



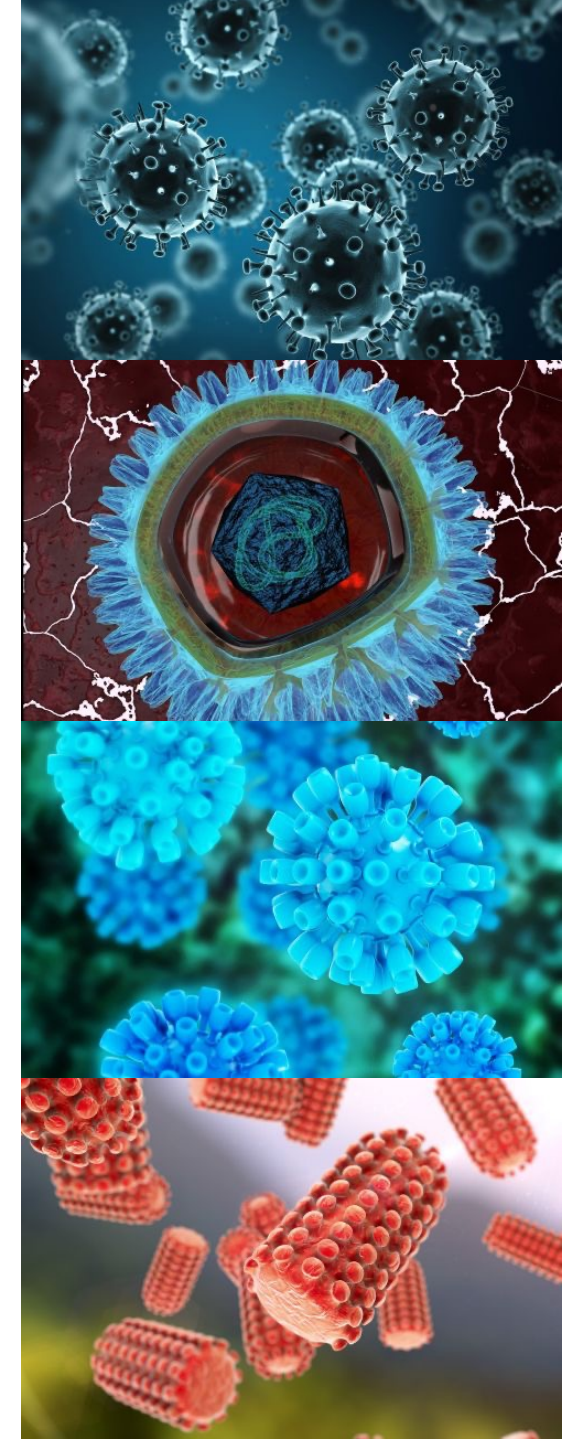
...not just one virus – every virus

Evrys Bio

CEO Lillian Chiang presenting

2023 BioPartnering Conference
Bio NJ – Somerset, NJ

Contact: John Kulp, Evrys Director of Business Development
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The Problem:

- > 200 viruses can cause disease in man
- 12 viral infections treated by marketed antivirals
- 20 viral infections addressed by marketed vaccines
- 26 viruses total we can defend in a pandemic
- > 170 viruses we can't

Today We Target One Virus at a Time

- Direct-Acting Antivirals (DAA):
 - Narrow spectrum, unlike antibiotics
 - A single viral mutation can confer resistance
- Vaccines:
 - Immune evasion by virus limits effectiveness
 - Poor effectiveness with weak antigens or immune system
 - Need to be administered long before exposure
 - Manufacturing bottle neck and may require cold chain logistics to distribute





...not just one virus - every virus

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



Unmet medical need poorly addressed by targeted antiviral approach

- >20 opportunistic infections threaten transplant recipients
 - lack of therapies to address pan-viral threats under immunosuppression
 - rare disease, specialty pharmaceutical, \$2-3 B/year
- Chronic viral hepatitis
 - >250 M individuals infected globally with hepatitis B (HBV)
 - virus-targeted therapies fail to provide sustained virologic response
 - >\$25 B/year based on HCV cure in 2014
- Pandemic preparedness (acute lethal RNA viruses)
 - Strategic National Stockpile (\$60 M/year)
 - COVID (\$18.9 B/year peak in 2022 for Paxlovid)
 - Viral escape and drug-resistance limits effectiveness of targeted therapies

