6	20.2	20.8	21.4
EBITDA	(13.8)	(2.1)	(3.5)	(1.4)	(3.6)	(10.6)	(5.5)	(4.1)	(11.0)	(21.2)	(41.8)	(49.5)	(55.0)	(61.3)	(60.1)	(20.0)	92.4	341.0	881.6	1,231.8	1,619.6	2,075.2	2,554.0	2,705.2	2,865.3	3,073.7
Accounts receivable	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Inventory	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Prepaid expense	(0.5)	0.4	0.5	0.6	0.0	0.4	(1.1)	1.0	0.4	(0.0)	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Accounts payable	0.5	(0.7)	(0.2)	(1.2)	0.0	(0.8)	1.2	0.2	0.0	0.0	1.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Accrued expense	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Deferred revenue	0.3	0.0	(1.3)	(2.0)	0.0	(2.7)	(0.7)	(0.7)	0.0	0.0	(1.3)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Lease liability	(0.5)	(0.7)	(0.0)	(0.0)	0.0	(0.0)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Cash interest	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Cash tax	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	(20.7)	(88.4)	(235.7)	(331.0)	(436.6)	(560.7)	(691.1)	(732.2)	(775.7)	(832.4)
Other	(0.0)	0.0	(0.0)	(0.1)	0.0	(0.1)	0.0	(0.0)	0.0	0.0	(0.0)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Cash from operations	(14.0)	(3.1)	(4.6)	(4.1)	(3.6)	(13.7)	(6.1)	(3.6)	(10.6)	(21.2)	(41.6)	(49.5)	(55.0)	(61.3)	(60.1)	(20.0)	71.7	252.6	645.9	900.8	1,183.0	1,514.5	1,862.9	1,973.0	2,089.6	2,241.3
Capex	(0.0)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	3.0	3.2	3.3	3.4	3.5	3.7	3.8	4.0	4.1	4.3	4.5	4.7	4.8
Free cash flow	(14.0)	(3.1)	(4.6)	(4.1)	(3.6)	(15.4)	(6.1)	(3.6)	(10.6)	(21.2)	(41.6)	(49.5)	(55.0)	(58.3)	(56.9)	(16.8)	75.1	256.1	649.6	904.6	1,187.0	1,518.6	1,867.2	1,977.5	2,094.2	2,246.2
Cash from operations	**(12.9)**	**(3.0)**	**(6.6)**	**(10.0)**	**(3.6)**	**(12.4)**	**(6.2)**	**(3.2)**	**(10.6)**	**(21.2)**	**(41.2)**	**(49.5)**	**(55.0)**	**(61.3)**	**(60.1)**	**(20.0)**	**71.7**	**252.6**	**645.9**	**900.8**	**1183.0**	**1514.5**	**1862.9**	**1973.0**	**2089.6**	**2241.3**
Cash from investing	**11.3**	**2.8**	**6.9**	**(6.3)**	**1.2**	**4.6**	**1.2**	**(3.3)**	**0.0**	**0.0**	**(2.1)**	**0.0**	**0.0**	**3.0**	**3.2**	**3.3**	**3.4**	**3.5**	**3.7**	**3.8**	**4.0**	**4.1**	**4.3**	**4.5**	**4.7**	**4.8**
Cash from financing	**0.0**	**0.0**	**2.3**	**22.3**	**(0.9)**	**23.8**	**0.6**	**25.4**	**32.9**	**0.0**	**32.9**	**70.5**	**141.0**	**141.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
F/X	**0.0**	**0.0**	**0.0**	**(0.0)**	**0.0**	**(0.0)**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Net change in cash	**(1.7)**	**(0.2)**	**2.6**	**6.0**	**(3.2)**	**16.0**	**(4.4)**	**18.9**	**22.3**	**(21.2)**	**(10.4)**	**21.0**	**86.0**	**82.7**	**(56.9)**	**(16.8)**	**75.1**	**256.1**	**649.6**	**904.6**	**1187.0**	**1518.6**	**1867.2**	**1977.5**	**2094.2**	**2246.2**
Cash, Beginning	**5.0**	**3.3**	**3.2**	**5.8**	**11.8**	**3.3**	**19.3**	**14.9**	**33.8**	**56.1**	**19.3**	**8.9**	**29.9**	**115.9**	**198.7**	**141.7**	**125.0**	**200.0**	**456.1**	**1105.7**	**2010.3**	**3197.3**	**4715.9**	**6583.1**	**8560.6**	**10654.8**
Cash, Ending	**3.3**	**3.2**	**5.8**	**11.8**	**8.6**	**19.3**	**14.9**	**33.8**	**56.1**	**34.9**	**8.9**	**29.9**	**115.9**	**198.7**	**141.7**	**125.0**	**200.0**	**456.1**	**1,105.7**	**2010.3**	**3197.3**	**4715.9**	**6583.1**	**8560.6**	**10654.8**	**12901.0**

Source: Company reports, Canaccord Genuity estimates

Figure 28: Oramed Pharmaceuticals, Inc. (ORMP) – balance sheet metrics ($MM)

