



# Annual General Meeting 2023

Management Update and Discussion

# Overview

1. Apabetalone Review: An Advanced Epigenetic Drug
2. Commercial Potential
3. Current Life Science Industry
4. Post COVID-19 Conditions Trial Update
5. BETonMACE2 Planning
6. Funding Option Example



Apabetalone:  
A Thoroughly Characterized, De-risked, Phase 3 Asset  
with a Track Record of Safety and Efficacy



Robust  
Intellectual  
Property  
Protection  
(to 2041)



Detailed  
**proteomic &  
transcriptomic**  
analyses – data  
room available



Over 40  
peer-reviewed  
publications  
(incl. **Cell, Nature,  
JAMA**)



**4200+ patient-  
years** of FDA-  
reviewed safety  
data



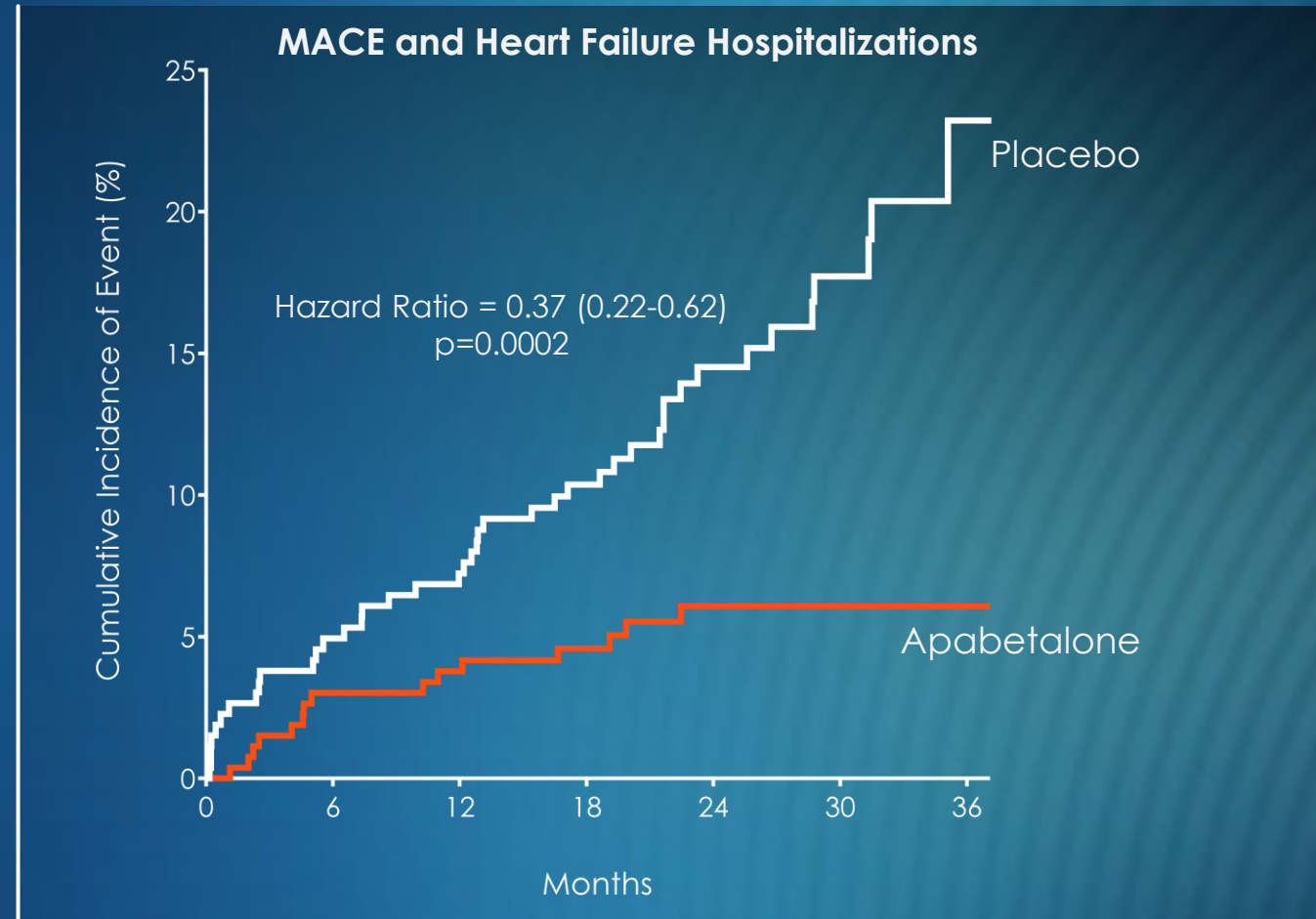
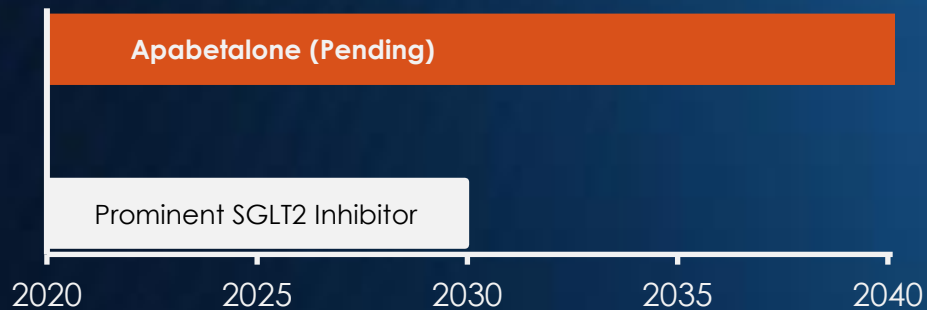
**US FDA**  
Breakthrough  
Therapy  
Designation

Apabetalone has robust clinical, scientific, and intellectual property support



# BETonMACE Clinical Result: Strong Synergy with SGLT2i & DPP4i

- Apabetalone demonstrated potential synergy with SGLT2 inhibitors & DPP4 inhibitors (next generation diabetes drugs)
  - Resverlogix has filed several patent applications related to combination
  - These pending combination claims would have patent life reach out to 2041
  - Potential to significantly extend market exclusivity

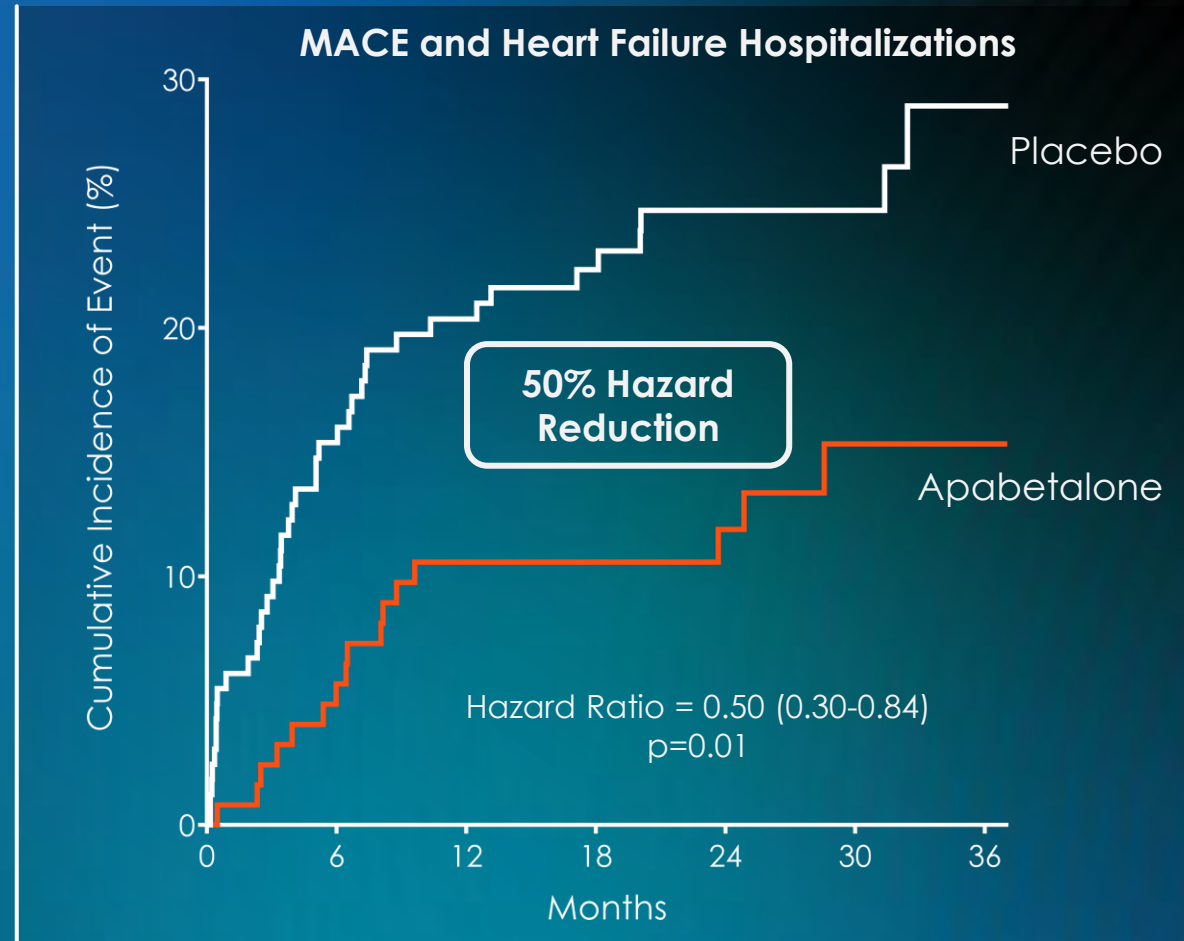


Major adverse cardiac event (MACE) is a composite endpoint of myocardial infarction, stroke, and cardiovascular death

SGLT2i or DPP4i Co-administration

## BETonMACE Clinical Result: Reduced MACE in CKD Patients

- In participants with chronic kidney disease (CKD), apabetalone was associated with fewer major adverse cardiac events (MACE) and fewer heart failure hospitalizations (HHF)
- MACE: 50% hazard reduction
- HHF: 52% hazard reduction



Major adverse cardiac event (MACE) is a composite endpoint of myocardial infarction, stroke, and cardiovascular death

