JPM Healthcare Conference
January 2021
NASDAQ: **IDYA**

IDEAYA Biosciences

Improving Lives Through Transformative Precision Medicines

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Certain statements in this presentation and the accompanying oral commentary are forward-looking statements. These statements relate to future events or the future financial performance of IDEAYA Biosciences, Inc. (the “Company”) and involve known and unknown risks, uncertainties and other factors that may cause the actual results, levels of activity, performance or achievements of the Company or its industry to be materially different from those expressed or implied by any forward-looking statements. In some cases, forward-looking statements can be identified by terminology such as “may,” “will,” “could,” “would,” “should,” “expect,” “plan,” “anticipate,” “intend,” “believe,” “estimate,” “predict,” “potential” or other comparable terminology. All statements other than statements of historical fact could be deemed forward-looking, including any expectations regarding the Company’s target discovery platform or new target validation efforts as creating opportunities for research and development initiatives; any projections of financial information, market opportunities, cash runway or profitability; any statements about historical results that may suggest trends for the Company's business; any statements of the plans, strategies, and objectives of management for development programs or future operations; any statements about the timing of preclinical research, clinical development, regulatory filings, manufacturing or release of data; any statements of expectation or belief regarding future events, potential markets or market size, technology developments, or receipt of cash milestones, option exercise fees or royalties; and any statements of assumptions underlying any of the items mentioned. The Company has based these forward-looking statements on its current expectations, assumptions, estimates and projections. While the Company believes these expectations, assumptions, estimates and projections are reasonable, such forward-looking statements are only predictions and involve known and unknown risks and uncertainties, many of which are beyond the Company's control. These and other important factors may cause actual results, performance or achievements to differ materially from those expressed or implied by these forward-looking statements. The forward-looking statements in this presentation are made only as of the date hereof. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of the Company in general, see the Company's periodic filings with the Securities and Exchange Commission (the "SEC"), including its Annual Report on Form 10-K for the year ended December 31, 2019, its Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, and any current and periodic reports filed thereafter. Except as required by law, the Company assumes no obligation and does not intend to update these forward-looking statements or to conform these statements to actual results or to changes in the Company's expectations.

This presentation concerns anticipated products that are under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration (FDA). It is currently limited by Federal law to investigational use, and no representation is made as to its safety or effectiveness for the purposes for which it is being investigated.

IDEAYA Biosciences Highlights

Leading Synthetic Lethality (SL) focused biotechnology company advancing transformative precision medicine therapies for cancer patients

- **Broad potential *First-in-Class* SL Pipeline advancing to the clinic and development candidate stage**, including IDE397 (MAT2A), PARG, & Pol Theta
- **Pharma Collaborations** with Pfizer & GSK, with over ~$3 billion in potential milestones
- **Strong Balance Sheet** with ~$288M in cash anticipated to fund operations into 2024 [1]
- **NASDAQ**: IDYA

- **Target 2021 Synthetic Lethality Catalysts**
  - IDE397 IND-filed, Best-in-Class Profile
    - Present +40 MTAP-deletion PDX Study data
    - Phase 1 FPI and Clinical Pharmacodynamic Data
    - Enable Clinical Combo w/ GSK Type I PRMT
  - Select PARG Development Candidate
  - Select Pol Theta Development Candidate
  - IDEAYA SL Investor Day hosted with GSK

(1) IDEAYA Form 10Q - Q3 2020 Financials

Synthetic Lethality

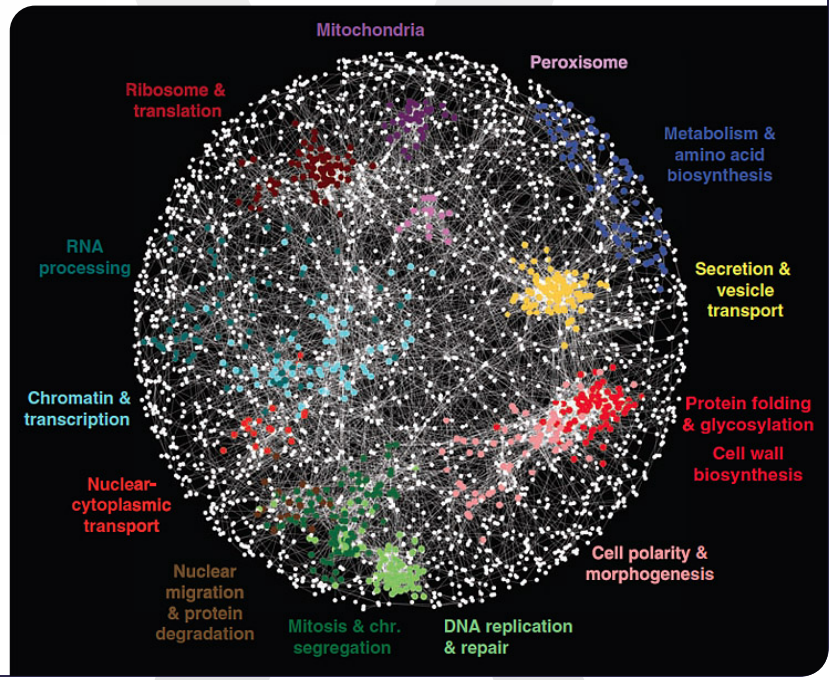
The Next Frontier in Precision Medicine Oncology

Synthetic Lethality provides a powerful approach to discover novel precision medicine therapies with patient biomarkers, including MTAP-deletion (~15% of solid tumors), BRCA/HRD (Breast, Prostate, Ovarian), and high-MSI (15% GI Cancers)

nature REVIEWS GENETICS

- **Synthetic lethality** occurs when the simultaneous perturbation of two genes results in cell death
- Synthetic lethal interactions with tumor-specific mutations (biomarker) may be exploited to develop anticancer therapies
- Large-scale screening for synthetic lethal targets has progressed through advances in molecular biology (e.g., RNA interference, CRISPR-Cas9 editing)

Nature Reviews Genetics, Vol. 18, 2017, Hieter, et al

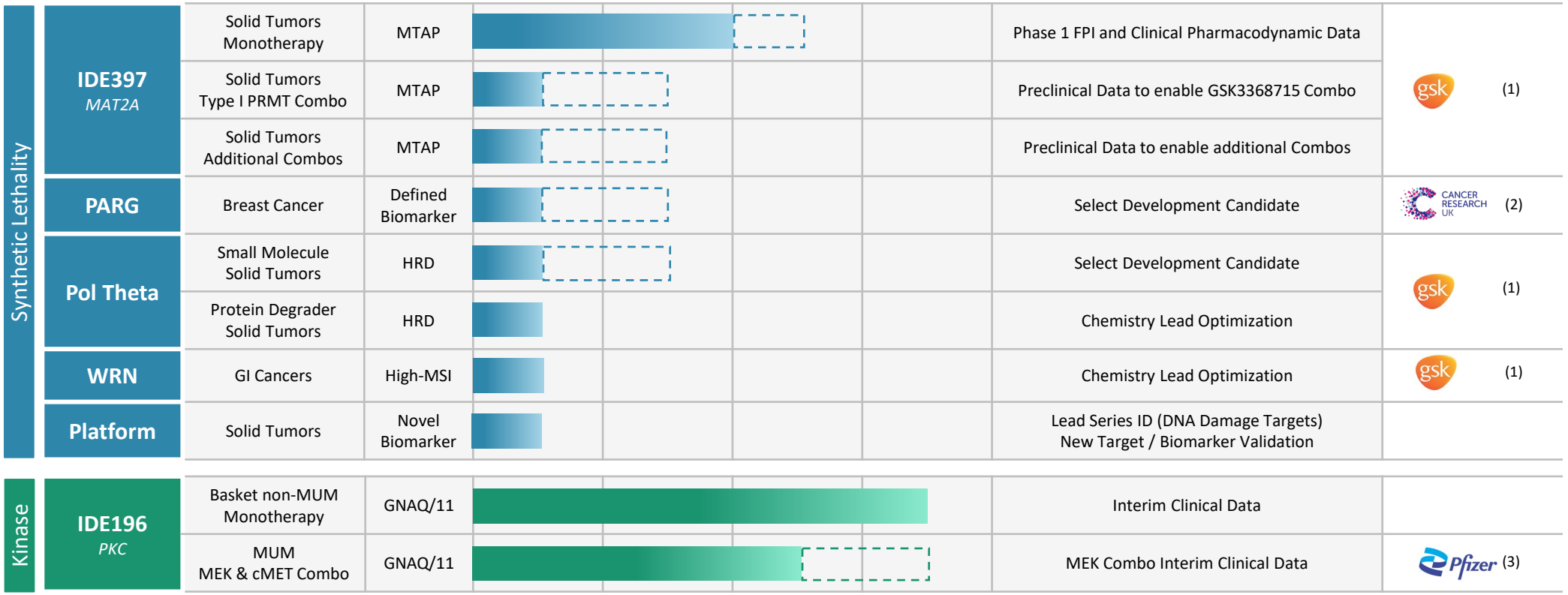


Reference: Charles Boone

IDEAYA's Precision Medicine Oncology Pipeline

Building the Industry Leading Synthetic Lethality Focused Biotechnology Company

Precision Medicine Pipeline



(1) Pursuant to GSK Collaboration, Option and License Agreement: MAT2A and WRN: 50/50 US Profits + ex-US Royalties; Polθ: Global Royalties
(2) Pursuant to CRUK Evaluation, Option and License Agreement, with ongoing Collaborative Research; IDEAYA controls all Commercial Rights
(3) Pursuant to Pfizer Clinical Trial Collaboration and Supply Agreement; IDEAYA retains all IDE196 Commercial Rights

