

# KAMADA INVESTOR PRESENTATION

NASDAQ & TASE: KMDA

April 2018

### FORWARD LOOKING STATEMENT



This presentation is not intended to provide investment or medical advice. It should be noted that some products under development described herein have not been found safe or effective by any regulatory agency and are not approved for any use outside of clinical trials.

This presentation contains forward-looking statements, which express the current beliefs and expectations of Kamada's management. Such statements involve a number of known and unknown risks and uncertainties that could cause Kamada's future results, performance or achievements to differ significantly from the prospected results, performances or achievements expressed or implied by such forward-looking statements. Important factors that could cause or contribute to such differences include, but are not limited to, risks relating to Kamada's ability to successfully develop and commercialize its pharmaceutical products, the progress and results of any clinical trials, the introduction of competing products, the impact of any changes in regulation and legislation that could affect the pharmaceutical industry, the difficulty of predicting, obtaining or maintaining U.S. Food and Drug Administration, European Medicines Agency and other regulatory authority approvals, the regulatory environment, restrains related to third parties' IP rights and changes in the health policies and structures of various countries, environmental risks, changes in the worldwide pharmaceutical industry and other factors that are discussed under the heading "Risk Factors" of Kamada's 2017 Annual Report on Form 20-F as well as in Kamada's recent Forms 6-K filed with the U.S. Securities and Exchange Commission.

This presentation includes certain non-IFRS financial information, which is not intended to be considered in isolation or as a substitute for, or superior to, the financial information prepared and presented in accordance with IFRS. The non-IFRS financial measures may be calculated differently from, and therefore may not be comparable to, similarly titled measures used by other companies. In accordance with the requirement of the SEC regulations a reconciliation of these non-IFRS financial measures to the comparable IFRS measures is included in an appendix to this presentation. Management uses these non-IFRS financial measures for financial and operational decision-making and as a means to evaluate period-to-period comparisons. Management believes that these non-IFRS financial measures provide meaningful supplemental information regarding Kamada's performance and liquidity.

Forward-looking statements speak only as of the date they are made, and Kamada undertakes no obligation to update any forward-looking statement to reflect the impact of circumstances or events that arise after the date the forward-looking statement was made, except as required by applicable securities laws. You should not place undue reliance on any forward-looking statement and should consider the uncertainties and risks noted above, as well as the risks and uncertainties more fully discussed under the heading "Risk Factors" of Kamada's 2017 Annual Report on Form 20-F as well as in Kamada's recent Forms 6-K filed with the U.S. Securities and Exchange Commission.

### **KAMADA – COMPANY PROFILE**



### COMMERCIAL STAGE BIOPHARMA

- Leader in plasma-derived protein therapeutics, focused on Alpha-1 Antitrypsin ("AAT") and specific hyper-immune IgGs
- 2 FDA approved products
  - Glassia® for AAT Deficiency (AATD); first FDA-approved liquid, ready-to-use IV AAT. Commercialized in the US through Shire plc.
  - KedRAB® for anti-rabies prophylaxis treatment. Commercialized in the US through Kedrion Biopharma.

# BUILDING PIPELINE/ IP

- Focused on global leadership in AAT Deficiency (AATD) through development, manufacturing, collaborations, and commercialization of innovative therapeutic approaches
- Inhaled AAT completed Ph2 (US) and Ph2/3 (EU), MAA withdrawn June 2017; FDA discussions re regulatory path forward; additional pivotal Phase 3 pending IND approval.
- AAT IV for other indications developed through strategic collaborations
- Fully integrated propriety manufacturing technology for extraction & purification of proteins from human plasma

### FINANCIAL SUMMARY

- 2017 Revenue: \$103 MM (represents 33% annual growth and exceeded annual guidance)
- 2018 Revenue Guidance: \$116-\$120MM
- Market Cap = ~\$186 MM<sup>1</sup>; Cash: \$43 MM; No Debt<sup>2</sup>
- Ticker: KMDA; Listed on TASE (2005) and Nasdaq (2013)
- Employees =  $413^2$

## HIGH VALUE PRODUCT PIPELINE



Product	Indication		Phase I	Phase II	Phase III Market	
Glassia® (IV AAT) *	AAT Deficiency	FDA approved (2010)				U.S. distribution through Shire
KamRab®/KedRab® (IM Anti-Rabies)	Prophylaxis for Rabies	FDA approved (2017)				U.S. distribution through
Inhaled AAT	AAT Deficiency <sup>1</sup>	EU Phase 2/3 (completed) MAA withdrawn (June 2017) US Phase 2 (completed) FDA review of path forward		>		May seek partner upon IND approval
D1-AAT (IV)	Type 1 Diabetes <sup>2</sup>	Phase 2 (completed)		>		Seeking partner for further development
G1-AAT (IV)	Graft vs Host Disease (GvHD) <sup>1</sup>	Phase 1/2 (completed)Phase 2 (initiation)		>		Ph2 in collaboration with MAGIC <sup>3</sup>
L1-AAT (IV)	Lung Transplant	Phase 2 (ongoing)		>		In collaboration with Shire plc

<sup>\*</sup> Recombinant AAT for AAT Deficiency in early development stages

3. Mount Sinai Acute GVHD International Consortium

<sup>1.</sup> Orphan drug designation (US & EU); 2. Orphan drug designation (US only);

Alpha-1 Antitrypsin Deficiency (AATD)



