## REVELATION BIOSCIENCES

Developing innovative therapeutics to address unmet needs

Corporate Presentation / January 2023

www.revbiosciences.com

## Forward-Looking Statements

This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. These forward-looking statements are generally identified by the words "anticipate", "believe", "expect", "estimate", "plan", "outlook", and "project" and other similar expressions. We caution investors that forward-looking statements are based on management's expectations and are only predictions or statements of current expectations and involve known and unknown risks, uncertainties and other factors that may cause actual results to be materially different from those anticipated by the forward-looking statements. Revelation cautions investors not to place undue reliance on any such forward-looking statements, which speak only as of the date they were made. The following factors, among others, could cause actual results to differ materially from those described in these forward-looking statements: the ability of Revelation to meet its financial and strategic goals, due to, among other things, competition; the ability of Revelation to grow and manage growth profitability and retain its key employees; the possibility that the Revelation may be adversely affected by other economic, business, and/or competitive factors; risks relating to the successful development of Revelation's product candidates; the clinical utility of an increase in intranasal cytokine levels as a biomarker of viral infections; the risk that our preclinical studies will not demonstrate sufficient positive data to support commencement of clinical trials; the risk that we may not fully enroll our clinical studies or enrollment will take longer than expected; risks relating to the occurrence of adverse safety events and/or unexpected concerns that may arise from data or analysis from our clinical studies; changes in applicable laws or regulations; expected initiation of the clinical studies, the timing of clinical data; the outcome of the clinical data, including whether the results of such study is positive or whether it can be replicated; the outcome of data collected, including whether the results of such data and/or correlation can be replicated; the timing, costs, conduct and outcome of our other clinical studies; the anticipated treatment of future clinical data by the FDA, the EMA or other regulatory authorities, including whether such data will be sufficient for approval; the success of future development activities for REVTx-100, REVTx-200, REVTx-300, REVTx-99b, REVDx-501, or any other product candidates; potential indications for which product candidates may be developed; the potential impact that COVID 19 may have on Revelation's suppliers, vendors, regulatory agencies, employees and the global economy as a whole; the ability of Revelation to maintain the listing of its securities on NASDAQ; the expected duration over which Revelation's balances will fund its operations; the ability of Revelation to obtain further financing and other risks and uncertainties described herein, as well as those risks and uncertainties discussed from time to time in other reports and other public filings with the SEC by Revelation.



## **Therapeutic Development Pipeline**

- Revelation has developed a robust pipeline of potential high-value products based on the activity of PHAD
- All current product candidates are based on PHAD. REVTx-100 and REVTx-300 are supported by preclinical data

Therapeutic Candidate	Discovery	Preclinical	Phase 1	Phase 2	Next Milestone
REVTx-100	Prevention of infection	post surgical			Initiate Phase 1a* study
REVTx-300	Prevention of of CKD	AKI, Treatment			Initiate Phase 1a* study
REVTx-200	Adjunct to IN vaccine	1			Readout from PEITHO nonclinical study
REVTx-99b	Food allergie	s			Initiate non-clinical study

\*Phase 1a is the same study, data will be used for REVTx-100 and REVTx-300



## PHAD is a Well-Defined TLR4 Agonist with Multiple Potential Applications



Modulation of Immune Response

Prevention and treatment of healthcare associated infection via trained immunity ((REVTx-100 (licensed from Vanderbilt University))

Treatment of acute and chronic inflammatory disease such as AKI, CKD and NASH (REVTx-300)

Recruit immune cells to the mucosa to augment the local and systemic adaptive immune response (REVTx-200)



Treatment of food allergies and allergic rhinitis (REVTx-99b)

✓ Revelation has developed proprietary formulations and methods of use to deliver phosphorylated hexaacyl disaccharide (PHAD®) systemically or to the local intranasal cavity to treat various diseases EVELATION



#### REVTx-100

For the Prevention of Healthcare Associated Infection

## **REVTx-100 Program Highlights**

#### Scientific Rationale



- Stimulation of the TLR4 TRIF pathway with REVTx-100:
  - Augments immune cell recruitment, which increases pathogen clearance
  - Downregulates the pro-inflammatory response allowing healing to take place
- Multiple preclinical studies performed demonstrating consistent reduction or prevention of infection (both gram negative and gram positive)

