BOUNDLESS BIO™

Unlocking a New Paradigm in Cancer Treatment via ecDNA-Directed Therapies (ecDTx)

Corporate Update

May 27, 2025

Nasdaq: BOLD

@BoundlessBio

Disclaimer: Forward-Looking Statements and Market Data

We caution you that this presentation contains forward-looking statements about us and our industry. All statements other than statements of historical facts contained in this presentation, including statements regarding our future results of operations and financial position, business strategy, research and development plans, the anticipated timing, costs, design and conduct of our ongoing and planned clinical trials and preclinical studies for our extrachromosomal DNA (ecDNA) directed therapeutic candidates (ecDTx), the timing of expected readouts, the potential therapeutic benefits of our ecDTx and the potential for them to be first-in-class, the timing and likelihood of regulatory filings and approvals for our ecDTx, the expected benefits of our portfolio prioritization, our ability to commercialize our ecDTx, if approved, the pricing and reimbursement of our ecDTx, if approved, the potential to develop future ecDTx, the potential benefits of strategic collaborations and our intent to enter into any strategic arrangements, the timing and likelihood of success, plans and objectives of management for future operations, future results of anticipated ecDTx development efforts and the sufficiency of our cash position to fund operations and milestones, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. In some cases, you can identify forward-looking statements by terms such as “anticipate,” “believe,” “contemplate,” “continue” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target” or “will, or the negative of these terms or other similar expressions. The inclusion of forward-looking statements should not be regarded as a representation by us that any of our plans will be achieved. Actual results may differ from those set forth in this presentation due to the risks and uncertainties inherent in our business, including, without limitation: we are early in our development efforts and our approach to discover and develop ecDTx to treat oncogene amplified cancers is novel and unproven; results from preclinical studies or early clinical trials not necessarily being predictive of future results; potential delays in the commencement, enrollment, data readouts or completion of clinical trials or preclinical studies or submission of an IND, including as a result of FDA feedback on our regulatory submission to support our planned clinical trial of the BBI-355 and BBI-825 combination; we may not realize the benefits expected from our portfolio prioritization and the streamlining of operations and workforce reduction, including our ability to conserve cash; our ability to retain key personnel; our dependence on third parties in connection with clinical trials, preclinical studies, ecDNA diagnostic development, and manufacturing; unfavorable results from clinical trials or preclinical studies; we may expend our limited resources to pursue a particular ecDTx and fail to capitalize on ecDTx with greater development or commercial potential; unexpected adverse side effects or inadequate efficacy of our ecDTx that may limit their development, regulatory approval, and/or commercialization; the potential for our programs and prospects to be negatively impacted by developments relating to our competitors, including the results of studies or regulatory determinations relating to our competitors; regulatory developments in the United States and foreign countries; we may use our capital resources sooner than we expect; our ability to obtain and maintain intellectual property protection for our ecDTx, ecDNA diagnostic, and technology; unstable market and economic conditions may adversely affect our business and financial condition and the broader economy and biotechnology industry; and other risks described in our filings with the Securities and Exchange Commission (SEC), including under the heading “Risk Factors” in our annual report on Form 10-K for the year ended December 31, 2024 and any subsequent filings with the SEC. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and we undertake no obligation to update such statements to reflect events that occur or circumstances that exist after the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

This presentation concerns therapeutic products that are or will be under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration. They are currently limited by federal law to investigational use, and no representation is made as to their safety or effectiveness for the purposes for which they are being investigated.

Trade names, trademarks and service marks of other companies appearing in this presentation are the property of their respective owners.

Summary of today's updates

- POTENTIATE study of BBI-355 (CHK1 inhibitor) will discontinue evaluating single agent BBI-355 in gynecologic tumors and BBI-355 in combination with an EGFR inhibitor, FGFR inhibitor, or CDK4/6 inhibitor in patients with cancers bearing amplification of *EGFR*, *FGFR*, or *CDK4/6*, respectively
- Boundless intends to evaluate BBI-355 in combination with BBI-825 (RNR inhibitor) in patients with cancers bearing oncogene amplifications
- BBI-940 has been declared as oral Kinesin degrader development candidate, with intention to file IND in 1H:26
- Boundless has streamlined its organization to reflect the new operational focus and eliminated ~20 positions
- Refined operations expected to provide cash runway into 1H:28

Boundless Bio (BOLD): clinical-stage public company establishing a new category in oncology that addresses oncogene amplified cancers

Oncogene amplified cancer:

- Significant unmet medical need (worse survival)
- Generally unresponsive to targeted therapy and immunotherapy
- ~1.3M new patients per year in major markets[1]

Extrachromosomal DNA (ecDNA):

- Cancer-specific circular DNA—a root cause of oncogene amplification
- Transformative emerging area of cancer biology
- Spyglass drug discovery platform leverages ecDNA to identify synthetic lethal targets in cancer

ecDNA-directed therapies (ecDTx):

- BBI-355: clinical stage oral CHK1 inhibitor
- BBI-825: clinical stage oral RNR inhibitor

} to be evaluated as a clinical combination

- BBI-940: oral kinesin degrader development candidate; expected IND filing in H1:26

1. United States, EU, and Japan

Spyglass reveals cancer targets, both novel and validated, that intersect distinct nodes of ecDNA lifecycle

CHK1

BBI-355 (clinical stage)

Novel, oral, selective inhibitor of CHK1

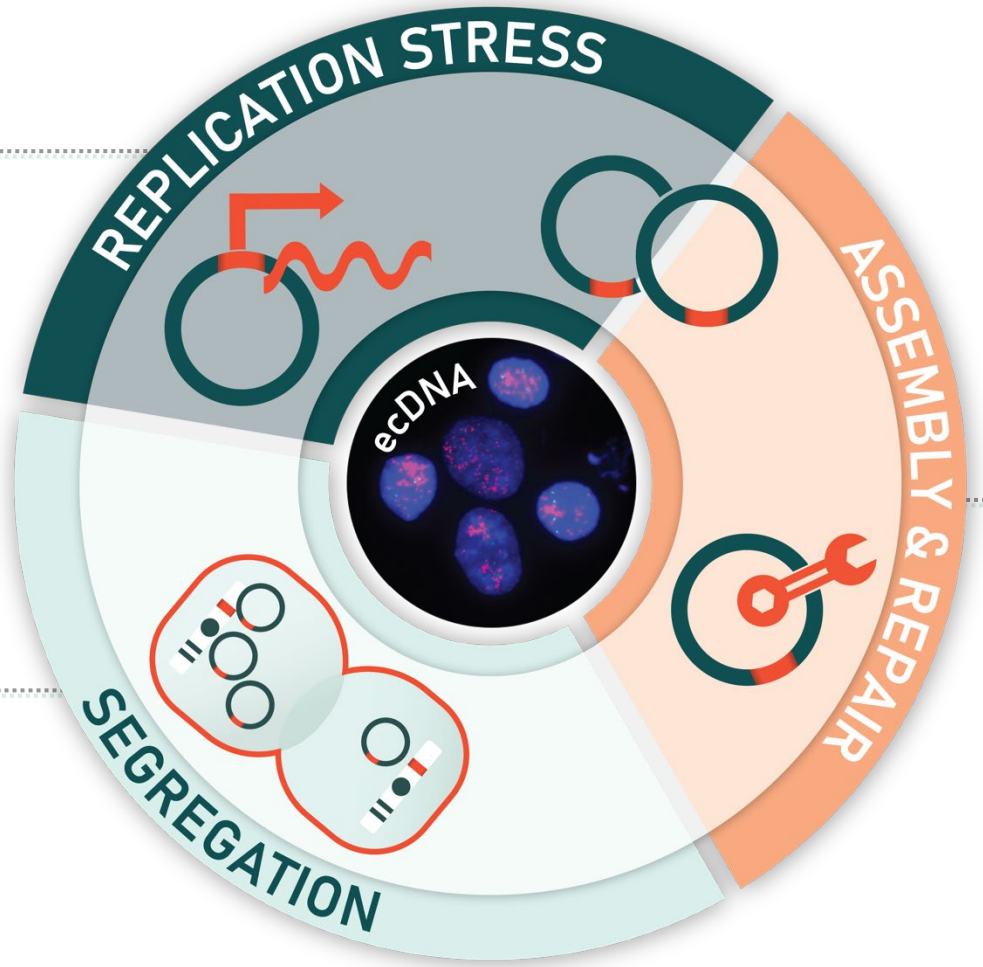
CHK1 is master regulator of replication stress, including that induced by ecDNA

Novel Kinesin

BBI-940 (IND-enabling studies)