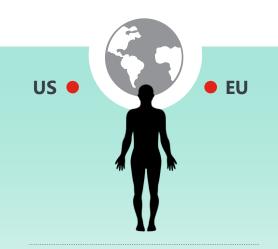
### **AAT DEFICIENCY**

## Potentially Lethal and Often Undiagnosed

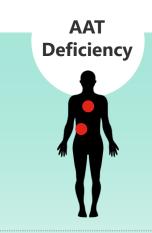




Genetic/Hereditary condition causing decreased levels of AAT in blood and tissues



Affects more then 100,000 people in the US and slightly lower number in Europe



# Predisposes to lung and liver diseases

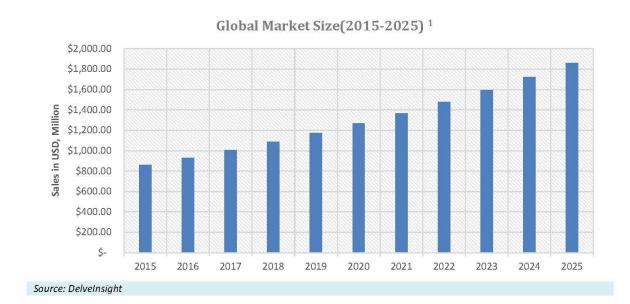
AAT deficiency-associated lung disease is characterized by airway obstruction and destructive changes in the lungs (Emphysema)

## **AAT DEFICIENCY (AATD) MARKET**

### Significant expansion opportunity



- Majority of patients suffering from AATD still remain undiagnosed & untreated
- Better diseases awareness and expanded diagnostics is contributing to increased demand
- Expected growth of US market approx. 8% annually<sup>1</sup>
- Greater AAT use in Europe and other geographies could further accelerate market growth
- Chronic therapy creates sustainable product revenue opportunity
- Average annual reimbursement (U.S.)
   ~\$80-\$100K per patient



• AATD prevalence <sup>1</sup>: ~115,000 (U.S.); ~72,000 (EU5) but only ~7,300 (U.S.) or ~1,800 (EU5) patients are treated <sup>1</sup>

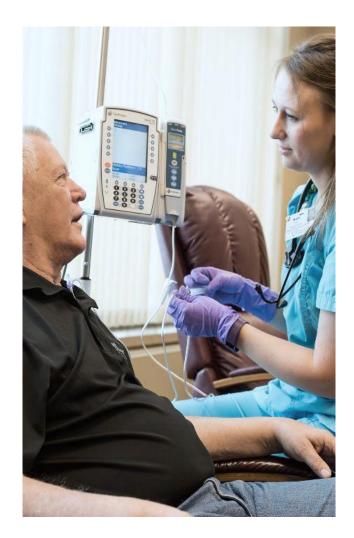
- Current market size is ~ \$1B WW
- Expected to reach \$1.8B by 2025

GLASSIA®:
Liquid AAT
for the
Treatment
of AAT
Deficiency



### **GLASSIA® IS A DIFFERENTIATED PRODUCT**





- Glassia® is the first liquid, FDA-approved ready-to-use, plasma-derived AAT product:
  - No reconstitution required
  - Reduces treatment time
  - Reduces risk of contamination and infection
- Kamada's highly purified liquid product is manufactured through a proprietary process
- Glassia<sup>®</sup> is sold in the U.S. by Shire plc
- Number of patients on Glassia increased by approx. 25% per year in each of 2014, 2015 and 2016
- Self-infusion approved by FDA in 2016

# GROWTH OF GLASSIA® DRIVEN BY STRATEGIC PARTNERSHIP WITH SHIRE



Significant Revenues to Kamada through 2020 followed by 20 Years of Royalties

Glassia® is sold in 5 countries, with majority of sales in the U.S.

- Minimum/max revenues of \$177MM/\$228MM to Kamada expected for 2018-2020
- Kamada manufactures and supplies Glassia to Shire through 2020
- Commencing on 2021, Shire to manufacture Glassia and pay royalties to Kamada through 2040
- Territory U.S., Canada, Australia and New Zealand
- Agreement covers all future AAT IV indications in the territory



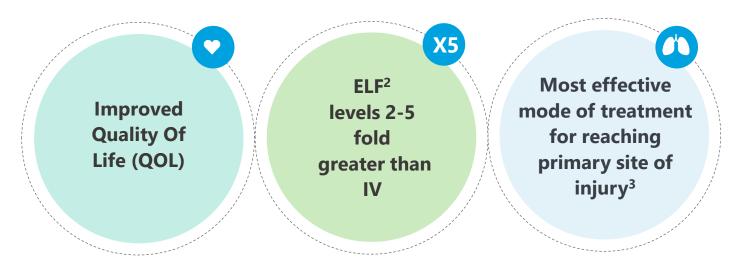


## **ANTICIPATED BENEFITS OF INHALED AAT**



Alpha-1 Foundation survey<sup>1</sup> confirms high level of patient's interest in Inhaled-AAT

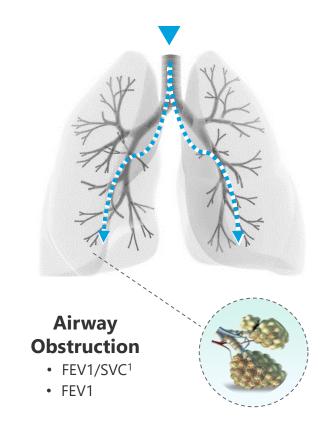
Inhaled AAT opportunity is estimated by Kamada at \$1B world wide