Intellectual
Property
Regulatory

Market

Next Steps

## US 11,389,465 (Licensed from Vanderbilt University). Additional related applications anticipated

Potential fast track, breakthrough designations possible. Potential for orphan status for certain indications

Large Market potential: Approximately 3% of hospital patients suffer at least one hospital associated infection (HAI) (~687,000 HAI annual cases in acute care settings resulting in ~72,000 deaths)<sup>1</sup>

Initiate Phase 1 healthy volunteer study in 2023

#### Pretreatment with PHADs Impart Protection from Gram Negative Bacterial Infection





Pre-treatment with MPLA and PHAD(s) demonstrated TLR4-mediated pathogen clearance Pre-treatment with MPLA or PHAD(s) demonstrated TLR4mediated increased leukocyte recruitment and reduced pro-inflammatory cytokines (IL-6, TNF- $\alpha$ ) in peritoneal cavity

**Study Design:** Mice were pre-treated (24 and 48 hours) with vehicle, MPLA (20ug), or PHADs (20ug) prior to infection with *P. aeruginosa*. All given IP. Cell counts assessed from peritoneal lavage 6 hours post infection. n = 7 to 10 animals per group.

#### Pretreatment with PHADs Impart Protection from Gram Positive Bacterial Infection



Pre-treatment with MPLA and PHAD(s) demonstrated improved pathogen clearance 3 days post infection

REVELATION

Pre-treatment with MPLA and PHAD(s) demonstrated improved survival

Study Design: Mice were pre-treated (24 and 48 hours) with vehicle, MPLA (1 mg/kg), or PHADs (1 mg/kg) prior to infection with S. aureus. All given IV. Bacterial counts assessed 3 days post infection. n = 7 to 10 animals per group.

### Biomarkers (cytokines) support the underlying mechanism of PHAD



• Significant reduction in pro-inflammatory cytokines indicates TRIF-biased signaling via TLR4 stimulation

Study Design: Mice were pre-treated (24 and 48 hours) with vehicle, MPLA (1 mg/kg), or PHADs (1 mg/kg) prior to infection with S. aureus. All given IV. Bacterial counts assessed 3 days post infection. n = 7 to 10 animals per group.

## The Impact of Surgical-Site Infections (SSI)

Surgical site infection (SSI) is the most common health care-associated infection following surgery and is associated with significant morbidity and mortality, transfer to an intensive care unit setting, prolonged hospitalizations, and hospital readmission<sup>6</sup>

## Up to 30%

Estimated SSI rate of patients undergoing colorectal surgery<sup>1</sup>

## 20%

SSI rate of all health care-associated infections in US hospitals<sup>2</sup>

## \$11k-26k

Cost of treatment per infection directly attributable to SSIs

## 7-11 days

Additional post-operative hospital days for patients with SSIs<sup>2</sup>

## 2-11x

Increased risk of death for SSI patient (up to 40% mortality after deep sternal infection)<sup>1</sup>

## US \$10bn; EU~€11bn

Estimated SSI-related incremental annual hospital costs in the US and EU<sup>3,4,5</sup>



DOI:10.1001/jamasurg
DOI:10.1086/676022
DOI: 10.1016/j.jamcollsurg.2016.10.029
~€11bn represents the midpoint of the range discussed in WHO Global guidelines on the prevention of surgical site infection. Nov 2016
DOI: 10.1086/501572

## Total US Addressable Market for REVTx-100 is over 6.3M Annual Procedures



Operations on the digestive system	3.8M
Operations on the urinary system	567K
Operations on the male genital system	360K
Operations on the female genital system	1.6M



## **REVTx-100 Development Plan**

- REVTx-100 has potential utility across multiple indications
- Revelation plans to develop REVTx-100 as a treatment for multiple indications through Phase 2
- Plan to strategic license and/or partner for Phase 3 studies and commercialization