Novel, oral degrader of Kinesin

Kinesin involved in segregation of DNA and critical for ecDNA segregation



RNR

(clinical stage) BBI-825

Novel, oral, selective inhibitor of RNR

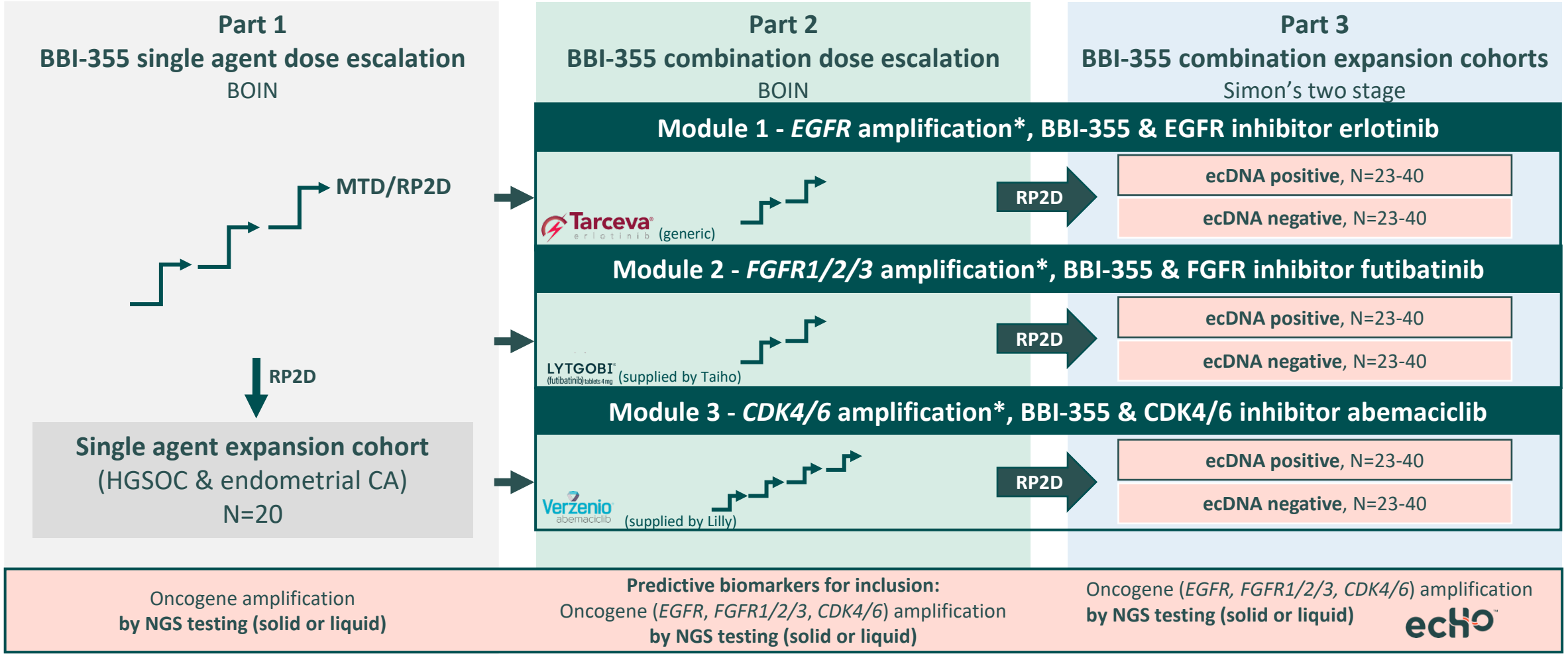
RNR is a rate-limiting enzyme for *de novo* synthesis of dNTPs, the raw materials of DNA, including ecDNA

CHK1: checkpoint kinase 1
dNTPs: deoxyribonucleotide triphosphates
RNR: ribonucleotide reductase

BBI-355: oral, selective CHK1 inhibitor

Targets replication stress in cancer

Phase 1/2 POTENTIATE study of BBI-355



"**POTENTIATE**" Study: Precision Oncology Trial Evaluating Novel Therapeutic Interrupting Amplifications Tied to ecDNA

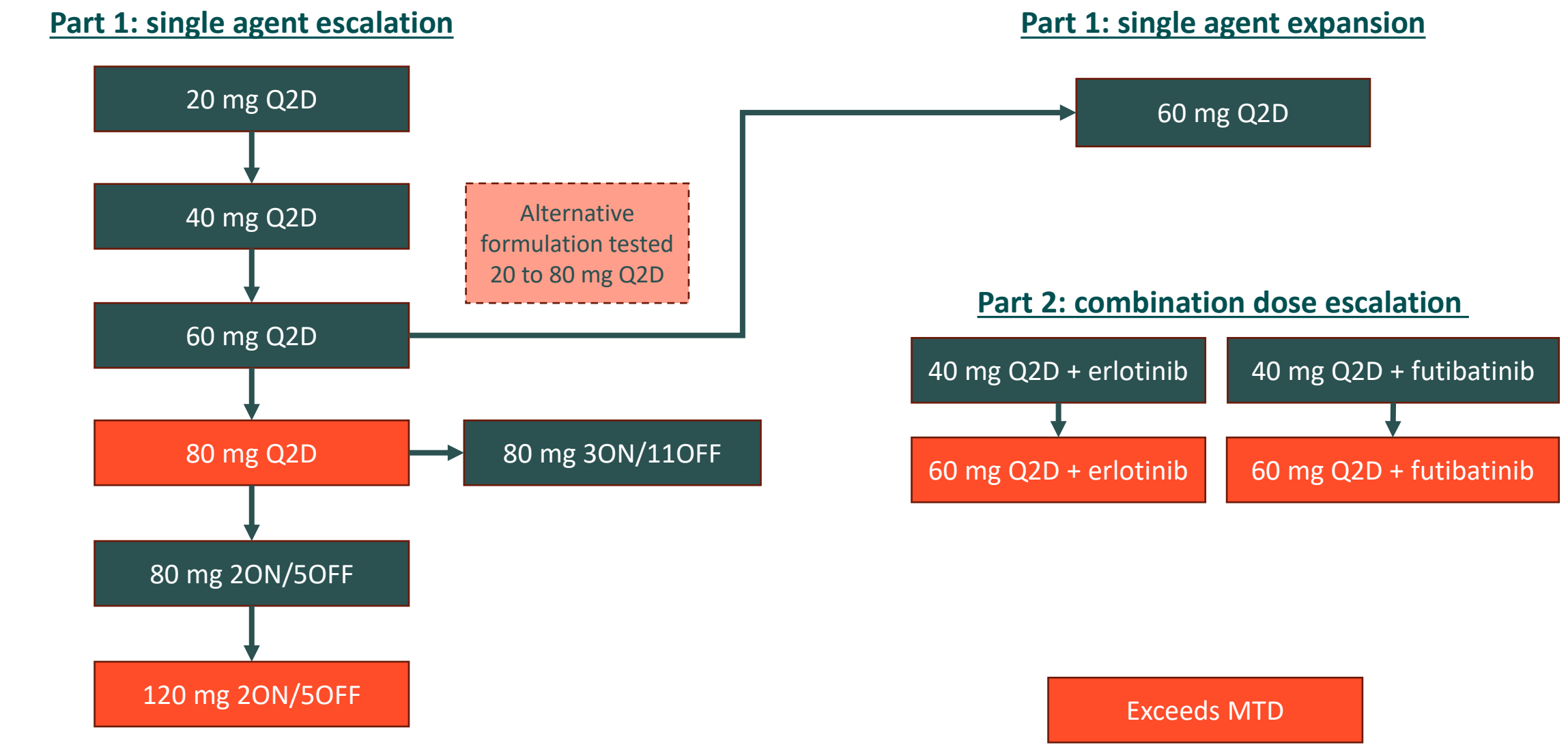
BOUNDLESS BIO

BOIN: Bayesian optimal interval design
HGSOC: High-grade serous ovarian carcinoma
MTD: Maximum Tolerated Dose; RP2D: Recommended Phase 2 Dose

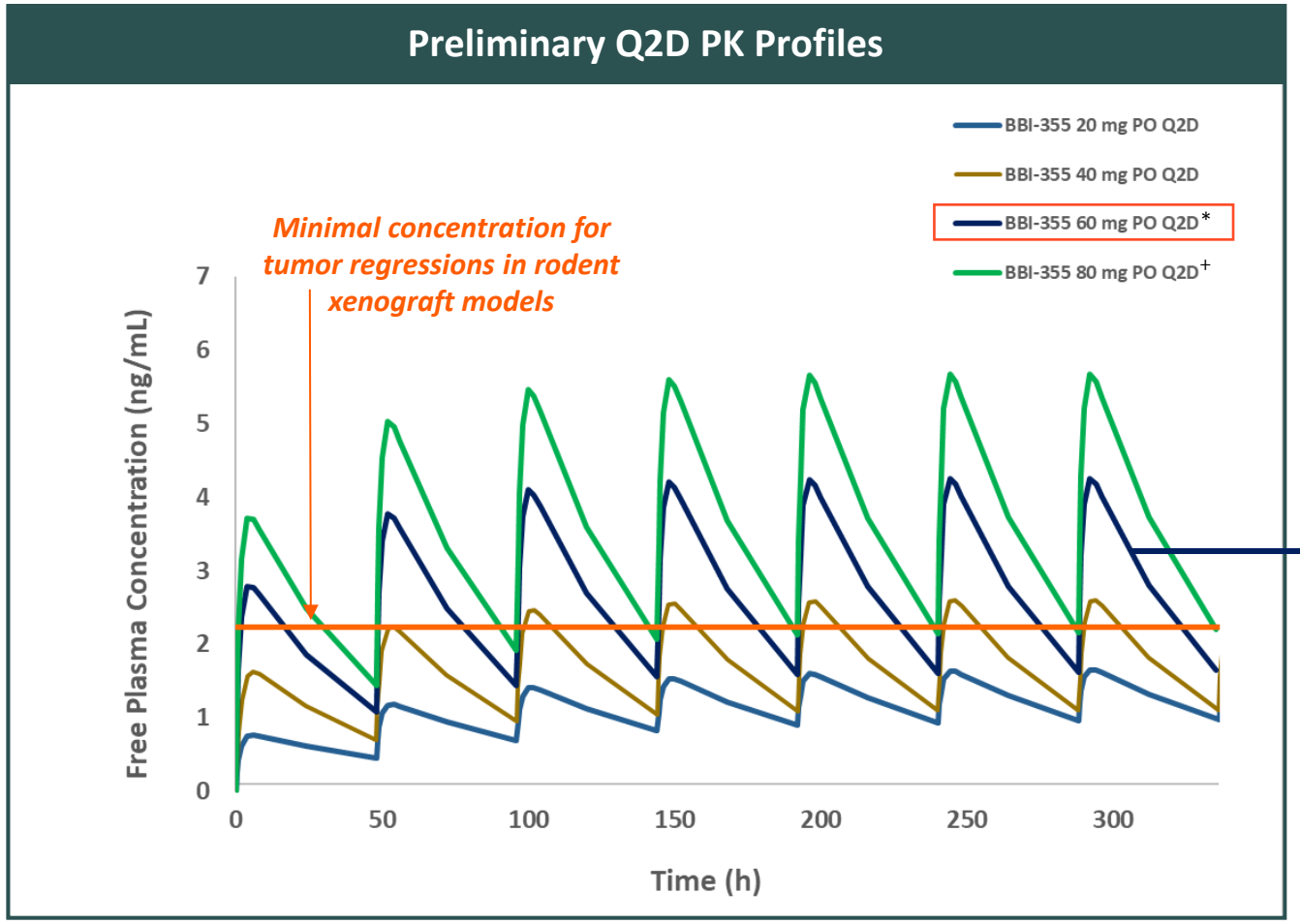
*Amplification of wildtype driver oncogene, patients with known pathogenic driver mutations or fusions of ANY oncogene are excluded