	2019	2020					2021E					2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E
		1Q	2Q	3Q	4Q	Year	1Q	2Q	3QE	4QE	Year															
Cash	3.3	3.2	5.9	9.3	19.3	19.3	14.9	33.8	56.1	34.9	34.9	29.9	115.9	198.7	141.7	125.0	200.0	456.1	1,105.7	2,010.3	3,197.3	4,715.9	6,583.1	8,560.6	10,654.8	12,901.0
Marketable securities	29.0	27.0	23.0	23.2	20.6	20.6	19.4	23.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total Cash	32.3	30.1	28.9	32.5	39.9	39.9	34.3	56.8	56.1	34.9	34.9	29.9	115.9	198.7	141.7	125.0	200.0	456.1	1,105.7	2,010.3	3,197.3	4,715.9	6,583.1	8,560.6	10,654.8	12,901.0

Source: Company reports, Canaccord Genuity estimates

Figure 29: Oramed Pharmaceuticals, Inc. (ORMP) - share count (MM)

	2019	2020					2021E					2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E
		1Q	2Q	3Q	4Q	Year	1Q	2Q	3QE	4QE	Year															
Basic shares, beginning	17.4	17.4	17.4	17.4	23.3	17.4	23.7	23.8	28.3	32.8	23.7	32.9	40.5	48.9	55.0	55.1	55.2	55.3	55.4	55.5	55.6	55.7	55.8	55.9	56.0	56.1
Option exercise, ATM, etc.	0.0	0.0	0.0	0.0	0.4	1.0	0.1	4.5	0.1	0.1	4.8	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Gross dollar value of stock offering	$0.0	$0.0	$0.0	$23.5	$0.0	$23.5	$0.0	$0.0	$35.0	$0.0	$35.0	$75.0	$150.0	$150.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Price per share	$0.00	$0.00	$0.00	$4.00	$0.00	$4.00	$0.00	$0.00	$8.00	$0.00	$8.00	$10.00	$18.00	$25.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00
Shares issued	0.0	0.0	0.0	5.9	0.0	5.9	0.0	0.0	4.4	0.0	4.4	7.5	8.3	6.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net change in basic shares	0.0	0.0	0.0	5.9	0.4	6.3	0.1	4.5	4.5	0.1	9.2	7.6	8.4	6.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Basic shares, ending	17.4	17.4	17.4	23.3	23.7	23.7	23.8	28.3	32.8	32.9	32.9	40.5	48.9	55.0	55.1	55.2	55.3	55.4	55.5	55.6	55.7	55.8	55.9	56.0	56.1	56.2
Weighted Average Basic Shares	17.4	17.4	17.4	20.3	23.5	20.5	23.7	26.0	30.5	32.8	28.3	36.7	44.7	51.9	55.0	55.1	55.2	55.3	55.4	55.5	55.6	55.7	55.8	55.9	56.0	56.1
Options & RSU/PSU/PSA/RSA	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Weighted average diluted shares	17.4	17.4	17.4	20.3	23.5	20.5	23.7	26.0	30.5	32.8	28.3	36.7	44.7	51.9	55.0	55.1	55.2	55.3	55.4	55.5	55.6	55.7	55.8	55.9	56.0	56.1

Source: Company reports, Canaccord Genuity estimates

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Investment Recommendation

Date and time of first dissemination: April 20, 2021, 05:04 ET

Date and time of production: April 20, 2021, 04:05 ET

Target Price / Valuation Methodology:

Oramed Pharmaceuticals - ORMP

We value shares of Oramed by employing a sum-of-the-parts analysis that includes programs where we believe clinical data is available to fairly determine the overall probability of success, as well as net cash on hand. Our estimates solely for the T2D program in the U.S. are used to generate our $27 12-month price target, and we view any additional programs such as T1D, NASH and T2D ex-U.S. as potential upside to our estimates.

Risks to achieving Target Price / Valuation:

Oramed Pharmaceuticals - ORMP

Clinical risk: Although ORMD-0801 has demonstrated clinical proof-of-concept in patients with T2D, the molecule is now being dosed in larger Phase III trials, and as more patients are exposed to drug over time there is the chance that issues could appear relating to efficacy, safety or both. While there is a significant amount of literature speaking to insulin use in treating T2D, ORMD-0801 is a unique orally delivered version of insulin and only through additional clinical trials can the molecule be further de-risked.

Regulatory risk: Given that there are currently no oral-insulin options approved for the treatment of T2D, the FDA is in new territory regarding the review of this type of molecule administration. The FDA continues to be unpredictable even with the review pathways, designations and outside panel reviews that can be employed during the review process.

Commercial risk: Given that there are currently no oral insulin therapeutics approved for the treatment of T1D and T2D, grasping the true commercial opportunity post-launch is difficult. The outcome of the two-Phase III trials and final labeling will be key to understanding the true market potential for ORMD-0801.

Competitive risk: The competitive landscape for T2D drug development is crowded. The opportunity to tap into a mature multi-billion-dollar market opportunity will result in the space remaining competitive. In addition to the overall T2D clinical landscape being competitive, specific to Oramed there are multiple players attempting to develop an oral delivery option for insulin.

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Global Stock Ratings (as of 04/20/21)

Rating	Coverage Universe		IB Clients
	#	%	%
Buy	601	64.48%	40.10%
Hold	159	17.06%	20.75%
Sell	14	1.50%	28.57%
Speculative Buy	143	15.34%	68.53%
	932*	100.0%	

*Total includes stocks that are Under Review

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Oramed Pharmaceuticals Rating History as of 04/19/2021

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