Phase	Target Indication <sup>1</sup>	Anticipated Timing	Use of Data
Preclinical	Тох	2023	Support US IND
Phase 1a	Healthy volunteers	2023	Support Phase 1b study for REVTx-100 and REVTx-300
Phase 1b	Post-surgical infection (abdominal)	2024	Support Phase 2 study
Phase 2	Post-surgical infection (abdominal)	2024/2025	Support Phase 3 study/Partnering discussion
Phase 2	Pneumonia (post sepsis)	2025	
Phase 2	Post burn <sup>2</sup>	TBD	
Phase 2	UTI	TBD	



## REVTx-100 Phase 1a/1b Draft Clinical Study Design

## Phase 1a: Healthy volunteers<sup>1</sup>

6 cohorts/8 subjects per cohort randomized 1:1 placebo vs drug:

Cohorts 1-5 - single ascending dose followed for 1 week

Readouts: safety and biomarker assessments

Cohort 6 – 5 daily doses at maximum tolerated dose followed for 1 week post last dose

Readouts: safety and biomarker assessments

Phase 1b: Patients undergoing elective abdominal colorectal surgery

30 subjects randomized 1:1:1 placebo: low dose group: high dose group

All doses 24 hours prior to surgery. Follow for 4 weeks

Readout: safety and biomarker assessments, including infection rate, duration, and severity.

REVELATION



#### REVTx-300

For the Treatment of Acute and Chronic Kidney Diseases

## **REVTx-300 Program Highlights**

#### Scientific Rationale

- Chronic and acute organ disease (AKI, CKD, NASH, and myocarditis) propagated by inflammation, followed by fibrosis, and ultimately loss of organ function
- Significant anti-fibrotic activity observed in preclinical AKI and CKD model with PHAD treatment



#### Intellectual Property

Market

Next steps

- Developed at/by Revelation. Patent applications covering formulations and methods of treating and preventing acute and chronic organ disease filed
  - CDC estimated 15% of US adults have CKD
  - CDC estimates an annual Medicare cost for CKD of \$87 billion
  - Conduct additional nonclinical studies for AKI, CKD, NASH, and myocarditis. Initiate Phase 1a study in 2023 (This is the same Phase 1a study as for REVTx-100, data will support both)

## REVTx-300 Reduces Fibrosis in Acute and Chronic Kidney Model (UUO in Rats)



† p < 0.05 vs UUO control

- Composite data represents the average of 3 anatomically distinct depths (10 images / depth / rat / group = ~60-65% of renal cortical area)
- Renal cortical fibrosis, expressed as Collagen Volume Fraction (CVF; via quantitation of PSR stained tissue sections) was increased in vehicle-treated UUO obstructed kidneys relative to sham-operated control
- SB-525334 attenuated UUO-induced increases in renal cortical CVF

#### **Key Results**

- Treatment with REVTx-300 resulted in a significant dose-dependent reduction in fibrosis
- The high dose group (0.9 mg/kg) reduced new collagen deposition (fibrosis) by 58% vs new collagen deposition observed in the no treatment UUO group (normalized to sham)

## REVTx-300 Antifibrotic Effect Likely Mediated by Reduction in TGF-B



#### Next Steps

Normal TNF- $\alpha$  range = 5-75pg/mL<sup>1,2</sup>

- Conduct additional nonclinical studies to further evaluate REVTx-300 for AKI, CKD, and NASH
- Phase 1 clinical study in 2023

REVELATION 1. Yin, J., et. al. Changes and significance of inflammatory cytokines in a rat model of cervical spondylosis". Experimental and Therapeutic Medicine 15.1 (2018): 400-406. 2. LI, Bo, et.al. Food Science and Technology (Campinas). 2017. 37. 10.1590/1678-457x.35716.