= Target Program Milestone through 2021

DDT = DNA Damage Target, WRN = Werner Helicase, Polθ = DNA Polymerase Theta, HRD = homologous recombination deficiency, MSI = microsatellite instability
PKC = protein kinase C, MUM = metastatic uveal melanoma

IDEAYA Team and Scientific Advisory Board

Proven Team & Scientific Thought Leaders in Precision Medicine Oncology

IDEAYA Executives & R&D Leadership

Yujiro Hata, M.B.A.
President, Chief Executive Officer, Director
FLEXUS BIOSCIENCES · Bristol-Myers Squibb · ONYX PHARMACEUTICALS · ENANTA Pharmaceuticals · AMGEN

Michael Dillon, Ph.D.
SVP, Chief Scientific Officer
Head of Research
NOVARTIS · Roche

Paul Stone, J.D.
SVP, Chief Financial Officer
5AM VENTURES · ILYPSA · AMGEN

Mark Lackner, Ph.D.
SVP, Head of Biology &
Translational Sciences
Genentech · EXELIXIS

Mick O'Quigley, M.B.A.
VP, Development Operations
Genentech · AMGEN

Paul Barsanti, Ph.D.
VP, Head of Drug Discovery
5AM VENTURES · nurix · NOVARTIS · CHIRON

Jason Throne, J.D.
SVP, General Counsel
neotract · THORATEC CORPORATION

IDEAYA Scientific Advisory Board

Alan D'Andrea, M.D.
IDEAYA SAB Chair
Harvard Medical School, Professor
Director, Center of DNA Damage and Repair, Dana Farber

William Sellers, M.D.
Broad Institute, Dana Farber, and Harvard, Professor
Novartis, Former Head Oncology Research,
SL Project Drive initiative

Frank McCormick, Ph.D.
UCSF, Professor and former Director,
Helen Diller Cancer Center
Former President AACR; Founder and CSO, Onyx

Trey Ideker, Ph.D.
UCSD, Professor, Co-Director Cancer Genomes & Networks
Program, Research in Dual-CRISPR and SL interaction maps

Brian Daniels, M.D.
Bristol Myers Squibb, Former SVP Global Development
& Medical Affairs

Elizabeth Swisher, M.D.
University of Washington, Professor; Co-Leader, Breast and
Ovarian Cancer Research Program, Seattle Cancer Care Alliance
Principal Investigator on multiple PARP inhibitor trials

Jeffrey Hager, Ph.D.
Former Chief Technology Officer, IDEAYA

IDEAYA BIOSCIENCES

IDEAYA and GSK Strategic Partnership

Landmark Partnership in Synthetic Lethality

Transformative Strategic Partnership

- Validates IDEAYA Synthetic Lethality platform
- Creates 3 strategic combination opportunities
- Advancing small molecules & protein degraders

Key Partnership Terms

- $100M cash upfront
- $20M equity investment as direct private placement
- $50M option exercise fee for MAT2A
- Over $3 billion in potential Milestone Payments, including approximately $1 billion per program
- 50/50 US profit share for MAT2A and Werner Helicase
- 20% development cost share for US profit share
- Royalties high single-digit to sub-teen double digit %

MAT2A (MTAP Deletion)

- Combo with GSK3368715 (Ph1), a Type I PRMT inhibitor
- $50M Option Fee, 50/50 US Profit Share & ex-US Royalties
- ~$1B potential Milestone Payments

Werner Helicase (MSI High)

- Combo with GSK's Dostarlimab, a PD-1 IO agent
- 50/50 US Profit Share and ex-US Royalties
- ~$1B potential Milestone Payments

Pol Theta (BRCA/HRD)

- Combo with GSK's Zejula™, a commercial PARP inhibitor
- GSK covers all Costs
- Global Royalties and ~$1B potential Milestone Payments

IDEAYA Form 8-K current report filed with the U.S. Securities and Exchange Commission on June 16, 2020; GlaxoSmithKline Q2 2020 Earnings Presentation

IDEAYA Synthetic Lethality Platform

Fully-Integrated Target, Biomarker, Drug Discovery and Translational Capabilities

SL Target & Biomarker Discovery and Validation

Bioinformatics, including AI Algorithms

Dual CRISPR, CRISPR, siRNA

Genetically Engineered Models

- 1st-in-class SL targets identified, such as Werner Helicase, Pol Theta and PARG
- DECIPHER™ - Dual CRISPR SL Library in DDR in collaboration with UCSD
- PAGEO™ - Paralogous Gene Evaluation in Ovarian in collaboration with Broad Institute

Drug Discovery and Pharmacological Validation

Structure Based Drug Design

Small Molecule Chemistry

Protein Degrader Capabilities

- Crystal structures for four SL programs obtained to enable structure-based design
- Potential best-in-class molecules discovered, including IDE397
- Protein degraders advancing for selected targets, including Pol Theta

Translational Research and Opportunity Expansion

Genomics – DNA and RNA Analysis

Proteomics – Protein Expression Profiling

Tissue (IHC, IF) and Liquid Biopsies Analysis

- Translational research to define clinical biomarkers
- Opportunity expansion through broad cell panel screening
- PD biomarker analysis to confirm target modulation and correlation with clinical activity

IDEAYA Synthetic Lethality Platform

Synthetic Lethality Target and Biomarker Discovery and Validation

Synthetic Lethality Target Discovery & Validation Platform

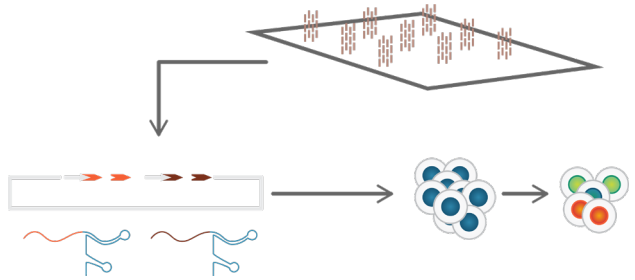
IDEAYA SL Platform integrates extensive proprietary and public data sets with orthogonal and complementary content

Bioinformatic analysis enables identification and validation of synthetic lethal target / biomarker interactions across vast datasets

Robust SL interactions validated genetically (Dual CRISPR, paralogues, isogenic pairs, CRISPR/siRNA), pharmacologically, & *in vivo*

DECIPHER™

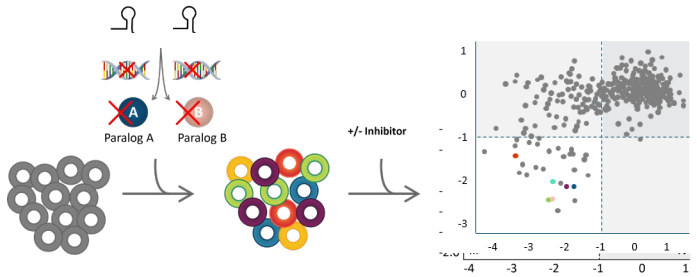
Dual CRISPR SL Library in DNA Damage Repair [2]



Evaluation of DNA Damage Targets synthetic lethal with tumor suppressor or oncogenes

PAGEO™

Paralogous Gene Evaluation in Ovarian Cancer [1]



Evaluation of SL targets in context of functionally redundant paralogous genes in ovarian cancer

Partnership Datasets

Cancer Dependency Map – Broad Institute

Foundation Insights™ – Foundation Medicine

depmap portal FOUNDATIONINSIGHTS™

Public Databases

IDEAYA data mining and analysis across data sets

PROJECTGENIE TCGA MSK-IMPACT™ Project Achilles BioPortal CCLE

[1, 2] IDEAYA Proprietary Libraries and Datasets – Strategic Collaborations with Broad Institute[1] and UC San Diego[2]

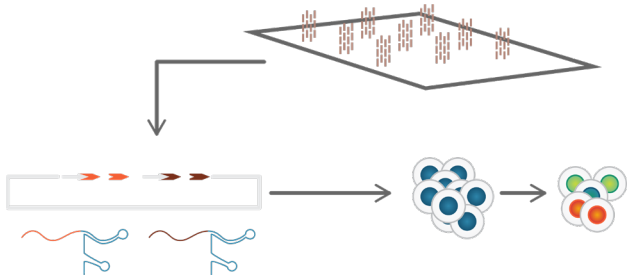
IDEAYA Synthetic Lethality Platform

Synthetic Lethality Target and Biomarker Discovery and Validation

DECIPHER™ Dual CRISPR Proprietary Synthetic Lethality Library

DECIPHER™

Dual CRISPR SL Library in DNA Damage Repair [1]