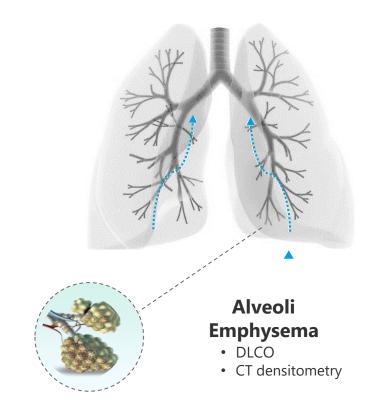
# INHALATION ENABLES DELIVERY OF AAT 5X HIGHER THAN INTRAVENOUS



**Inhaled AAT ~ 50%** of the dosage reaches **airway tree** and alveoli

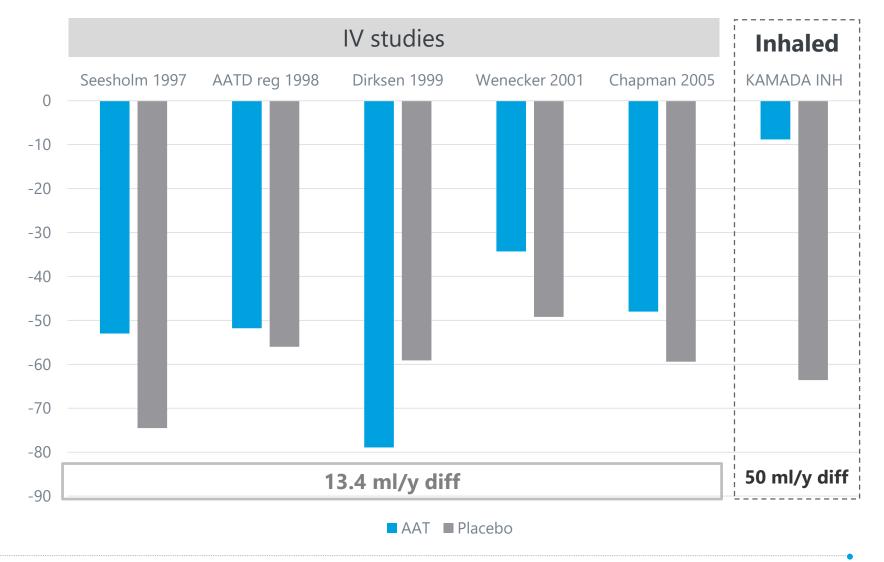


**Intravenous AAT** ~ **2%** of the dosage reaches alveoli and **airway tree** 



# INHALED AAT SLOWED FEV1<sup>1</sup> DETERIORATION BETTER THAN FORMER IV TRIALS

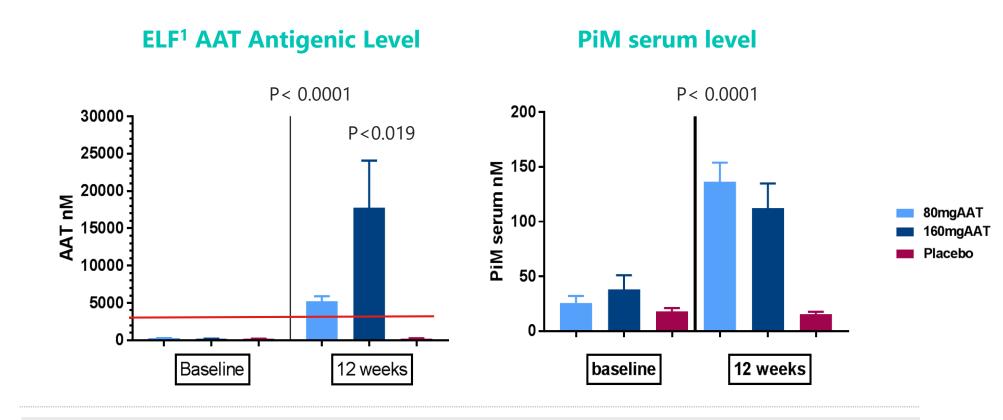




### **INHALED AAT PHASE II U.S.**



ELF AAT Antigenic Level & Inhibitory Capacity Increased Significantly

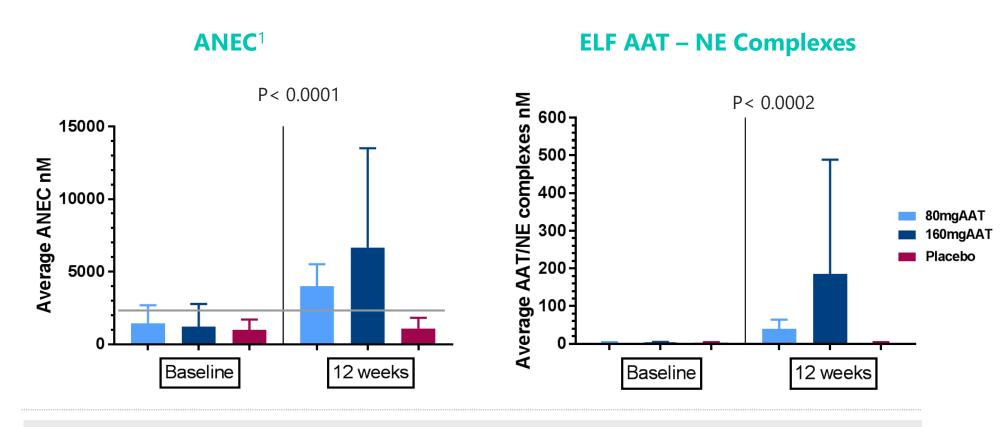


AAT ELF level is reasonably likely to predict clinical benefit

### **INHALED AAT PHASE II U.S.**



ELF AAT-NE complexes & Inhibitory Capacity Increased Significantly



Inhaled AAT is the most effective means to restore AAT inhibitory capacity in the airways (ANEC<sup>1</sup> & AAT-NE Complexes)