## Reduction in TGF- $\beta$ Has Been Shown to Be a Predictive Surrogate Clinical Biomarker and Potential Therapeutic Target for Reduction of Fibrosis and Treatment of Cancer

- TGF-β has been correlated with fibrosis in multiple clinical populations, including acute kidney injury, chronic kidney disease, NASH, and myocarditis. TGF-β is also a driver of tumor growth, and increased levels have been observed in cancer patients.<sup>1,2,3,4</sup>
- Multiple therapies targeting the reduction in TGF- $\beta$  have been pursued, with mixed results:
  - ALK5 inhibitors
    - Effective in blocking TGF- $\beta$  activity via binding to TGF- $\beta$  receptor
    - Major safety hurdles valvulopathy and bone dysplasia in preclinical models
    - Galunisertib furthest in development (oncology indication), discontinued in 2020, no reason provided (Eli Lilly)
  - Anti-TGF-β MAb
    - Multiple ongoing studies, several halted due to futility
  - Anti-sense oligonucleotides
    - Multiple ongoing studies, several halted
- Complete knock down of TGF- $\!\beta$  likely associated with adverse events
- Safety profile of MPLA and observed tolerability of PHAD may afford wider therapeutic window compared to other anti-fibrotic treatments that target reduction in TGF- $\beta$

<sup>1.</sup> Mohy doi: <u>10.1016/j.mgene.2014.08.002</u>

## **AKI Epidemiology**

- In the US, 1% of all hospital admissions have AKI on admission<sup>1</sup>
- During hospitalization, the approximate incidence rate of acute kidney injury is 2 to 5% and it develops in up to 67% of patients admitted in the intensive care unit<sup>1</sup>
- AKI is an important contributor to increased hospital stay duration and patient morbidity <sup>2,3,4</sup>



Age-standardized incidence of hospitalizations with acute kidney injury<sup>6</sup> among men and women aged  $\geq$ 20 years with and without diabetes — United States, 2000–2014<sup>5</sup>

1. Acute Kidney Injury Abhinav Goyal; Parnaz Daneshpajouhnejad; Muhammad F. Hashmi; Khalid Bashir

Winther-Jensen M, Kjaergaard J, Lassen JF, Køber L, Torp-Pedersen C, Hansen SM, Lippert F, Kragholm K, Christensen EF, Hassager C. Use of renal replacement therapy after out-of-hospital cardiac arrest in Denmark 2005-2013. Scand Cardiovasc J. 2018 Oct;52(5):238-243
Park S, Lee S, Lee A, Paek JH, Chin HJ, Na KY, Chae DW, Kim S. Awareness, incidence and clinical significance of acute kidney injury after non-general anesthesia: A retrospective cohort study. Medicine (Baltimore). 2018 Aug;97(35):e12014.
Kirkley MJ, Boohaker L, Griffin R, Soranno DE, Gien J, Askenazi D, Gist KM., Neonatal Kidney Collaborative (NKC). Acute kidney injury in neonatal encephalopathy: an evaluation of the AWAKEN database. Pediatr Nephrol. 2019 Jan;34(1):169-176.

CDC Trends in Hospitalizations for Acute Kidney Injury — United States, 2000–2014

6. Acute kidney injury identified by the following International Classification of Diseases, Ninth Revision, Clinical Modification codes: at least one diagnostic code of 584 or at least one procedure code of 39.95 or 54.98 and excluding the following codes: V45.1, V56.0, V56.31, V56.32, and V56.8.



## AKI as a Result of Cardiac Surgery

Acute kidney injury is a major medical problem that is of particular concern after cardiac surgery.<sup>1</sup> Additionally, evidence suggests that even slight postoperative increases in serum creatinine levels are associated with a significant increase in the risk of death.<sup>2</sup>

#### Up to 31%

Of patients undergoing cardiac surgery with no prior CKD develop post operative AKI<sup>3</sup>

#### 50%

Death rate of patients that develop post operative AKI<sup>2</sup>

## \$42.6k

Average cost of treatment directly attributable to  $\mathsf{A}\mathsf{K}\mathsf{I}^2$ 

## 4-7 days

Additional hospital days for patients with postoperative AKI<sup>2</sup>

#### **8**x

Increased risk of death for patients that develop postoperative AKI<sup>3</sup>

## 79%

Rate of postoperative AKI patients that develop a least one other complication<sup>2</sup>



## **AKI and CKD Markets**



- Hospital addmission with AKI
- AKI during hospitalization
- AKI during intensive care
- Cardiac Surgeries
- CKD Patients

Source: Cardiac Surgeries: <u>https://idataresearch.com/over-900000-cardiac-surgeries-performed-every-year-in-the-united-states/</u> AKI: DOI: 10.2147/IJNRD.S167477 DOI: 10.1097/ACO.000000000000422 DOI: 10.214470/1678-9741-2018-0084 CKD: CDC Trends in Hospitalizations for Acute Kidney Injury — United States, 2000–2014