Evaluation of DNA Damage Targets synthetic lethal with tumor suppressor or oncogenes

DECIPHER™ DDR Library 1.0

~225 Non-Overlapped Genes

~12,000 Gene Pairs per Cell Line
67 TSG/OG's and 176 DDR Targets

Curated Breast / Lung Cell Lines

DECIPHER™ Genes

>20 Novel Drug Targets Identified

Target Validation Ongoing

[1] Developed in Collaboration with UCSD, Principal Investigator – Dr. Trey Ideker

IDEAYA is Advancing the Next Generation of Potential *First-in-Class* Synthetic Lethality Programs

IDEAYA Synthetic Lethality Pipeline

IDE397 (MAT2A/MTAP) Lead SL Program IND Filed

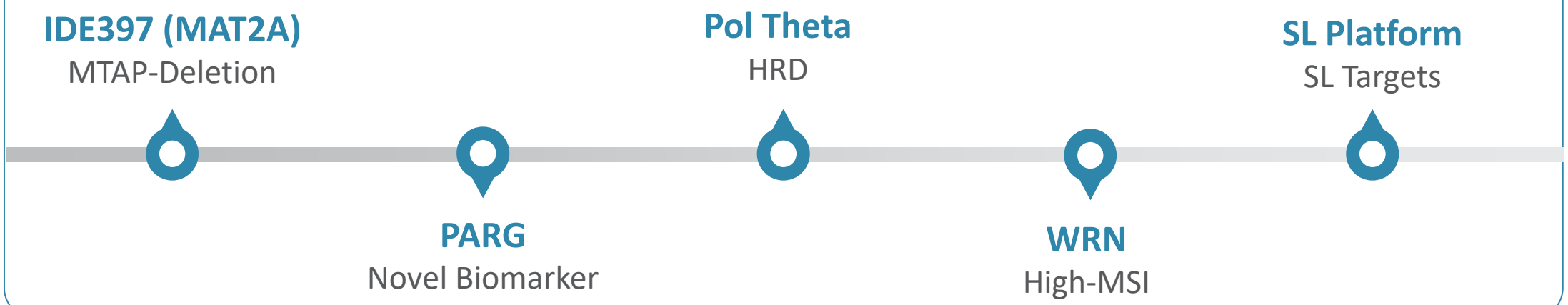
Potential First-in-Class Monotherapy and First-in-Class / Best-in-Class Combination Therapies (Type I PRMT, Taxanes)

Targeting PARG and Pol Theta Development Candidates in 2021

PARG monotherapy efficacy in multiple tumor types; Pol Theta + PARPi combination regressions in BRCA2-/- xenograft

IDEAYA Synthetic Lethality Investor Day 2021

IDEAYA to host with GlaxoSmithKline

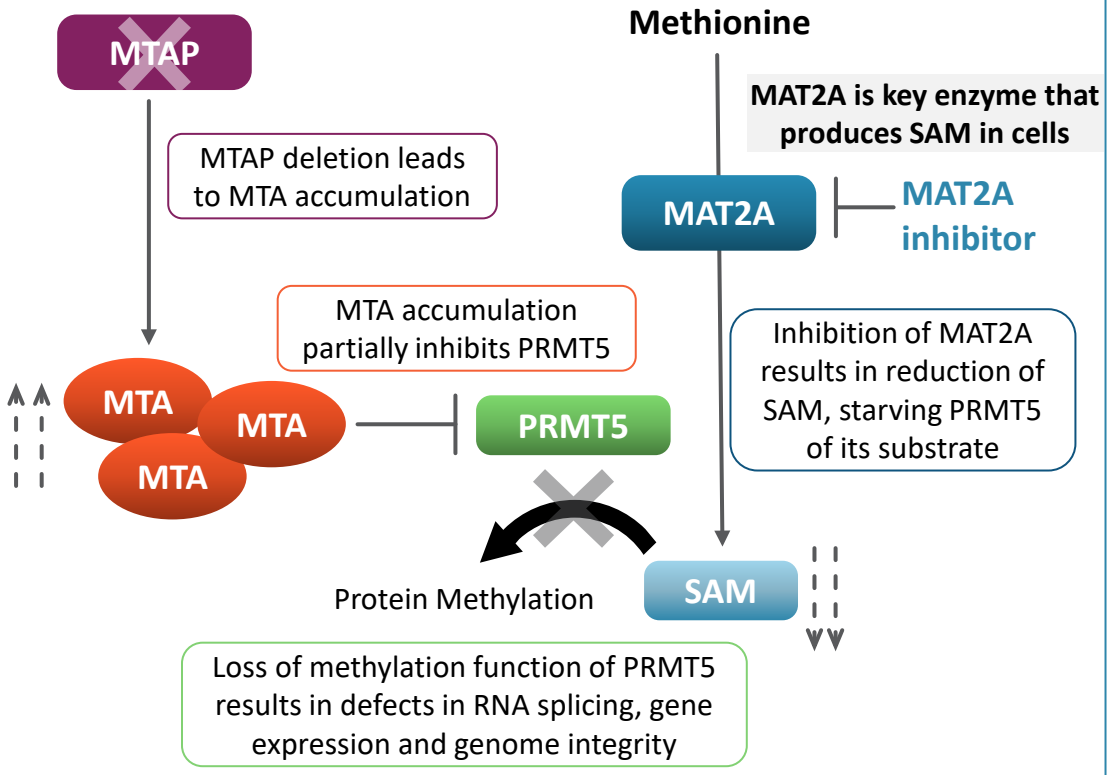


HRD = Homologous Recombination Deficiency, MSI = Microsatellite Instability

MAT2A Inhibition is Synthetic Lethal with MTAP Deletion

MTAP Deletion Prevalence ~15% of all Solid Tumors

MTAP-MAT2A Synthetic Lethality Biology



MTAP Deletion Prevalence

Cancer Type	N	MTAP Deletions (%)
Glioblastoma	592	41
Mesothelioma	87	32
Esophageal	95	28
Bladder	411	26
Pancreatic	184	22
Melanoma	448	16
Lung Cancer (NSCLC)	1053	15
Head and Neck	523	14
Sarcoma	255	10
Esophagogastric	514	10
Diffuse Glioma	513	9
Breast	1084	3
Ovarian	585	3
Adrenocortical	92	3
Thymic	123	3
Hepatocellular	369	3
Renal non-clear cell	348	2

Data from The Cancer Genome Atlas in cBioPortal

IDE397: MAT2A Development Candidate

Clinical Evaluation of IDE397 – Differentiated Profile and Selective for MTAP-/- Cell Lines

IDE397 Target Product Profile

IDE397 demonstrates *in vivo* efficacy and PD modulation at 5 to 30mg/kg

- AG270 published preclinical dose typically 200mg/kg [1]

IDE397 has not caused preclinical liver injury or increased bilirubin

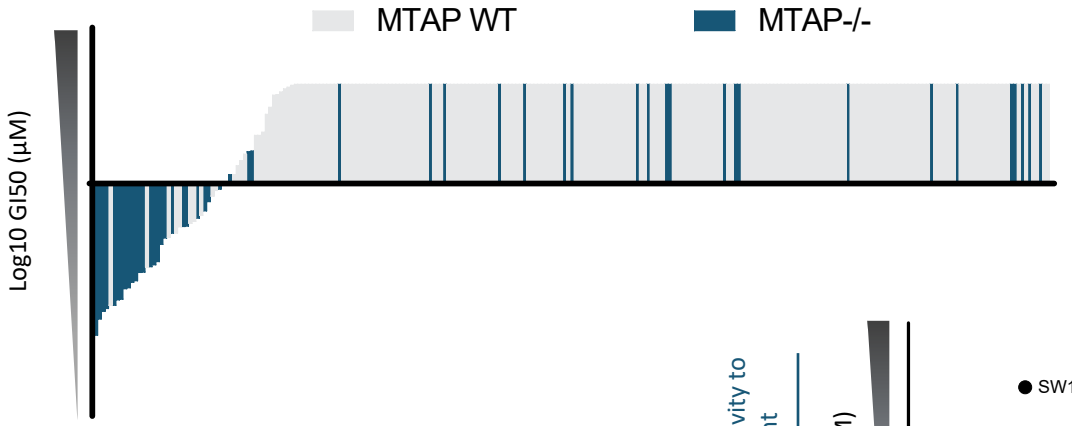
- Liver injury not observed in tox studies
- Not an inhibitor of UGT1A1 (AG270 noted to inhibit UGT1A1) [1]

IDE397 has favorable physical properties, including solubility

- AG-270 observed non-linear exposure >200mg QD (GI absorption)

(1) Agios, AACR 2019, Keystone 2019, Triple Meeting 2019 (Webcast Call Q&A)