Part 3 Simon's optimal two-stage design (Goal 1st stage RR ≥ 2/23)

POTENTIATE dose escalation schema: monotherapy and combination



Human PK data of BBI-355 showed 60 mg Q2D is minimum dose required to achieve exposure that is reliably in the therapeutically active range



60 mg Q2D required for robust pharmacology

AUC: area under the curve
PO: oral
Q2D: every two days

*Tolerated as single agent but not in combination
+ Not tolerated as single agent

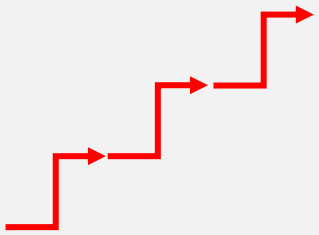
BBI-825: oral, selective RNR inhibitor

Targets DNA assembly and repair in cancer

BBI-825-101 (STARMAP): First in human Ph1/2 study

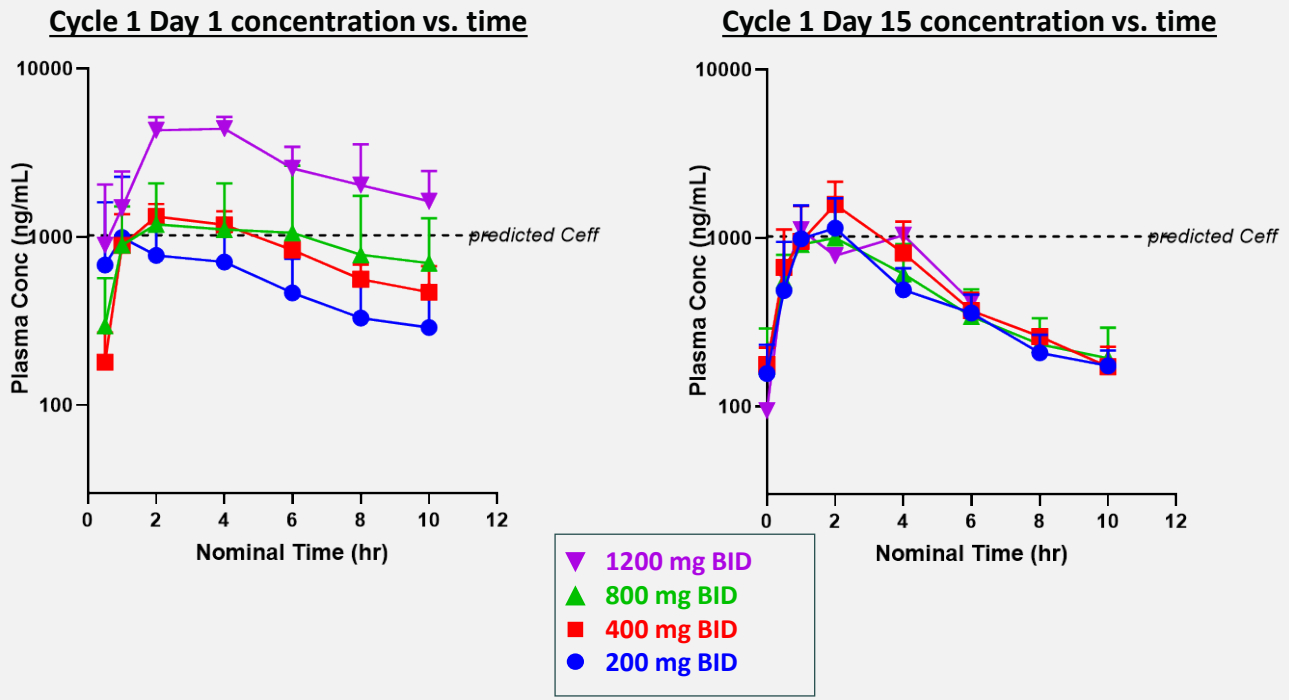
Steady-state PK exposure following Q2D dosing is not in therapeutically active range

Part 1
BBI-825 single agent dose escalation



Dosing PO BID

Part 1 human pharmacokinetics (PK)
BBI-825 single agent Cycle 1, Day 1 and Day 15



Rapid absorption, with dose-dependent increase in exposure on Day 1; Reduced exposure at steady-state on Day 15

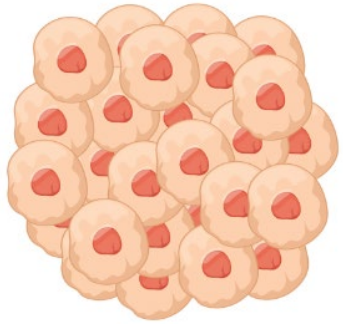
Ceff calculated based on exposures associated with tumor growth inhibition in rodent xenograft models of MAPK-induced resistance

BBI-355 / BBI-825: novel replication stress combination

Highly synergistic replication stress combination with reduced toxicity risk

RNR inhibition, in combination with CHK1 inhibition, in oncogene amplified cells results in imbalanced dNTP pools, increased replication stress, and synergistic cytotoxicity

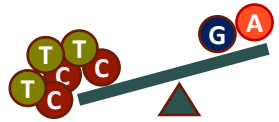
Metabolic reprogrammed
De novo addicted "Warburg"
Oncogene amplified tumor cells



- *De novo* dNTP pathway dominant
- Elevated replication stress

1

RNRi



dTTP/dATP

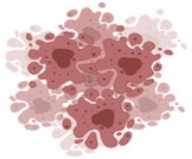
Imbalanced dNTP pools
High replication stress

ssDNA
Stalled forks
S-phase arrest

pCHK1-S296/345

DDR mediated
resolution & growth

Cell death

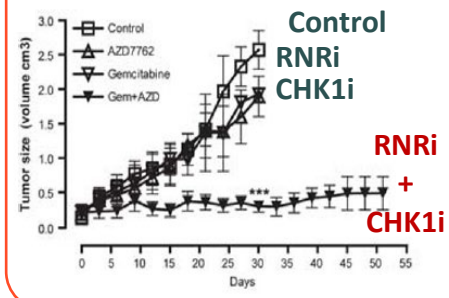


Replication/mitotic
catastrophe

CHK1i

2

Synergistic activity
in combination



Warburg effect: metabolic shift where cancer cells prefer glycolysis (over normal oxidative phosphorylation), leading to *de novo* synthesis of nucleotides (dNTPs)

DDR: DNA damage and repair
dNTP: deoxyribonucleotide triphosphates
ssDNA: single strand DNA

Bartucci et al. Cell Death & Diff. 2011
AZD7762: CHK1i
Gemcitabine: RNRi (non-selective)

Historical evidence demonstrating benefit of CHK1 inhibitor and (non-selective) RNR inhibitor combination

- Gene encoding **CHK1** (CHEK1) demonstrates strong co-dependency with the RNR regulatory component, **RRM2**, reflecting a synthetic lethal relationship
- Numerous structurally distinct RNR and CHK1 inhibitors demonstrate **enhanced activity over monotherapy**

Clinical proof of concept of CHK1i + RNRi

Drug (Target)	Objective responses in tumors
SRA737 (CHK1i) + gemcitabine*	Ovarian, rectal, anogenital SCC, cervical, SCLC
GDC-0575 (CHK1i) + gemcitabine^	TNBC, soft tissue sarcoma, NSCLC
No responses using SRA737 or GDC-0575 monotherapy	

Subtherapeutic dose of non-selective RNRi (low dose gemcitabine) potentiated selective CHK1i, resulting in clinical responses across multiple indications

SCC: squamous cell carcinoma
SCLC: small cell lung cancer

NSCLC: non small cell lung cancer
TNBC: triple negative breast cancer

*Jones, Clin Canc Res 2023
^Italiano, Ann Onc 2018

Both doses used low dose gemcitabine with intermittent weekly combo dosing

While adding non-selective RNRi to CHK1i increased anti-tumor activity, it also increased hematologic toxicity

CHK1i treatments	Monotherapy Safety Gr3+	Combination with gemcitabine Safety Gr3+
SRA737 • Monotherapy RP2D 800 mg QD • Combo: SRA 737 + LDG (250mg/m^2)	Neutropenia 10% Thrombocytopenia: 2%	**Neutropenia: 17%** **Thrombocytopenia: 10%** **Anemia: 12%**
GDC-0575 • Monotherapy MTD 60 mg • Combo: GDC-0575 + IDG (500 mg/m^2)	Neutropenia: 19% Thrombocytopenia: 5% Anemia: 5%	**Neutropenia: 79%** **Thrombocytopenia: 14%** **Anemia: 31%**

- **Adding non-selective RNRi (gemcitabine) to CHK1i (SRA737 or GDC-0575) enhanced clinical response rates**
- **However, combination also increased the rate of Gr3+ hematologic toxicities**
- **Thus, combination with a non-selective RNRi did not improve the therapeutic index over CHK1i monotherapy**

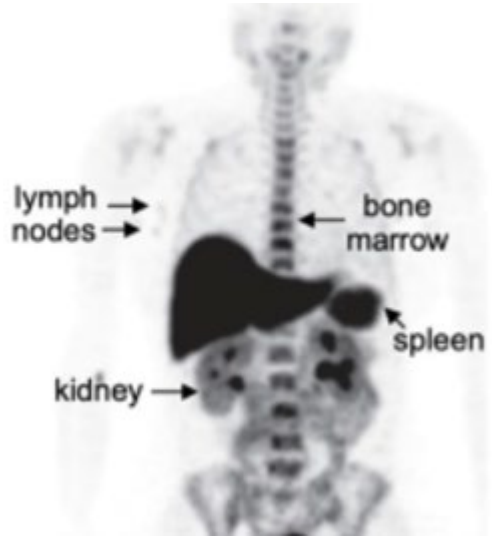
Therapeutic opportunity to maximize the potential of combining selective RNRi and CHK1i by minimizing impact to hematopoietic cells and enhancing the replication stress vulnerability in oncogene amplified cancer

