BOUNDLESS BIO™

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

Corporate Presentation

December 2024

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), ecDNA diagnostic candidate, and other development programs, the timing of expected readouts, the potential therapeutic benefits of our ecDTx, the timing and likelihood of regulatory filings and approvals for our ecDTx, 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 directed against ecDNA in 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; 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 quarterly report on Form 10-Q for the quarter ended March 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.

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

Oncogene amplified cancer:

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

ecDNA:

- Cancer-specific circular DNA—a root cause of oncogene amplification
- Transformative emerging area of cancer biology
- Spyglass drug discovery platform identifies ecDNA synthetic lethalities

ecDNA-directed therapies (ecDTx):

- BBI-355: oral CHK1 inhibitor, Phase 1/2 initial clinical POC data expected in 2H 2025
- BBI-825: oral RNR inhibitor, Phase 1/2 trial not to advance at this time
- ecDTx 3: targets novel kinesin, advancing toward development candidate by mid-2025
- ECHO diagnostic identifies ecDNA+ cancers to enable patient selection

Experienced team:

- Track record of precision oncology drug and diagnostic approvals, multi-$B M&A
- Leading ecDNA scientific founders, board, advisors
- Cash runway into 2027; funding BBI-355 through initial POC data and key milestones for ecDTx 3

1. United States, EU, and Japan

ecDTx: ecDNA-directed therapy
ECHO: ecDNA Harboring Oncogenes; BBI's proprietary ecDNA diagnostic

ecDNA are cancer-specific, circular units of DNA that are a frequent driver of oncogene amplified cancer

Normal chromosome

EGFR

Unaltered gene

Transformation to cancer

Altered oncogene

Mutation

EGFR

OR

Fusion

BCR

ABL

- ~14-18% of cancer patients have mutations or fusions
- 40+ FDA approved TKIs
- ~$20B in annual sales

Amplified oncogene

Chromosomal amplification

EGFR

extrachromosomal DNA (ecDNA) amplification

EGFR EGFR EGFR EGFR

- 25% of cancer patients have amplified oncogenes
- No approved therapies, except HER2 inhibitors (over $10B in annual sales)
- **~50% of high-copy number amplifications are on ecDNA**

NEXT FRONTIER OF ONCOLOGY

~1.3m patients per year[1]
Oncogene amplified cancer

~750k patients per year[1]
ecDNA-enabled cancer

TM

TKI: tyrosine kinase inhibitor

1) Patients in US, EU, and Japan; numbers of patients based on third-party sources and internal estimates

Next-generation precision oncology pipeline targets ecDNA to address high unmet need cancer patients

ecDTx: Therapeutic Candidates echo: Diagnostic Candidate

CHK1: checkpoint kinase 1
ecDTx: ecDNA-directed therapy
RNR: ribonucleotide reductase

ECHO: ecDNA Harboring Oncogenes; BBI's proprietary ecDNA diagnostic

Accomplished leadership team has proven experience delivering value for patients and shareholders

Zachary Hornby

Chief Executive Officer, President, Director

ignyta · Roche · Fate Therapeutics · Halozyme · Neurocrine Biosciences · Rozlytrek (entrectinib 100mg | 200mg capsules)

Christian Hassig, PhD

Chief Scientific Officer

Sierra Oncology · Sanford Burnham Prebys · kalypsys · Scripps Research · Ojjaara (momelotinib 200 mg · 150 mg · 100 mg tablets)

Klaus Wagner, MD/PhD

Chief Medical Officer

INHIBRX · Genentech · Novartis · The University of Texas MD Anderson Cancer Center (Making Cancer History®) · Tarceva® erlotinib

Neil Abdollahian

Chief Business Officer

CIDARA Therapeutics · Trius Therapeutics · AVANIR Pharmaceuticals · IONIS

Jessica Oien, JD

Chief Legal Officer

CIDARA Therapeutics · Otonomy · élan · Somaxon Pharmaceuticals

Extended management team experience

LOXO Oncology at Lilly · MERCK · Herceptin HYLECTA™ (trastuzumab and hyaluronidase-oysk) injection for subcutaneous use · Retevmo® (selpercatinib capsules 40 mg · 80 mg) · VITRAKVI® (larotrectinib) 25-mg/100-mg capsules, 20-mg/mL oral solution

