

ACS Entrepreneurs Spotlight

Moderator Ken Polk

Panelists
Jamie Bacher
Steven Isaacman
Darcy Prather
Alon Singer



MTDIA: An Orally Available Small Molecule Transition State Inhibitor for Triple Negative Breast Cancer

(Technology originated from the laboratory of Vern Schramm
at the Albert Einstein College of Medicine)

Steve Isaacman, Ph.D.
Founder & CEO
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**Healthy Company
Funded Through 2018
With No Debt**

<i>* in thousands</i>	2013	2014
Revenue (\$)	1,053	1,566
EBITDA (\$)	160	326
% Growth	N/A	104.06%

Triple Negative Breast Cancer (TNBC)

High Rate of
Metastasis

Occurs in Young
Women (<40 years)

230,000 Breast
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10-20%
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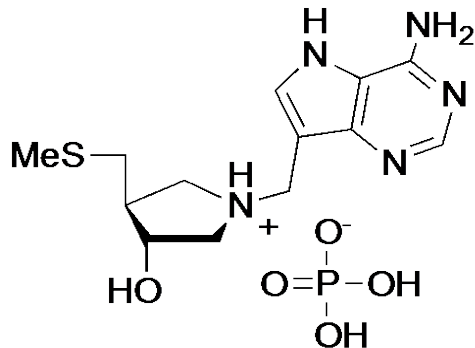
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OUR SOLUTION



MTDIA
 $K_i^* = 86 \text{ pM}$

Transition State Inhibitor
of the MTAP Enzyme

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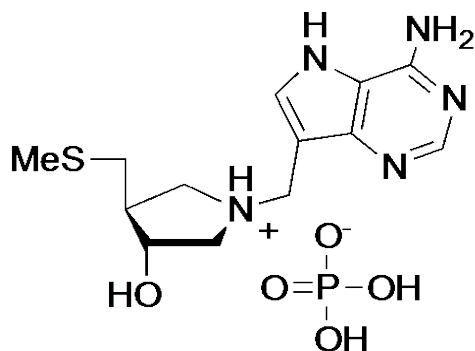
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- Non-toxic, orally available