## **REVTx-300 Development Plan**

- REVTx-300 has potential utility across multiple indications
- Plan is to develop REVTx-300 as a treatment for multiple indications through Phase 2
- Plan to strategic license and/or partner for Phase 3 studies and commercialization
- Tox data from REVTx-100 will also support the AKI indication below

Phase	Indication	Anticipated Timing	Use of Data
Preclinical	AKI (I/R)	2023	Support IND
Preclinical	CKD	2023	Support IND
Preclinical	NASH	2023	Support additional indication
Phase 1a	Healthy volunteer	2023	Support Phase 1b study for REVTx-100 and REVTx-300
Phase 1b	AKI <sup>1</sup>	2024	Support Phase 2 study
Phase 2	AKI <sup>1</sup>	2024/2025	Support Phase 3 study/Partnering discussion
Phase 2	CKD <sup>1</sup>	2025	
Phase 2	NASH <sup>1</sup>	TBD	



## REVTx-300 Phase 1a/1b Draft Clinical Study Design

## Phase 1a: Health volunteers<sup>1</sup>

6 cohorts/8 subjects per cohort randomized 1:1 placebo vs drug:

Cohorts 1-5 - single ascending dose followed for 1 week

Readouts: safety and biomarker assessments

Cohort 6 – 5 daily doses at maximum tolerated dose followed for 1 week post last dose

Readouts: safety and biomarker assessments

**Phase 1b: Patients undergoing elective cardiac surgery** 30 subjects randomized 1:1:1 placebo: low dose group: high dose group

All doses 24 hours prior to surgery. Follow for 4 weeks

Readouts: safety and biomarker assessments. Includes rate of AKI, duration, and severity





#### REVTx-200

Intranasal Adjunct for Improved Intramuscular (IM) Vaccination

## **REVTx-200 Program Highlights**

#### Scientific Rationale

Traditional IM Immunization Alone:

- Increased systemic antibodies (IgG)
  - Systemic protection
- Weak mucosal antibodies (IgA)
  - Poor mucosal protection
  - Transmission still active
- Clinical biomarker data supports proposed mechanism of action

#### Potential Market<sup>1</sup>



#### Next Steps

- Nonclinical POC (PEITHO) study readout
- Conduct additional non-clinical study to optimize dosing regimen
- REVTx-200 may have potential utility with multiple vaccines
- Secure strategic licensing and/or partnering opportunities for Phase 2 studies and commercialization

IM Immunization + REVTx-200:

- Increased systemic antibodies (IgG)
  - Systemic protection
- Improved mucosal antibodies (IgA + IgM)
  - Robust mucosal protection
  - Transmission blunted/blocked



## **Financial Overview**

## **Financial Overview**

Cap Table	Shares
Common Stock	23,536,070
Public Warrants (REVBW)	10,511,597
Warrants <sup>1</sup>	12,031,444
Roll-over RSU's	257,047
Options granted <sup>2</sup>	352,313
Equity Pool (available for grant)	942,108
Fully Diluted	47,630,579

Beneficial holders	Percent
George Tidmarsh, M.D., Ph.D. (Chairman)	8.9%
All other management	6.7%
Total management	15.6%
5% or Greater	
George Tidmarsh, M.D., Ph.D. (Chairman)	8.9%
AXA IM Prime Impact Fund	8.3%

1. Includes (i) 8,333,334 Private Warrants w/exercise of \$0.60, (ii) 165,976 Roll-over Warrants w/exercise of \$2.68, (iii) 2,586,667 Common Stock Warrants w/exercise of \$3.29, (iv) 362,134 Placement Agent Warrants w/exercise of \$3.29, and 583,333 Placement Agent Warrants w/exercise of \$0.75.

2. Includes 156,492 options granted on 2/25/2022 w/exercise of \$1.40 and 195,821 options granted on 7/29/2022 w/exercise of \$0.563

# REVELATION BIOSCIENCES

For more information please visit <u>www.revbiosciences.com</u>

Thank you!