Chronic Kidney Disease Population



# Apabetalone: Realizing the Untapped Potential of Epigenetics

## WITHOUT ALTERING DNA

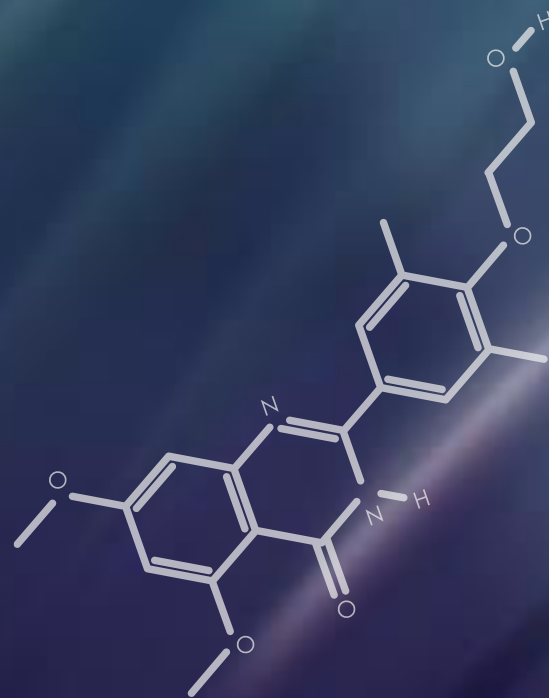
- Apabetalone regulates expression of disease-causing genes

## EPIGENETIC MECHANISM

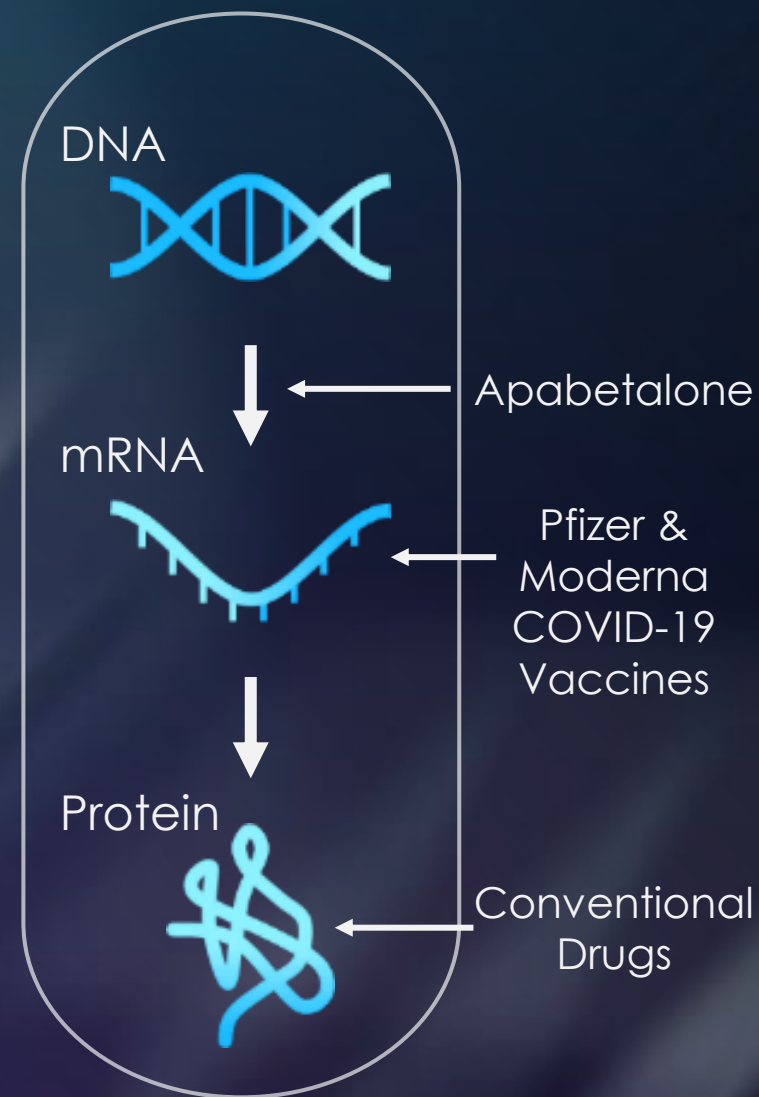
- Through inhibition of BET proteins, apabetalone acts at the level of gene transcription

## ACTING UPSTREAM

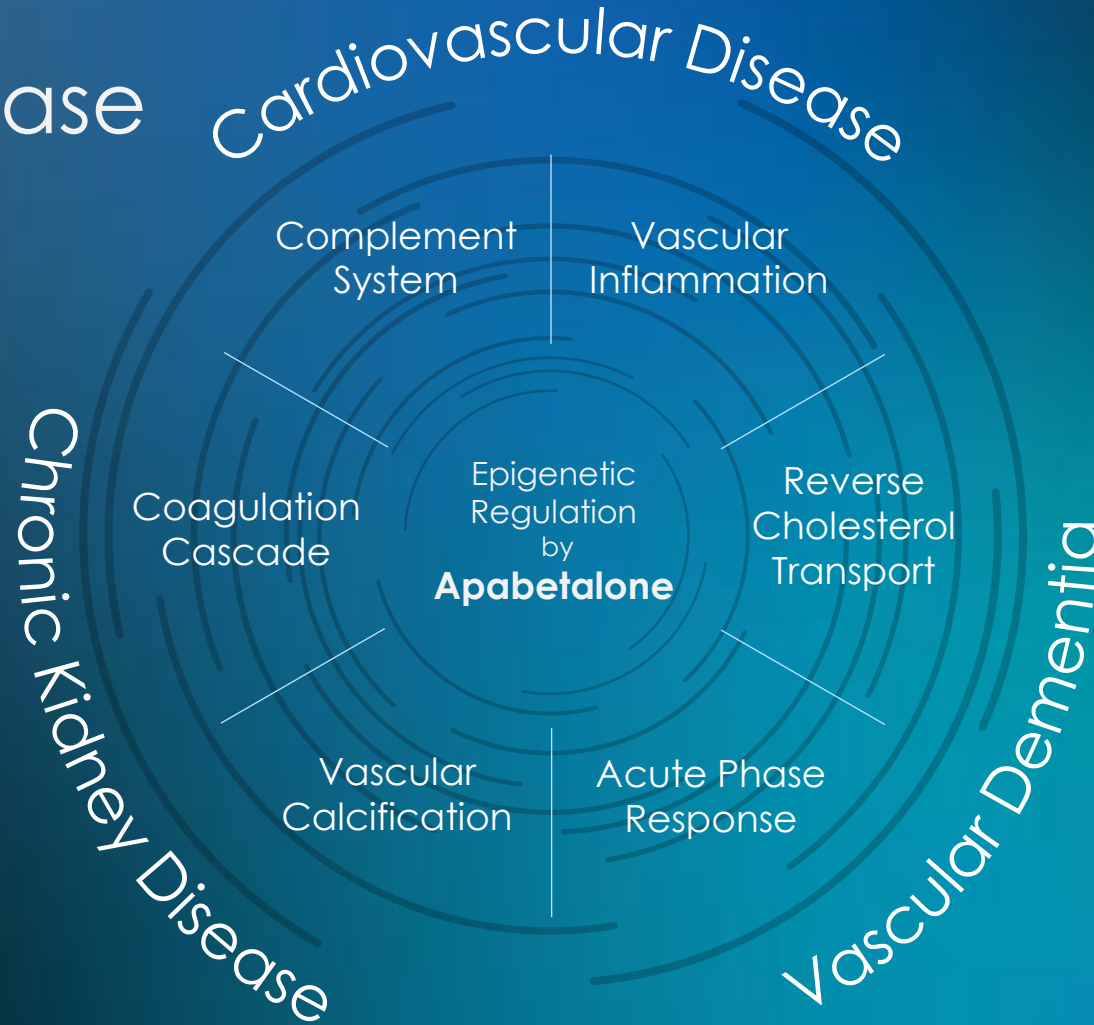
- Conventional pharmaceuticals target single proteins, while apabetalone can benefit multiple dysregulated pathways



RESVERLOGIX



# Apabetalone: Regulating Vascular Disease



Multiple pathways contribute to the development and progression of vascular disease

Apabetalone counters the dysregulation of genes that drive chronic illness

Many of the same pathways contribute to the development of Post COVID-19 Conditions



Four Pillars:

# Therapeutic Product Development



1



## Intellectual Property & Academic Support

- Multiple patents
- Coverage to 2041
- Over 40 publications



2



## Regulatory Approval Pathway

- Breakthrough Therapy Designation
- Additional indications under review



3



## Commercialization Strategy & Capacity

- Expanded partnership with EVERSANA™
- Detailed commercialization work in place



4



## Financing

- Industry-wide decrease in M&A and IPO activity
- Alternate non-equity options being pursued













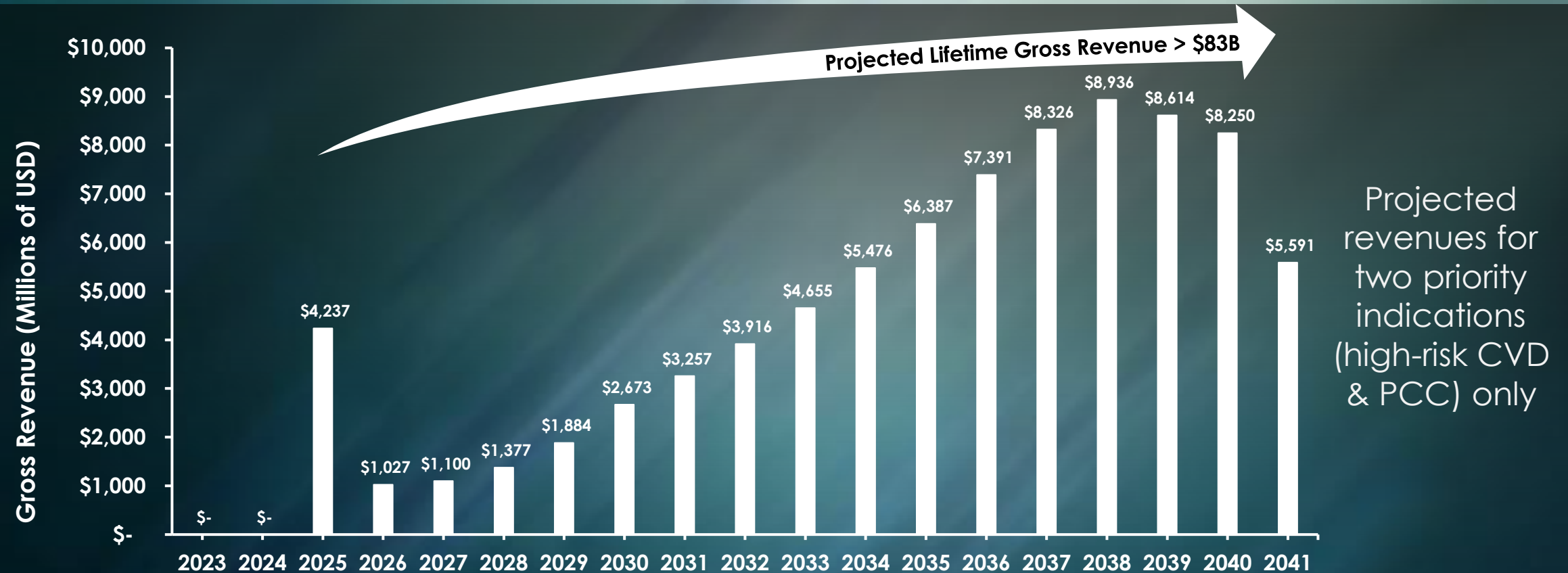
# Commercial Potential

## Commercial Opportunity: Multiple Unaddressed Indications

- Apabetalone addresses critical unmet need in high-risk patients with few available treatment options
- Multiple benefits across expanded indications provides an unprecedented commercial opportunity