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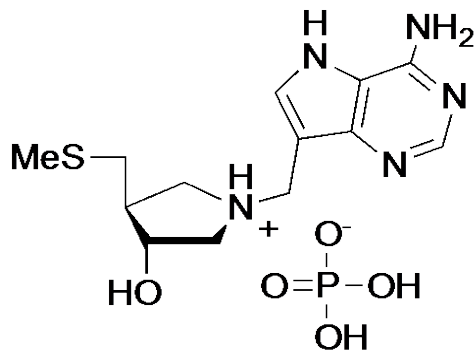
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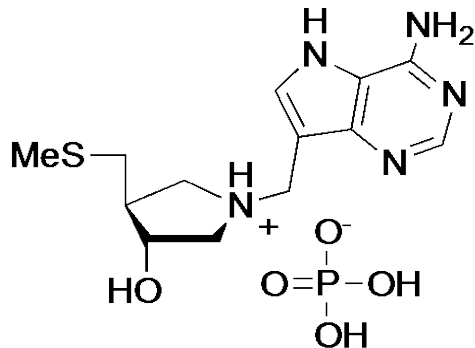
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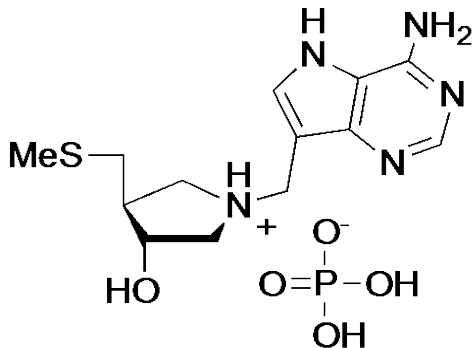
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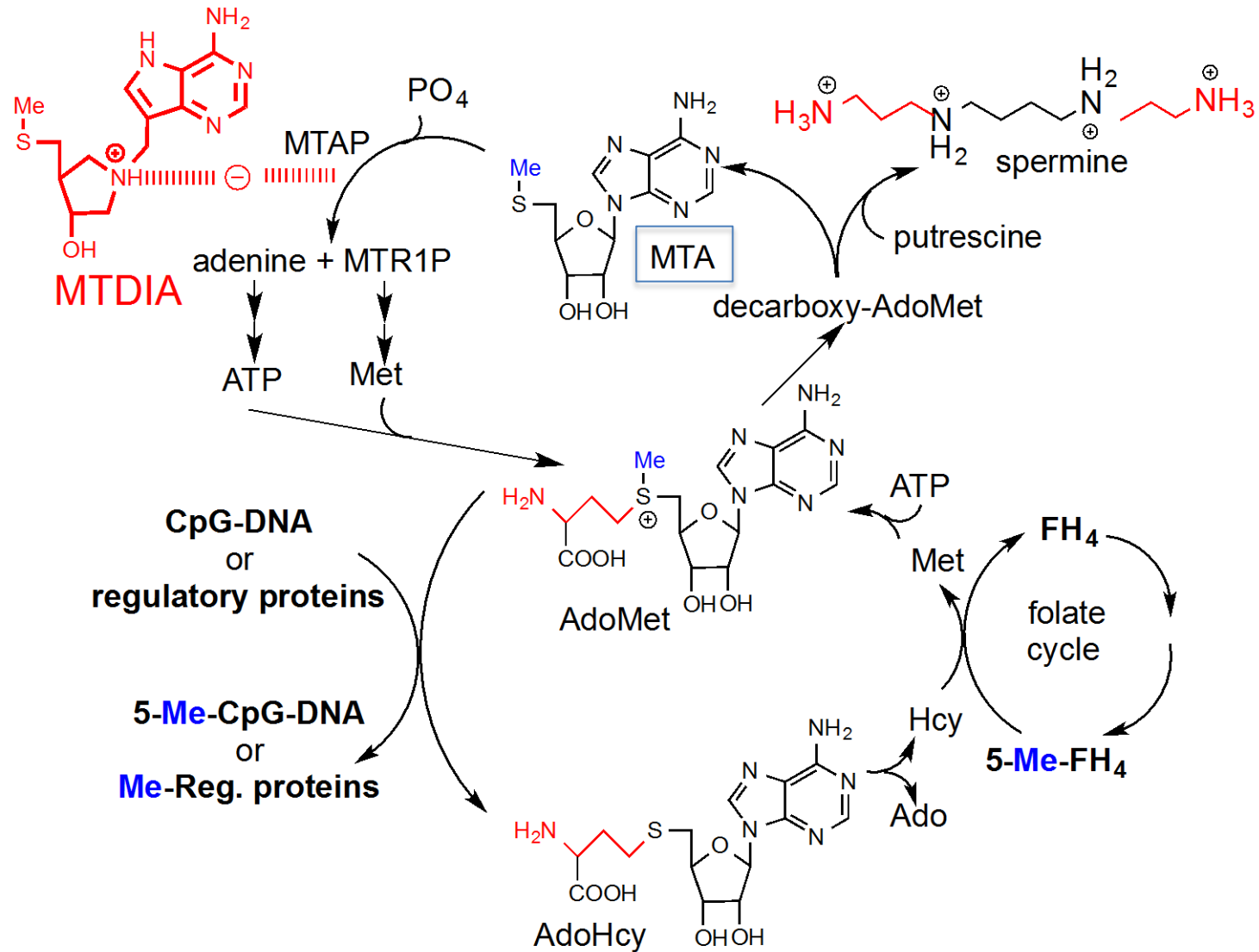
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- Expected to clear IND within 12 months