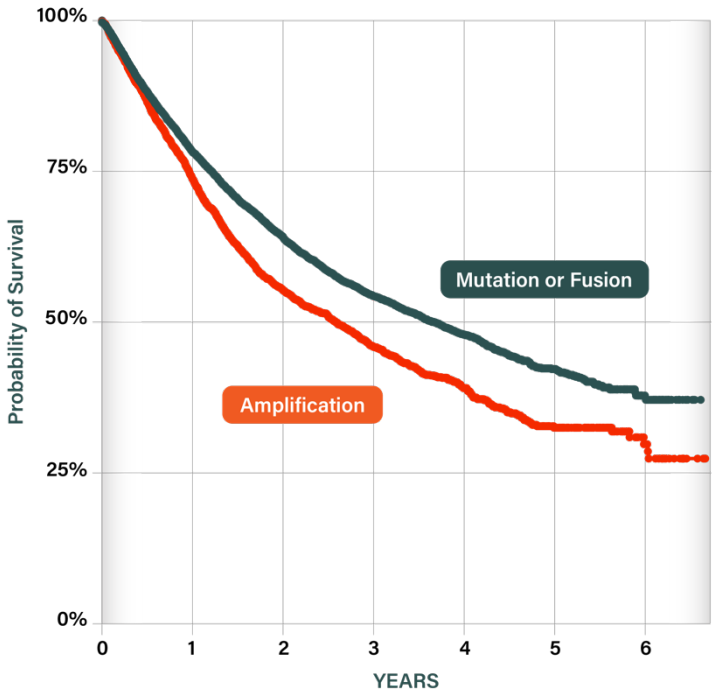
Significant unmet need in oncogene amplified cancers

Cancers with oncogene amplifications: more aggressive, difficult to treat, and worse prognosis

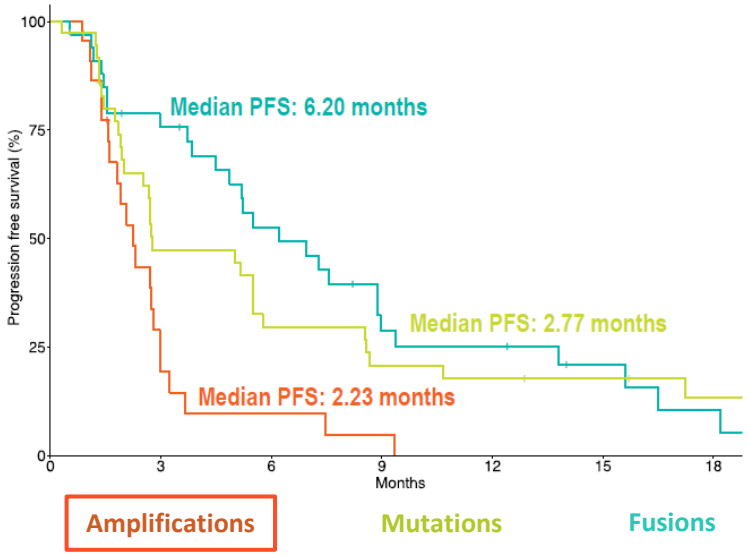
Oncogene amplified cancers

- Oncogene amplification is a type of oncogenic alteration where extra copies (>2) of an oncogene (e.g., *EGFR*) drive tumor growth or resistance
- Patients with oncogene amplifications have worse survival than other cancer patients
- Unlike other alterations, oncogene amplified tumors are generally unresponsive to targeted therapies and immunotherapies

Survival of cancer patients, segmented by oncodriver status[1]



PFS of cancer patients with *FGFR* alterations treated with FGFR inhibitors



*Patients with primary or metastatic cancers with **amplifications, point mutations, skipping deletions or fusions** of these genes: AR, ALK, ARAF, BRAF, CCND1, CDK4, CDK6, EGFR, ERBB2, FGFR1, FGFR2, FGFR3, FGFR4, HRAS, IDH1, IDH2, KIT, KRAS, MAP2K1, MAP2K2, MAP2K4, MDM2, MET, MYC, NF1, NRAS, NTRK1, NTRK2, NTRK3, PDGFB, PDGFRA, PDGFRB, PIK3CA, RAF1, RET, ROS1*

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1. cBioPortal analysis using MSK-IMPACT (N=14,674 patients) and MSK-MET (N=1,115 patients) data; p-value = < 0.0001
PFS: progression free survival

Pobel et. al. *ESMO TAT Virtual Congress*. 2021

Despite advancements in precision medicine, cancers with gene amplifications generally do not respond to targeted therapies