Kristeleit et al., BJC 2023
Jones et al., Clin Canc Res 2023
Italiano, Ann Onc 2018

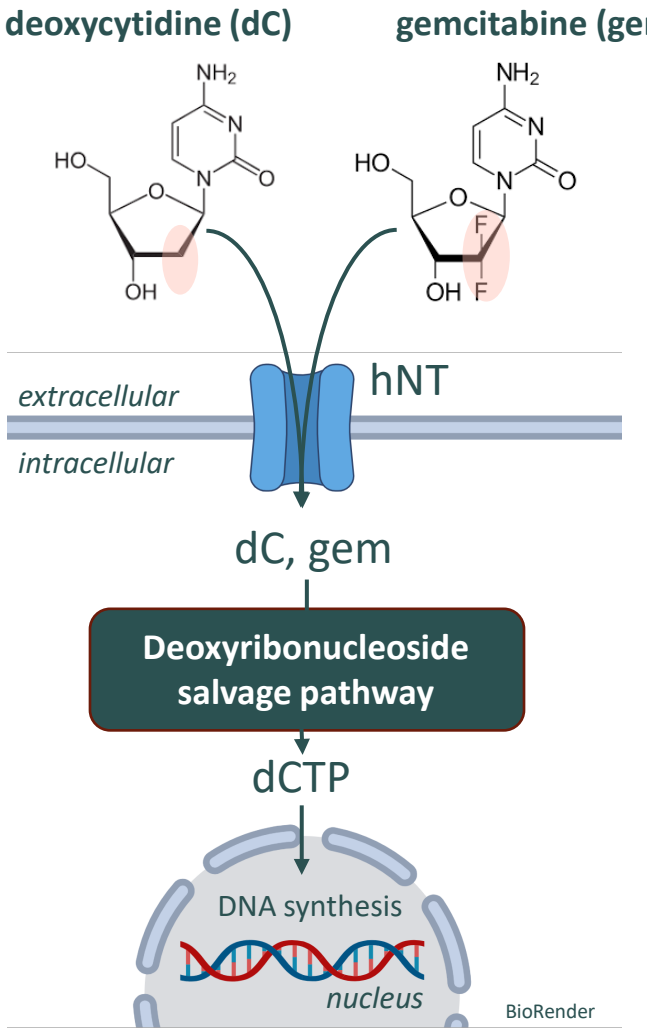
IDG: intermediate dose gemcitabine
LDG: low dose gemcitabine

BBI-825, a selective, non-nucleoside RNRi may improve tolerability and potential therapeutic index in combination with CHK1i

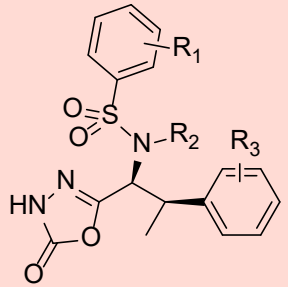
Gemcitabine, and other nucleosides, are **actively transported** into cells reliant on the dNTP **salvage pathway**



Thus, nucleoside analogs **accumulate** in normal tissues, including **bone marrow**



Selective RNR dimerization inhibitor



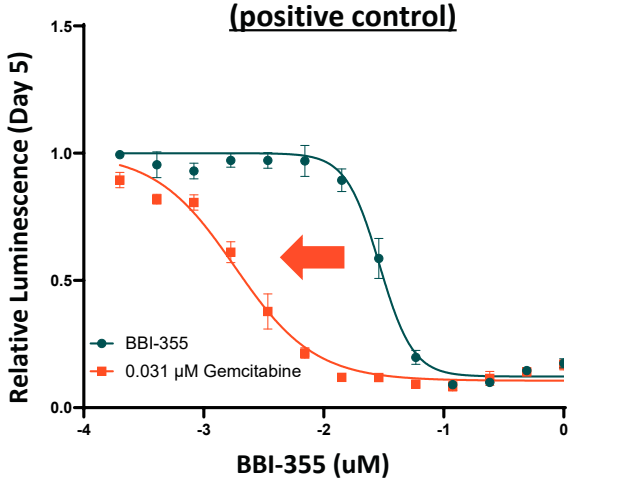
BBI-825 is structurally unrelated to nucleosides, thereby **avoiding accumulation in normal proliferating tissues** that are primarily dependent on the dNTP salvage pathway

Abousaway et al., Nanotheranostics 2021

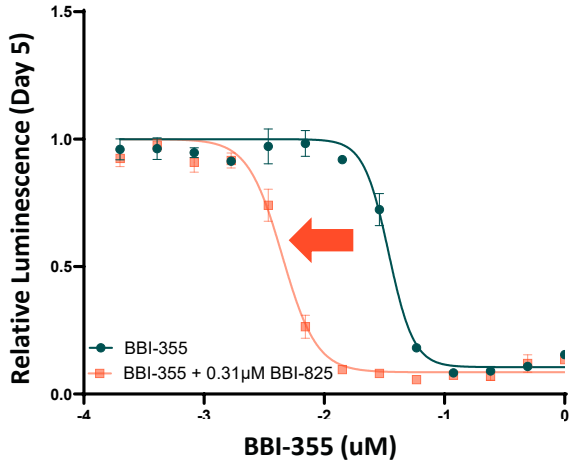
dCTP: deoxycytidine triphosphate
DI: dimerization inhibitor
hNT: human nucleoside transporter

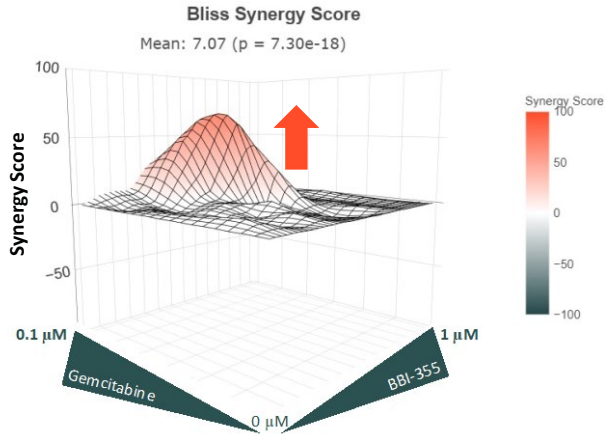
BBI-825 (selective RNRi) demonstrated synergistic activity when combined with BBI-355 in cancer cells

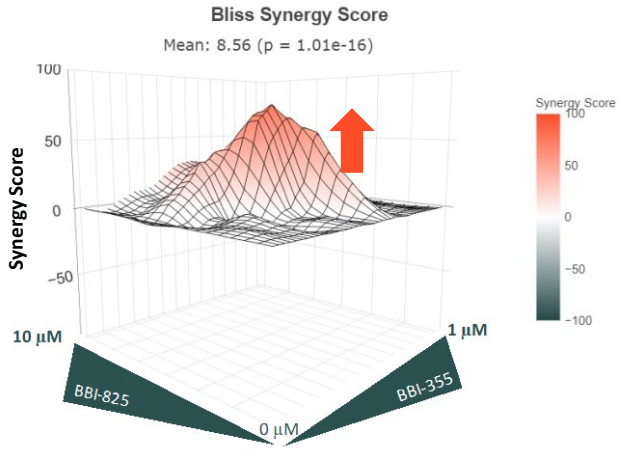
In vitro sensitivity of BBI-355 + gemcitabine (positive control)



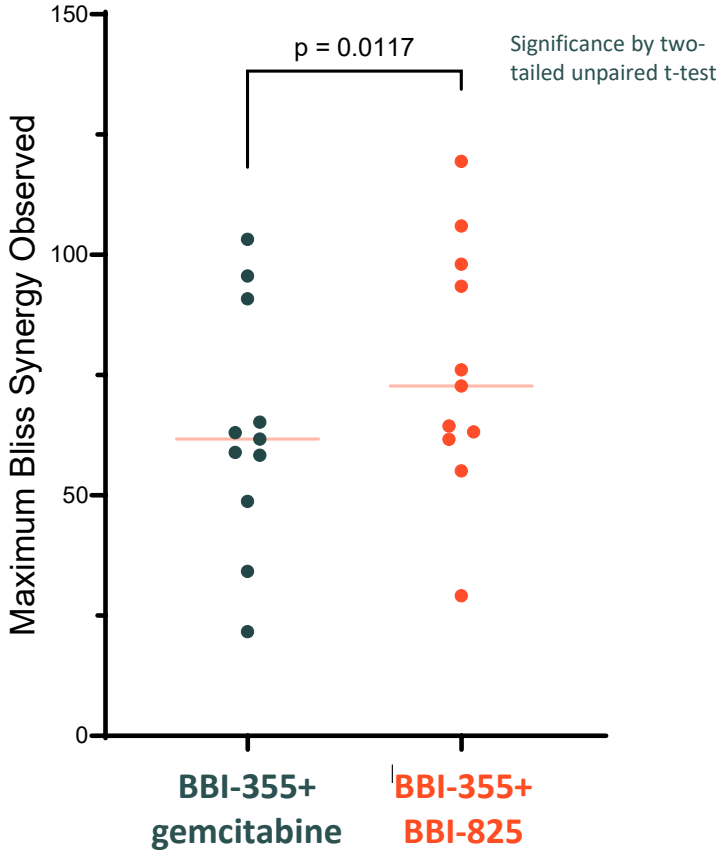
In vitro sensitivity of BBI-355 + BBI-825