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

Evrys Product	Disease Condition	Viruses to Be Covered
EV-100	viral infection in immunosuppressed transplant recipients	DNA viruses: CMV, other beta and gamma herpes viruses, e.g., EBV, HHV-6, and other opportunistic viruses
EV-200	chronic hepatitis B	Hepatitis viruses: persistent HBV genome (cccDNA) and HAV, HCV, HDV, HEV
EV-300	medical countermeasure (MCM)	Lethal RNA viruses: Ebola, Marburg, encephalitis viruses, lassa fever virus, other alpha-, arena-, and filoviruses
EV-300	pan-respiratory infections	Respiratory RNA viruses: influenza A and B, respiratory syncytial virus, and coronaviruses

>\$50 M of Awarded Government Support for Evrys Pipeline

	Validated Target	Drug Discovery	Preclin POC	Process Development	Complete CMC IND-enablement	IND	Market Approval
EV-100 TRANPLANT INFECTIONS	\$8 M past and current awarded government grants/contracts					Apr-24	2027
EV-200 VIRAL HEPATITIS	\$4 M		2023 Q4			2025	
EV-300 MEDICAL COUNTERMEASURE	\$35 M		2023 Q2			2025	
EV-300 PAN-RESPIRATORY INFECTIONS	\$4 M						

The U.S. government is a critical stakeholder in infectious disease providing visibility to patients, physicians, drug companies, payers, the FDA... Non-dilutive funding from DHHS and DoD is a profit center for Evrys research and development. Development success predicts future government contracts to de-risk manufacturing and market risk.

EV-100 for cytomegalovirus prophylaxis to manage infection in immunosuppressed transplant recipients

- Rapid path to Proof of Concept (Phase 2a)
 - CMV viral load is a validated biomarker and approvable outcome
 - EBV, HHV-6, adenovirus, ... as 2° endpoints
- Attractive U.S. market for CMV prophylaxis (NDA)
 - Rare disease, specialty pharmaceutical
 - CMV comprises ~40% of transplant viral infections
 - \$3.2 B annually to manage CMV complications and organ rejection
 - Broad-spectrum against other opportunistic viruses will drive utilization and downstream label expansion to non-CMV infections*
 - Providing high barrier to resistance and preclinically active in combination with branded antivirals losing exclusivity in 2024-2026

**Evrys clinical advisory board: C. Kotton, MGH, M. Boeckh, Fred Hutch; R. Whitley, UAB; P. Griffiths, U. London*

EV-100: A Game-Changer for CMV

Drug: <i>mechanism</i>	Pan-Viral Profile	EC ₅₀ (μM)	MAX INH at EC ₉₉	Viral Genes conferring resistance	Length of U.S. exclusivity from Orange Book
EV-100: <i>human SIRT2 inh</i>	CMV, EBV, respiratory & hepatic viruses	0.7	>100-fold	None	1 st issued patent expiry in 2038

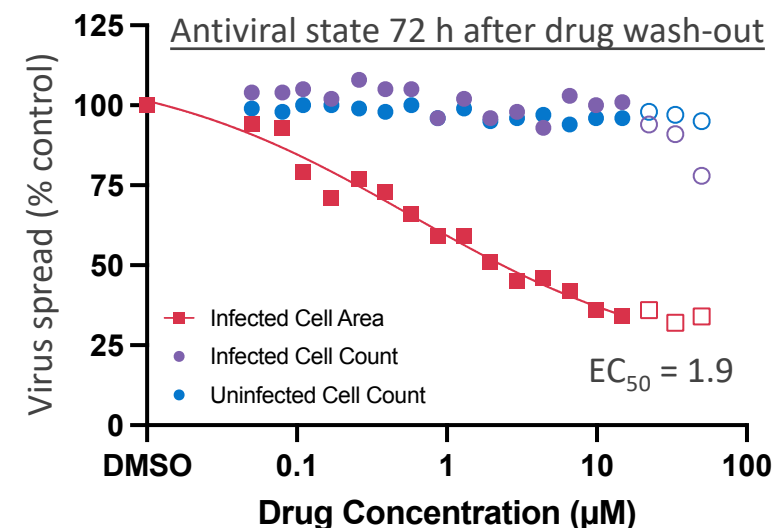
Marketed drugs:

valganciclovir: <i>nucleoside analog</i>	CMV, HSV	2.6	28-fold	UL54, UL97	generic
maribavir: <i>viral protein kinase inh</i>	CMV, EBV	0.25	24-fold	UL97	Takeda 2026
letermovir: <i>viral terminase inh</i>	CMV	0.003	4-fold	UL56	Merck 2024 (oral) 2033 (injectible)
cidofovir: <i>viral DNA pol inh</i> (tox-limited)	CMV, HSV	0.64	>100-fold	UL54	generic
foscarnet: <i>pyrophosphate mimic</i> (tox-limited)	CMV, HSV	200	n.d.	UL54	generic

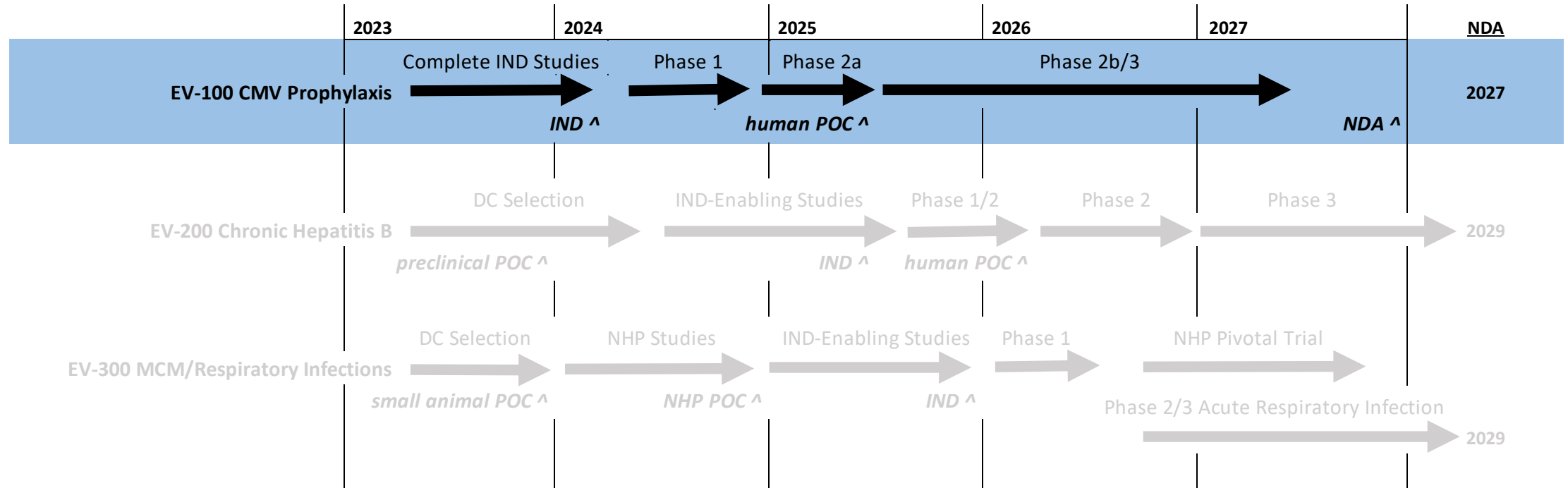
EV-100 Broad-Spectrum with Long-Lasting Pharmacodynamic Effect