	<p><b>Type 2 Diabetes Patients with Low HDL-C and Recent ACS</b></p>	<p><b>Type 2 Diabetes Patients with Low HDL-C, Cardiovascular Disease, and Chronic Kidney Disease (eGFR &lt;60)</b></p>	
	<p><b>Post COVID-19 Conditions (PPC)</b></p> <p><b>Two priority indications moving forward immediately</b></p>	<p><b>End Stage Renal Disease (eGFR &lt;15), Receiving Dialysis Treatment, with Elevated ALP (≥80 U/L)</b></p>	
	<p><b>Pulmonary Arterial Hypertension</b></p>	<p><b>Type 2 Diabetes Patients with Low HDL-C, Cardiovascular Disease, and Non-Alcoholic Fatty Liver Disease</b></p>	
	<p><b>Elderly (&gt;65 years) with Dementia or Amyloid Burden (AD) (MoCA Score ≤21)</b></p>	<p><i>Other future potential indications include orphan diseases, neuromuscular diseases, HIV, and others</i></p>	

# Commercial Opportunity: Targeting Massive Markets



Source: RVX Internal Projections and Forecasts based on global reports. Mid case revenue projections for T2DM, Low HDL-C, Recent ACS, and Post- COVID-19 Conditions markets highlighted.

## Commercial Opportunity Comparison: A Potential Blockbuster

- With dramatic improvements in cardiac outcomes, a long exclusive runway, and no major competitors, apabetalone is a potential game changer in cardiovascular therapeutics
- Expansion to multiple promising indications could provide further revenue streams

	<b>Lipitor®</b> (atorvastatin)	<b>Apabetalone</b> (with SGLT2i or DPP4i)
<b>MACE Reductions</b>	~30%	63%
<b>Major Competitors</b>	6	0
<b>Peak Annual Sales</b>	\$13Bn (2006)	>\$8Bn (est. Very Conservative)





# Current Condition of the Life Sciences Industry

The Good, The Bad & The Ugly!



## Industry Perspective: Pharma M&A was Down in 2022

- 2022 was a difficult year for the financial markets and for the pharmaceutical industry specifically
- Due to macroeconomic trends, and the over-capitalization of biotechnology companies in early 2021, both deal values and volume were down industry-wide
- Analysts expect a return to normalcy before the end of 2023, and a ramp up in pharma investments as companies prepare for a looming patent cliff in the late 2020s

Combined Value (2022):

**US\$158.5Bn**

**41%**

Decrease in Pharma  
M&A Deal Value  
Compared to 2021

Combined Volume (2022):

**258 Deals**

**30%**

Decrease in Pharma  
M&A Deal Volume  
Compared to 2021

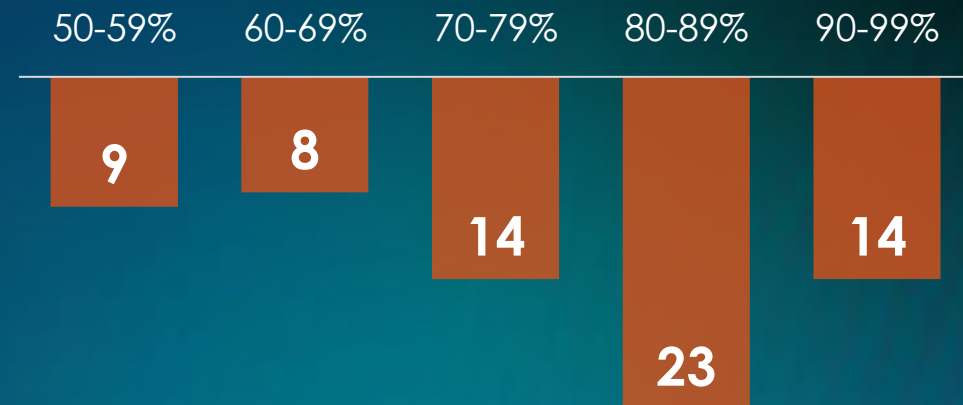


# Biotechnology – an Industry in Difficult Times

- The volume of biotech initial public offerings (IPOs) and the funds raised by these offerings declined in 2022 and the first half of 2023

Year	IPOs	Funds Raised
2023*	7	\$924.6MM**
2022	21	\$2,229.5MM
2021	104	\$14,803.0MM

## Price Drops of 2021 Biotech IPOs



- Many biotech companies with IPOs in 2021 have share prices significantly below their IPO price
- Only 9 of 104 are above their IPO price (the average increase among these 9 is 180%)



\*As of June 15, 2023

\*\*Excludes J&J wholly-owned spinout (May 2023)

Source: Biopharma Dive

# Upcoming Patent Cliff: Pharma is Motivated to Replace Expiring IP

- Between 2023-2030, almost all major pharma companies will see patents expires on some of their blockbuster drugs
- Combined, these companies could lose over **US\$200 billion** in sales by 2030



# Upcoming Patent Cliff: Pharma is Motivated to Replace Expiring IP

- Many of the drugs with expiring IP are indicated for conditions in which RVX and ZEN compounds may offer some benefit
- Major SGLT2 inhibitors will lose exclusivity in 2025 (Farxiga), 2027 (Invokana), and 2028 (Jardiance)