BLISS assessment of synergy across cancer cell line panel



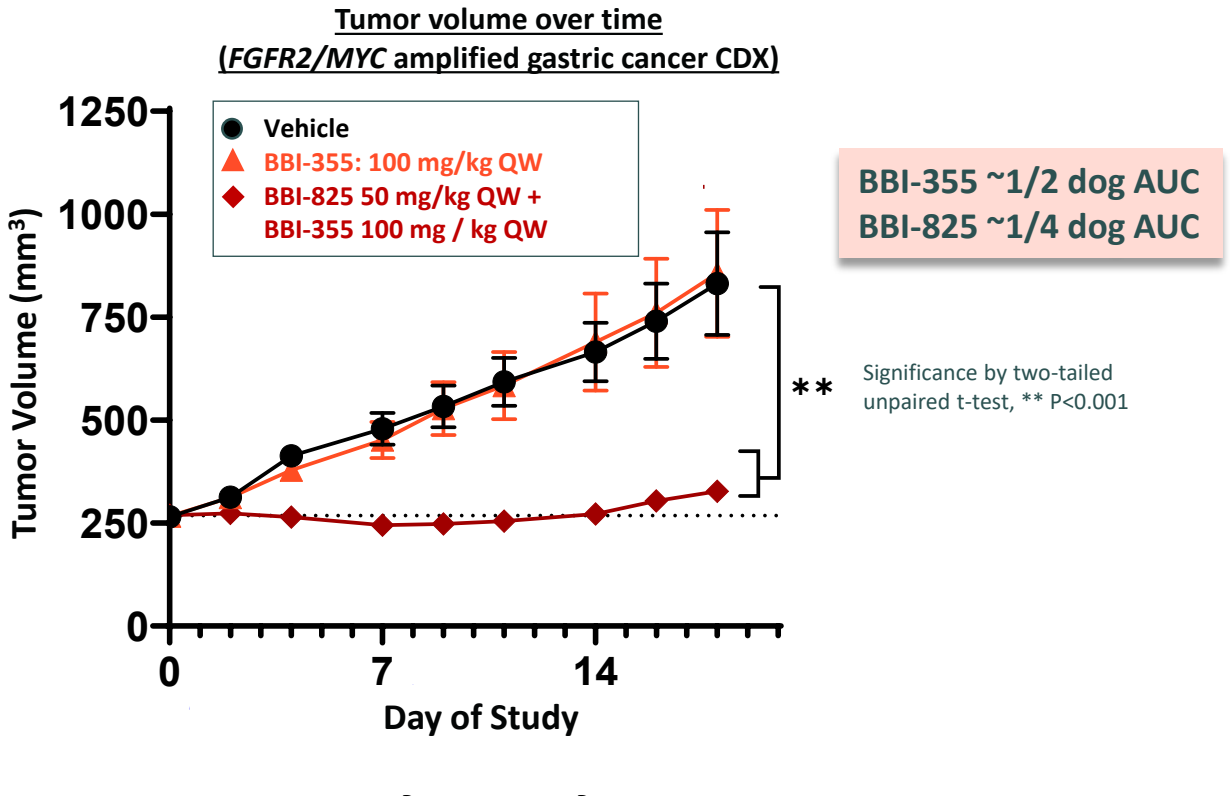
Unlike gemcitabine, BBI-825 in combination with BBI-355 was well tolerated in pilot dog toxicology study

Selective RNRi has reduced risk of hematological toxicity in combination with BBI-355

		LDG + BBI-355	BBI-825 + BBI-355
Clinical Observations		1 treatment cycle in 14 days Exceeds MTD	2x weekly treatment cycle, 14 days No clinical signs
Complete Blood Count (CBC)*		**LDG:** Normal range (max decline 55%, D5) **BBI-355:** Mild neutropenia (max decline 75%, D5) **Combo:** **Severe neutropenia** (max decline 90%; D5) In surviving animals, all values recovered to baseline @ D14	**BBI-825:** Normal range (max decline 18%, D14) **BBI-355:** Mild neutropenia (max decline 81%, D8) **Combo:** **Normal range** (max decline 62%, D5) All values recovered to baseline @ D14
		Combination Not Tolerated	**Combination Well Tolerated**

*Median values (n=3) except for LDG + BBI-355 combo, n=1 D5-D14
LDG: low dose gemcitabine(300mg/m^2)

The combination of BBI-825 with BBI-355, with weekly dosing, led to substantial anti-tumor activity in mouse xenografts at dose levels that had minimal single agent activity



BBI-355 ~1/2 dog AUC
BBI-825 ~1/4 dog AUC

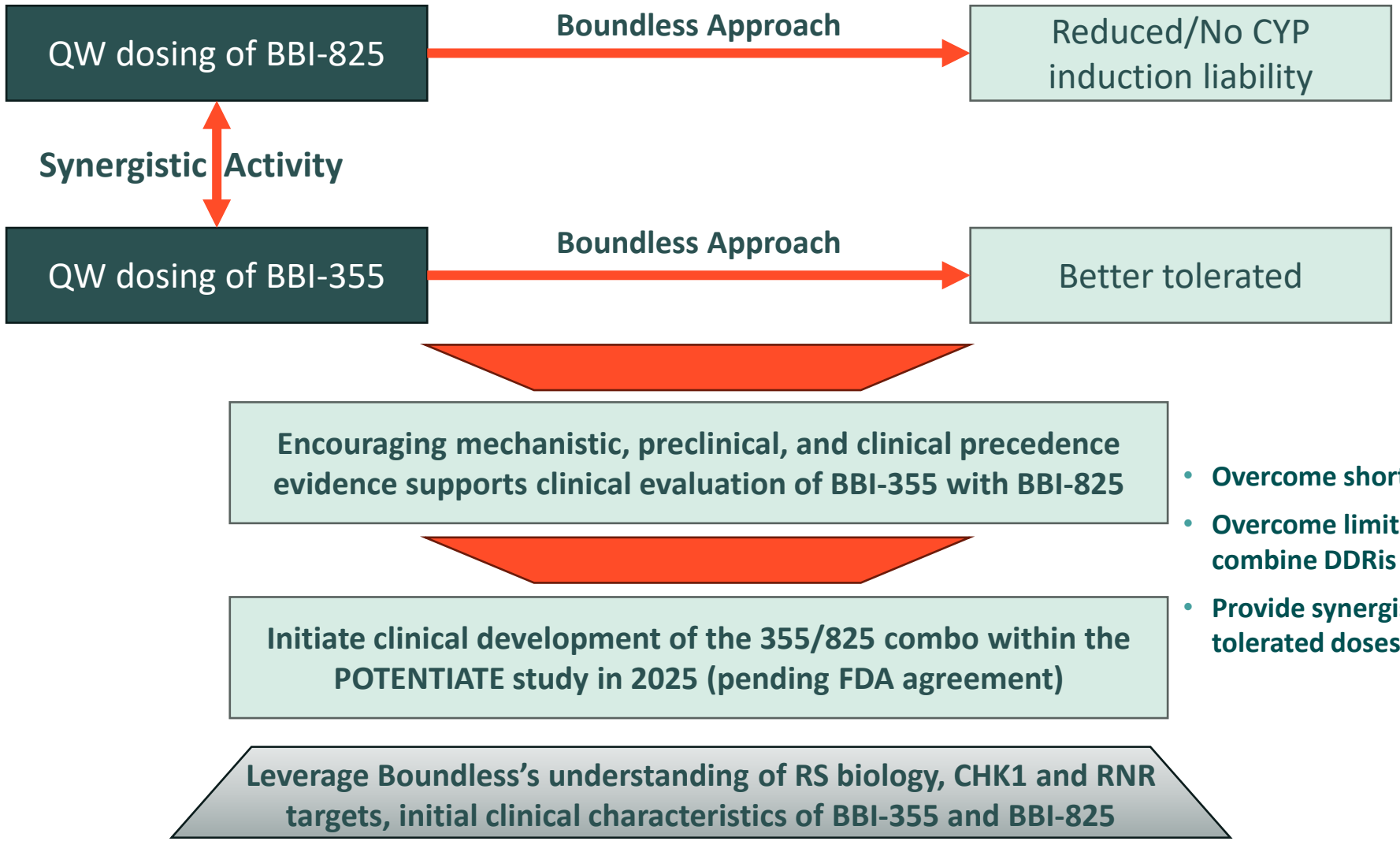
Significance by two-tailed unpaired t-test, ** P<0.001

- **Once weekly combination of BBI-825 and BBI-355 resulted in tumor growth inhibition, including regressions**
- **Generally, well tolerated (<10% weight loss); exposures below those that were well tolerated in dogs**

QW: once weekly

Prior study determined BBI-825 monotherapy achieves partial 69% TGI in this model with Q2D dosing [~2-fold higher weekly exposure]

Summary of rationale for 355/825 combo and next steps

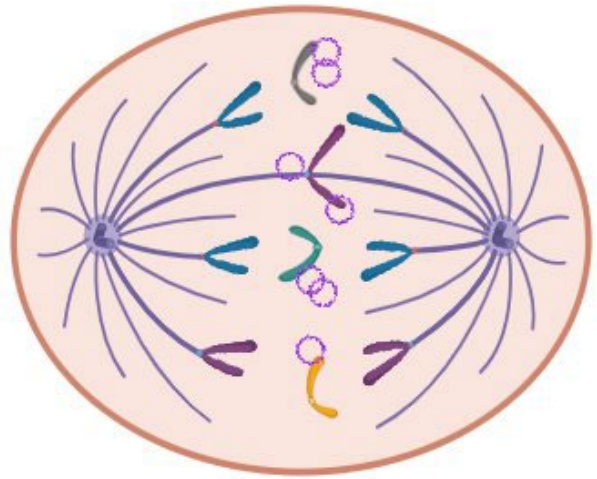


- **Overcome shortcomings of either agent alone**
- **Overcome limitations on prior attempts to combine DDRis with RNRis**
- **Provide synergistic anti-tumor activity at tolerated doses**

BBI-940: novel kinesin oral degrader

Targets DNA segregation in cancer

Targeting a novel kinesin that regulates DNA segregation and viability of ecDNA bearing cells