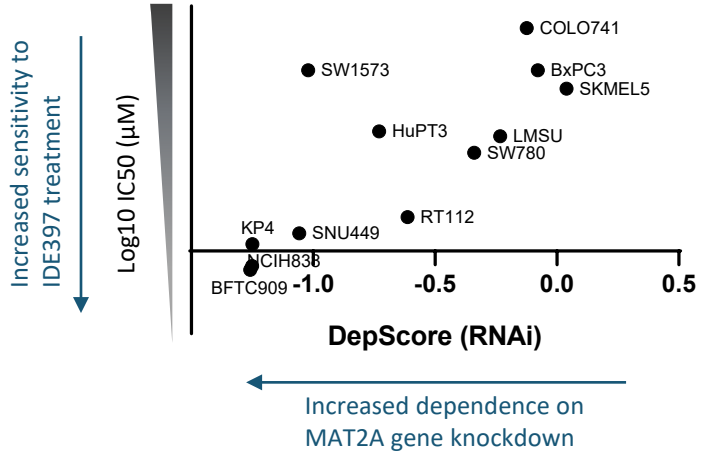
IDE397 is Selective for MTAP-/- Cell Lines



MTAP-/- cell lines are sensitive to IDE397

MTAP WT cell lines are insensitive

Pharmacological inhibition correlates with MAT2A genetic knockdown

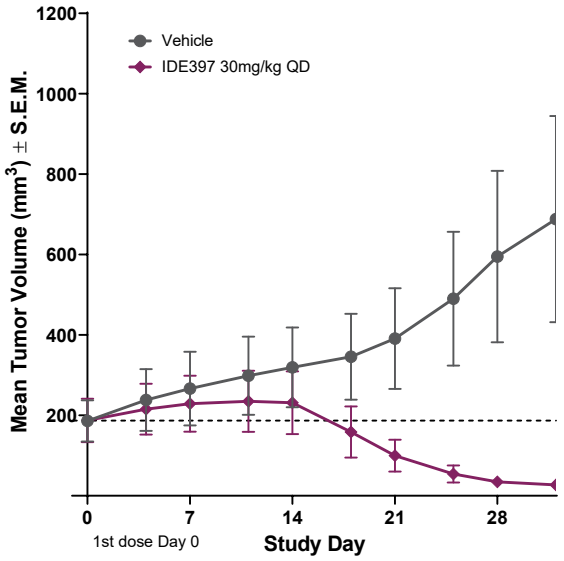


IDEAYA Data

IDE397 PDX Study of >40 MTAP-/- Models in Multiple Indications

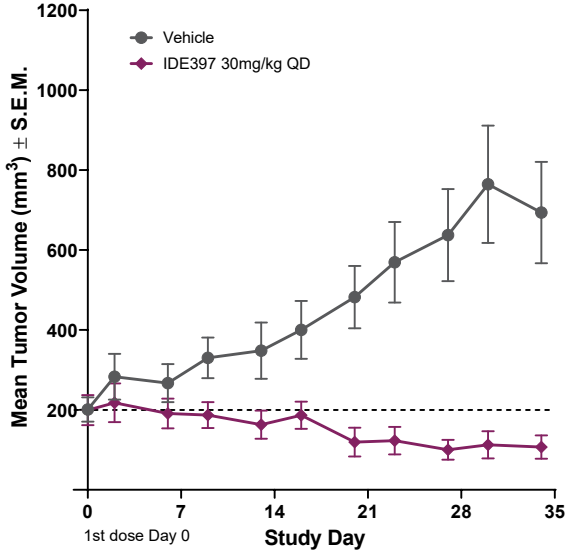
Monotherapy Tumor Regressions & Significant TGI Across Multiple Solid Tumor Types [1]

Bladder PDX Model



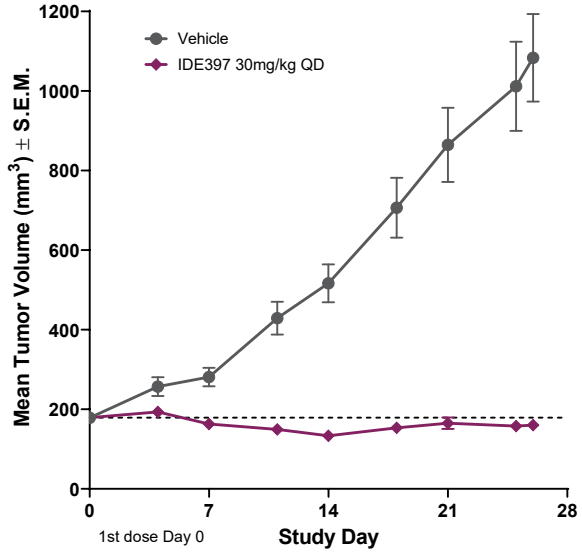
IDEAYA Data

Gastric PDX Model



IDEAYA Data

Esophageal PDX Model



IDEAYA Data

IDE397 evaluation in Patient Derived Xenograft (PDX) models with homozygous MTAP deletions in Solid Tumors

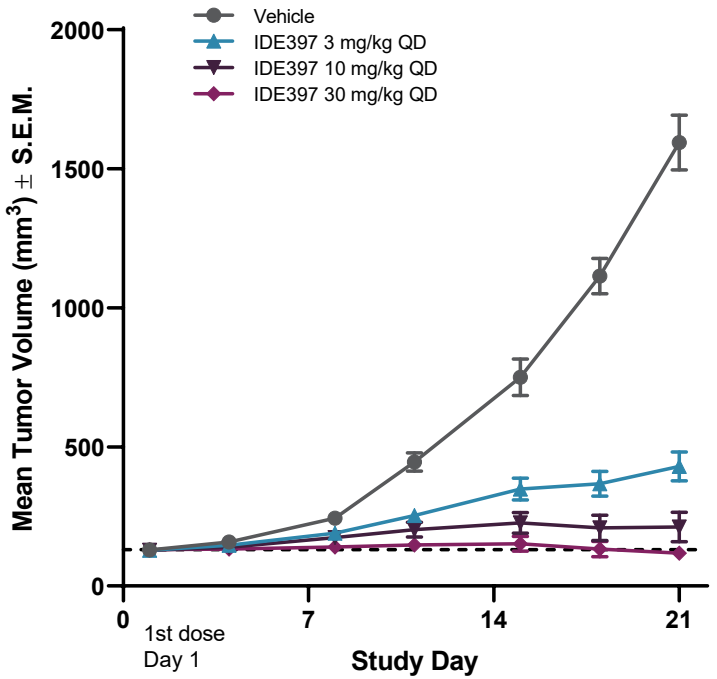
- Tumor Regressions (≥ 100% TGI) observed in multiple PDX models and across multiple indications
- ≥ 75% Tumor Growth Inhibition (TGI) observed in ~ 50% of models and across major solid tumor types

(1) IDEAYA PDX Study data targeted to be presented in peer-reviewed setting in 2021

IDE397 Monotherapy Demonstrates Tumor Regressions in NSCLC

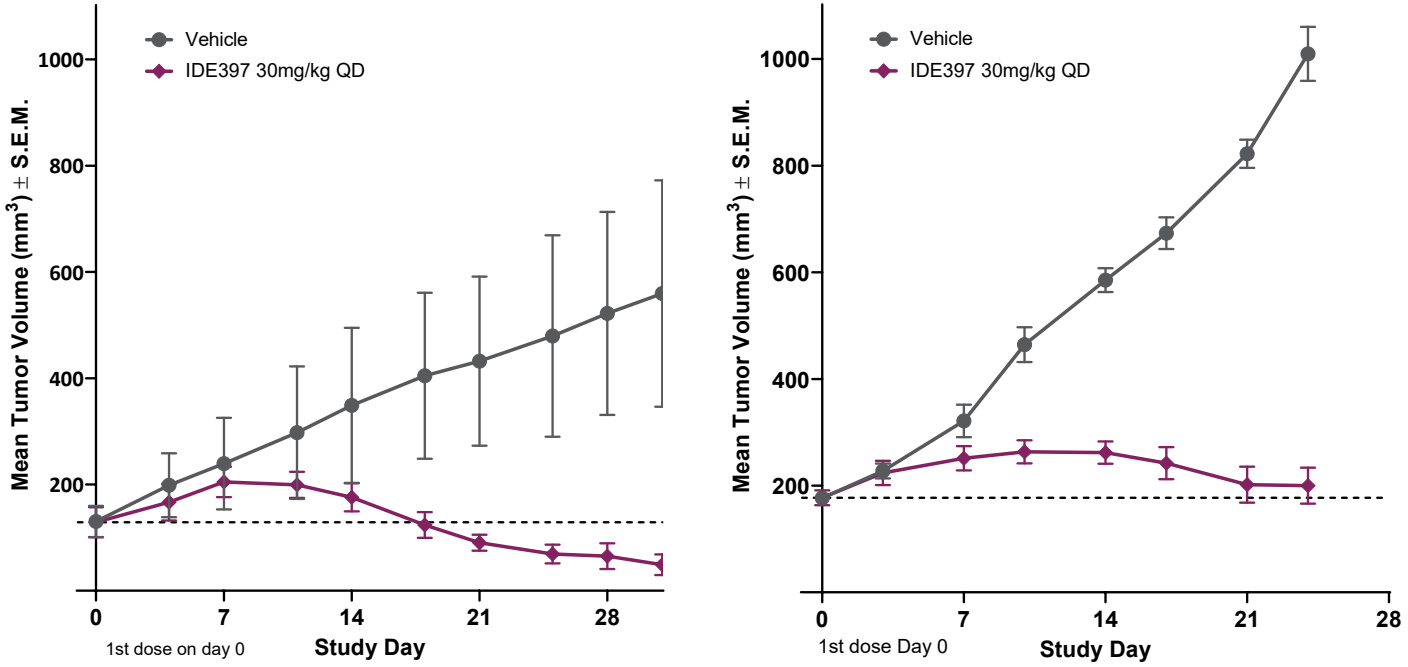
Tumor stasis to regressions in endogenous MTAP-/- CDX and PDX NSCLC Models [1]