RVX

ZEN

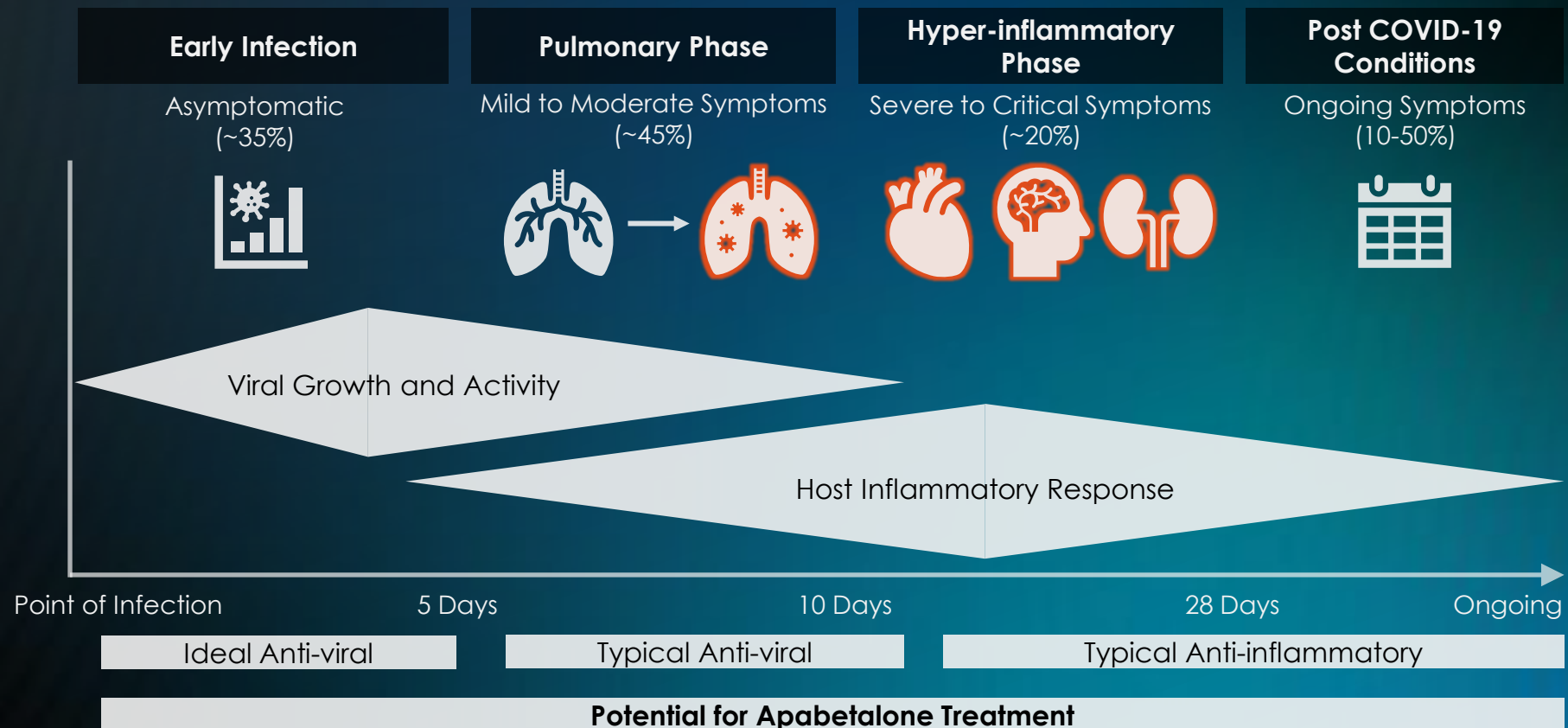


# Post COVID-19 Conditions Trial

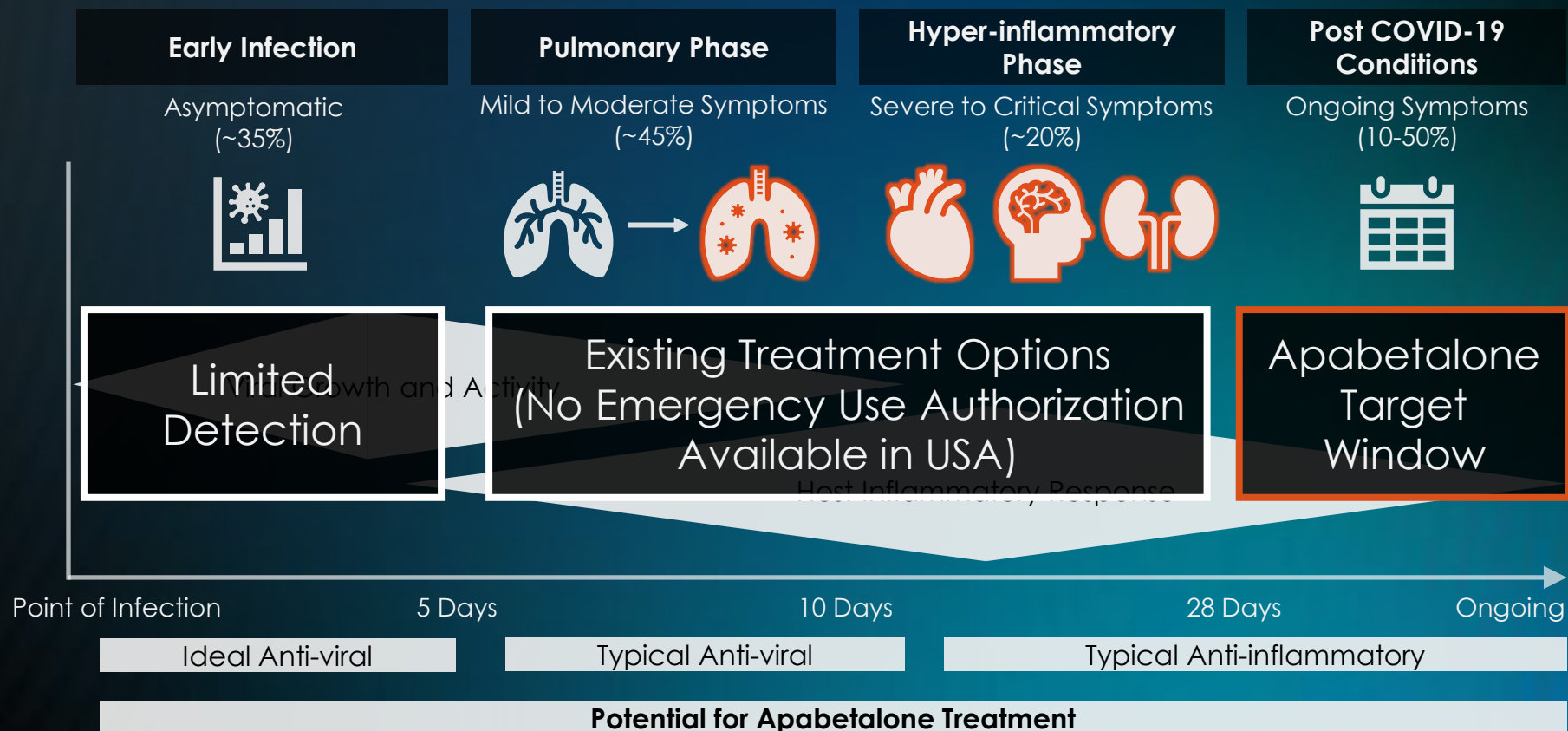
Addressing the evolving challenges of the global pandemic



# COVID-19: Apabetalone and Disease Progression

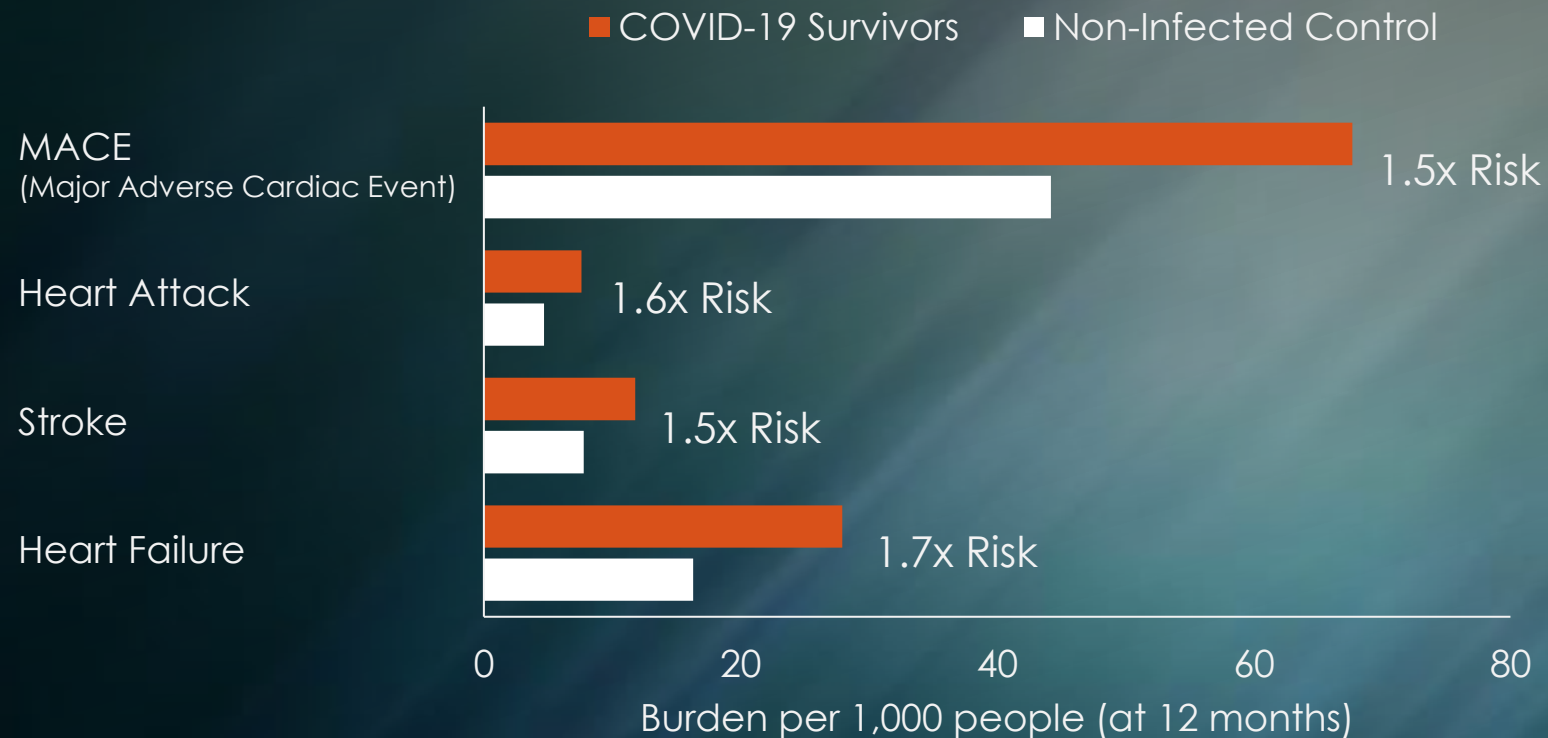


# COVID-19: Apabetalone and Disease Progression



Post COVID-19 Cardiovascular Outcomes:

# Increased Burden of Multiple Cardiovascular Events



People who contract COVID-19 have a 50%-70% greater risk of severe cardiac events in the first year after their infection than people who never contracted COVID-19

Adapted from: Xie et al. 2022 (Nature Medicine)

MACE is a composite endpoint of myocardial infarction, stroke, and cardiovascular death



# Post COVID-19 Cardiovascular Outcomes: A Growing Body of Literature Supports Long-Term Risks

Numerous high-quality peer-reviewed publications have independently confirmed increased risk of negative cardiovascular outcomes following COVID-19 infection

**nature medicine** ARTICLES  
<https://doi.org/10.1038/s41591-022-01689-3>  
 Check for updates

**OPEN**  
**Long-term cardiovascular outcomes of COVID-19**

Yan Xie<sup>1,2,3</sup>, Evan Xu<sup>1,4</sup>, Benjamin Bowe<sup>1,2</sup> and Ziyad Al-Aly<sup>1,2,5,6,7</sup>

*The*  
**American Journal of Cardiology**

**Risk of Cardiovascular Events After COVID-19**

Larisa G. Tereshchenko, MD, PhD ✉ • Adam Bishop, BS • Nora Fisher-Campbell, BA • ...  
 Inga Van Buren, BA • Jessica Wallace, BA • Akram Khan, MD • Show all authors

**thebmj**

**Risk of persistent and new clinical sequelae among adults aged 65 years and older during the post-acute phase of SARS-CoV-2 infection: retrospective cohort study**

Ken Cohen<sup>1</sup>, Sheng Ren, senior manager of data science<sup>1</sup>, Kevin Heath, senior medical director for payment integrity and clinical analytics<sup>2</sup>, Micah C Dasmariñas, data scientist<sup>1</sup>, Karol Giuseppe Jubilo, data scientist<sup>1</sup>, Yinglong Guo, director of data science<sup>1</sup>, Marc Lipsitch, professor<sup>3</sup>, Sarah E Daugherty, senior principal research scientist<sup>1</sup>

**Heart**

**Cardiovascular disease and mortality sequelae of COVID-19 in the UK Biobank**

Zahra Raisi-Estabragh<sup>1, 2</sup>, Jackie Cooper<sup>1</sup>, Ahmed Saleh<sup>1</sup>, Betty Raman<sup>3</sup>, Aaron Mark Lee<sup>1</sup>, Stefan Neubauer<sup>3</sup>, Nicholas C. Harvey<sup>4, 5</sup>, Steffen E. Petersen<sup>1, 2, 6, 7</sup>

**PLOS MEDICINE**

**Cardiometabolic outcomes up to 12 months after COVID-19 infection. A matched cohort study in the UK**

Emma Rezel-Potts, Abdel Douiri, Xiaohui Sun, Phillip J. Chowienczyk, Ajay M. Shah, Martin C. Gulliford ✉

**eClinicalMedicine**  
 ARTICLES | VOLUME 53, 101619, NOVEMBER 2022

**Long-term cardiovascular outcomes in COVID-19 survivors among non-vaccinated population: A retrospective cohort study from the TriNetX US collaborative networks**

Weijie Wang • Chi-Yen Wang • Shioh-Ing Wang<sup>1</sup> • James Cheng-Chung Wei<sup>1</sup> ✉ • Show footnotes

**PLOS ONE**

**One-year cardiovascular outcomes after coronavirus disease 2019: The cardiovascular COVID-19 registry**

Luis Ortega-Paz ✉, Victor Arévalos ✉, Diego Fernández-Rodríguez, Victor Jiménez-Díaz, Jordi Bañeras, Gianluca Campo, Miguel Rodríguez-Santamarta, José Francisco Díaz, Claudia Scardino, Zaira Gómez-Álvarez, Alberto Pernigotti, Fernando Alfonso, Ignacio J. Amat-Santos, [ ... ], on behalf of the CV COVID-19 registry investigators ✉ [ view all ]



# Post COVID-19 Conditions: Scientific Advisory Board

- A team of highly engaged, experienced, and respected COVID-19 clinical trial investigators
- Infectious Disease, Critical and Emergency Care Specialists



**JUDITH S. CURRIER, MD**  
Professor of Medicine  
Division Chief, Infectious Diseases  
Director, UCLA Clinical AIDS  
Research and Education  
UCLA Health  
Los Angeles, California



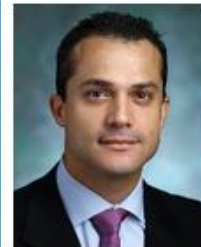
**PRINCY N. KUMAR, MD, FIDSA, MACP**  
Professor of Medicine and Microbiology  
Chief, Division of Infectious Diseases and  
Tropical Medicine  
Senior Associate Dean of Students  
Georgetown University School of Medicine  
Washington, District of Columbia