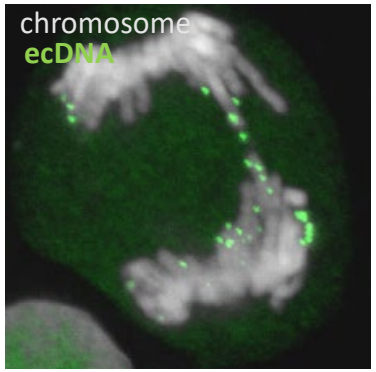
ecDNA (no centromere)

centrosome

chromosome

microtubule

ecDNA 'hitchhikes' with chromosomes during mitosis

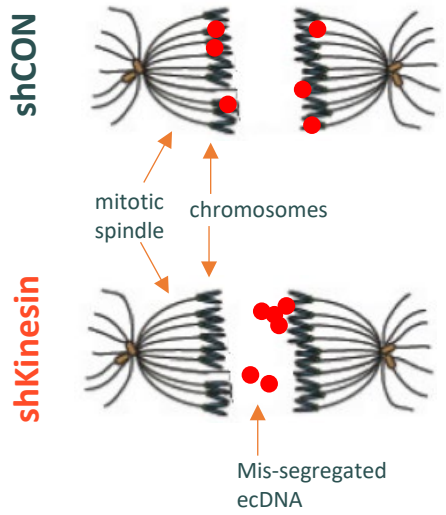


Oobatake and Shimizu, Genes Chrom Canc 2019

- Chromosome segregation is primarily dependent on interactions between the mitotic spindle microtubules and the centromere
- ecDNA lack centromeres and likely rely on distinct mitotic machinery for proper segregation
- Spyglass has revealed a kinesin that is non-essential for chromosome segregation in healthy cells but is essential for proper ecDNA segregation in cancer cells
- Genetic knockdown of "kinesin" reduced ecDNA and showed synthetic lethality and anti-tumor activity in multiple cancer models
- We are not aware of any other efforts to drug this kinesin

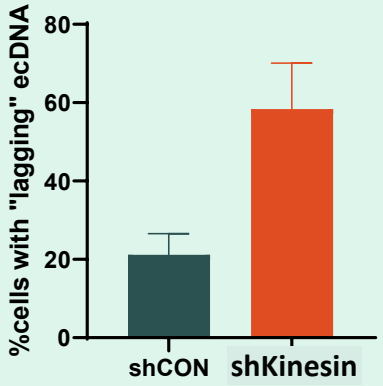
Genetic knockdown of Kinesin resulted in mis-segregation of ecDNA during mitosis and reduced cellular ecDNA levels over time

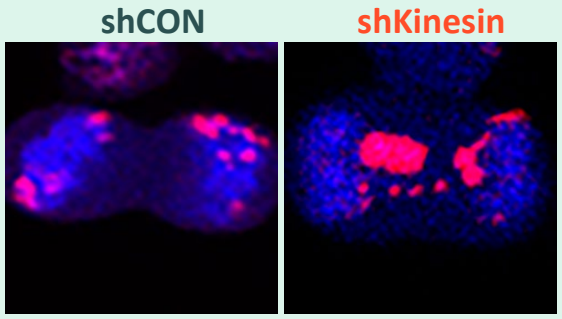
Model for Kinesin inhibition



Kinesin may interact with ecDNA and chromosomes, independently of centromeres, to align DNA at the metaphase plate and promote segregation during mitosis

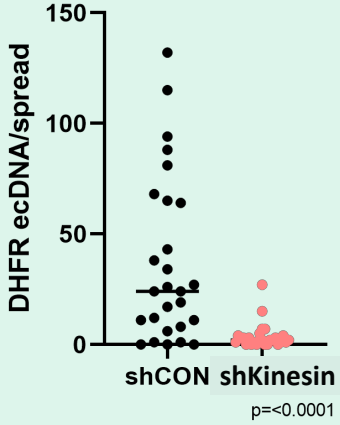
ecDNA displayed a "lagging" phenotype during mitosis in the absence of Kinesin

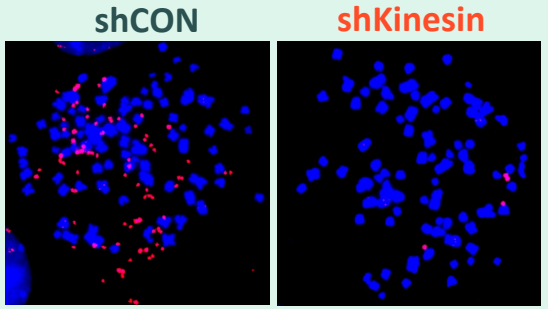




DAPI (DNA) / *DHFR* (ecDNA)

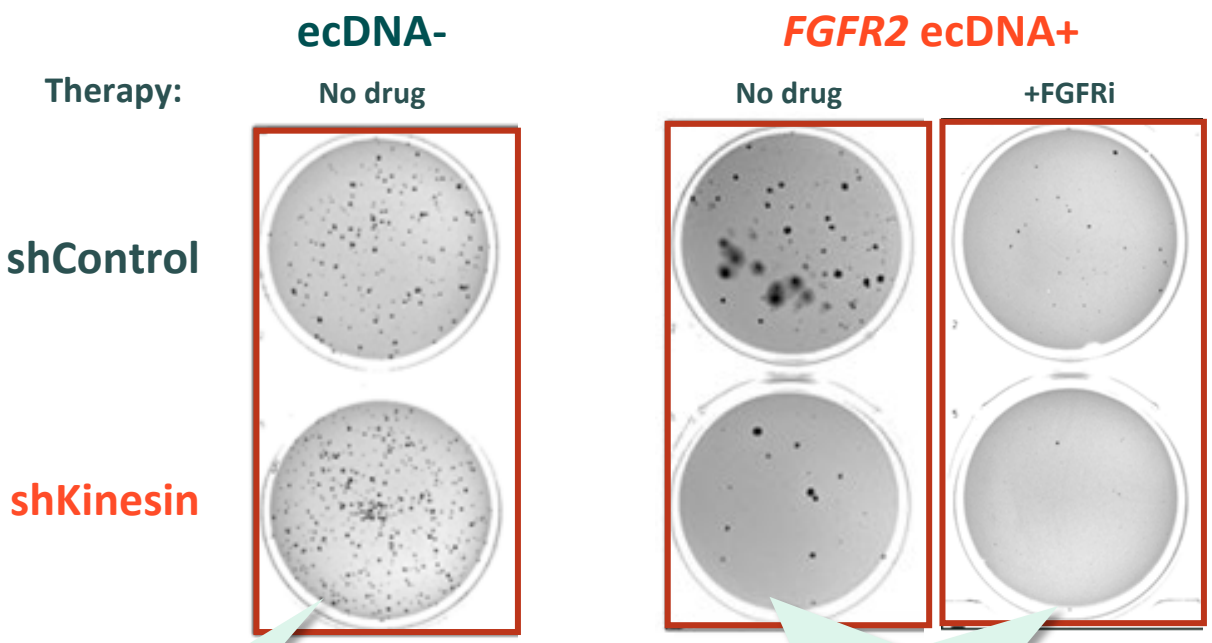
Kinesin was needed to sustain high levels of ecDNA in cancer cells



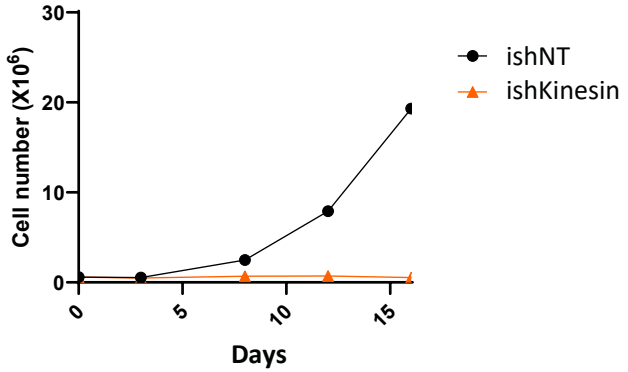


DAPI (DNA) / *DHFR* (ecDNA)

Genetic inactivation of Kinesin resulted in significant anti-proliferation of oncogene amplified tumor cell lines



Anti-tumor activity in *MYCN* amplified cancer cell line



No negative impact on colony growth in ecDNA- cells

Kinesin KD resulted in significant reduction in viability of ecDNA+ cells. Combination with targeted therapy substantially abrogated colony formation

Genetic inhibition resulted in antiproliferation and cytotoxicity in multiple cancer cell lines

KD: knockdown

Boundless identified a novel inhibitor scaffold via multiple high-throughput screens of >1M compounds
Extensive medicinal chemistry effort optimized potent, cell-active, heterobifunctional degraders

HTS/HTL

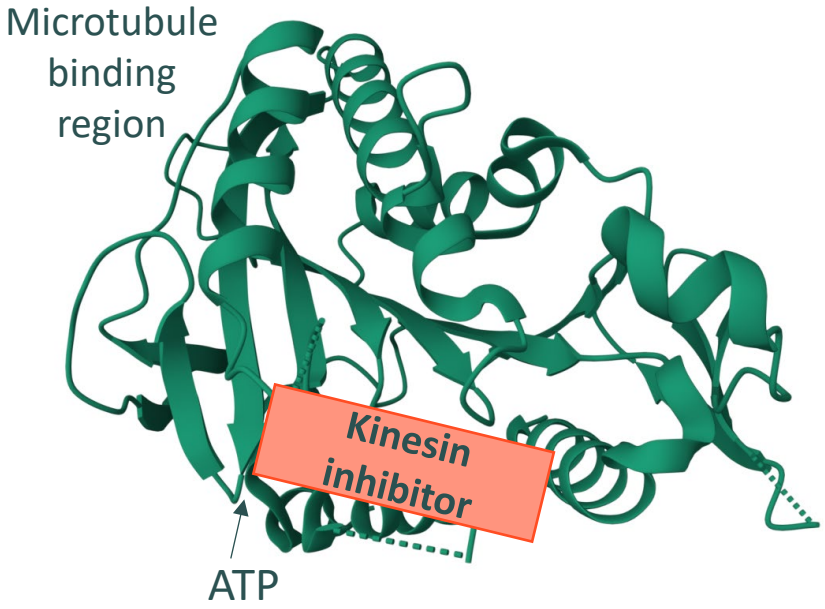
uM biochemical inhibitor series

Inhibitor/ligand SAR

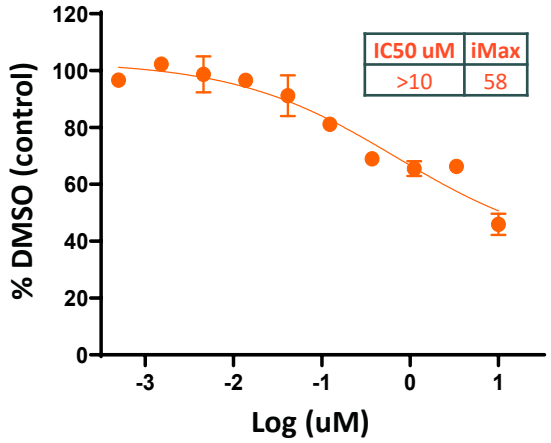
- nM inhibitors
- Selective motor domain binding
- Weak cellular activity

