

...not just one virus – every virus

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Old approaches fail to flatten the curve



- Vision: Shelf-stable, easily manufactured, ready-for-use pills to cure current and future viral infection
- **Mission:** Build a pipeline of breakthrough antiviral drugs that provide unique <u>broad-spectrum treatment modalities</u> and <u>address the problem of drug resistance</u>
- Strategy: Target the infected cell instead of the virus



Evrys products define new markets by addressing the infection condition that can be caused by many viruses

Evrys Product	Development Stage	Disease Condition	Viruses to Be Covered	^a Competitor Therapy
EV-100	IND-enabling pre-clinical development	viral infection in immunosuppressed transplant patients	CMV, other herpes viruses (e.g., EBV), polyomaviruses (e.g., BKV)	CMV only
EV-200	lead optimization	chronic hepatitis B	HAV, HBV, HCV, HDV, HEV	HBV or HCV (not both)
EV-300	lead optimization <i>(DoD use)</i>	medical countermeasure (MCM) for acute lethal infection	Ebola, Marburg, encephalitis viruses, lassa fever virus, other alpha-, arena-, and filoviruses	vaccines for select viruses
EV-300	lead optimization <i>(civilian use)</i>	pan-respiratory infections	influenza A and B, respiratory syncytial virus, adenoviruses, coronaviruses, other respiratory viruses	influenza only (e.g., Tamiflu)

^a Viruses covered by standard-of-care competitor antiviral drugs unless otherwise indicated (e.g., vaccines)



Evrys Bio Overview

- Doylestown, PA since 2013
- \$12 M investor financing to date
 - Pharma-savvy angels: CEO, C-level execs, Mid-Atlantic Bio Angels, Keiretsu, BOHE
 - 2 Strategic Investors: ShangPharma & BioArdis
- \$47.1 M* non-dilutive financing
 - 11 Awarded Government Grants/Contracts
- Strong I.P. including issued patents
- World-class management team and advisors

*Cumulative total since 2013 including milestone payments not yet triggered



BIODURO



KEIRETSU









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Lillian Chiang, PhD, MBA Founder, CEO & President



Serial entrepreneur: Millennium, Purdue, Aestus, Kadmon

Thomas Shenk, PhD Founder, Chairman of the Board

Princeton Professor: founded ImClone, MeiraGTx, Novalon, Cadus, PMV

Steve Holtzman, Board Advisor

Former CBO Biogen, CEO Infinity, CEO Decibel Therapeutics

Richard Whitley Board Director and Clinical Advisor

Infectious disease Key Opinion Leader, Gilead Board Director



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Stacy Remiszewski, PhD Vice President, Research Former Section Head Roche Oncology Chemistry

Matthew Todd, PhD Director, Enzyme Biology and Biophysics Former Director, Janssen Lead Discovery

Aaron Dubberley Director, Intellectual Property Former Mt. Sinai Asst. Director of I.P.

Karen Monzon, MBA Controller

Former Director, Fidelity Investments

John L. Kulp, PhD Director, Business Development



Evrys Pipeline: First IND in 2023



*EV-200 and EV-300 currently funded by NIAID and DTRA, respectively.



Host-Target: Human Sirtuin Proteins

- Sirtuins SIRT1-7 are multifunctional enzymes that regulate transcription, genome stability, cellular signaling, and energy metabolism in response to the metabolic status of the cell
- Viral infection disrupts the metabolic status of the cell and depend on sirtuin regulated functions to replicate productively
- SIRT2 modulators (nicotinamide, sirtinol, cambinol, AGK2) can engage cellular reprogramming to inhibit cytomegalovirus^{1,2}, hepatitis A virus³, hepatitis B virus^{4,5}, *Listeria*^{6,7}, *Salmonella*⁸, *Tuberculosis*⁹
- Evrys SIRT2 targeted drugs are allosteric inhibitors if SIRT2 were a multifunctional Swiss army knife, Evrys SIRT2-targeted drugs modify some functions, such as the scissors, to stop viral replication, but do not completely knock out all functions of the knife required for cellular integrity of uninfected cells.
- SIRT2 KO mouse is healthy and less susceptible to infection¹⁰

^{1,2}Mao 2016, Koyuncu 2014, ³Kanda 2015, ^{4,5}Piracha 2018, Yu 2018, ^{6,7}Eskandarian 2013, Pereira 2018, ⁸Gogoi 2018, ⁹Bhaskar 2020, ¹⁰Ciarlo 2017



Evrys portfolio of well-characterized broad-spectrum antivirals

- EV-100 in IND-enablement
- > 800 compounds synthesized
 - 5 validated Chemical Scaffolds with issued patents on 2, modulating a family of cellular proteins called sirtuins
- Platform technologies
 - Host target-engagement, antiviral mechanism-ofaction, computational chemistry, biophysics
- Extendable and customizable to other viruses
 - viral hepatitis (EV-200)
 - medical countermeasures (EV-300)
 - respiratory viruses (EV-300)

Co-Crystal Structure of Evrys LEAD Bound to SIRT2





EV-100: First Clinical Target - cytomegalovirus

- Rapid path to Proof of Platform and FDA approval
 - **<u>CMV viral load</u>** is a validated biomarker and approvable endpoint
 - Proof of Concept: antiviral effectiveness in transplant patients with active CMV infection
 - First indication (orphan): non-inferiority CMV prophylaxis
- Attractive U.S. market for a small biotech
 - CMV comprises ~40% of transplant viral infections
 - \$3.2 B annually to manage CMV complications and organ rejection including > \$1 B in antivirals
 - Broad-spectrum against other herpes and polyomaviruses <u>will drive</u> <u>utilization</u> and downstream label expansion to non-CMV infections
 - Preclinically blocks reactivation from latency and lytic replication of Epstein Barr virus