**CARLOS DEL RIO, MD**  
Executive Associate Dean  
Distinguished Professor  
Emory School of Medicine  
Atlanta, Georgia



**TIFFANY M. OSBORN, MD,  
MPH, FCCM, FACEP, FAEM**  
Professor of Surgery  
and Emergency Medicine  
Barnes Jewish Hospital  
St. Louis, Missouri



**FRANCO R. D'ALESSIO, MD**  
Associate Professor Of Medicine  
Johns Hopkins University  
Attending Physician  
Johns Hopkins Hospital  
Baltimore, Maryland



**BARRY ZINGMAN, MD**  
Professor  
Albert Einstein College of Medicine  
Bronx, New York

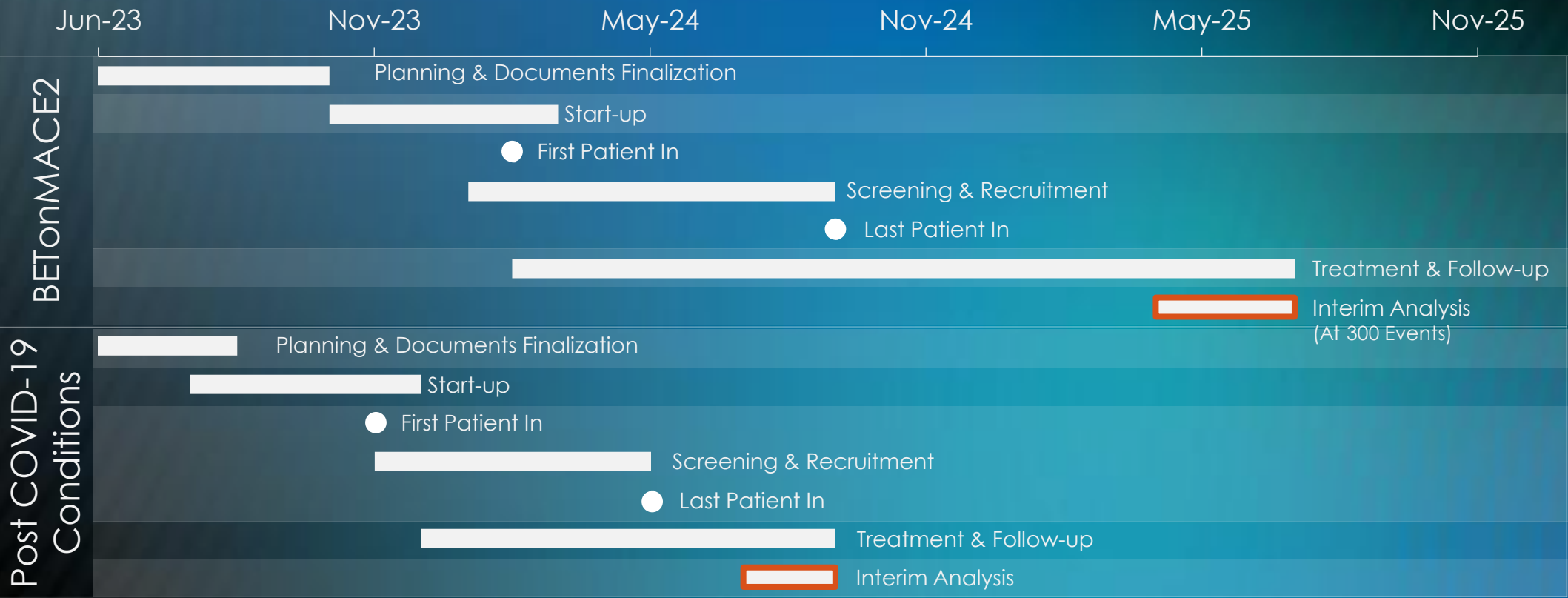




# BETonMACE2 Clinical Program

A registration-enabling clinical study of apabetalone  
with FDA Breakthrough Therapy Designation

# Clinical Trial Timelines: Accelerated Development with Interim Analyses



Projected timelines to interim analysis only, subject to change

# EVERSANA™: Flexibility in Commercialization



EVERSANA™



We partnered with EVERSANA™ to support the development of apabetalone through their complete commercialization services



# Clinical Programs: Recent Advancements

We are a global leader in the development of epigenetic therapies for the treatment of chronic disease

**Cell**  
Article

**BET inhibition blocks inflammation-induced cardiac dysfunction and SARS-CoV-2 infection**

Richard J. Mills<sup>1</sup>, Sean J. Humphrey<sup>2</sup>, Patrick R.J. Fortuna<sup>1</sup>, Mary Lor<sup>1</sup>, Simon R. Foster<sup>1</sup>, Gregory A. Quaife-Ryan<sup>1</sup>, Rebecca L. Johnston<sup>1</sup>, Troy Dumenuil<sup>1</sup>, Cameron Bishop<sup>1</sup>, Rajeev Rudraraju<sup>3,4,5</sup>, Daniel J. Rawle<sup>1</sup>, Thuy Le<sup>1</sup>, Wei Zhao<sup>5</sup>, Leo Lee<sup>5</sup>, Charley Mackenzie-Kludas<sup>5</sup>, Neda R. Mehdiabadi<sup>6</sup>, Christopher Halliday<sup>7</sup>, Dean Gilham<sup>7</sup> ... James E. Hudson<sup>1,20</sup> 

**JAMA | Original Investigation**

**Effect of Apabetalone Added to Standard Therapy on Major Adverse Cardiovascular Events in Patients With Recent Acute Coronary Syndrome and Type 2 Diabetes**  
A Randomized Clinical Trial

Kausik K. Ray, MBChB; Stephen J. Nicholls, MBBS, PhD; Kevin A. Buhr, PhD; Henry N. Ginsberg, MD; Jan O. Johansson, MD, PhD; Kamyar Kalantar-Zadeh, MD; Ewelina Kulikowski, PhD; Peter P. Toth, MD, PhD; Norman Wong, MD; Michael Sweeney, MD; Gregory G. Schwartz, MD, PhD; for the BETonMACE Investigators and Committees

**biomedicines**



Article

**Bromodomain and Extraterminal Protein Inhibitor, Apabetalone (RVX-208), Reduces ACE2 Expression and Attenuates SARS-Cov-2 Infection In Vitro**

Dean Gilham<sup>1,†</sup>, Audrey L. Smith<sup>2,†</sup>, Li Fu<sup>1,†</sup>, Dalia Y. Moore<sup>2,‡</sup>, Abenaya Muralidharan<sup>3,‡</sup>, St. Patrick M. Reid<sup>3</sup>, Stephanie C. Stotz<sup>1</sup>, Jan O. Johansson<sup>1</sup>, Michael Sweeney<sup>1</sup>, Norman C. W. Wong<sup>1</sup>, Ewelina Kulikowski<sup>1,†</sup> and Dalia El-Gamal<sup>2,\*,†</sup> 

**Cardiovascular Diabetology**

**Relation of insulin treatment for type 2 diabetes to the risk of major adverse cardiovascular events after acute coronary syndrome: an analysis of the BETonMACE randomized clinical trial**

Gregory G. Schwartz<sup>1,‡</sup>, Stephen J. Nicholls<sup>2</sup>, Peter P. Toth<sup>1,4</sup>, Michael Sweeney<sup>5</sup>, Christopher Halliday<sup>5</sup>, Jan O. Johansson<sup>5</sup>, Norman C. W. Wong<sup>5</sup>, Ewelina Kulikowski<sup>5</sup>, Kamyar Kalantar-Zadeh<sup>5</sup>, Henry N. Ginsberg<sup>5</sup> and Kausik K. Ray<sup>5</sup>

**CJASN**  
Clinical Journal of the American Society of Nephrology

**Effect of Apabetalone on Cardiovascular Events in Diabetes, CKD, and Recent Acute Coronary Syndrome**  
Results from the BETonMACE Randomized Controlled Trial

Kamyar Kalantar-Zadeh<sup>1,‡</sup>, Gregory G. Schwartz<sup>2</sup>, Stephen J. Nicholls<sup>3</sup>, Kevin A. Buhr<sup>4</sup>, Henry N. Ginsberg<sup>5</sup>, Jan O. Johansson<sup>6</sup>, Ewelina Kulikowski<sup>6</sup>, Kenneth Lebioda<sup>6</sup>, Peter P. Toth<sup>7,8</sup>, Norman Wong<sup>6</sup>, Michael Sweeney<sup>6</sup> and Kausik K. Ray<sup>9</sup> on behalf of the BETonMACE Investigators

**Cardiovascular Diabetology**

**Apabetalone and hospitalization for heart failure in patients following an acute coronary syndrome: a prespecified analysis of the BETonMACE study**

Stephen J. Nicholls<sup>1</sup>, Gregory G. Schwartz<sup>2</sup>, Kevin A. Buhr<sup>3</sup>, Henry N. Ginsberg<sup>4</sup>, Jan O. Johansson<sup>5</sup>, Kamyar Kalantar-Zadeh<sup>6</sup>, Ewelina Kulikowski<sup>6</sup>, Peter P. Toth<sup>7,8</sup>, Norman Wong<sup>6</sup>, Michael Sweeney<sup>5</sup> and Kausik K. Ray<sup>9</sup> on behalf of the BETonMACE Investigators

**JAD** Journal of Alzheimer's Disease

**Cognitive Effects of the BET Protein Inhibitor Apabetalone: A Prespecified Montreal Cognitive Assessment Analysis Nested in the BETonMACE Randomized Controlled Trial**

Jeffrey Cummings<sup>1,†</sup>, Gregory G. Schwartz<sup>2</sup>, Stephen J. Nicholls<sup>3</sup>, Aziz Khan<sup>4</sup>, Chris Halliday<sup>5</sup>, Peter P. Toth<sup>6</sup>, Michael Sweeney<sup>6</sup>, Jan O. Johansson<sup>6</sup>, Norman C. W. Wong<sup>6</sup>, Ewelina Kulikowski<sup>6</sup>, Kamyar Kalantar-Zadeh<sup>6</sup>, Kenneth Lebioda<sup>6</sup>, Henry N. Ginsberg<sup>6</sup>, Bengt Winblad<sup>1,†</sup>, Henrik Zetterberg<sup>1,†,§,||,m</sup> and Kausik K. Ray<sup>6</sup>