### **INHALED AAT: MOVING FORWARD**



US



- In discussions with the FDA addressing concerns and obtaining guidance on the clinical/ regulatory pathway for the Inhaled AAT in the U.S.
- Expecting FDA discussions to materialized by Mid-2018
- Planning to initiate a Phase 3 study thereafter, pending IND approval





- Phase 2/3 completed; Study endpoints were not met
- MAA submitted based on data showing Lung Function Improvements; MAA withdrawn in June 2017 as EMA viewed data as insufficient for approval
- Plan to resubmit MAA after next Phase 3 study is successfully completed



### KamRAB/KedRAB

### Human Rabies Immune Globulin







- FDA Approval August 2017
- Product launch: Q1/2018 in collaboration with Kedrion
- ~40,000 post-exposure prophylaxis treatments administered each year, representing ~\$100 million market opportunity<sup>1</sup>

#### **U.S. Opportunity:**

Strategic agreement with Kedrion S.p.A for the clinical development and marketing of KedRAB in U.S.



#### Worldwide

- More than 1.5MM Vials sold to date (2ml) = ~ 300,000 people treated w/w
- Major markets: India, Thailand, Israel, Russia
- Approved Supplier of the WHO
- November 2017: Signed new \$13 MM supply for 2018-2020

#### **WHO** estimates:

~10 million people worldwide require medical treatment against rabies each year after being exposed to an animal suspected of rabies infection



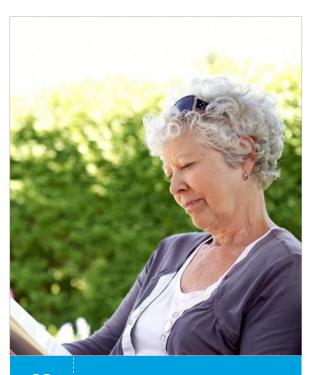
# **IMMUNE-MODULATORY INDICATIONS**







**Graft versus Host Disease** 

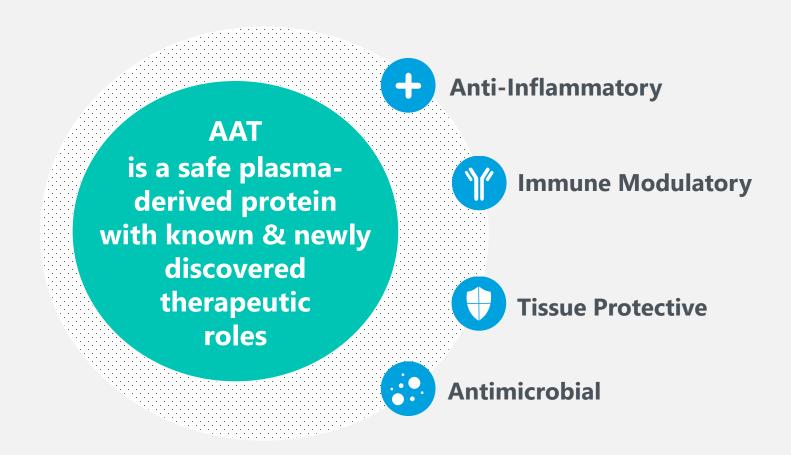


03

**Lung Transplantation** 

# AAT SERVES AS AN EXCITING POTENTIAL THERAPY FOR MULTIPLE INDICATIONS





Excellent safety profile, encouraging clinical and pre-clinical experience coupled with biochemical rationale may position AAT as a high-potential future treatment in various indications.



AAT to Treat Newly Diagnosed Type-1 Diabetes

01

# AAT (IV) AS POTENTIAL TREATMENT FOR NEWLY DIAGNOSED TYPE-1 DIABETES PATIENTS



#### MARKET OPPORTUNITY **AAT IMPACT EXPECTED BENEFITS Type-1 Diabetes** Studies have shown **Preservation of beta cells** Occurs when the immune system that AAT protects correlates with reduced risk attacks and destroys beta cells in beta cell islets of long-term complications the pancreas More than 10 million suffer from Delays the progression of DCCT<sup>2</sup> indicated that patients autoimmune diabetes Type 1 diabetes globally with C-peptide on MMTT ≥0.2 Inhibits insulitis and beta-cell pmol/mL were less likely to 100,000 new patients/year diagnosed globally develop retinopathy and apoptosis In the U.S. alone: 3 million Decreases beta-cell hypoglycemia complications<sup>3</sup> patients, with 30,000 new inflammation Higher / sustained levels of Cpatients diagnosed annually<sup>1</sup> peptide correlate with reduced incidences of the microvascular complications<sup>3</sup>

<sup>23</sup> 

### **PHASE II STUDY**



Phase II Completed:
Double-Blind,
Randomized,
Placebo-Controlled,
Multicenter Study



# Study objective

### Design

### **Endpoints**

### **Results**

- To evaluate the efficacy and safety of plasmaderived, Alpha-1 Antitrypsin (AAT) in the treatment of newly diagnosed Type 1 Diabetes patients
- Two doses, placebo controlled, randomized with 70 pediatric and young adult patients.
   One year study
- Beta cell preservation (C-peptide AUC),
   HbA1C, hypoglycemic events and insulin daily dose
- In the pre-determined subgroup of patients between the ages of 12-18 years old, a trend toward better efficacy was demonstrated in the high dose arm of AAT (120mg/kg)
- In the overall study population no significant treatment effect was observed.