NSCLC Endogenous MTAP-/- CDX Model



IDEAYA Data

NSCLC MTAP-/- PDX Models



IDEAYA Data

Robust dose dependent PD modulation observed in NSCLC CDX Model

(1) IDEAYA PDX Study data targeted to be presented in peer-reviewed setting in 2021

IDE397 + Type I PRMT (GSK3368715) Combination Rationale

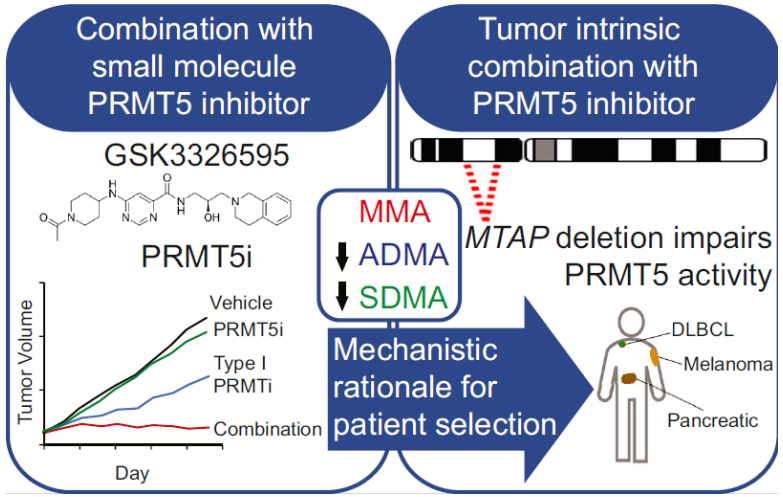
IDEAYA / GSK Partnership Enables Compelling Clinical Combo to Pursue MTAP-/- Tumors

IDE397 + Type I PRMT Combination Rationale

Cancer Cell

Anti-tumor Activity of the Type I PRMT Inhibitor, GSK3368715, Synergizes with PRMT5 Inhibition through MTAP Loss

GSK Publication



Dual ADMA plus SDMA reduction enhances preclinical anti-tumor activity in MTAP-deletion *in vivo* models

- Type I PRMT inhibitor GSK3368715 reduces ADMA levels
- MAT2A or PRMT5 inhibition reduces SDMA levels, as Type II PRMT inhibitors
- MAT2Ai has potential for higher Therapeutic Index vs. PRMT5i in MTAP-deleted tumors through MAT2A/MTAP Synthetic Lethality

Mohammad et al., GSK, Cancer Cell July 2019

IDEAYA & GSK Collaboration Activities

IDE397 + GSK3368715 preclinical combination efficacy & tolerability studies

- Preliminary data supports ADMA and SDMA hypothesis for Type I and Type II combination
- Targeting IDE397 plus GSK3368715 clinical combination initiation following demonstration of clinical PD modulation for IDE397

IDEAYA and GSK collaboration enables potential industry leading clinical combination to pursue MTAP-deletion

IDEAYA / GSK collaboration provides mutual exclusivity on MAT2A target

IDE397 Monotherapy in MTAP-Deletion: Phase 1 Clinical Trial Execution

Patient Selection, Trial Design and Pharmacodynamic (PD) Biomarkers

IDE397 Biomarker Driven Phase 1 Clinical Plan

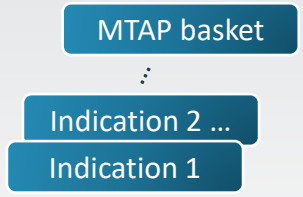
Diagnostic Biomarkers

Patient Selection

MTAP Gene Deletion and Protein Level Confirmation

- MTAP Deletion detected by commercial and institutional NGS screening panels
- MTAP IHC assay developed and validated across multiple tumor types in collaboration with Roche Ventana

Dose Escalation



Cohort Expansion

Monotherapy Tumor Type Selections Clinical Combinations

- IDE397 PDX study in +40 MTAP-deletion models to inform tumor type selection
- Evaluate clinical combinations, including GSK3368715 (Type I PRMTi) and Taxanes

Pharmacodynamic Biomarkers

Clinical PD / Target Engagement

Targeting Clinical PD Data in 2021

- SAM Assay commercially available for peripheral & tumor SAM detection by LC/MS
- SDMA Assay being established for tumor SDMA detection by ELISA/IHC

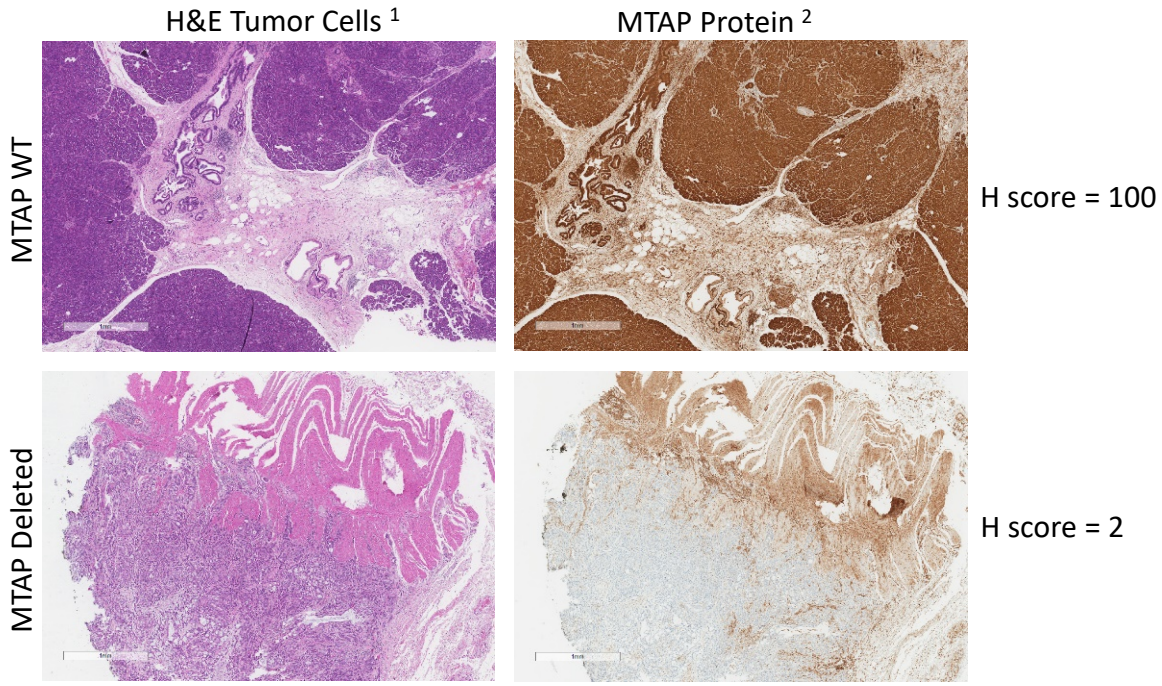
MTAP-Deletion Represents ~15% of all Solid Tumors

~75,000 Patients per Year in US, EU5, and Japan

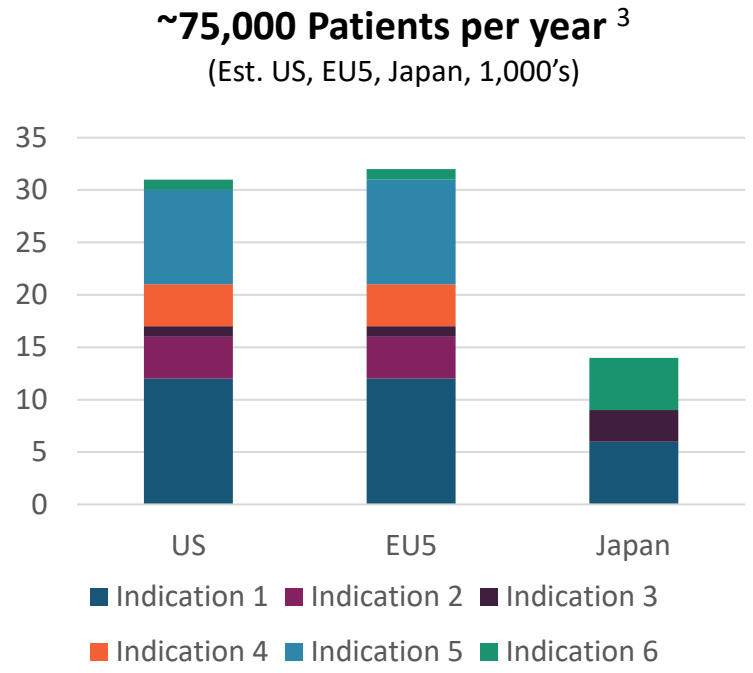
Patient Selection: Based on NGS and/or IHC to identify patients with MTAP-deletion