MTDIA INHIBITS MTAP AND CAUSES ANTI-CANCER EFFECTS

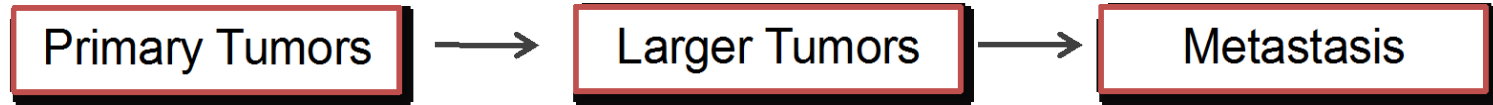


Sole function of the MTAP enzyme is to metabolize MTA

Altered gene expression (epigenetic change) is required for cancer progression

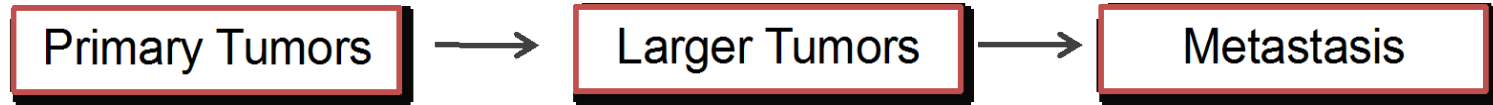


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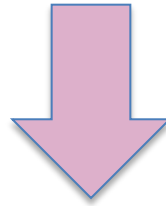


A single dose of MTDIA (5 mg/kg) systemically inhibits MTAP for > 24 h

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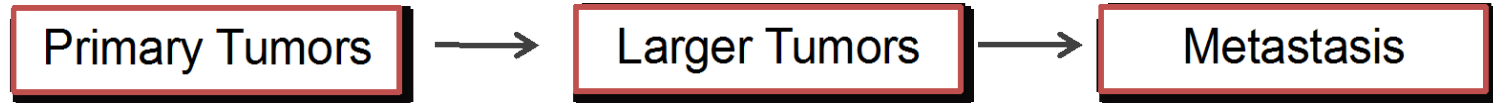


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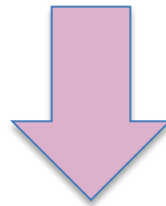


MTA accumulates in the whole-body to therapeutic levels

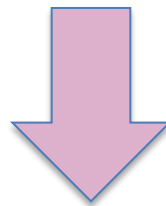
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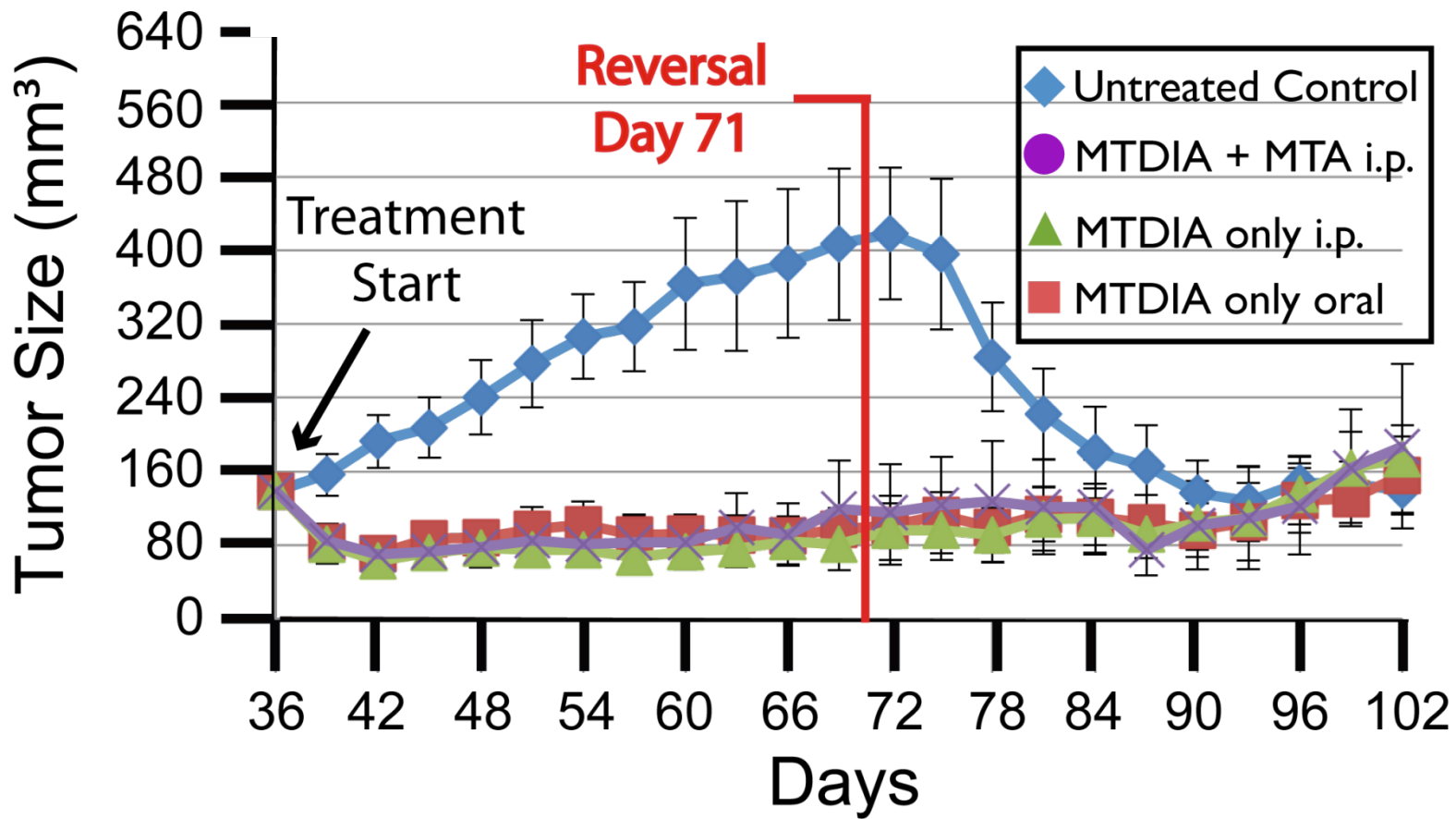