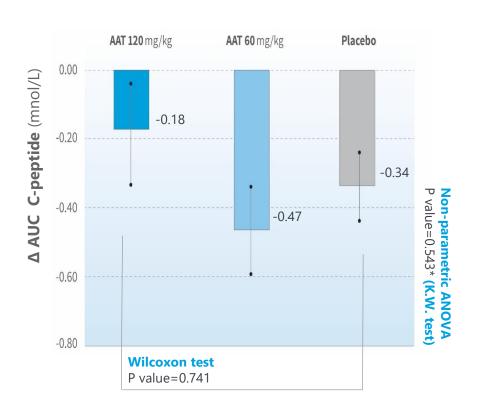
### **BETA CELL FUNCTION AND INSULIN AT 1 YEAR**

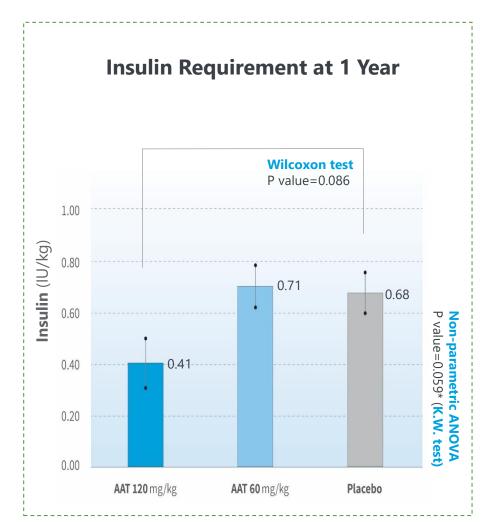


Subgroup Analysis, Ages 12-18

# Beta-Cell Function by MMTT AUC C-peptide at 1 Year

Δ Stimulated AUC

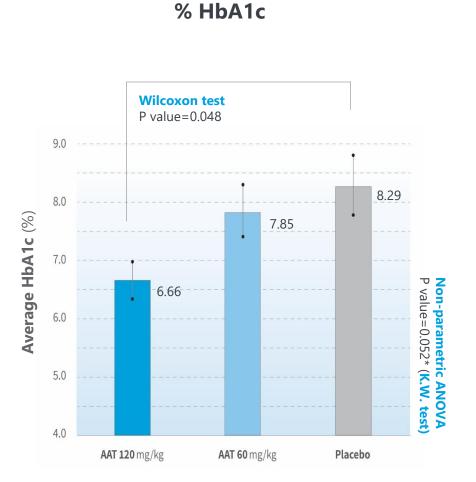


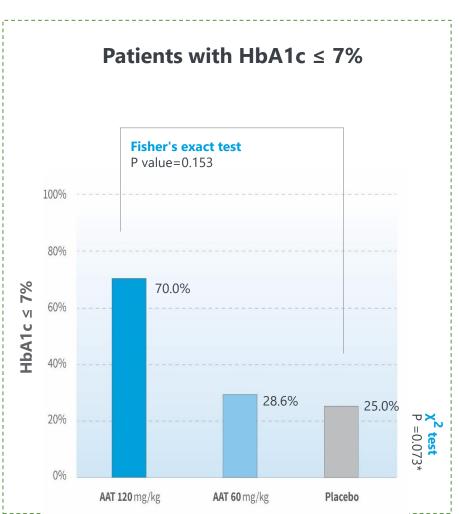


## **GLYCEMIC CONTROL RESULTS AT 1 YEAR**



Subgroup Analysis, Ages 12-18





# "AAT COULD BE AN EFFECTIVE TREATMENT OPTION FOR NEWLY DIAGNOSED 12-18 YEARS OLD T1D PATIENTS"





Peter Gottlieb, M.D.,

Professor of Pediatric and Medicine,
Barbara Davis Center for Diabetes,
University of Colorado School of
Medicine and a leading member in
TrialNet, an NIH-sponsored network of
institutions and researchers dedicated
to the prevention of type-1 diabetes.

"Given this study was not powered to show efficacy, the results are very encouraging.

These findings suggest that administration of AAT could be an effective treatment option for newly diagnosed T1D patients who are 12-18 years old. The results of this subgroup are intriguing and warrant further studies in a larger population.

Subgroup segmentation by age is common in this complicated disease, and the fact that we see the same positive trend in this age group for all three measures – C-peptide, daily insulin requirement, and HbA1C – suggests that the **results are consistent and could be promising.**"

## **AAT FOR T1D - NEXT STEPS**



- Full data set analysis and publication
- Regulatory advice (US/EU)
- Seek strategic partner for collaboration in further product development





**AAT to Treat Graft versus Host Disease** 

## **GRAFT VERSUS HOST DISEASE (GVHD):**



A Major Complication in Hematopoietic Cell Transplantation

# DEADLY SIDE EFFECTS

30-40%	of bone marrow transplantations will develop acute GvHD
40-50%	of acute GvHD will not respond to steroid treatment (SR-aGvHD)
~70%	mortality rate of patients with SR-aGvHD



# SEARCHING FOR AN EFFECTIVE TREATMENT

Standard of care prophylaxis exhibits poor efficacy/severe AE's

No FDA-approved specific drug for GvHD indication – An Unmet Medical Need

Estimated Market Size<sup>1</sup>: ~ \$500 MILLION

### AN EARLY-BIOMARKER PREDICTS LETHAL GVHD



Study performed by Matthew J. Hartwell, et al., the Icahn School of Medicine at Mount Sinai <sup>1</sup> suggests that a biomarker algorithm can identify patient at high risk of lethal GvHD and nonrelapse mortality in advance of symptoms onset

No laboratory test can predict the risk of nonrelapse mortality (NRM) or severe GvHD after hematopoietic cellular transplantation (HCT) prior to the onset of GVHD symptoms.