# Funding Option Example





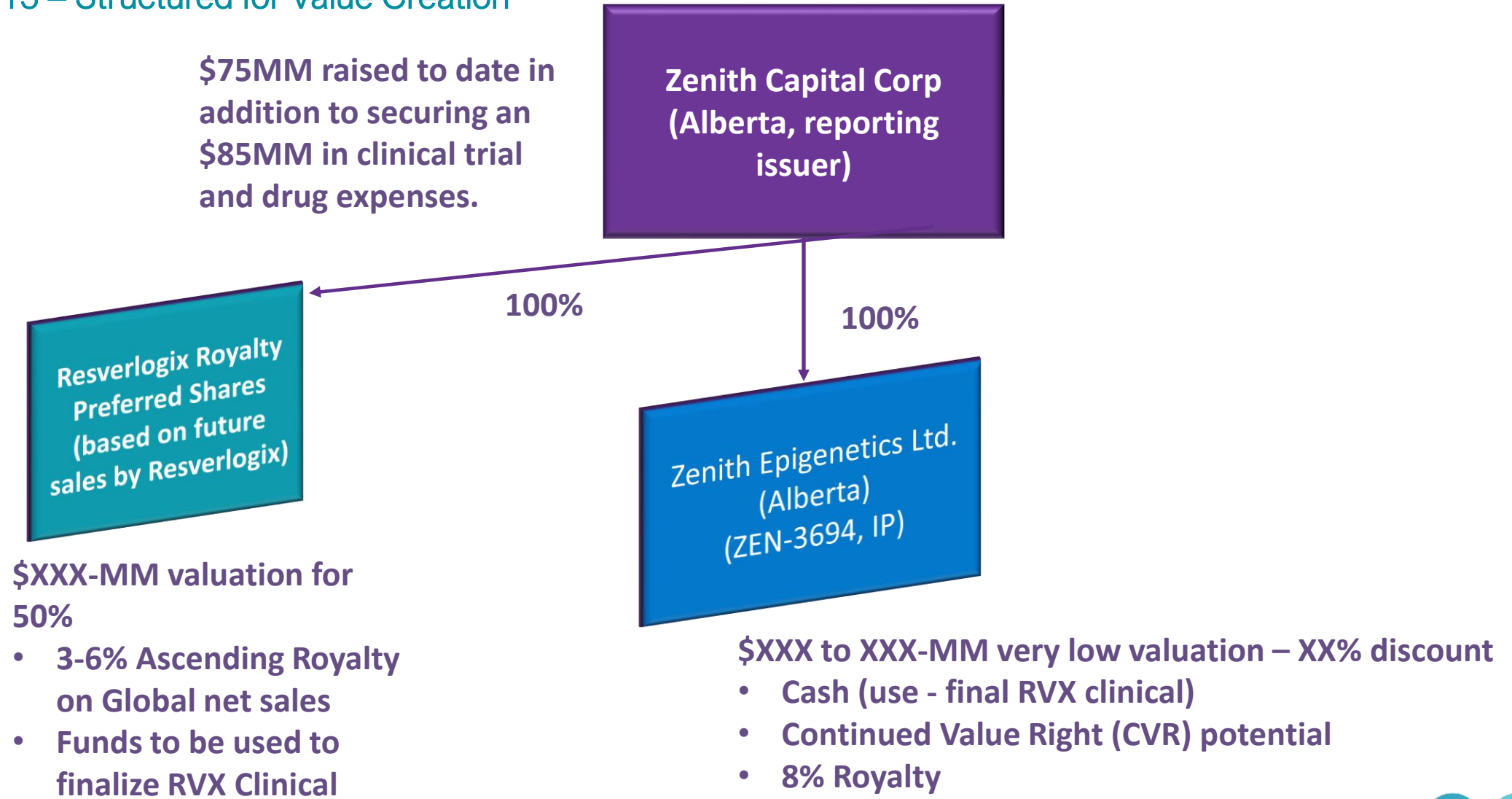
# Corporate Strategy

Value Creation Strategies for 2023 - Divergence!



# Corporate Structure – Two Major Assets

Formed in 2013 – Structured for Value Creation



# Corporate Structure – Two Major Assets

Formed in 2013 – Structured for Value Creation

\$75MM raised to date in addition to securing an \$85MM in clinical trial and drug expenses.

Zenith Capital Corp  
(Alberta, reporting issuer)

100%

100%

Resverlogix Royalty Preferred Shares  
(based on future sales by Resverlogix)

In discussions

\$XXX-MM valuation for 50%

- 3-6% Ascending Royalty on Global net sales
- Funds to be used to finalize RVX Clinical

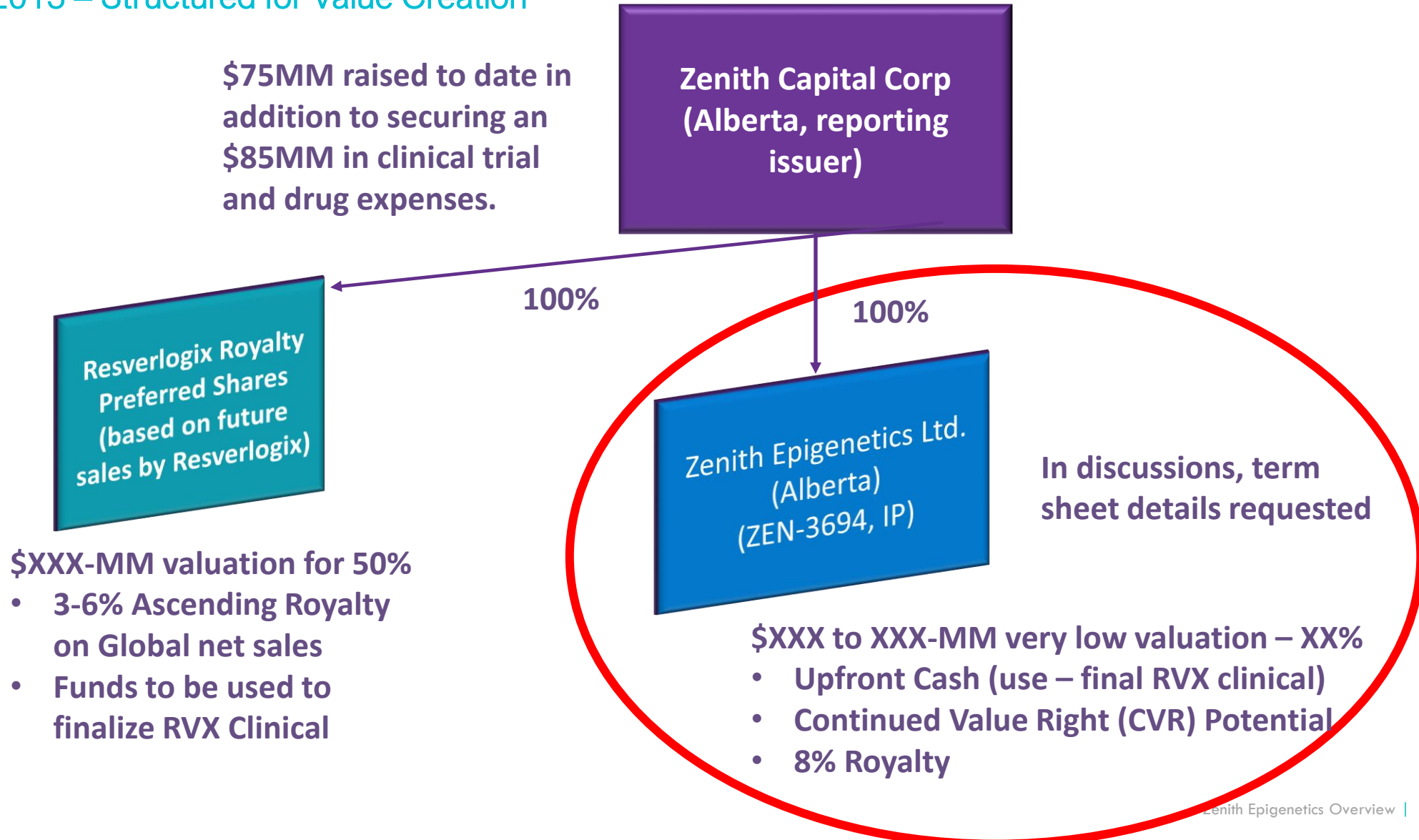
Zenith Epigenetics Ltd.  
(Alberta)  
(ZEN-3694, IP)

\$XXX to XXX-MM very low valuation – XX% discount

- Cash (use – final RVX clinical)
- Continued Value Right (CVR) Potential
- 8% Royalty