Patient Population: ~75,000 patients per year in US, EU5 and Japan

MTAP IHC Assay Developed with Roche Ventana



Addressable MTAP-Deletion Patient Population



(1) H&E stain identifies various types of cells represented by deep purple color in tumor biopsies
(2) MTAP stain identifies MTAP protein levels with semi-quantitative scoring (e.g., 100 = high, 1 = low)
(3) IDEAYA Analysis

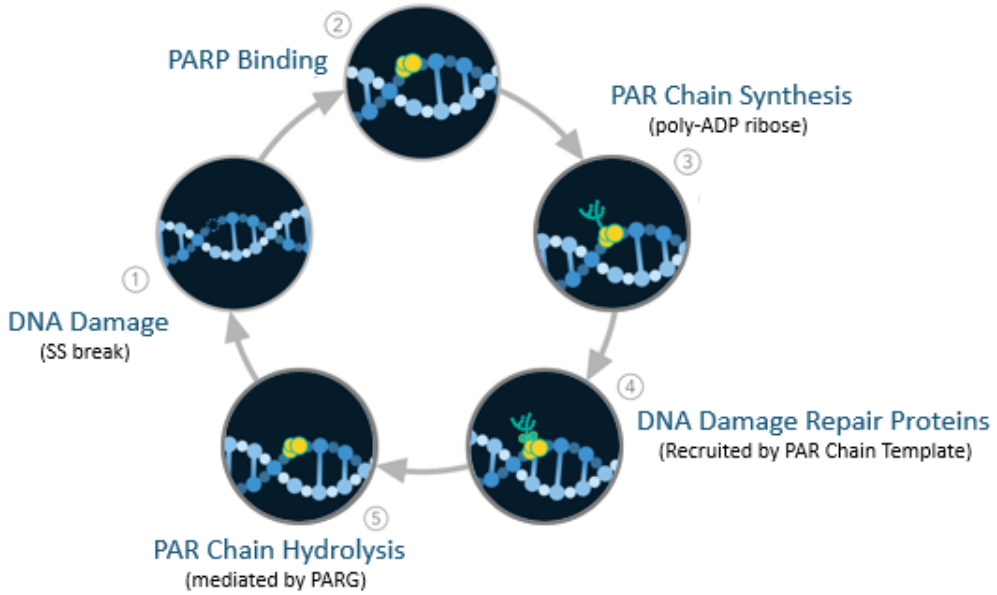
PARG Synthetic Lethality Program

Targeting Development Candidate in 2021

PARG Biology

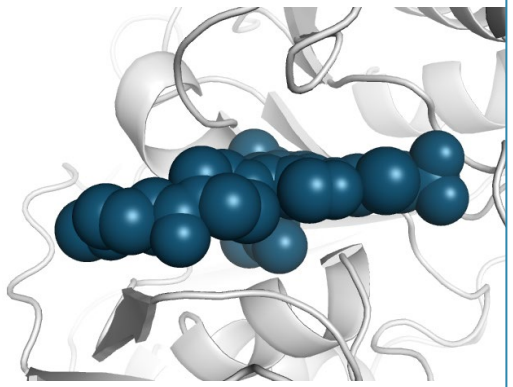
Novel target in Clinically Validated Pathway

Poly(ADP-ribose) glycohydrolase (PARG) regulates DNA repair by hydrolyzing PAR chains in final step of DDR cycle



PARG Drug Discovery Program

First in class lead optimization program guided by structure-based drug design



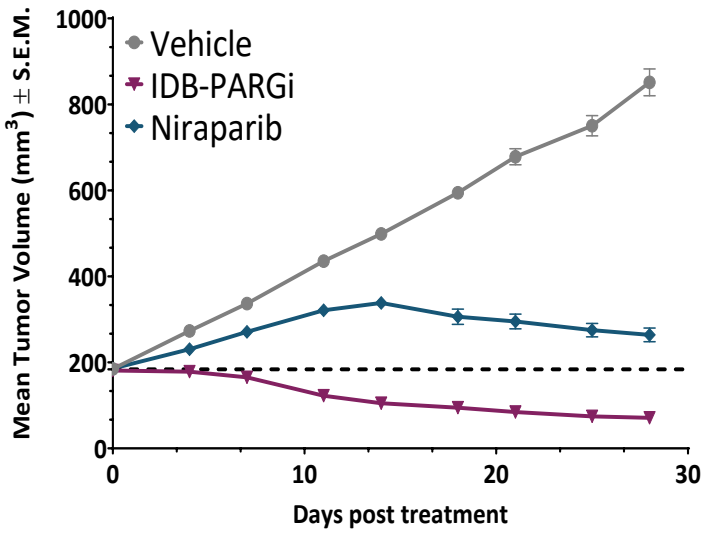
- Multiple potent cellularly active compounds demonstrate *in vitro* and *in vivo* PAR accumulation (PD) and *in vivo* efficacy in defined biomarker setting
- Collaboration with Bill Sellers lab (Broad) established to identify additional genetic sensitizers to PARGi

IDEAYA Data

IDB-PARGi Demonstrates Tumor Regressions in Defined Biomarker Setting

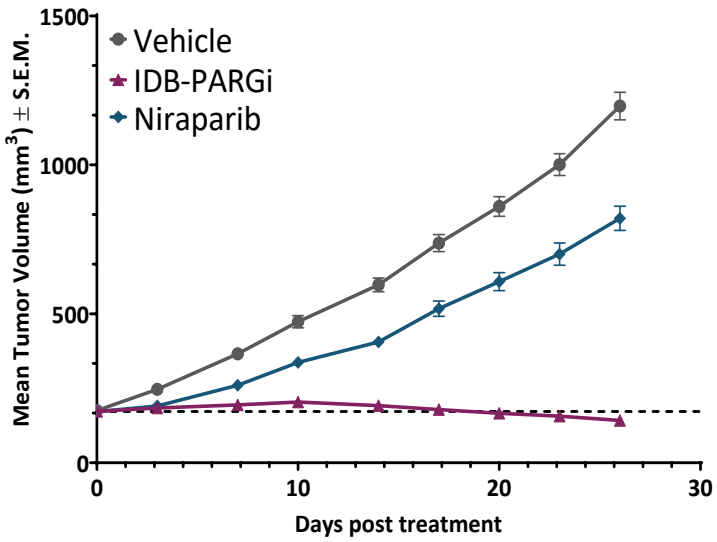
Monotherapy Regressions in Multiple Indications with enhanced activity vs. PARP Inhibitor

Tumor Type 1 CDX Model



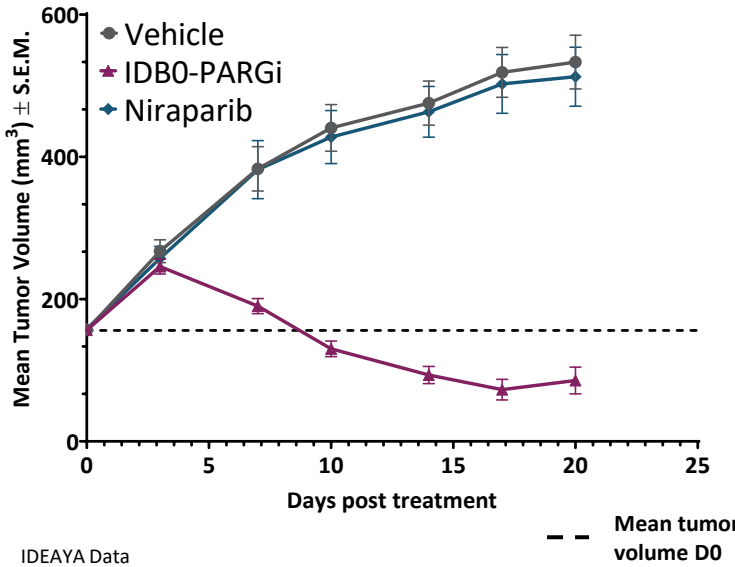
IDEAYA Data

Tumor Type 2 CDX Model



IDEAYA Data

Tumor Type 3 CDX Model



IDEAYA Data

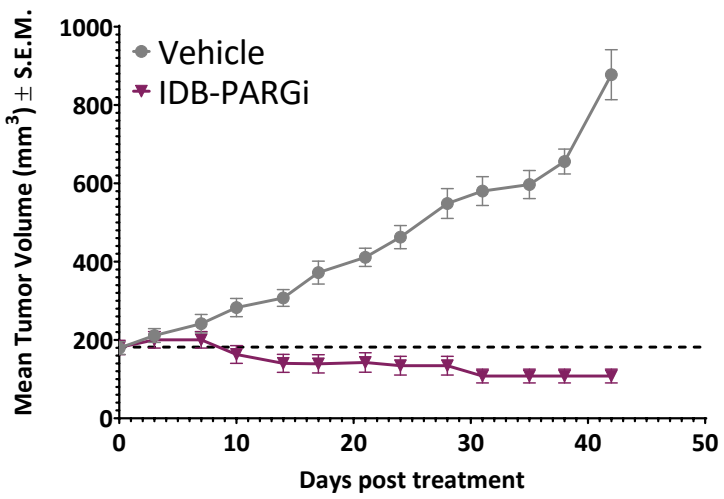
Evaluation of IDB-PARGi in Cell-line Derived Xenograft (CDX) Models across Multiple Indications