#### **Method**

Patient blood samples on day 7 after HCT were obtained from a multicenter set of 1,287 patients, and 620 samples were assigned to a training set. We measured the concentrations of 4 GVHD biomarkers (ST2, REG3 $\alpha$ , TNFR1, and IL-2R $\alpha$ )

#### **Results**

A 2-biomarker model (ST2 & REG3 $\alpha$ ) concentrations identified patients with a cumulative incidence of 6-month NRM of 28% in the high-risk group and 7% in the low-risk group (P<0.001). GVHD-related mortality was greater in high-risk patients (18% vs. 4%, P<0.001), as was severe gastrointestinal GVHD (17% vs. 8%, P<0.001). The same algorithm can be successfully adapted to define 3 distinct risk groups at GVHD onset.

#### **Conclusion**

A biomarker algorithm based on a blood sample taken 7 days after HCT can consistently identify a group of patients at high risk for lethal GVHD and NRM.

### **NEXT STUDY OF AAT (IV) FOR GVHD**



### Collaboration with Mt. Sinai to evaluate AAT for preemption of aGvHD

### **Proof-of-Concept Study:**

- Open label single arm multicenter study to be conducted in 5 US centers which are members of Mount Sinai Acute GVHD International Consortium (MAGIC)
- Study is co-funded by Mount Sinai and Kamada, and is sponsored by the Icahn School of Medicine at Mount Sinai (ISMMS)
- Led by Prof James L.M. Ferrara, MD, and Prof. John Levine, MD, MS

Kamada has exclusive rights to develop and commercialize AAT for preemption of GvHD using the MAGIC Biomarkers

# Innovative approach

- Biomarker based algorithm to diagnose patients at risk to develop steroid-resistant GvHD (SR-GvHD) at day 7 after bone marrow transplantation (BMT).
- Early intervention could prevent patients from further disease deterioration

### **Study objective**

 To assess the safety and preliminary efficacy of IV AAT as preemptive therapy in patients at high risk for the development of SR-GvHD after BMT

### Design

 30 patients treated with IV AAT for 2 months with a follow-up period of 1 year after BMT

### **Endpoints**

 Proportion of High Risk patients who develop SR-GvHD by day 100 post BMT, as well as safety, severity of GvHD, mortality, etc.

This study replaces the previously planned phase II/III study which was designed to treat aGvHD patients in First Line setting



03 **AAT to Treat Lung Transplantation** 

# ADVANCING THE LUNG TRANSPLATATION OPPORTUNITY





# Lungs have the highest rate of rejection among transplanted solid organs

~33% will experience acute rejection within the first year ~50% will develop chronic rejection within the first 5 years

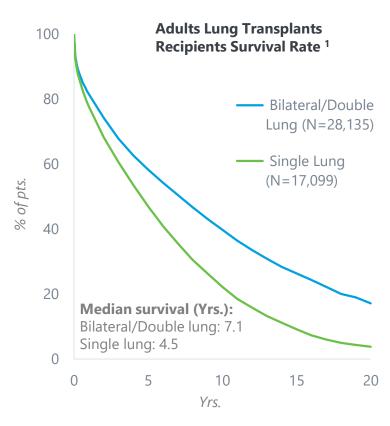


# No new treatment options have been made available for years

Physician feedback indicates strong need for improved post-transplant therapies over existing options (toxicity, immunosuppressive)



Kamada initiated the first clinical trial designed specifically to prevent lung transplant rejection



### Potential Market Size<sup>2</sup> ~ \$400-500 MILLION

### **ON-GOING PHASE II STUDY WITH AAT IV**



### For Prevention of Lung Transplant Rejection

### **Phase II:**

Prospective, open label, standard-ofcare (SOC) controlled, randomized, parallel group single center study

In collaboration with Baxalta/Shire led by Prof. Mordechai Kramer, Rabin Medical Center, Israel

Study objective	<ul> <li>To assess the safety of AAT IV and the effect on rate and severity of acute and chronic lung rejection as well as pulmonary infections, in subjects undergoing first lung transplantation</li> </ul>
Design	30 lung transplant recipients randomized 2:1 to receive AAT IV on top of standard-of-care (SOC) or SOC alone, for 48 weeks plus 12 months of follow-up period

### **Endpoints**

**Interim results** (16 Pts; 6 months)

- Safety: Related adverse events (AEs)
- Efficacy: Changes in FEV1 from baseline and overall effect, incidence and rate of acute lung rejection
- IV AAT demonstrated favorable safety and tolerability profile in 10 patients during first six months of treatment, consistent with previously observed results in other indications.

"Preclinical data published in Blood suggest that IV AAT has an immunomodulatory and anti- inflammatory mechanism of action that would support its efficacy in the prevention of lung transplant rejection" (Prof. Mordechai Kramer)



### **DISTRIBUTION SEGMENT**



## Exclusive distributor in Israel of leading biopharmaceutical companies

Medical Field	Product/Brand Name	Description
Immunology	Intratect & Gammaplex <sup>1</sup>	Gamma-globulins 5% IV
Hospital & Critical Care	Vialabex/Zenalb/Albiomin <sup>1</sup>	Human serum Albumin
Hospital & Critical Care	Heparin sodium injection	Heparin sodium 5000 IU/ml
	Ixiaro	Japanese encephalitis vaccine
Infectious Disease	Varitect <sup>1</sup>	Varicella zoster IgG
	Megalotect <sup>1</sup>	CMV IgG
Hematology and	Optivate <sup>1</sup>	Coagulation Factor VIII (human)
Hemophilia	Replenine <sup>1</sup>	Coagulation Factor IX (human)
	Foster	Beclometasone+ Formoterol inhaled
Respiratory	Bramitob	Tobramycin, inhaled
	Provocholine	Methacholine, inhaled
Liver	Zutectra <sup>1</sup>	Hepatitis B IgG S.C
Liver	Hepatect <sup>1</sup>	Hepatitis B IgG I.V