TARGETED THERAPY	TARGET	APPROVED	NO APPROVAL
IBRANCE palbociclib; Verzenio abemaciclib; KISQALI ribociclib 200 mg tablets	CDK4/6	HR+/HER2- breast cancer → ✗	Amplification
IRESSA gefitinib; GILOTRIF (afatinib) tablets; RYBREVANT (amivantamab-vmjw) Injection for IV Use | 350 mg/7 mL (50 mg/mL); Tarceva erlotinib; TAGRISSO osimertinib; EXKIVITY mobocertinib 40 mg capsules	EGFR	L858R NSCLC T790M NSCLC Exon 19 deletion NSCLC Exon 20 insertion NSCLC → ✗	Amplification
Balversa (erdafitinib) 3, 4, 5 mg tablets; Pemazyre (pemigatinib) tablets 13.5mg·9mg·4.5mg; LYTGOBI (futibatinib) tablets	FGFR	*FGFR3* mutation bladder cancer *FGFR2/3* fusion cholangiocarcinoma → ✗	Amplification
TABRECTA (capmatinib) tablets 150 mg · 200 mg; TEPMETKO (tepotinib)	MET	Exon 14 skipping NSCLC → ✗	Amplification

A new approach is needed to treat cancers driven by oncogene amplifications

Across most oncogenes, patients with gene amplified tumors derive little benefit from targeted therapies

Targeted therapies have not been approved for,
nor demonstrated robust clinical activity in, most oncogene amplified cancers*

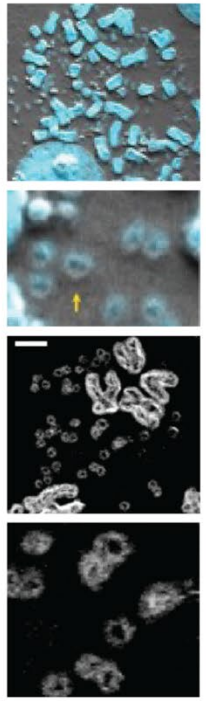
ORR: overall response rate
NSCLC: non-small cell lung cancer

*HER2+ cancers excluded, as they are successfully addressed by HER2 inhibitor therapies

ecDNA: a key driver of oncogene amplifications

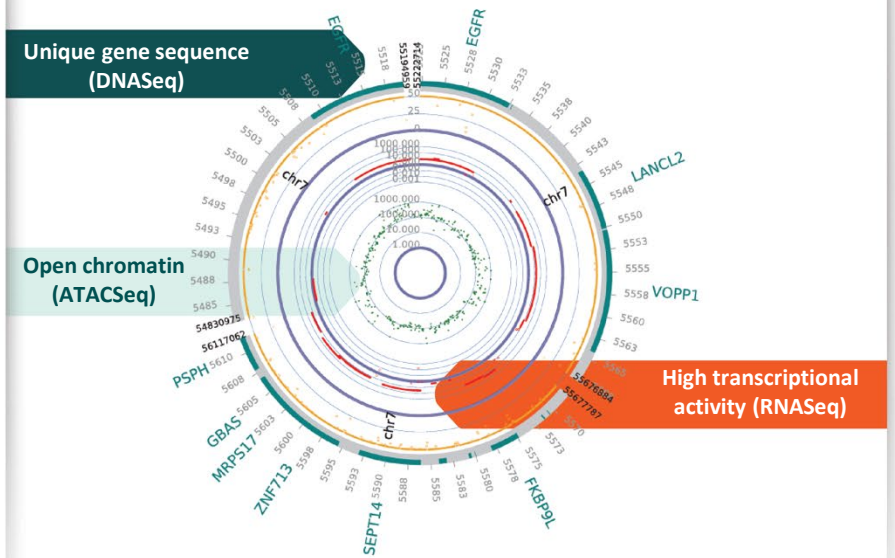
ecDNA are a primary driver of oncogene amplified cancers and enable resistance to targeted therapies

ecDNA are circles of DNA, distinct from chromosomes, that amplify full-length genes and regulatory elements



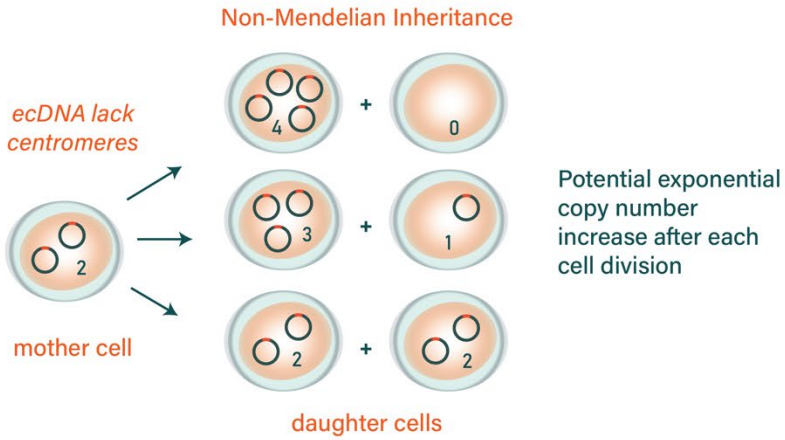
Large size: 2 – 5 Mbp

Circular shape of ecDNA enhances transcriptional activity, leading to high oncogene expression