# Corporate Structure – Two Major Assets

Formed in 2013 – Structured for Value Creation



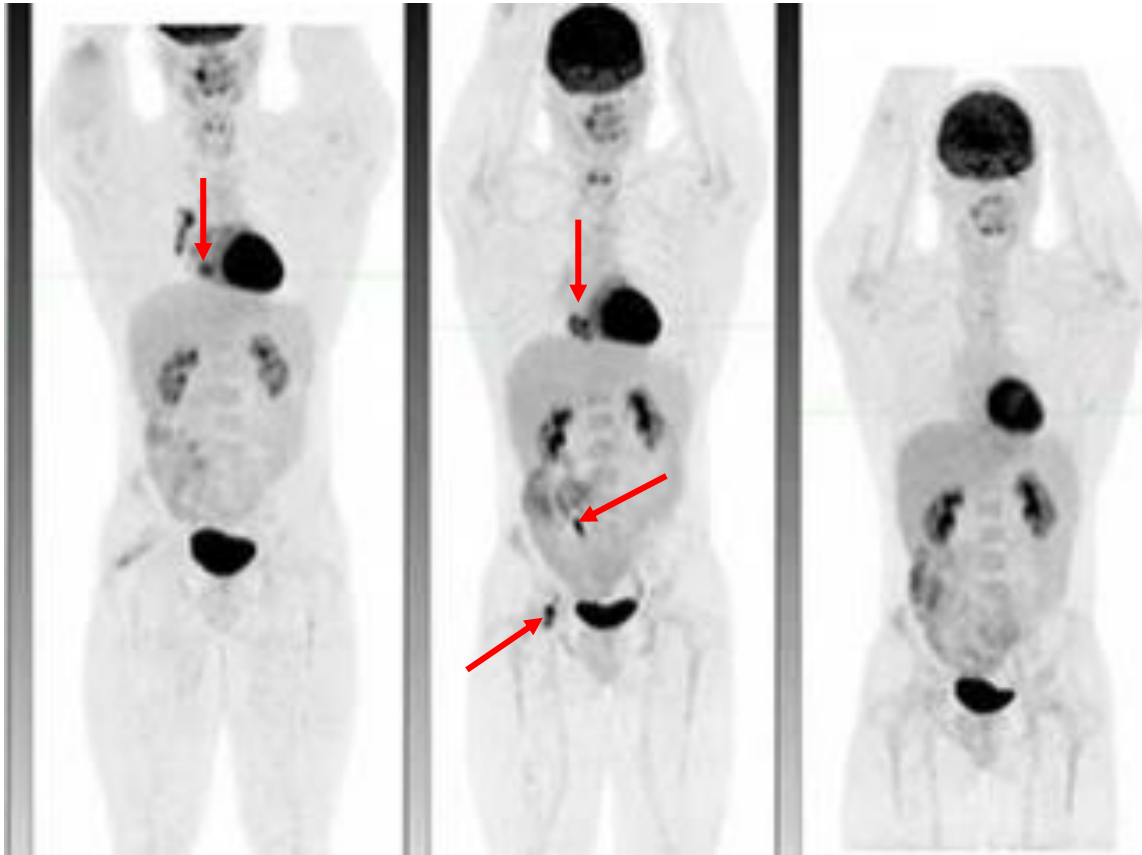


# Near CR with ZEN-3694 in Nut Midline Carcinoma Patient

10/5/22

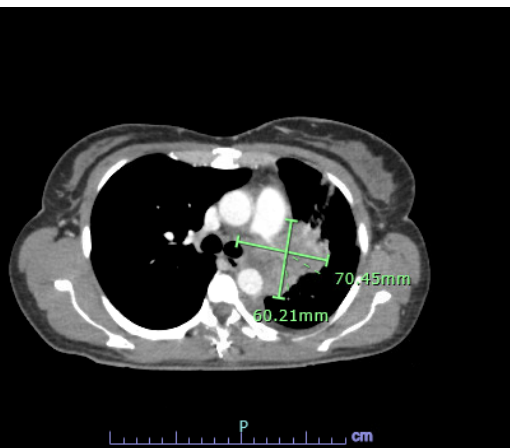
12/9/22

3/7/23

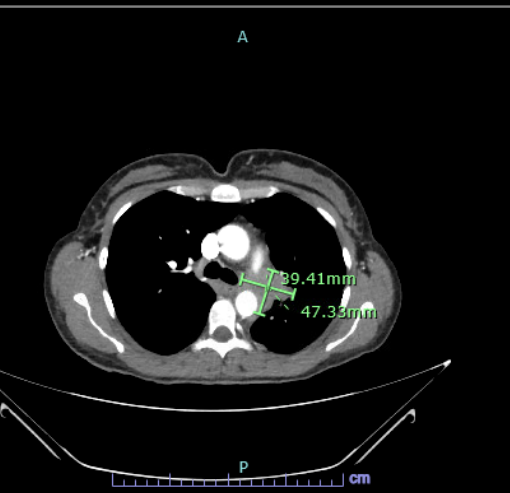


- Progressing on bone and lung lesions prior to treatment
- 12/18/22 : Single agent ZEN-3694 treatment started at 48mg/qd
- Dose interruption due to diarrhea in Cycle 1
- ~2/2/23 : ZEN-3694 dose increased to 48mg BID – is being tolerated
- 3/7/23: Scans show a near complete response
- Patient continuing on 48mg BID

# Thoracic NUT Carcinoma Patient on compassionate use ZEN-3694



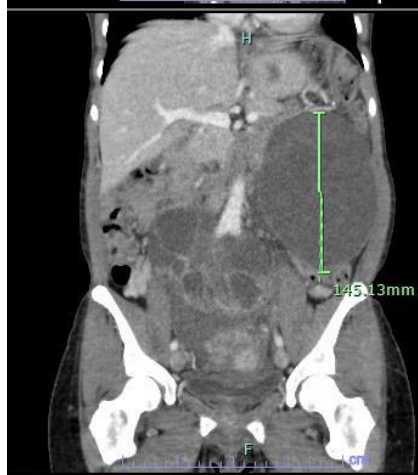
09/18/22  
Lung  
lesion:70.45mm



02/07/23  
Lung  
lesion:47.33mm



12/01/22  
Abdominal  
lesion:160mm

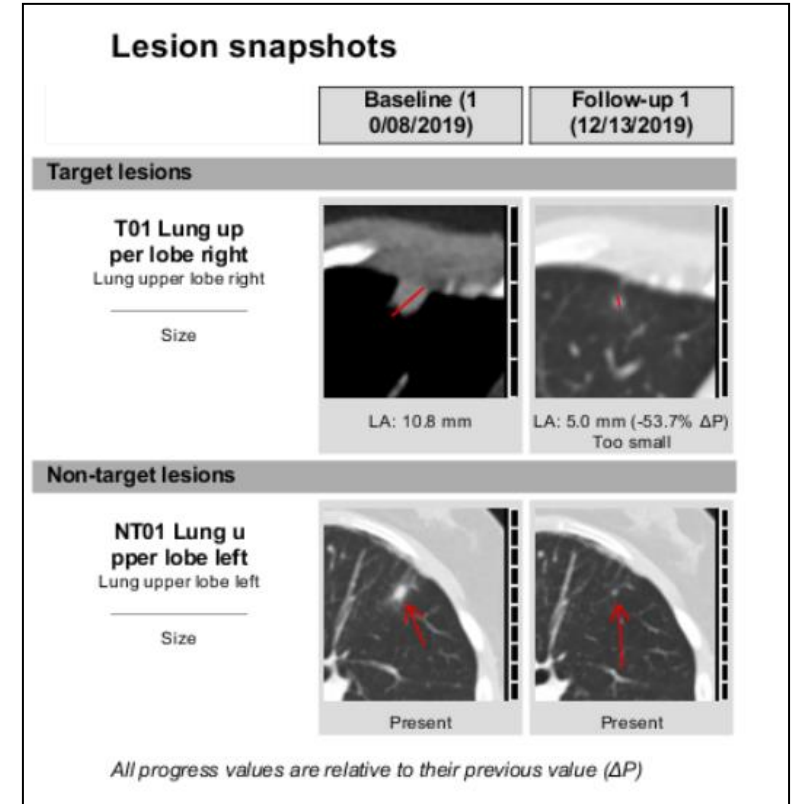
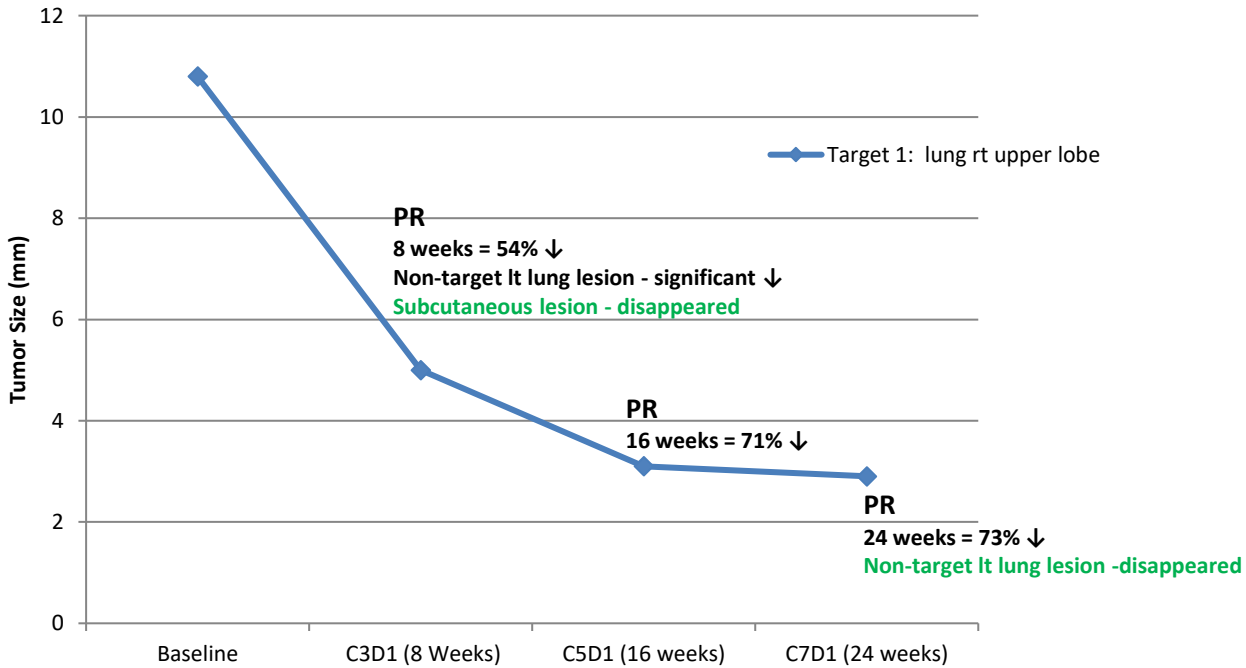


02/23/23  
Abdominal  
lesion:145mm

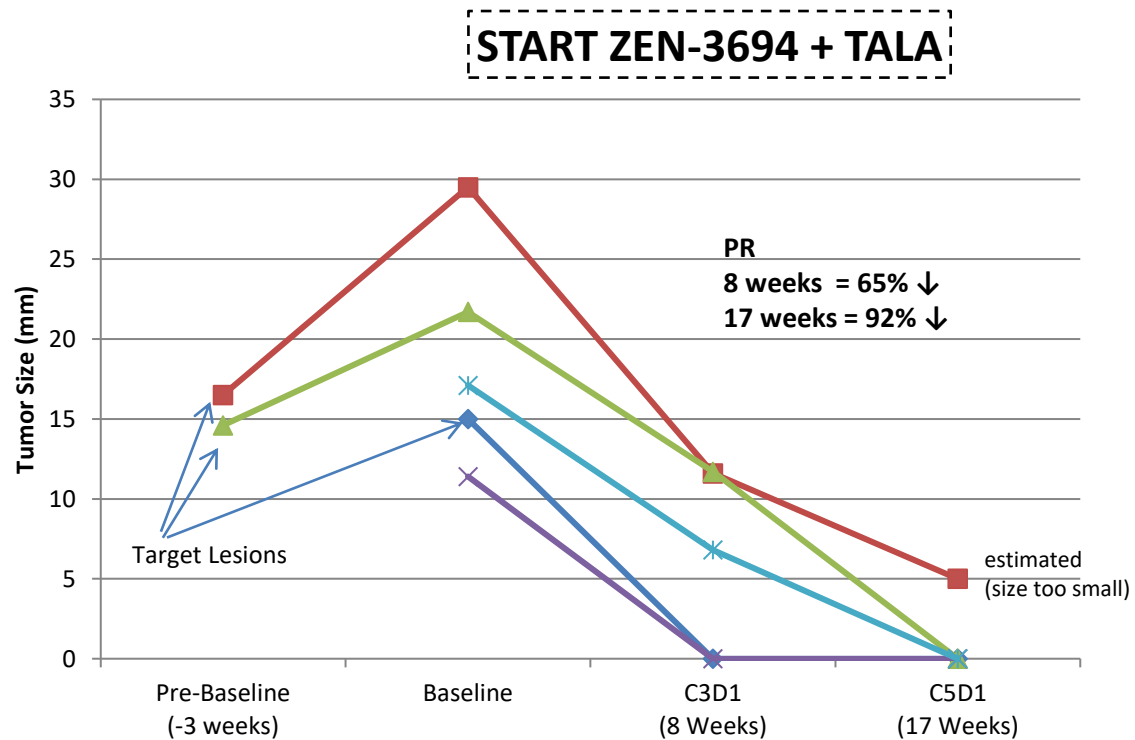
Clinical History: PDL1+, Thoracic NUT carcinoma