Additional products are under registration with the Israeli MOA









# **INCREASING REVENUES AND GROSS PROFITS**

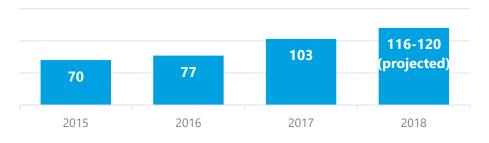


2017 Exceeded
Revenues Guidance
of \$100M

2018 Revenues
Guidance
\$116-120M;
Profitable

US \$ MM	FY 2015 Audited	FY 2016 Audited	% <b>YoY</b> 2016/2015	FY 2017 Audited	% <b>YoY</b> 2017/2016
Proprietary Products	43	56	30%	80	42%
Distribution Products	27	21	-22%	23	8%
<b>Total Revenues</b>	70	77	10%	103	33%
<b>Gross Profit</b>	16	22	38%	32	50%
<b>Gross Profit (%)</b>	23%	29%		31%	
R&D	(17)	(16)		(12)	
S&M and G&A	(11)	(11)		(13)	
<b>Operating Profit (Loss)</b>	(12)	(5)		7	
Net Profit (Loss)	(11)	(7)	36%	7	200%
Adjusted EBITDA <sup>1</sup>	(6)	(1)		11	

### Revenues (US\$MM)



# **EXPECTED 2018 MILESTONES**



Initiating next GvHD study in collaboration with Mt. Sinai Hospital and the MAGIC consortium	Q1/2018 √
Rabies product launch in the U.S.	Q1/2018 √
Inhaled AAT for AAT Deficiency: <ul><li>Approved IND for registration trial in US</li><li>Scientific Advice in EU</li></ul>	Mid 2018
Initiating inhaled AAT for AATD phase III study (subject to IND approval)	H2/2018
Interim report for Phase II for lung transplant trial (1 year treatment)	H2/2018
Advancing type-1 diabetes program through collaboration	H2/2018
Achieve \$116-120 million in annual revenues, profitable, cash flow positive	2018



### KAMADA INVESTMENT HIGHLIGHTS



- Commercial stage global biopharmaceutical company focused on Alpha-1 Antitrypsin Deficiency (AATD) and Specific Hyper-Immune IgGs
- 2017 revenues at \$103MM. 2018 guidance of strong 13-17% revenue growth
- Two FDA approved products
  - **Glassia**® for AATD; Marketed in the US by Shire plc; Unique and differentiated product profile in a fast growing market
  - **KedRab** for Post-Exposure Prophylaxis Anti-rabies; marketed in the US by Kedrion
- Strategic partnerships with industry leaders -> Shire, Kedrion, Biotest and PARI
- Novel inhaled AAT developed as a second generation product for AATD
  - Planning a phase 3 study, pending approved IND
- IV AAT pipeline for additional orphan indications (T-1D, GvHD & Lung Transplant)
- Proprietary platform technology for the extraction and purification of proteins from human plasma;
- cGMP compliant, FDA-approved manufacturing facility
- Distributed biopharmaceutical products segment in Israel
- Strong Financial Profile with Growing Profitability; \$43M cash & forecast positive cash flow in 2018









Kamada Investor Presentation / April 2018

### **APPENDIX A**



#### **Appendix A: Reconciliation of Non-IFRS Measures**

Adjusted EBITDA is defined as net income (loss), plus income tax expense, plus financial expense, net, plus depreciation and amortization expense, plus non-cash share-based compensation expenses, plus or minus income or expense in respect of exchange and translation differences and derivatives instruments not designated as hedging, and plus one-time management compensation payment.

We present adjusted EBITDA because we use this non-IFRS financial measure to assess our operational performance, for financial and operational decision-making, and as a means to evaluate period-to-period comparisons on a consistent basis. Management believes this non-IFRS financial measure is useful to investors because: (1) they allow for greater transparency with respect to key metrics used by management in its financial and operational decision-making; and (2) they exclude the impact of non-cash items that are not directly attributable to our core operating performance and that may obscure trends in the core operating performance of the business.

Non-IFRS financial measures have limitations as an analytical tool and should not be considered in isolation from, or as a substitute for, our IFRS results. We expect to continue reporting non-IFRS financial measures, adjusting for the items described below, and we expect to continue to incur expenses similar to certain of the non-cash, non-IFRS adjustments described below. Accordingly, unless otherwise stated, the exclusion of these and other similar items in the presentation of non-IFRS financial measures should not be construed as an inference that these items are unusual, infrequent or non-recurring. Adjusted EBITDA is not a recognized term under IFRS and does not purport to be an alternative to any other IFRS measure. Moreover, because not all companies use identical measures and calculations, the presentation of adjusted EBITDA may not be comparable to other similarly titled measures of other companies.

(US\$K, Unaudited) _	YE2015	YE2016	YE2017
Net Income (Loss)	(11,270)	(6,733)	6,901
Taxes on income	0	1,722	269
Financial expenses (income), net	471	(343)	(338)
Depreciation and amortization			
expense	3,227	3,501	3,523
Share-based compensation charges Expense (income) in respect of currency exchange and translation differences and derivatives	1,907	1,071	483
instruments, net	(625)	(127)	612
Adjusted EBITDA	(6,290)	(909)	11,450

# INHALED AAT – IN THE WORDS OF THE KEY OPINION LEADERS



### EU Phase 2/3:

"The study results demonstrated primarily that the overall treatment effect on lung functions, is of significant clinical value. This study is the first study ever that is indicative of inhaled AAT's ability to potentially reduce lung inflammation as expressed by its preservation of lung function and the changes shown in symptoms."