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Accumulated MTA has anti-cancer effects by disrupting metabolism, and altering epigenetic controls in tumor cells

TNBC (MDA-MB-468) XENOGRAFTS IN MICE



Days 36 - 71

Days 71 - 102

◆	Vehicle Control	MTDIA i.p. 30 mg/kg
●	MTDIA i.p. 12.6 mg/kg + MTA 25 mg/kg	Treatment Withdrawn @ day 71
▲	MTDIA i.p. 24 mg/kg	Treatment Withdrawn @ day 71
■	MTDIA oral 30.5 mg/kg	Treatment Withdrawn @ day 71

MTDIA HAS BROAD ANTI-CANCER ACTIVITY IN MICE

Cell line	Tumor Type	Mouse strains	Implant site	MTDIA (mg/kg)	
				I.P.	P.O.
MDA-MB-468	TNBC	NCr-nu	orthotopic	6	21
MDA-MB-231	TNBC	NCr-nu	orthotopic	16	30
A549	NSCLC	Rag ² / _γ C ^{-/-} , NCr-nu	Foot pad	5	9
H358	NSCLC	NCr-nu	subQ flank	10	16
FaDu	Head & Neck	NOD/SCID, NCr-nu	Foot pad	5	9, 21
HeLa	Cervical	NCr-nu	Foot pad	5	9
Colo205	Colon	NCr-nu	subQ flank	2	23
PC3	Prostate	Rag ² / _γ C ^{-/-}	Foot pad	5	9

Market Size

- \$9B global breast cancer market (9.8% growth rate)
- \$3.6B global TNBC treatment market (11.6% growth rate)
- \$1.7B metastatic TNBC treatment market (5.1% growth rate)

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Revenue Projection

Treatment Cost of \$50k / year	Year	Market Share	Breast	TNBC	Metastatic TNBC
Independent 3 rd party analysis	1	2.0%	\$470M	\$188M	\$89M
	2	7.0%	\$1.48B	\$592M	\$281M
	3	14%	\$3.13B	\$1.25B	\$592M
	4	24%	\$3.38B	\$1.35B	\$1B
	5	39%	\$8.45B	\$3.38B	\$1.6B

Cytotoxic chemotherapy

- Primary tumors respond.
- Modest activity in metastatic TNBC.
- Highly toxic with deleterious side effects.

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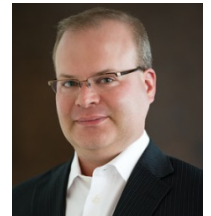
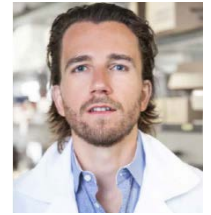
PARP Inhibitors

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MTDIA Advantages

- Broadly effective with low toxicity and novel MOA.
- Protected by an extensive patent estate through 2030.
- Broad community support and non-dilutive investments.
- Barrier to entry is financial – to accelerate development.