Degrader optimization

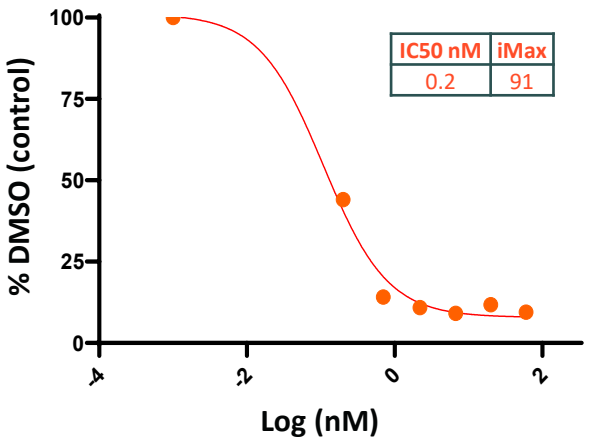
- nM PROTAC degraders
- Robust cellular and *in vivo* activity



Kinesin motor domain bound to inhibitor



Potent inhibitors



Potent degraders

HTL: hit-to-lead
HTS: high throughput screen
SAR: structure activity relationship

BBI-940 achieved Boundless's Kinesin degrader target product profile (TPP)

Product Preclinical Property	TPP	BBI-940
Route of administration **PO bioavailability (mouse/rat/dog)**	Oral >20%	✓
***In vitro* potency (HiBit DC_{50}/DC_{90}, Dmax%)**	<10nM/<100nM, >90%	✓
CYPi	>1uM	✓
hERG	>1000x over target	✓
PD Response (*in vivo* % degradation)	>80%	✓

Oral Druggable Space beyond Lipinski's Rule of Five*

BBI-940 selected as the Development Candidate

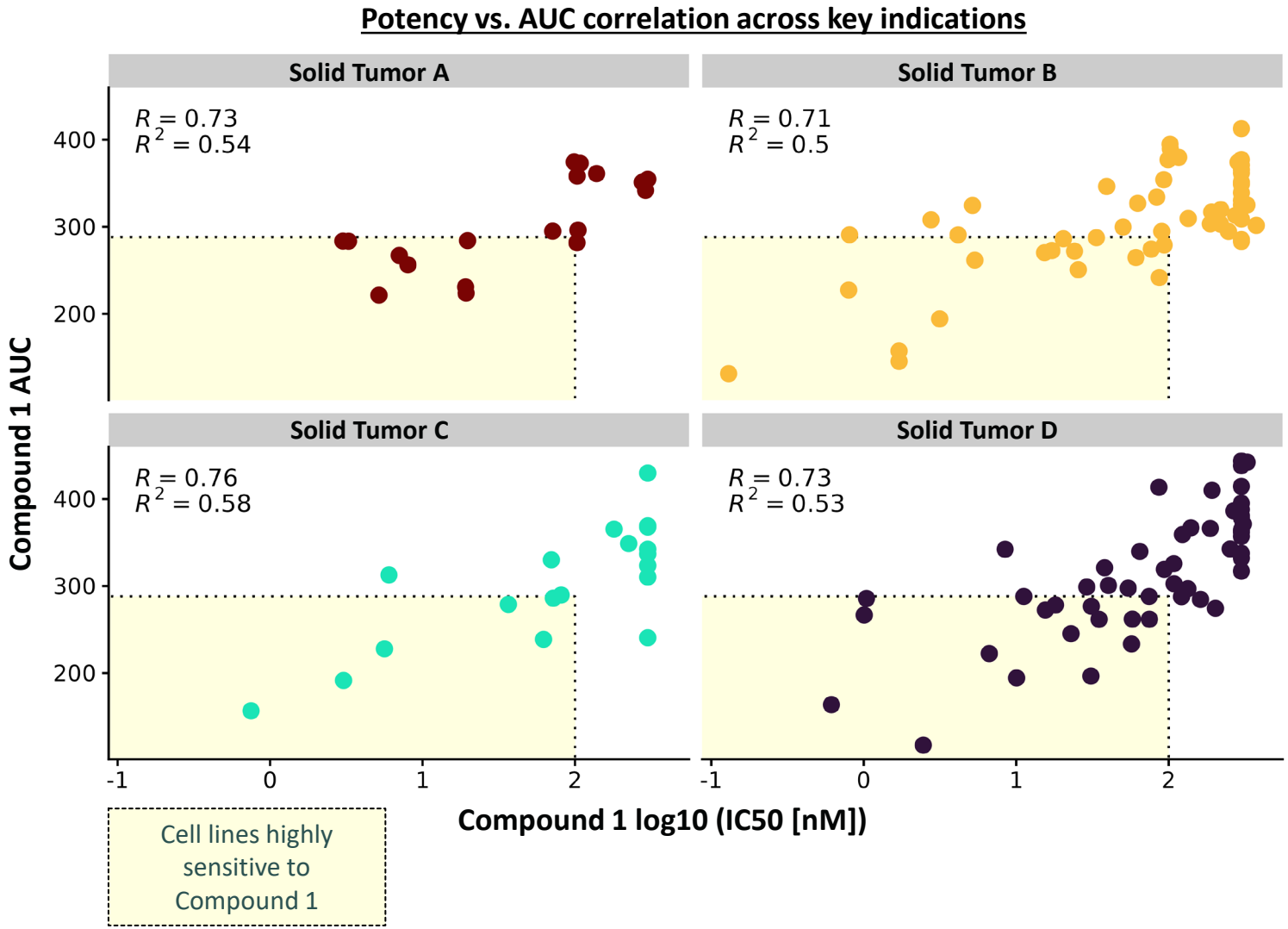
*Commonly used to develop oral degraders

HBA: hydrogen bond acceptors
HBD: hydrogen bond donors
xLogP: hydrophobicity

MW: molecular weight
RB: rotatable bonds
TPSA: topological polar surface area

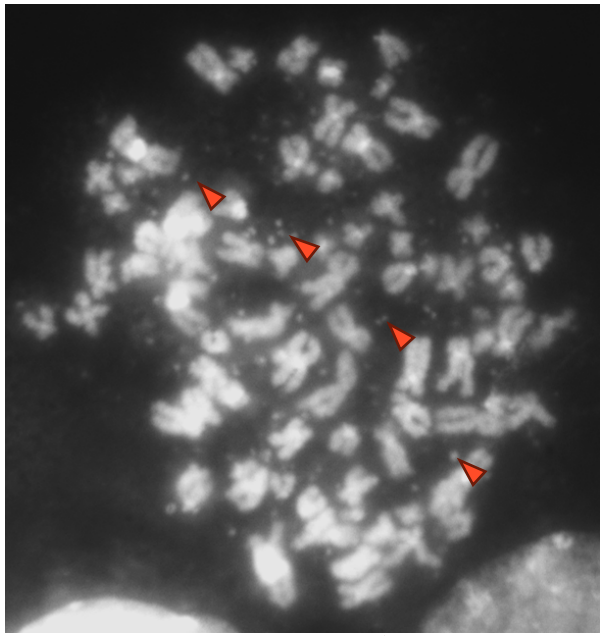
In vitro screen identified multiple tumor types with high sensitivity to Kinesin degradation

- **270+ cell line anti-proliferation screen evaluated sensitivity to lead oral Kinesin degraders**
- **Data demonstrated significant sensitivity (low nM EC_{50}) correlated with low AUC values in a subset of cell lines across various tumor types**