Prof. Jan Stolk, MD, Department of Pulmonology, Leiden University Medical Center, Principal Investigator of the Phase 2/3 clinical trial and acting Chairman of the Alpha 1 International Registry (AIR) "The study analysis suggests exciting results that may lead to wider acceptance of the inhaled route of administration of alpha- 1 antitrypsin augmentation therapy, which could be a real breakthrough for AATD patients."

Robert A. Sandhaus, Ph.D., M.D., FCCP, Founder and Director of the Alpha1-Antitrypsin Deficiency Program at National Jewish Health in Denver, Colorado, and the Clinical Director of the Alpha-1 Foundation

"These new analyses confirm the clinicallymeaningful lung function improvement seen with inhaled AAT patients in this study. These results are impressive and underscore the initial findings from this study. In my opinion, inhaled AAT has shown to be an efficacious treatment for this orphan disease."

*Prof. Kenneth Chapman*, M.D., Director of the Canadian Registry for the Alpha-1 Antitrypsin Deficiency (Asthma and Airway Centre in Toronto Western Hospital, University of Toronto) and an investigator in the Phase 2/3 clinical trial.

#### **US Phase 2:**

"The results of this study are extremely compelling. Based on the results of this study, it is clear that inhaled AAT is the most effective mode of treatment for reaching the primary sites of potential lung injury, and restoring AAT inhibitory capacity. I look forward to the start of a pivotal study in the U.S. to confirm these results."

Professor Mark Brantly, MD, the Primary Investigator in this study who serves as a Vice Chair of Research, Department of Medicine, Chief Division of Pulmonary, Critical Care and Sleep Medicine, Professor of Medicine, Molecular Genetics and Microbiology at the University of Florida College of Medicine and Alpha One Foundation Research Professor.

# **INHALED AAT PHASE II/III TRIAL - POST-HOC RESULTS**



Spirometry Measures (MMRM<sup>1</sup>)

Lung Function	Least Squa (SEM) (Chan 50 from I		
ranction	AAT (N=84)	Placebo (N=81)	P-Value <sup>1</sup> (Changes at Week 50)
FEV <sub>1</sub> (L)	-12mL	-62mL	0.0956
<b>FEV</b> <sub>1</sub> (% of predicted)	-0.1323	-1.6205	0.1032
FEV <sub>1</sub> /SVC (%)	0.6183	-1.0723	0.0132

Least Squa (SEM) n Overall treat		
AAT (N=84)	Placebo (N=81)	P-Value <sup>1</sup> (Overall Effect)
+15mL	-27mL	0.0268
0.5404	-0.6273	0.0658
0.6230	-0.8715	0.0074

# **CLINICAL DEVELOPMENT FOR NEWLY DIAGNOSED TYPE-1 DIABETES: NEW EXCITING PROSPECTS**



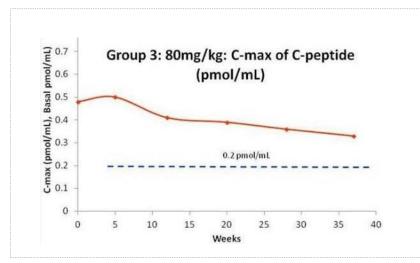
Phase I/II: Open Label Study to evaluate the safety, tolerability and efficacy of AAT on beta cell preservation and glycemic control on newly diagnosed T1D pediatric patients (N=24)

AUC% for C-peptide decreased 23% from baseline vs. ~40-50% expected decrease after 12-15 months from diagnosis

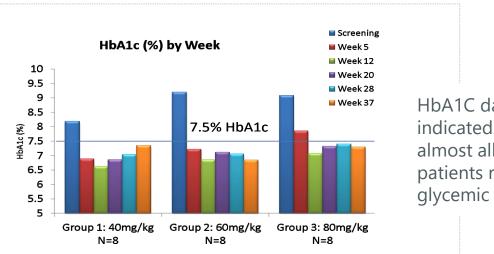
Specific diabetes antibody levels decreased in all groups from baseline to study completion, a decrease that may indicate an immune modulatory effect

At end-of-study, 38% of patients decreased insulin dose

All subjects completed the study. No Serious AEs occurred. AEs were mild and mostly infusion-related (fatigue, headache)



End-of-study slope analysis of C-peptide [max] and C-peptide [AUC] revealed no significant changes from baseline



HbA1C data indicated that almost all patients reached glycemic control

## **GVHD PROOF-OF-CONCEPT STUDY WITH AAT (IV)**

**Results** 



For Graft-Versus-Host Disease (published 1/2016)

### Phase I/II study:

Open label of 24 patients with steroid-resistant GvHD bone- following allogeneic marrow stem cell transplant

Study Design	4 dose groups - 15 day regimen. Doses given on days: 1, 3, 5, 7, 9, 11, 13 and 15

Primary % of patients who experience no toxicity and in whom GVHD is stable or improved

- Encouraging preliminary clinical results;
- Stool AAT levels showed a decrease in intestinal AAT loss, suggesting healing of the bowel mucosa

**BEFORE** Duodenits suspect severe upper and lower GVHD

AFTER 8 DOSES OF AAT Moderate mucosal denudement and edema noted throughout the duodenum