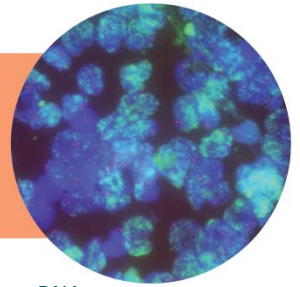


Active Gene Expression

ecDNA asymmetrically segregate during mitosis, enabling exponential copy number increase or decrease during cellular division



Protein products of genes amplified on ecDNA can provide a fitness advantage – driving cancer growth and resistance

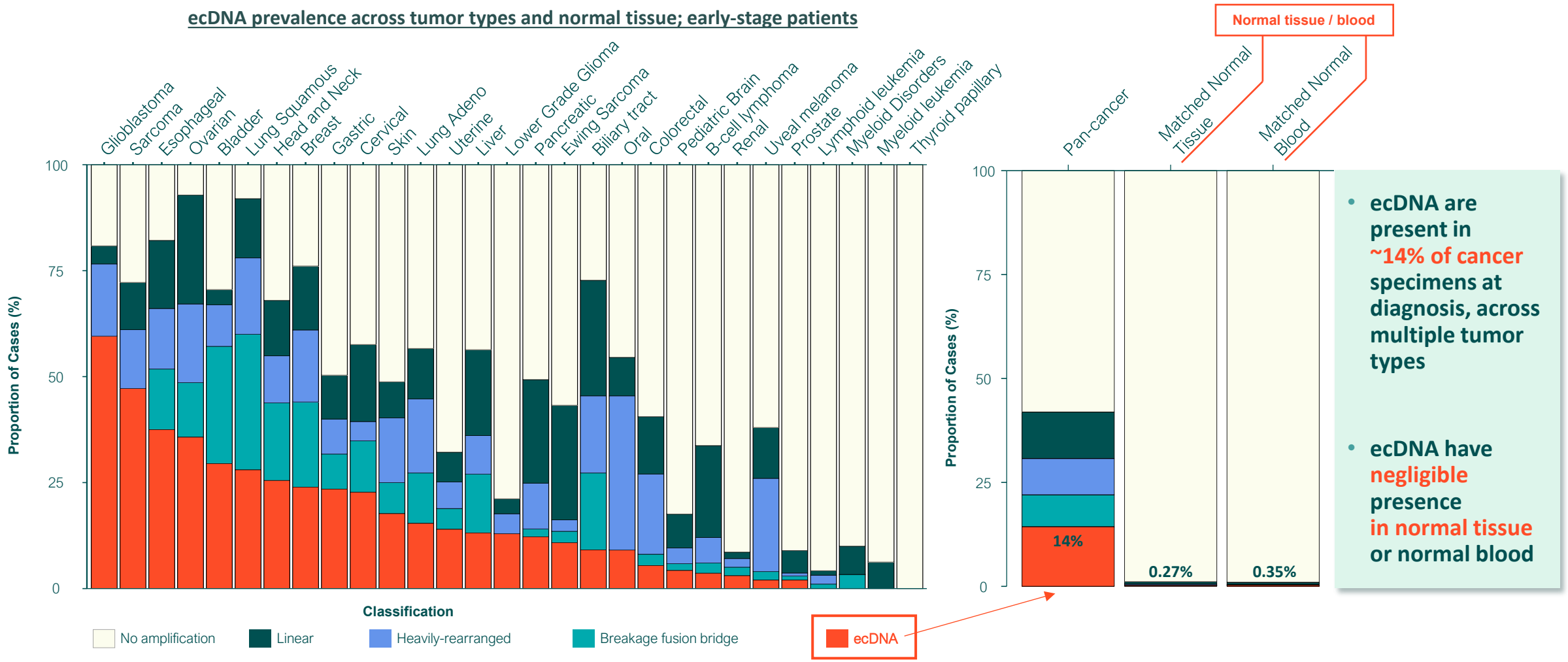


MYCN amplifications on ecDNA in pediatric neuroblastoma

Mbp: mega base pairs

Wu, Turner… Verhaak, Chang, Bafna, Mischel. 2019 Nature

ecDNA are detected broadly across different cancer types, but not in normal tissue or blood