- Tumor regressions and enhanced Tumor Growth Inhibition (TGI) relative to Niraparib (PARPi) observed
- *In vivo* efficacy observed in PARPi resistant CDX Models

PARG Breast Cancer PDX Study in Defined Biomarker Setting

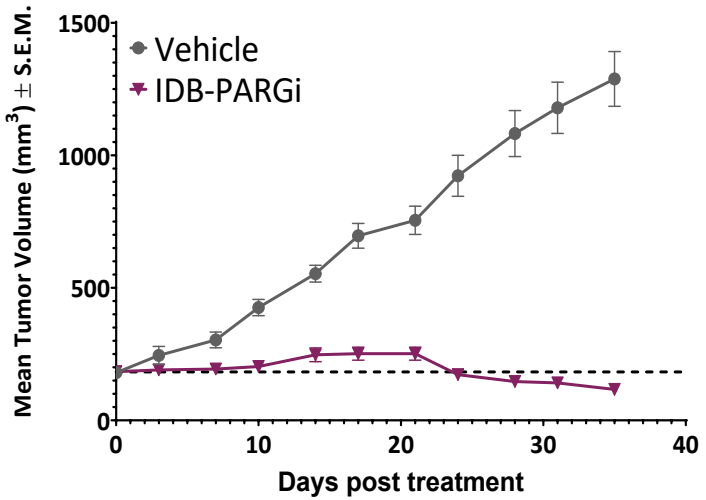
Monotherapy Tumor Regressions observed in Multiple PDX Models

Breast Cancer PDX Model



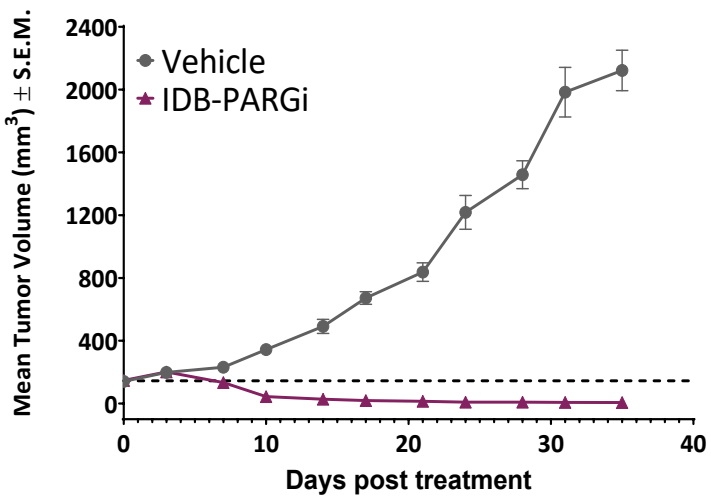
IDEAYA Data

Breast Cancer PDX Model



IDEAYA Data

Breast Cancer PDX Model



IDEAYA Data

Mean tumor volume D0

Evaluation of IDB-PARG in Patient Derived Xenograft (PDX) Models in Breast Cancer

- Tumor Regressions (≥ 100% TGI) observed in multiple PDX models with defined genetic and subtyping profiles
- Enhanced Tumor Growth Inhibition (TGI) relative to Niraparib (PARPi) observed in some models

(1) PDX Study data targeted to be presented in a peer-reviewed setting in 2021

Pol Theta Synthetic Lethality Program

Targeting Development Candidate in 2021

Pol Theta Synthetic Lethality with BRCA/HRD

DNA polymerase theta (Pol Theta) promotes DNA repair by Microhomology-Mediated End-Joining (MMEJ) an error-prone mutagenic DNA repair pathway

MMEJ is active, and Pol Theta is overexpressed, in HRD cancer cells (e.g. BRCA1/2) making Pol Theta a SL target in HRD cancers

PARP1 & Pol Theta are both involved in MMEJ mediated DNA repair supporting a synergistic effect

IDEAYA Pol Theta inhibitors show selective cell viability effects in DLD1 BRCA2-/- vs. wildtype cell lines

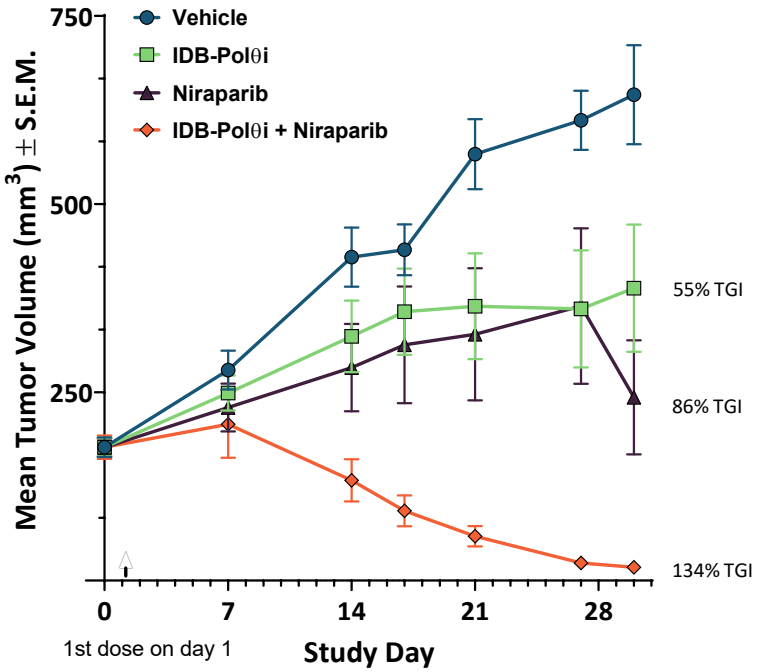
Advancing both small molecule inhibitors and protein degraders

IDEAYA Data

Pol Theta ATPase inhibitor *In Vivo* Activity

Pol Theta inhibitor in combination with niraparib demonstrates significant tumor regression in DLD1 BRCA2-/- xenograft model

Regressions observed for all animals dosed within combination study



IDEAYA Data

Werner Helicase Synthetic Lethality Program

Candidate Biomarker: High-MSI (15% GI Cancers and 16% CRC) [1]

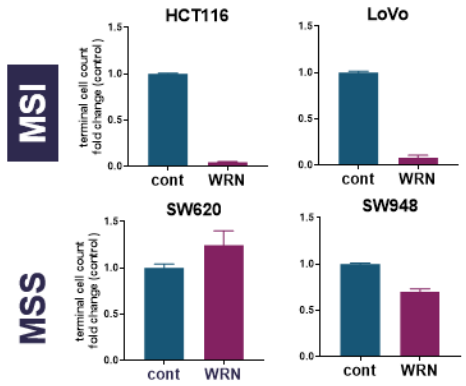
Werner Helicase Synthetic Lethal with High-MSI

CellPress

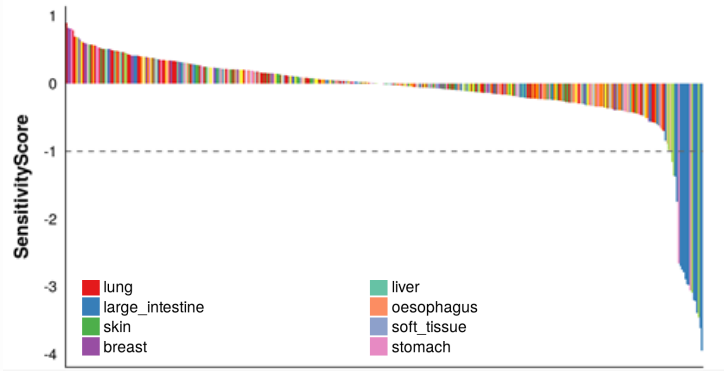
Werner Syndrome Helicase is Required for the Survival of Cancer Cells with Microsatellite Instability