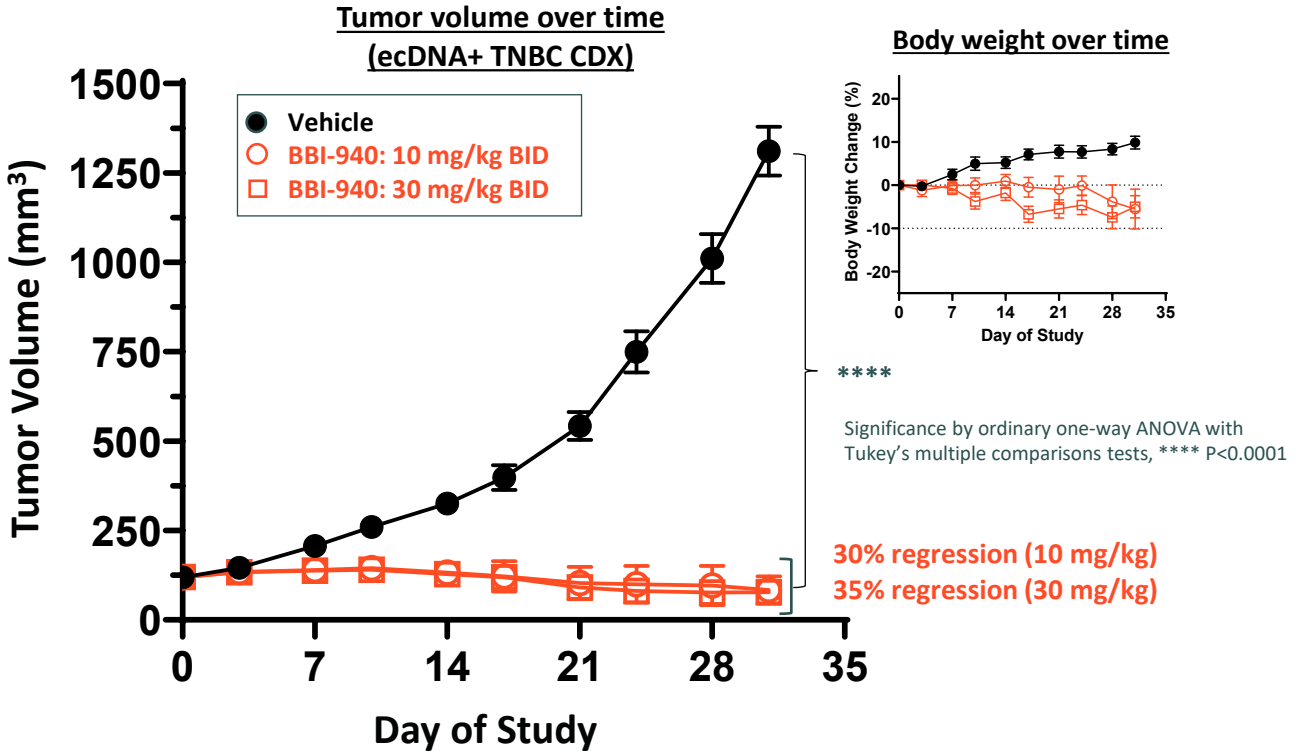


AUC: area under curve
Compound 1: close analog to BBI-940

BBI-940 induced tumor regressions in TNBC xenograft model



Referring to ecDNA



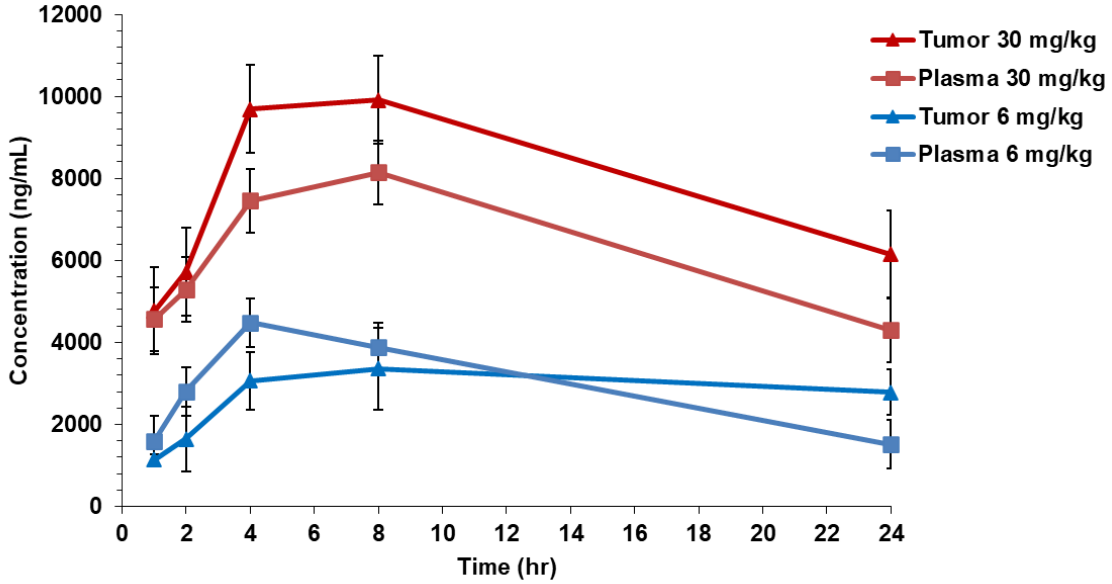
Significance by ordinary one-way ANOVA with Tukey's multiple comparisons tests, **** P<0.0001

- Monotherapy regression demonstrated with oral administration in a gene amplified ecDNA+ TNBC model
- BBI-940 demonstrated sustained regressions at both doses tested
- BBI-940 generally well tolerated (body weight loss <10%)

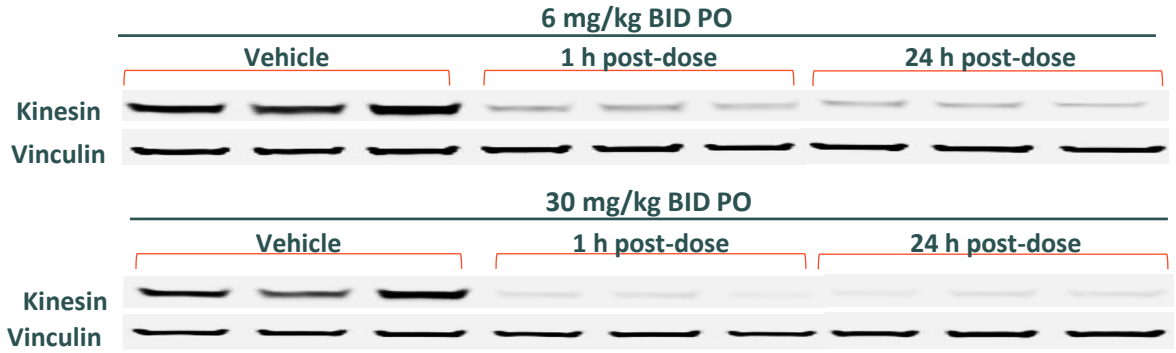
TNBC: triple-negative breast cancer

PK/PD of Kinesin oral degraders consistent with anti-tumor activity

Mean plasma and tumor concentration over time



Tumoral Kinesin protein after 5.5 days of Compound 1 dosing



- Orally administered Kinesin degraders displayed dose-proportional exposure, with good tumor penetration
- Tumor free concentrations sustained for dosing duration sufficient to drive 70-80% degradation

Compound 1: close analog to BBI-940

Boundless Bio: leveraging novel cancer biology to advance unique-in-class development strategies

Runway extension

- On Friday, Boundless eliminated ~20 positions, representing ~1/3 of our workforce
- With $138M of cash and equivalents on the balance sheet as of March 31, 2025, focused operations are expected to provide cash runway into 1H:28

Boundless Bio is leading a compelling and differentiated approach to address oncogene amplified cancers

Dedicated to Oncogene Amplified Cancers by Targeting Unique Cancer Biology

- **Oncogene amplifications**: one of cancer's highest unmet medical needs, represents expansive addressable market
- **ecDNA**: a root cause of amplification; Boundless Bio's unique lens into differentiated cancer biology
- **Spyglass**: ecDNA-focused platform to discover novel drug targets for oncogene amplified cancer
- **ecDTx**: multiple potentially first-in-class therapeutic programs

Fortress Position, Track Record of Success, Well-Funded

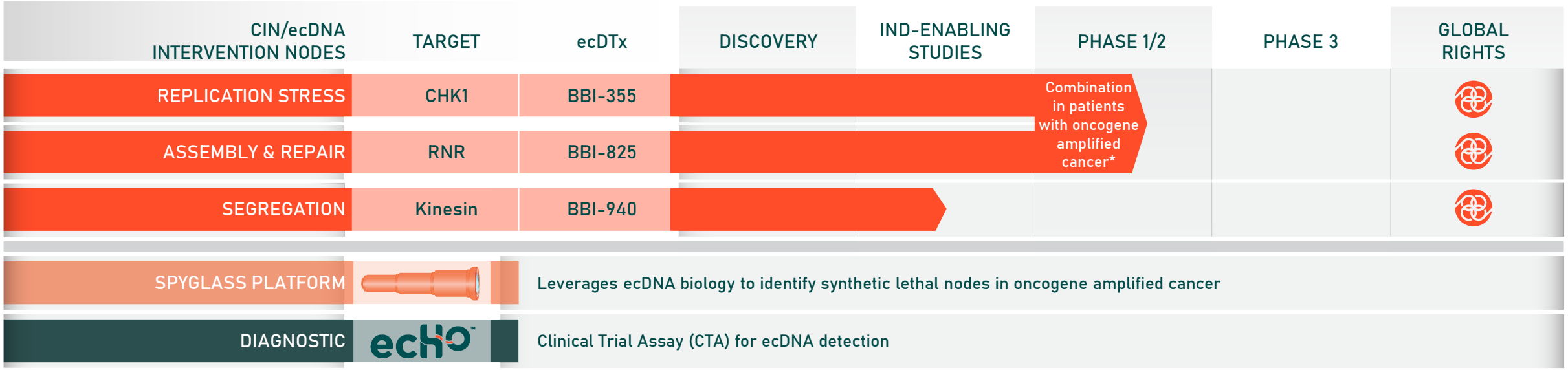
- Founded by world's leading ecDNA experts; led by experienced management team with a track record of precision oncology drug approvals and multi-$B M&A
- All ecDTx internally discovered and wholly-owned
- Approximately $138M in cash and equivalents*, expected to provide cash runway into 1H 2028

Multiple Highly-Differentiated Value Drivers

ecDTx	Target	Intervention Node	Anticipated Milestones
BBI-355 / BBI-825	CHK1 & RNR	Replication Stress; DNA Assembly & Repair	Initial clinical POC from Phase 1/2 POTENTIATE trial within existing cash runway
BBI-940	Kinesin	DNA Segregation	Submit IND in 1H 2026. Initial clinical POC from first-in-human clinical trial within existing cash runway

*Total pro forma cash, cash equivalents, and short-term investments as of 3/31/2025

Next-generation precision oncology pipeline to address high unmet needs in oncogene amplified cancer



ecDTx: Therapeutic Candidates echo™: Diagnostic Candidate

CIN: chromosomal instability
ecDNA: extrachromosomal DNA
ecDTx: ecDNA-directed therapy

CHK1: checkpoint kinase 1
RNR: ribonucleotide reductase
ECHO: ecDNA Harboring Oncogenes; BBI's proprietary ecDNA diagnostic

*BBI-355+BBI-825 combination study to commence pending U.S. regulatory clearance

BOUNDLESS BIO

Unbound by convention, bound to save lives

www.boundlessbio.com
@BoundlessBio