Virus	Virus Family	FLS-359 EC ₅₀	EV-100 EC ₅₀	Comparator EC ₅₀	Comparator Standard of Care (SOC)
Zika	flavivirus	0.4		3.9	amodiaquine
HCoV-OC43	beta coronavirus	0.5	0.4	1.6	hydroxychloroquine
CMV	beta herpesvirus	0.6	0.7	1.4	ganciclovir (SOC)
SARS-CoV2	beta coronavirus	0.6	0.4	0.07	remdesivir (SOC)
Influenza A	orthomyxovirus	<u>1.2</u>		<u>0.71</u>	ribavirin
Influenza B	orthomyxovirus	1.2		> 25	oseltamivir (SOC)
HCoV-229E	alpha coronavirus	1.6		0.04	remdesivir
Ad5	adenovirus	1.6		3.1	cidofovir
Influenza A ^R	orthomyxovirus	2.5		9	oseltamivir (SOC)
Epstein-Barr	gamma herpesvirus	3.8		43	ganciclovir
HBV	hepadnavirus	5.2	3.2	0.03	tenofovir (SOC)
RSV	orthopneumovirus	6.7		16.1	ribavirin

Shown EC₅₀ concentration in μM providing 50% maximal antiviral effectiveness. Underlined indicates EC₉₀ reported.
CC₅₀ drug concentration across assays was $\geq 10\text{-}100\ \mu\text{M}$, the highest concentrations tested.



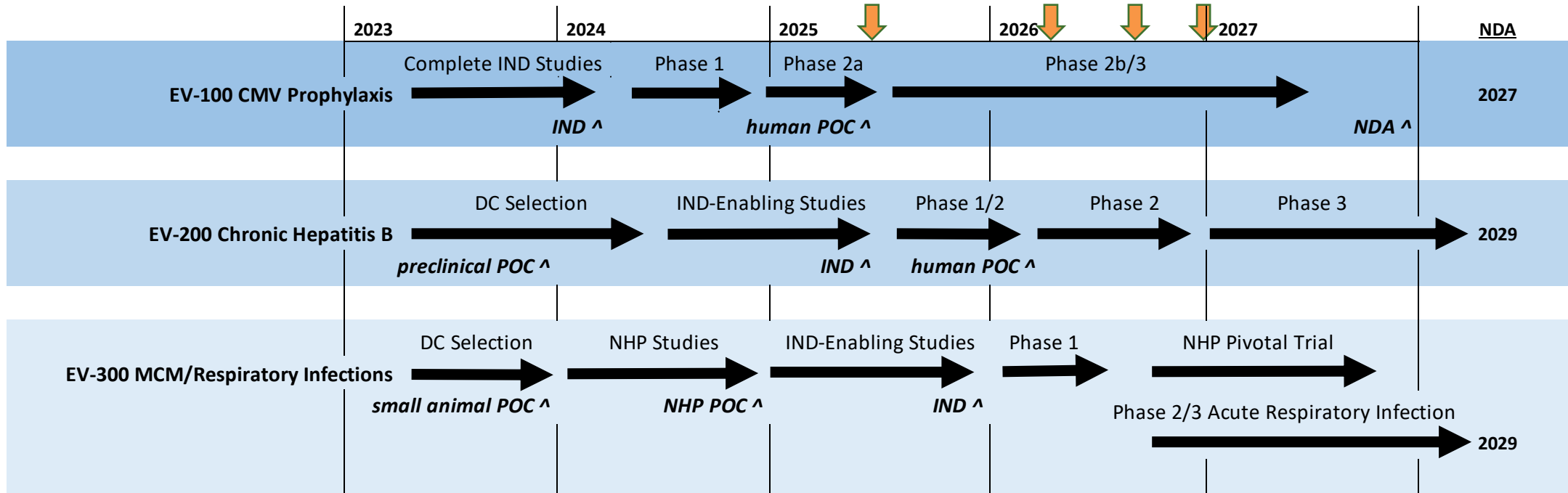
EV-100 Timeline to NDA in 2027



EV-100 Summary

- Evrys Bio has a pipeline of host-targeted antivirals addressing unmet need and EV-100 is our first clinical-stage product
- EV-100 has potential to become market leader by providing broad-spectrum antiviral effectiveness and a high barrier to virally acquired drug resistance for management of opportunistic infection in immunosuppressed transplant patients
- Seeking partner for EV-100 with pivotal trial achievable by 2027
- Revenue generating company with strong engagement of the government as a current and future stakeholder, seeking investment to scale to the clinic and exit