- ecDNA are present in ~14% of cancer specimens at diagnosis, across multiple tumor types
- ecDNA have negligible presence in normal tissue or normal blood

Analysis of WGS data from >3,000 tumor and matched normal samples from donors to TCGA and PCAWG

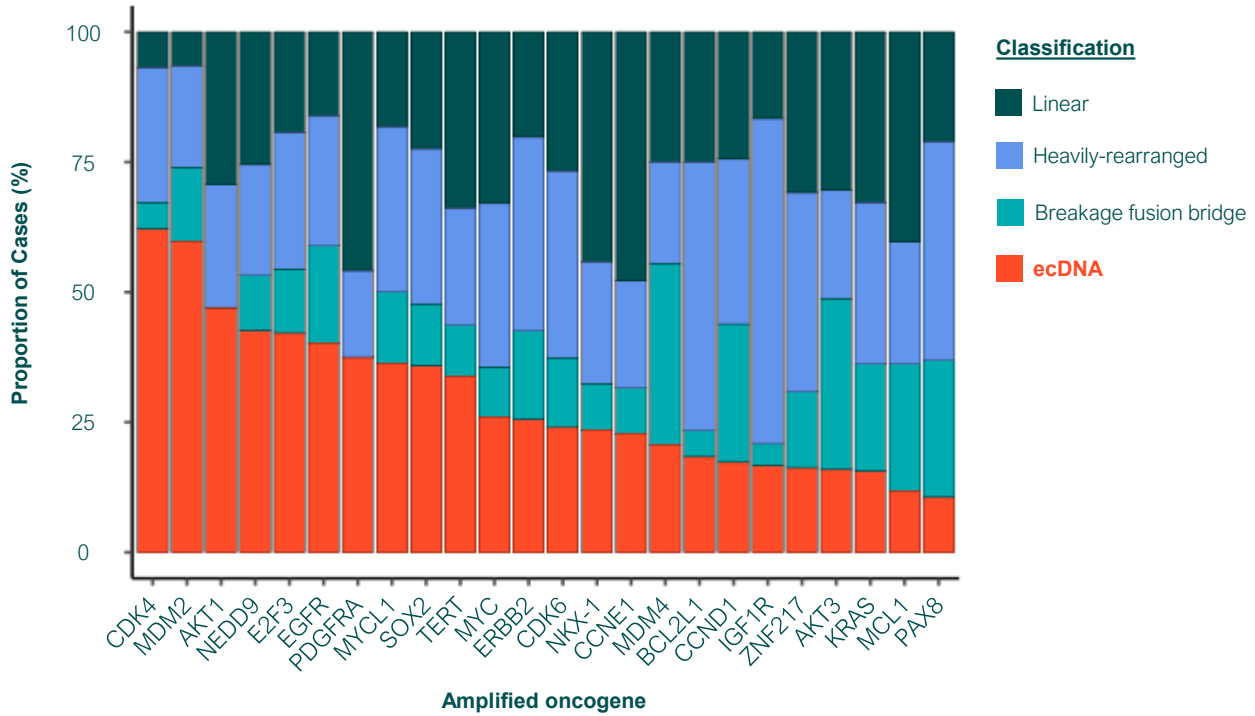
Kim, Nguyen, Turner, et al. 2020 Nature Genetics

PCAWG: Pan-Cancer Analysis of Whole Genomes
TCGA: The Cancer Genome Atlas
WGS: Whole Genome Sequencing

Cancer's most common high copy number oncogene amplifications frequently occur on ecDNA; when they do, it is associated with worse survival