- Started cis/etop 10/4/22
- Added ZEN-3694 on cycle 2 (48mg) 10/25/22
- ZEN increased to 60 5:2 11/15/22
- Completed 6 cycles of cis/etop and 5 cycles ZEN-3694 on 1/19/23
- Started pembrolizumab+ ZEN (60 5:2) on 2/7/23
- Surgical resection of abdominal and liver mass 2/28/23
- Resumed pembro + ZEN

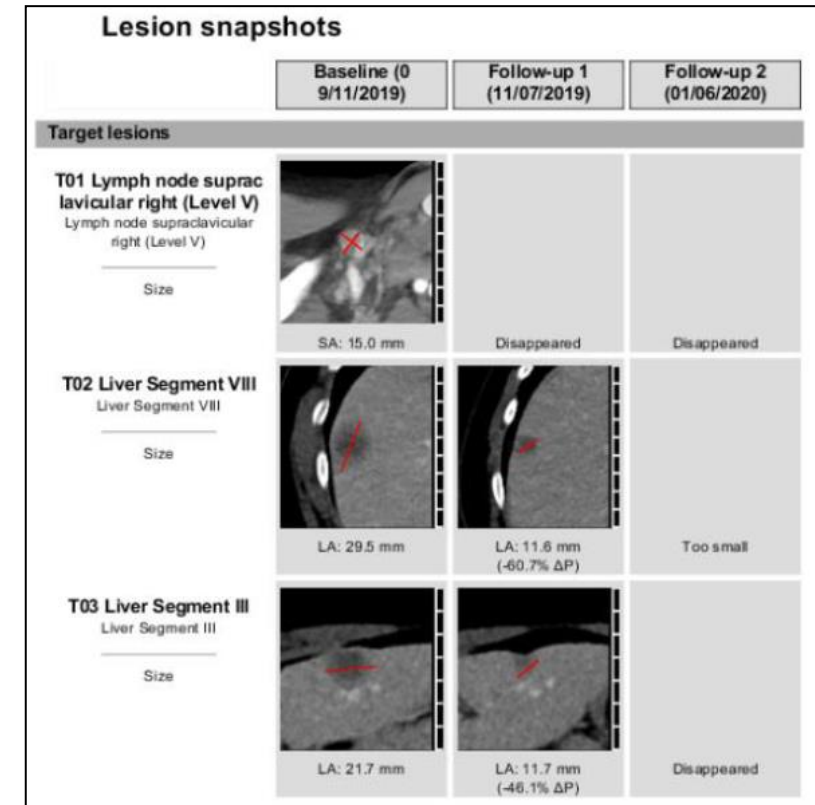
# Inhouse Clinical Trial Result - 73% decrease in Lung Lesions (Triple Negative Breast Cancer that metastasized to the Lungs)



# Inhouse Clinical Trial Result - 92% decrease in Liver Lesions (Triple Negative Breast Cancer that metastasized to the Liver)



- ◆ Target 1: Supraclavicular rt. lymph node
- Target 2: Liver segment VIII
- ▲ Target 3: Liver segment III
- ✕ Non-Target 1: Cervical lymph node
- ✧ Non-Target 2: Liver





# Exceptional Responders in Triple Combo Clinical Trial (Prostate Cancer mCRPC Metastasized to Bone and Liver)

Cohort B patient CR: **100%** Disappearance of bone lesions

Cohort A patient PR: **60%** decrease in liver lesions

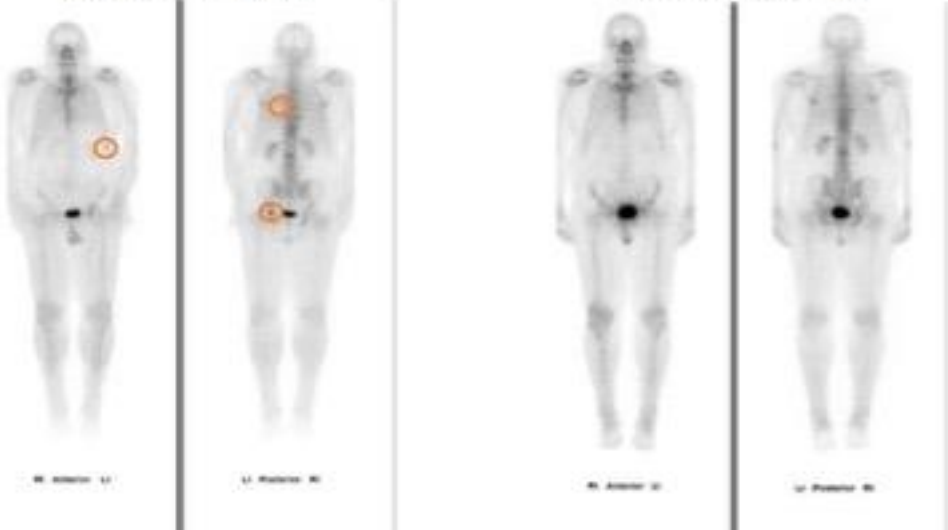
## Exceptional Responder

59 yo male with adenocarcinoma underwent prostatectomy and previously progressed on Bicalutamide and Abiraterone. He continues to have a sustained PSA50 response since C3D1 and a CR since May 2022.



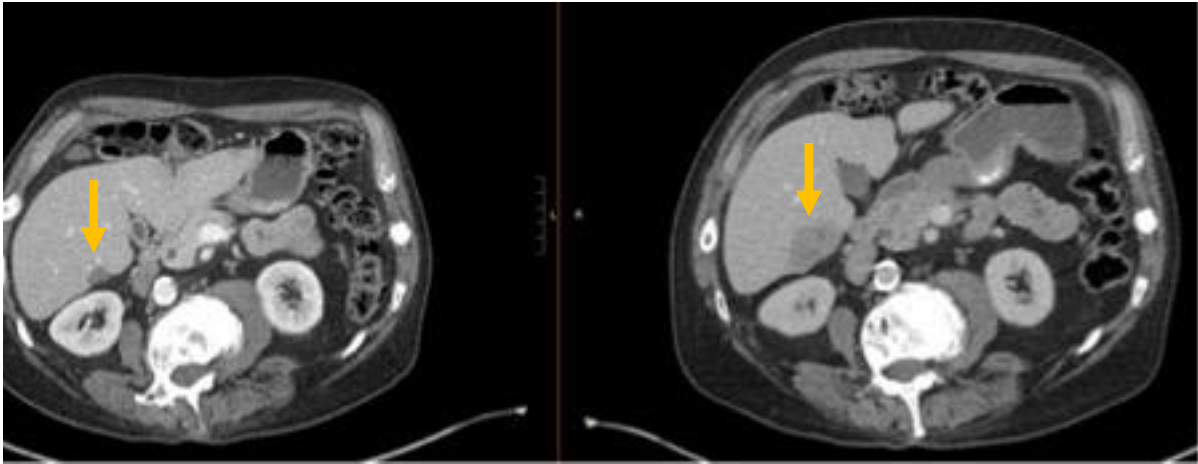
Bone Scan March 2021

Bone Scan August 2022



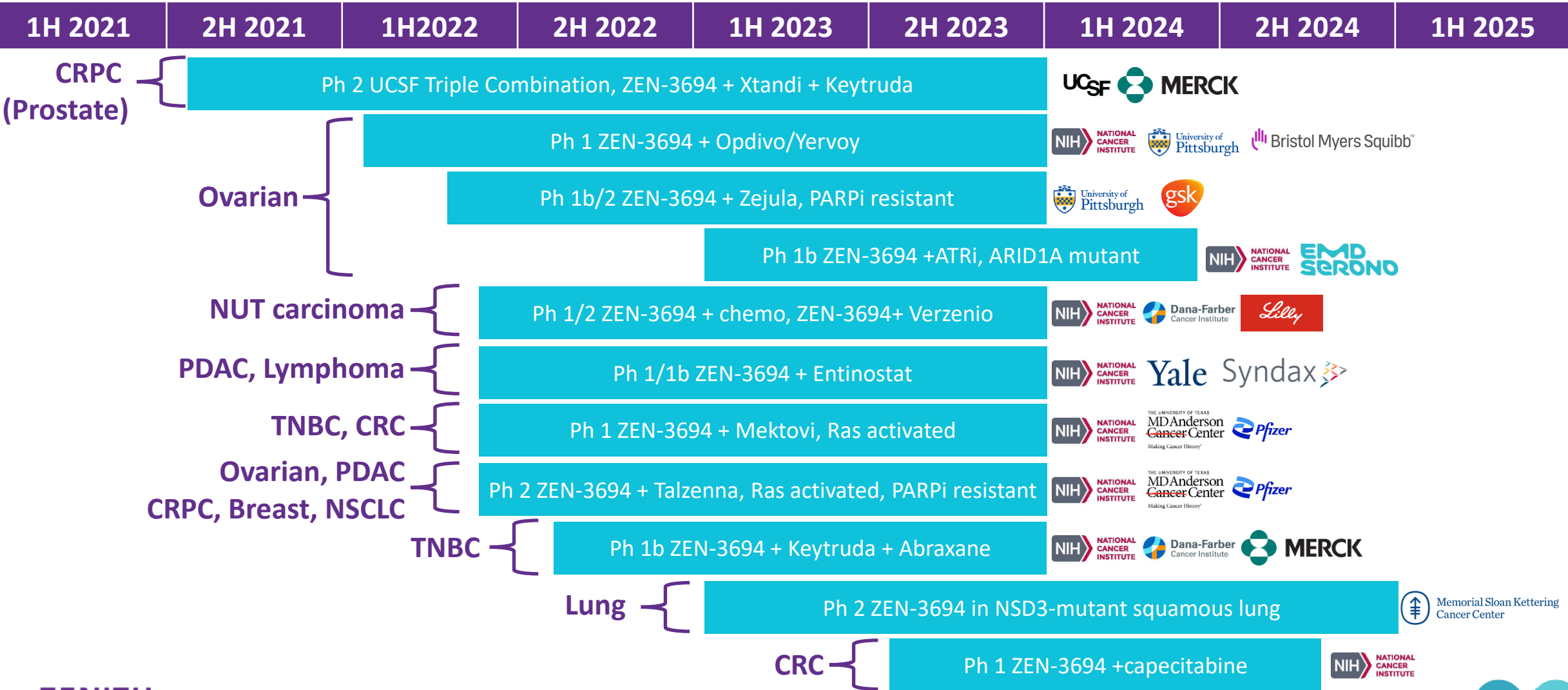
Post cycle 3

Baseline



# Investigator Sponsored and National Cancer Institute Trials (13 additional exterior run trials paid for by our collaborators)

Advance to registration enabling studies in multiple additional indications and combinations upon proof-of-concept data





## Contact

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