10

EV-100: A Game-Changer for CMV

Drug mechanism	Pan-Viral Profile	EC ₅₀ (μΜ)	MAX INH at EC ₉₉	Time to virus detection after block-release	Response to high viral load	Viral Genes conferring resistance	Human Dose (mg/kg)
EV-100 human SIRT2 inh	CMV, EBV, BKV, JCV, others	0.7	>100-fold	> 96 hours	No change in EC ₅₀ as viral dose increases	None known	4
Marketed drugs:							
Valganciclovir (SOC) nucleoside inh	CMV, HSV	2.6	28-fold	72 hours	EC ₅₀ is increased as viral dose increases	UL54, UL97	15
Letermovir (SOC) viral terminase inh	CMV	0.003	4-fold	24 hours	ongoing spread	UL56	8
Cidofovir <mark>(tox-limited)</mark> viral DNA pol inh	CMV, HSV	0.64	>100-fold	> 96 hours	n.d.	UL54	5
Foscarnet (tox-limited) pyrophosphate mimic	CMV, HSV	200	n.d.	n.d.	n.d.	UL54	90



EV-200: Potential to contribute to functional cure of hepatitis B chronic infection

Reduction of HBV cccDNA, S and E antigens, and RNA





EV-300 aims to flatten the curve



EV-300: \$34.3 M Contract validates platform

Medical Counter Measure (MCM) to treat lethal acute Alphaviruses, Arenaviruses, and Filoviruses

- June 30, 2021: DTRA contract
- \$34.3 M, 5⁺ years from lead selection to human Phase 1
- Market approval via Animal Rule
- Evrys retains all commercialization
 - Government MCM stockpile
 - Evrys funded civilian acute panrespiratory virus infections



EV-300: Broad effectiveness against diverse respiratory viruses

Virus	Virus Family	Cell Line (CC ₅₀)	Evrys LEAD EC ₅₀	Comparator EC ₅₀	Comparator Standard of Care (SOC)	Assay performed by
HCoV-OC43	beta coronavirus	human MRC5 (> 25)	0.54	1.6	hydroxychloroquine	Evrys Bio
SARS-CoV2	beta coronavirus	human Calu 3 (16)	0.64	0.07	remdesivir (SOC)	USAMRIID
Influenza A	orthomyxovirus	human HNBE (> 100)	<u>1.2</u>	<u>0.71</u>	ribavirin	NIAID DMID
Influenza B	orthomyxovirus	canine MDCK (> 5)	1.2	> 25	oseltamivir (SOC)	Evrys Bio
HCoV-229E	alpha coronavirus	human MRC5 (> 25)	1.6	0.04	remdesivir	ImQuest
Ad5	adenovirus	human MRC5 (> 25)	1.6	3.1	cidofovir	Evrys Bio
Influenza A ^R	orthomyxovirus	canine MDCK (> 5)	2.5	9	oseltamivir (SOC)	Evrys Bio
MERS	beta coronavirus	human MRC5 (> 20)	4.1	0.07	remdesivir	USAMRIID
RSV	orthopneumovirus	human MRC5 (> 25)	6.7	16.1	ribavirin	Retrovirox
Shown EC $_{50}$ concentration in μ M providing 50% maximal antiviral effectiveness. Underlined indicates EC $_{90}$ reported. CC $_{50}$ drug concentration in						

µM resulting in 50% cytotoxicity; ">" indicates highest concentration tested.



Evrys is operating nearly cash neutral

- U.S. Government (Govt) funding is a profit center for Evrys' R&D
- Govt contracts and advanced purchase commitments for the Strategic National Stockpile will derisk Evrys' manufacturing and market risk
- Evrys' Govt network provides visibility to all infectious disease stakeholders (patients, physicians, drug companies, payers, FDA)

Evrys Bio, LLC 2021 Profit and Loss	
Income	
U.S. Government Grant/Contract Income	
Transplant Infections (NIH R44AI114079)	2,024,641
Influenza (NIH R44Al122488)	81,406
Medical Countermeasure (OTA No. W15QKN1691002)	920,153
Hepatitis B (NIH R44Al157725)	123,273
Total U.S. Government Grant/Contract Income	3,149,473
Other Income	208,069
Interest Earned	147
Total Revenue	3,357,689
Expenses Salary & Benefits Expense Research Supplies Equipment Expense Professional Fees (External Consultants) External Contract Research Expense Rent & Utilities G&A Expenses (excluding Salary & Benefits Expense) Intellectual Property Expense	1,731,809 203,658 30,449 367,909 1,323,198 156,646 60,213 49,723
Other Legal Expense	78,701
Total Expense	4,002,305
Net Income	(644,616)
Average Monthly Burn	(53,718)
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Seeking investment to scale to the clinic



- EV-100 (transplants) to proof of concept (POC) in man
- EV-200 (HBV) to POC in man
- EV-300 (MCM) to POC in non-human primate (NHP) and ready for pivotal trials
- EV-300 (respiratory) to IND

*EV-200 and EV-300 currently funded by NIAID and DTRA, respectively.



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Evrys Bio Summary

- Transformational technology, strong I.P., huge unmet need
- Inventor, Team, Advisors, and Investors with track record
- Leveraged investment with government funding development
- Tipping point of technology with preclinical proof-of-concept
- Seeking investment to scale to clinical proof-of-concept and first liquidity opportunity for investors