Investment to scale to the clinic and exit



↓ Potential Exit Triggers

- 2025: EV-100 acquisition after human POC
- 2025: EV-200 acquisition at IND
- 2026: EV-200 acquisition after human POC
- 2026: EV-300 contract development, manufacturing, and sales revenues to the government
- 2026: IPO

Evrys Bio

- Doylestown, PA since 2013
- \$12.5 M investor financing to date
 - Pharma-savvy angels: CEO, C-level execs, Ben Franklin, Mid-Atlantic Bio Angels, Keiretsu, BOHE
 - 2 Strategic Investors: ShangPharma & BioArdis
- \$50.1 M* non-dilutive financing
 - 12 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*

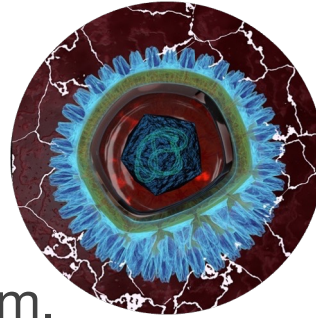




Expert Team

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

Richard Whitley
Board Director and Clinical Advisor

Infectious Disease Key Opinion Leader,
Gilead Board Director

Steve Holtzman, Board Advisor

Former CBO Biogen, CEO Infinity,
CEO Decibel Therapeutics

Debra Yu, Business Advisor

Former President Lian Bio



Stacy Remiszewski, PhD
Vice President, Research

Former Director, Roche Oncology
Chemistry.

Matthew Todd, PhD
Head of Enzyme Biology and Biophysics

Former Director, Janssen Lead Discovery.

Aaron Dubberley
Head of Intellectual Property

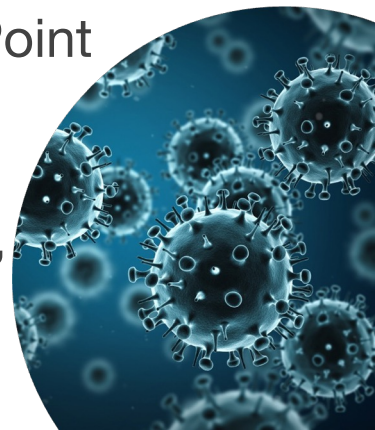
Former Mt. Sinai Asst. Director. of I.P.

John Kulp, PhD
Director, Business Development

Serial entrepreneur, CEO Conifer Point

Steven Ma, PhD, PMP
Director, Operations

Former Project Management, NRx,
CHDI Foundation, PPD, Lonza



Evrys Bio Summary

- Transformational technology, strong I.P., huge unmet need
- Inventor, Team, Advisors, and Investors with track record
- Leveraged investment with government as partner
- Tipping point of technology with first clinical-stage product
- Seeking investment to scale to the clinic and exit