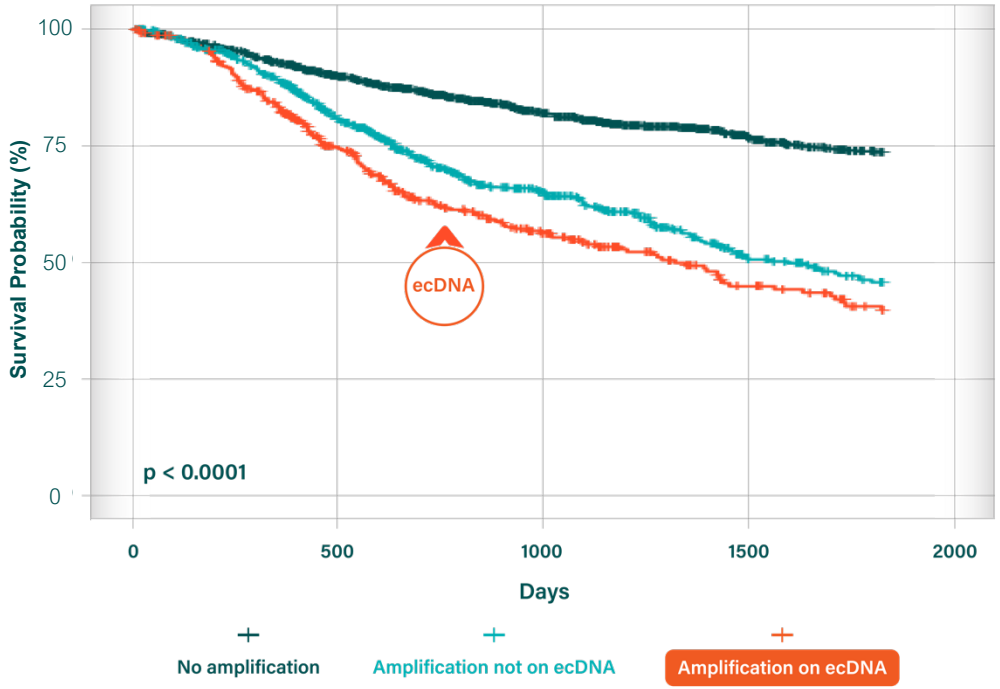
~54% of high-copy number oncogene amplifications are detected on ecDNA

Most frequently amplified oncogenes, segmented by amplification type



Patients with oncogene amplification *on ecDNA* have worse survival

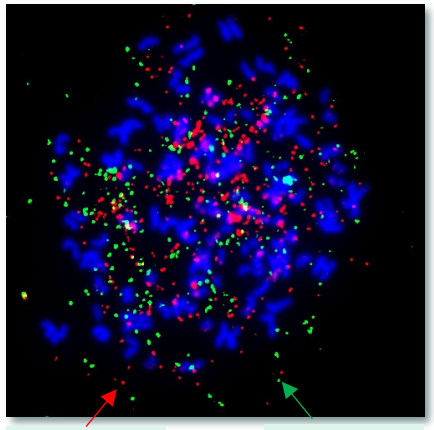
Survival of cancer patients, segmented by gene amplification status



Adapted from Kim, Nguyen, Turner, et al. 2020 Nature Genetics
High copy number defined as ≥8 gene copies for this analysis

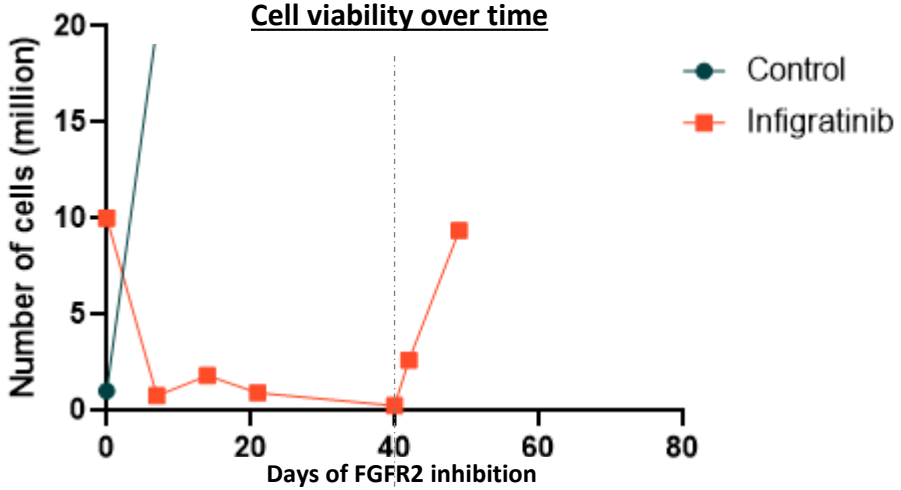
ecDNA enable cancer cells to resist therapies by rapidly adapting oncogene dependency

Gastric cancer cells pre-treatment

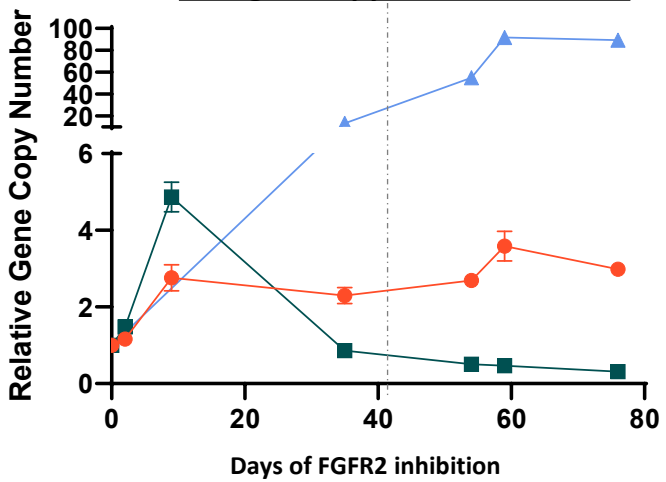


FGFR inhibitor (infigratinib)