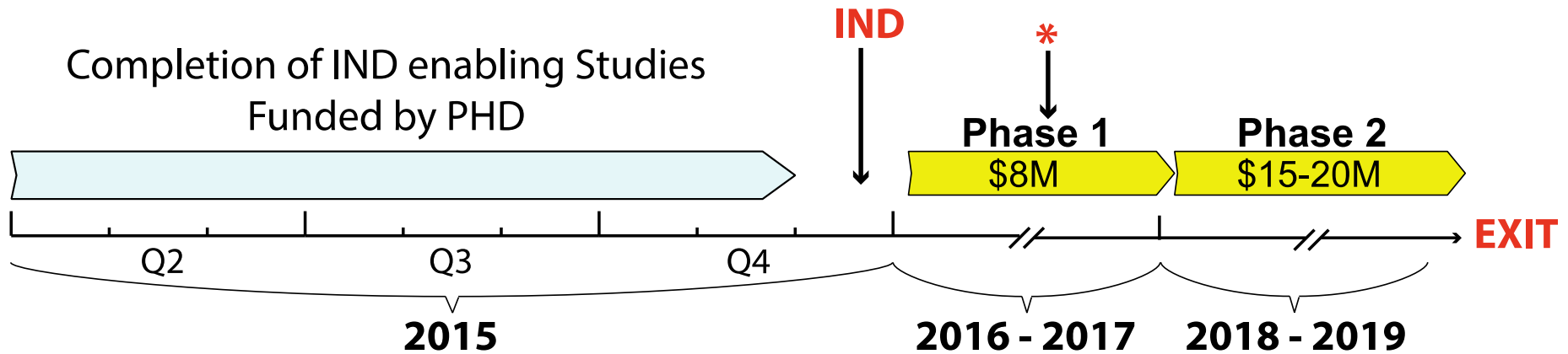
Management



- **Steven Isaacman, Ph.D., Founder & CEO**
 - PI on 10 awards.
 - Develop and commercialized several products globally.
- **Tom Cirrito, Ph.D., Corporate Development**
 - Former executive at Stemline Therapeutics.

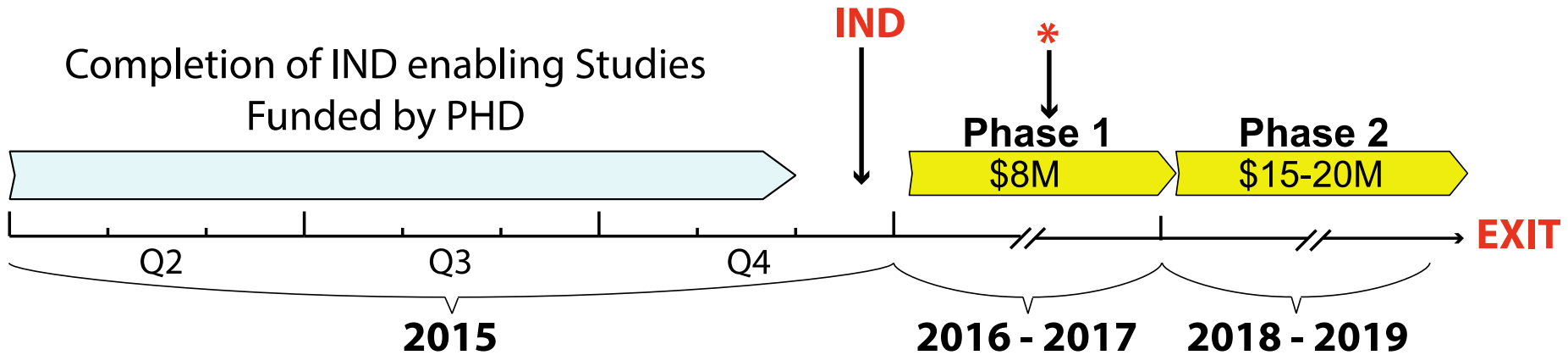
Advisory Board

- **Vern Schramm, Ph.D., Chair Biochemistry**
 - Faculty at the Albert Einstein College of Medicine.
 - Inventor of the MTDIA technology.
- **Joseph Sparano, M.D., Medical Oncologist**
 - Clinical oncologist at Montefiore University Hospital.
 - Specialist in breast cancer.
- **Alex Lyubimov, M.D., Ph.D., D.A.B.T.**
 - Pre-clinical oncology expert.
 - Successfully submitted 25 oncology INDs



Next Steps

- PHD is seeking **\$8M** to fund a Phase 1 clinical trial.
- Spin out MTDIA technology into a NewCo.
- ROI of > 20x upon completion of Phase 2 clinical studies.