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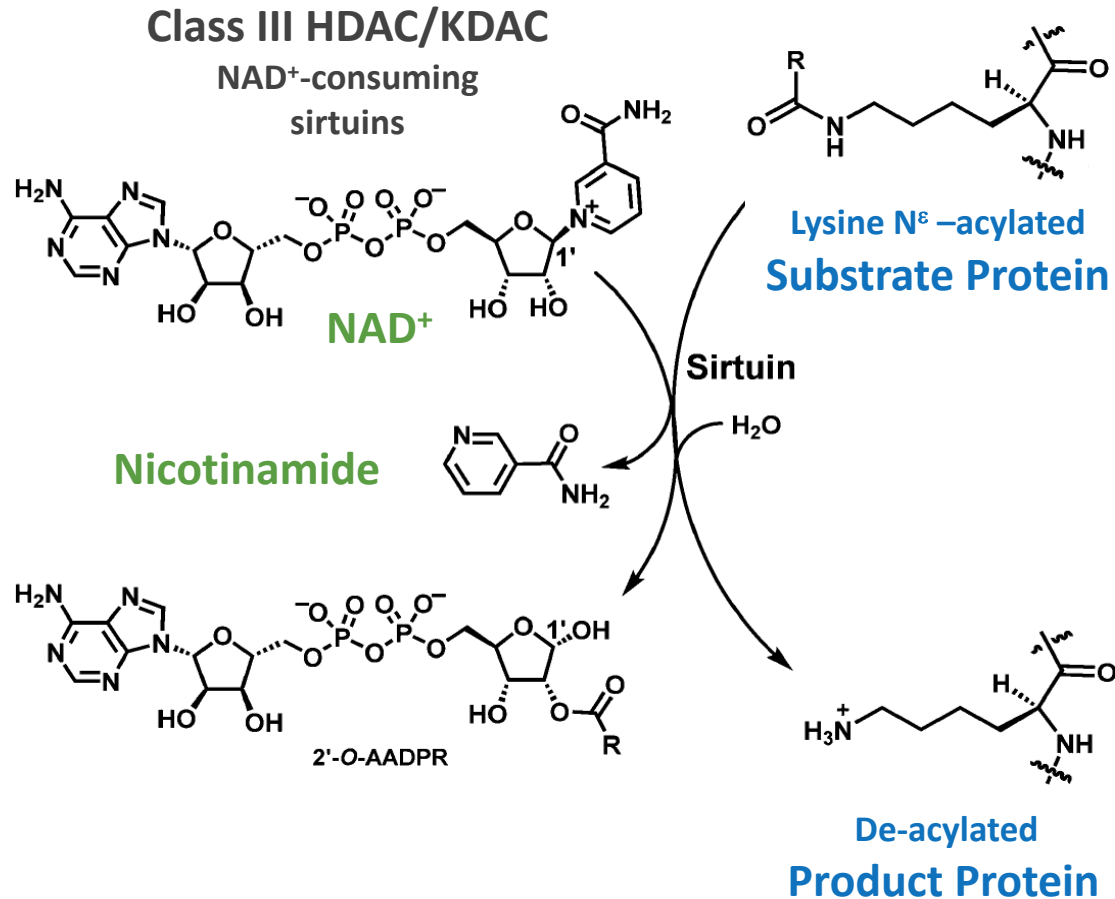
Appendix

EV-100 Target: Human Sirtuin 2 Protein

- Sirtuins are Class 3 histone de-acetylases 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 depends 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

SIRT2: NAD⁺-dependent lysine acylase



Cellular substrates of SIRT2 PTM (post-translational modification) required for productive viral infection

Epigenetics: H3K56, H3K18, H4K16, H4K20, p300, Tip60

Stress regulation: p53, FOXO1, FOXO3a, NF-κB, CDK9, NEDD4 (c-Myc), PGAM2, HIF-1a

Cell-cycle: CDH1, CDH2, BUBR1, PRSET7

Metabolism: PEPCK1, ENO1, ALDOA, GKRP, G6PD, AKT

Cellular reorganization: α-tubulin, keratin 8, Par-3, Slug



Drug Candidate EV-100 Summary

- SIRT2 selective
- Better than standard-of-care
 - Broad-spectrum activity
 - Blocks development of resistance
 - Can be combined
 - Superior virologic control
 - Prevents virus rebound
 - Long-lasting pharmacodynamics
 - Effective independent of viral load
- Oral bioavailability
- Acceptable ADME
- In vivo target engagement and efficacy
- NOAEL in mice 300 mpk daily for 7 d
- > 6-fold therapeutic window
- Chemistry suitable for manufacturing
 - 6-step synthesis
 - non-GMP batch in June

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

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