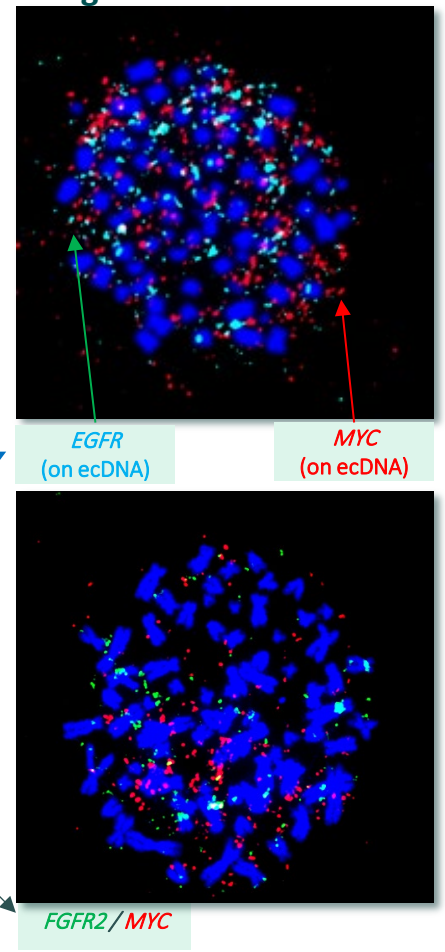
Cell viability over time



Oncogene copy number over time



FGFR inhibitor resistant gastric cancer cells

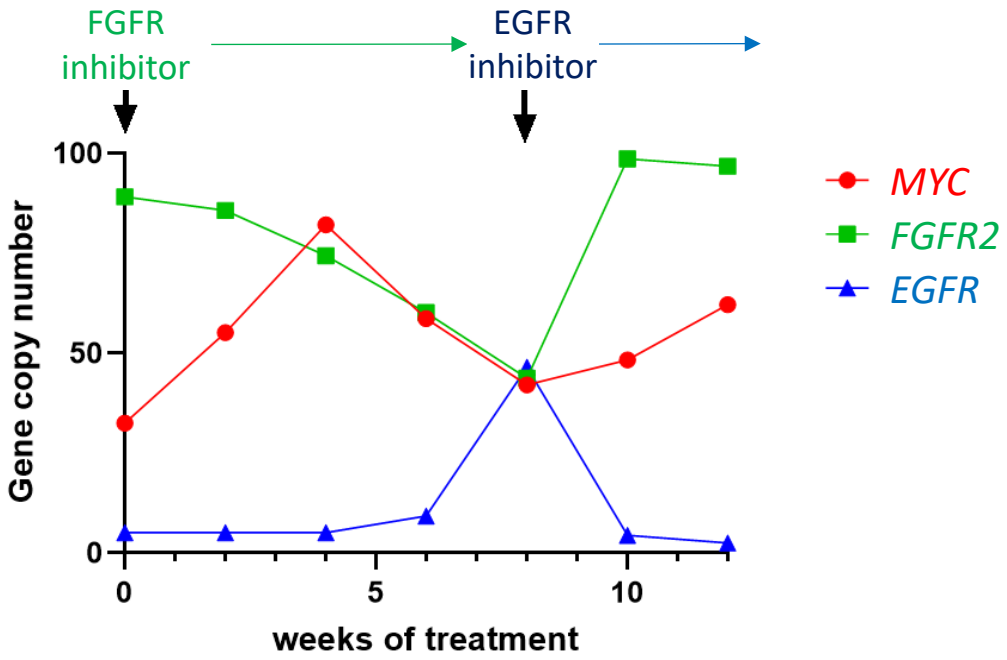


In this model, ecDNA enable gastric cancer cells to rapidly switch oncogene dependency from *FGFR2* to *EGFR* under therapeutic pressure