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We are a unique partner

- PHD is funded through 2018, eligible for an additional \$10M through the NCI SBIR program, and will continue to contribute funds to compliment your investment.



Thanks for listening!

Steve Isaacman, Ph.D.
Founder & CEO

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KALION, INC.

KALION

ACS Entrepreneur Spotlight
Sept. 18, 2015

Darcy Prather

Everyday Products Come from Chemical Building Blocks (\$400B market size)



Major Building Blocks

Oil Based

- Ammonia
- Benzene
- C-4
- Chlor-Alkali
- Ethylene Chain
- Methanol
- Propylene
- Toluene
- Xylene

Renewable

- PLA?



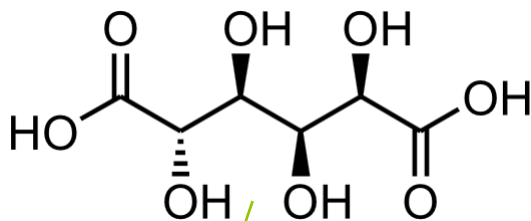
Glucaric Acid: A Renewable Platform With >\$15 Billion Addressable Markets

Super Absorbent Polymers



Detergents

Glucaric Acid



Adhesives



Nylons



Coatings



Glucaric Costs

- \$10/lb today



\$1/lb
Kalion

Our Workers – *E. coli*



Glucaric Acid Production

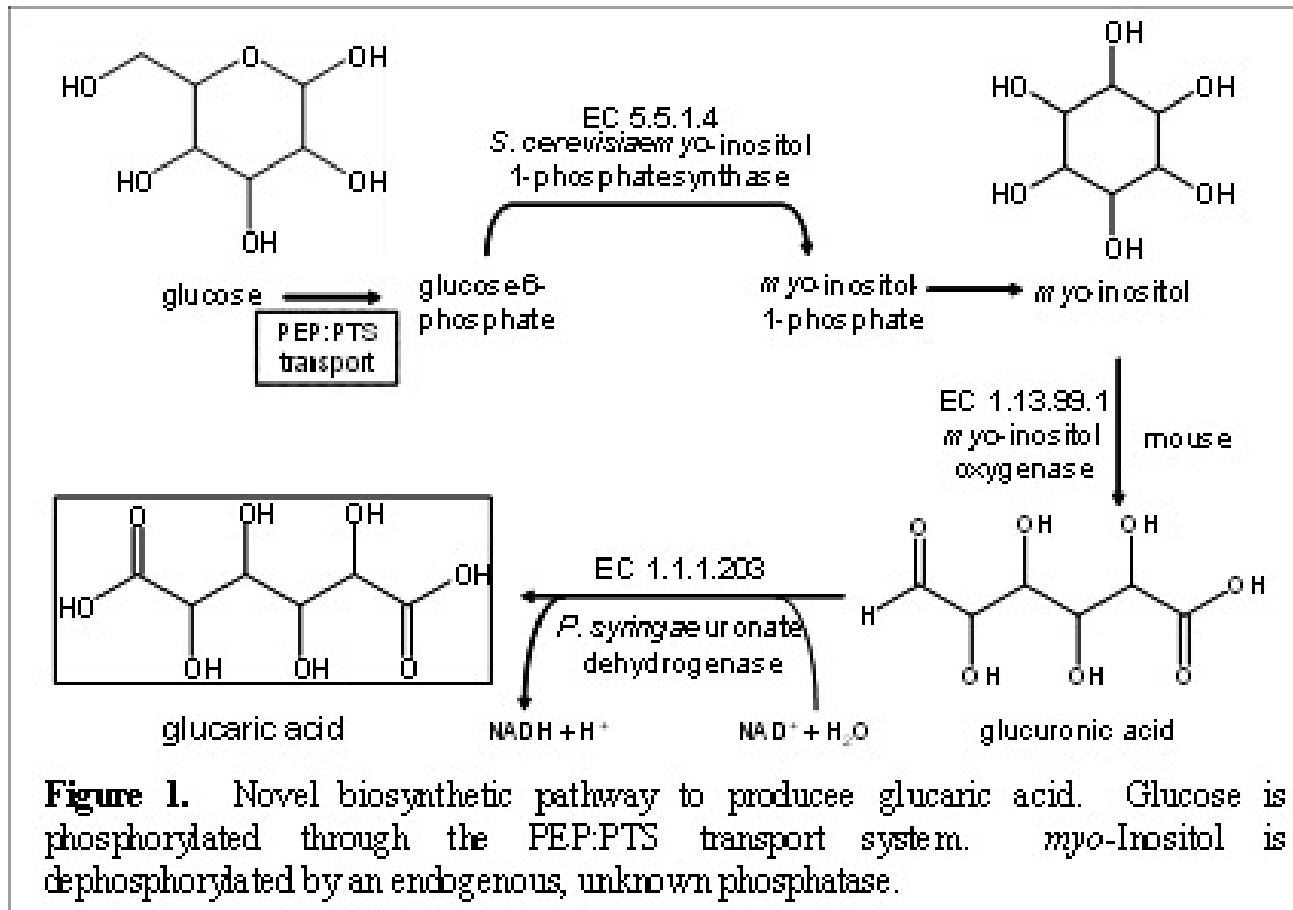


Figure 1. Novel biosynthetic pathway to produce glucaric acid. Glucose is phosphorylated through the PEP:PTS transport system. *myo*-Inositol is dephosphorylated by an endogenous, unknown phosphatase.

Glucaric Acid Competitive

- Maximum theoretical yield

$$\frac{1 \text{ mol glucaric acid}}{\text{mol glucose}} = \frac{1.17 \text{ g glucaric acid}}{\text{g glucose}}$$



Standard Yields

**12-14 Cents of Sugar per pound of
Glucaric Acid**

The Kalion Team



- **Darcy Prather**, Founder, President, CEO
 - McKinsey, Great Lakes Industrial Technology Advisory Board, Rhodes Scholar, MA Oxford, SBs MIT – EE, STS