IDEAYA Publication

Cell Press, iScience, March 2019, Hager et al



Project Drive: WRN is essential in MSI-High cancer cell lines



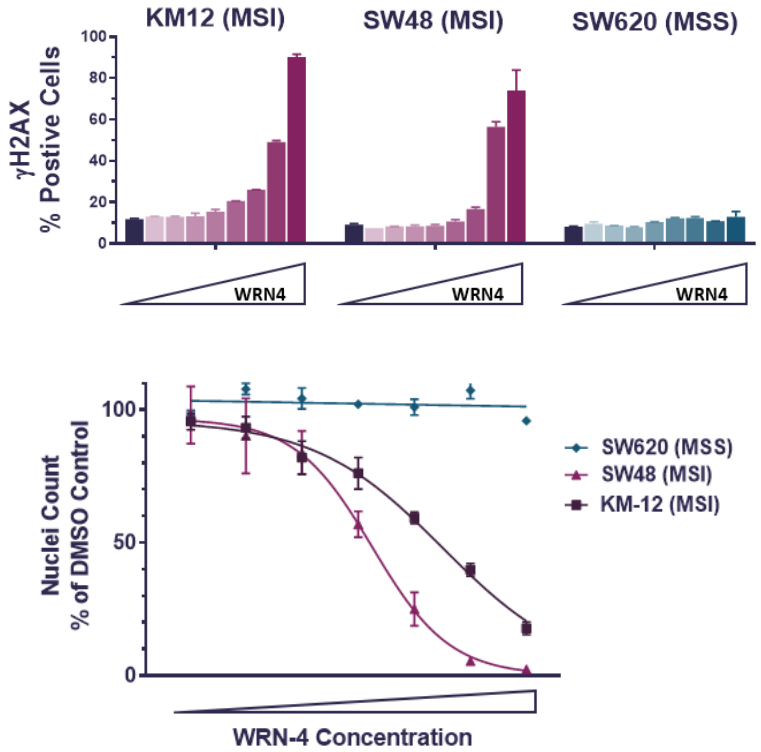
Project Drive

Werner Inhibitor Cellular PD and Viability

PD-marker: dose dependent increase of DNA damage marker γH2AX

Cell viability: MSI-high specific cell viability effect; no effect in MSS cell lines

***In vivo* efficacy**: demonstrated WRN inhibitor *in vivo* PD and efficacy



IDEAYA Data

[1] Cancer Res., November 1998

[1] Cancer Res., November 1998

IDE196 Phase 1/2 Clinical Program Summary

PKC Inhibitor Targeting *GNAQ/GNA11* Hotspot Mutation Tumors

Metastatic Uveal Melanoma (MUM)
IDE196 Combination Therapies

MUM Indication: Focus on Clinical Combos

- IDE196 + MEK (binimetinib) & IDE196 + cMET (crizotinib)
- IDE196 + MEK & IDE196 + cMET preclinical synergy demonstrated[2]

Study goal is to enhance IDE196 mono clinical activity in MUM

- IDE196 mono BID (30 pts), ~73% Disease Control Rate & ~13% ORR[1]

Pfizer Clinical Trial Collaborations for MEK & cMET combos

Interim data anticipated 2021

GNAQ/GNA11 Basket Trial (Non-MUM)
IDE196 Monotherapy

Ph2 Monotherapy Expansion Initiated in Skin Melanoma

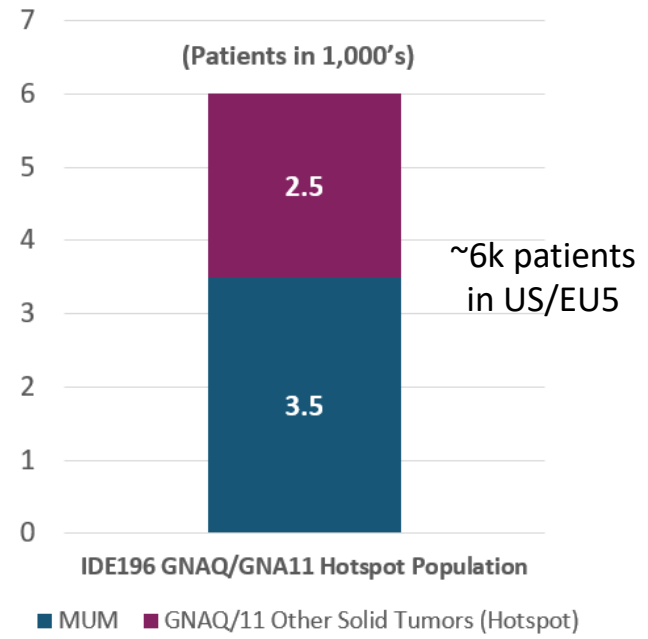
- 100% DCR & 1 confirmed PR in first 4 patients[3]

Enrolled Lung Cancer GNAQ/11 patient

Interim data anticipated 2021

No FDA approved therapies for MUM or GNAQ/11 mutation patients

Addressable GNAQ/11 Patients (US/EU5)



[1] Novartis Data, AACR 2019 [2, 3] IDEAYA Data

Building The Premier Synthetic Lethality Focused Precision Medicine Oncology Biotech in 2021 and Beyond

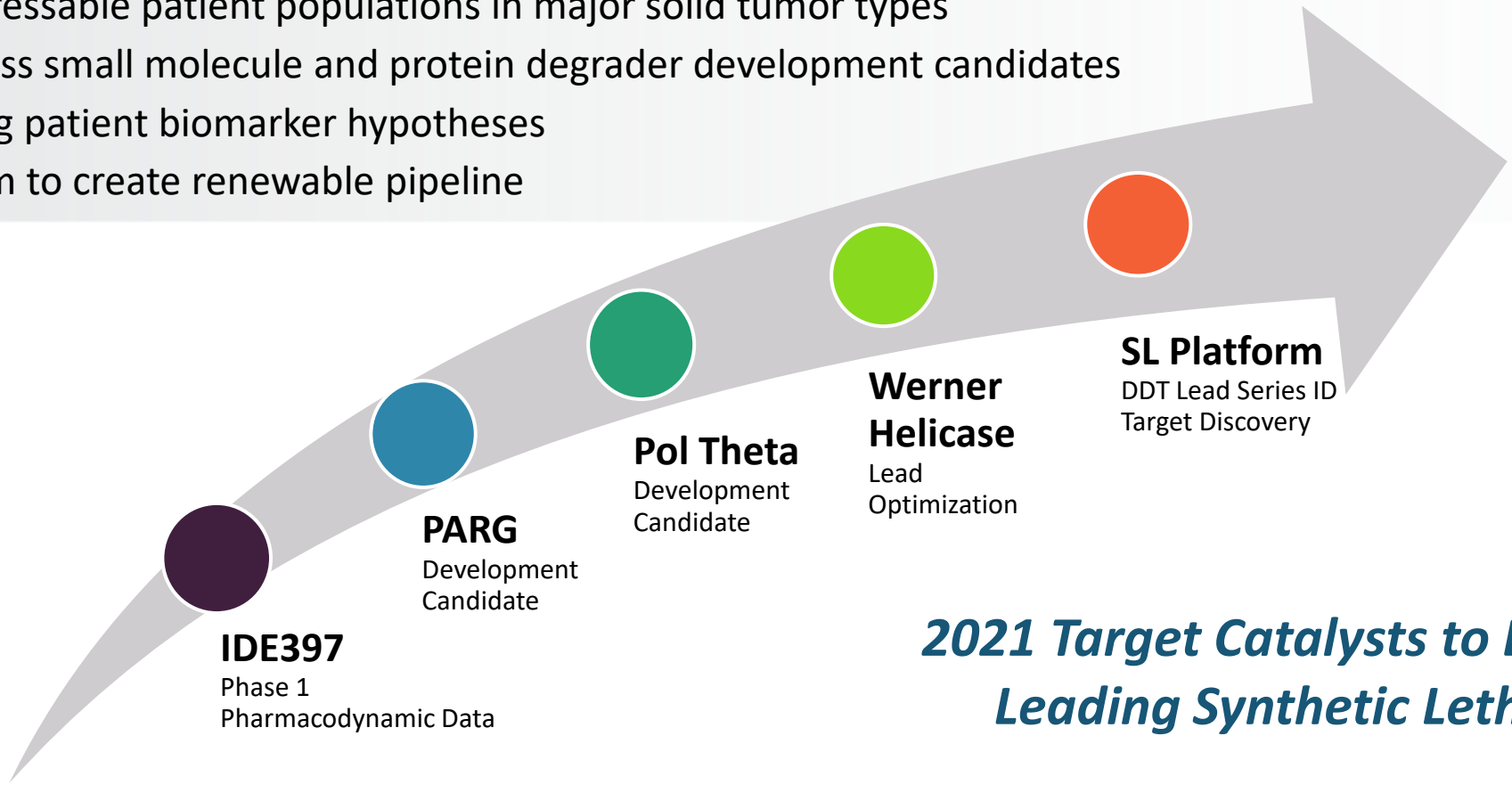
Focus on *First-in-Class* Synthetic Lethality Programs to Deliver Patient Breakthroughs

Large addressable patient populations in major solid tumor types

Best-in-class small molecule and protein degrader development candidates

Compelling patient biomarker hypotheses

SL platform to create renewable pipeline



2021 Target Catalysts to Build Industry Leading Synthetic Lethality Pipeline

DDT = DNA Damage Target