- **Neal Connors**, Founder, CTO
 - 17 yrs Merck Bio-process R&D, past President Society for Industrial Microbiology, PhD Microbiology and Biotechnology Ohio State



- **Kristala Prather**, Founder, Key Advisor
 - Associate Professor Chemical Eng. MIT, 4 yrs Merck BioProcess R&D, Chem Eng. Ph.D Berkeley, SB MIT



- **Alan Watson**, VP Business Development
 - 25+ yrs Corporate & Startup Business Experience, SmartCells, Cubist, Elixir, GE, PhD Chemistry, MBA

SAB Members

John Gavenonis, DuPont Performance Polymers, Global Technology Manager – **Renewable / Sustainable** (RS) Materials Global Manufacturing Technology Manager – Kalrez® / Vespel® Parts (60 engineers, 8 plants) Sales/Marketing – Global Health

Stephen W. Drew, former VP of Operations at Merck, Member National Academy of Engineering, Consultant to pharma and financial companies (e.g., Kleiner Perkins Caufield & Byers, Bristol Myers Squibb)

Jay Keasling, Prof. of Chem. and Biomolecular Eng. UC Berkeley, CEO Joint BioEnergy Institute, Founder (Amyris, Codon Devices, Lygos, LS9), Member National Academy of Engineering

Charlie Cooney, Prof. of Chem. Eng. MIT; board member of Genzyme, Polypore International, LS9, BioProcessors, and Biocon; founding faculty director of the Deshpande Center and the International Innovation Initiative

Key Steps

Flasks



2005-
2010
MIT



Benchtop



2014-15
Kalion



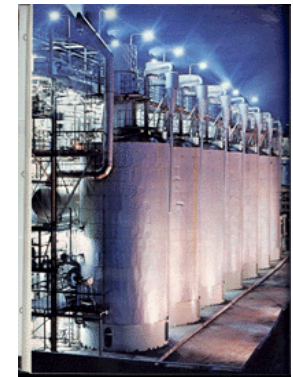
500 L Scale



2016-17
Kalion



Commercial
Fermentations



Sales 2017
Partners

Darcy Prather

President

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