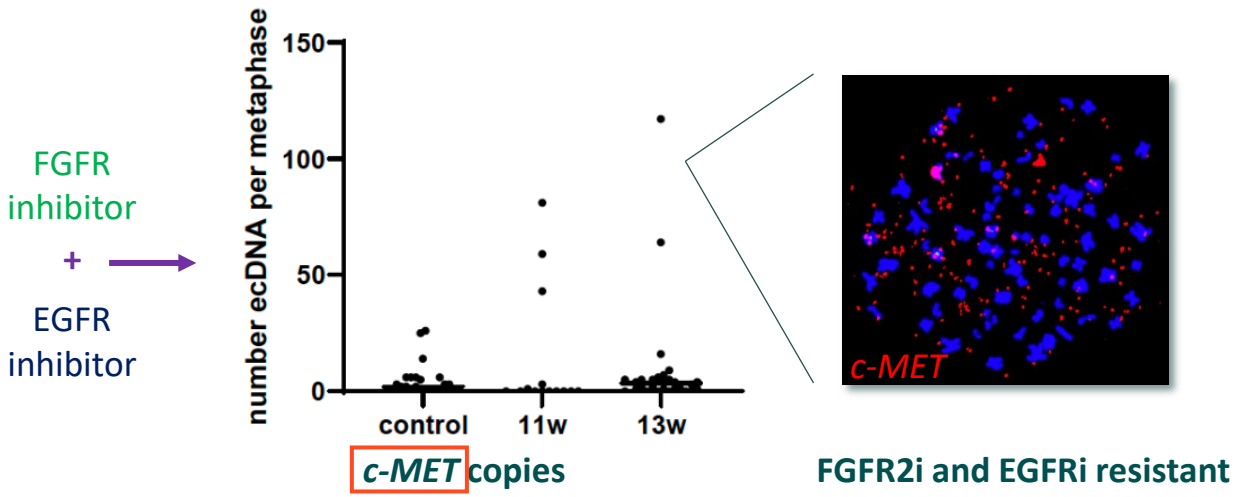
Turner, et al. Cancer Res 2021.

Tumors employ ecDNA to rapidly enable new oncogenic drivers, even under combination target inhibition

Oncogene copy on ecDNA changes dynamically in response to *sequential targeted therapeutic pressure*



New oncogene populations can arise on ecDNA in response to *combination targeted therapeutic pressure*



Inhibition of EGFR results in return of *FGFR2* => ecDNA amplification supports oncogenesis

Simultaneous dual inhibition of FGFR2 and EGFR leads to ecDNA driven amplification of new oncogene (*c-MET*)

Only targeting oncogenes amplified on ecDNA is a futile therapeutic approach due to ecDNA-enabled process of continuous and rapid oncogene dependency switching

Turner, et al. Cancer Res 2021.

Driving a new treatment paradigm by targeting ecDNA pathways that enable tumor evolution and resistance

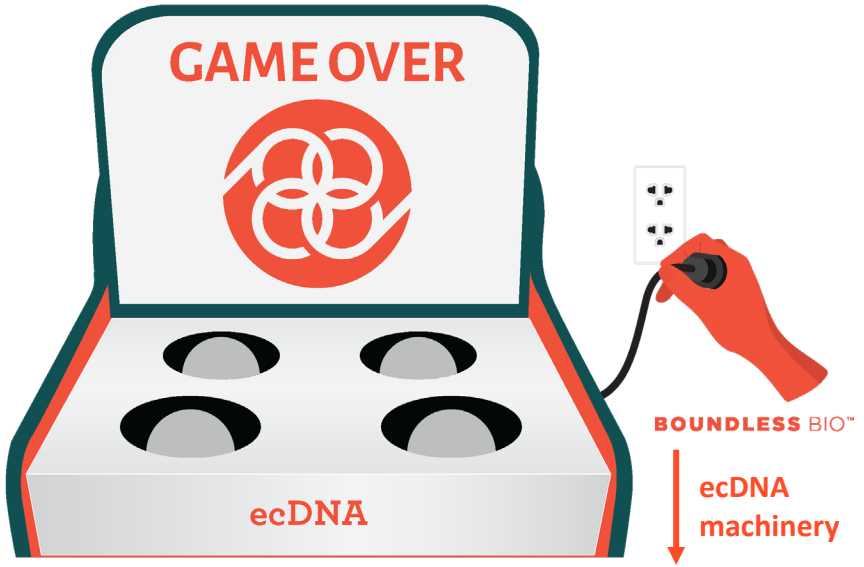
Traditional Targeted Therapy:

Develop targeted inhibitors against activated oncodriver targets, but cells typically develop **resistance**

Applying traditional targeted therapy approach to ecDNA enabled cancers is clinical 'Whac-a-Mole'

Next Generation Precision Oncology:

Exploit underlying vulnerabilities in **ecDNA-driven cells** to drug targets essential for ecDNA functionality in cancer

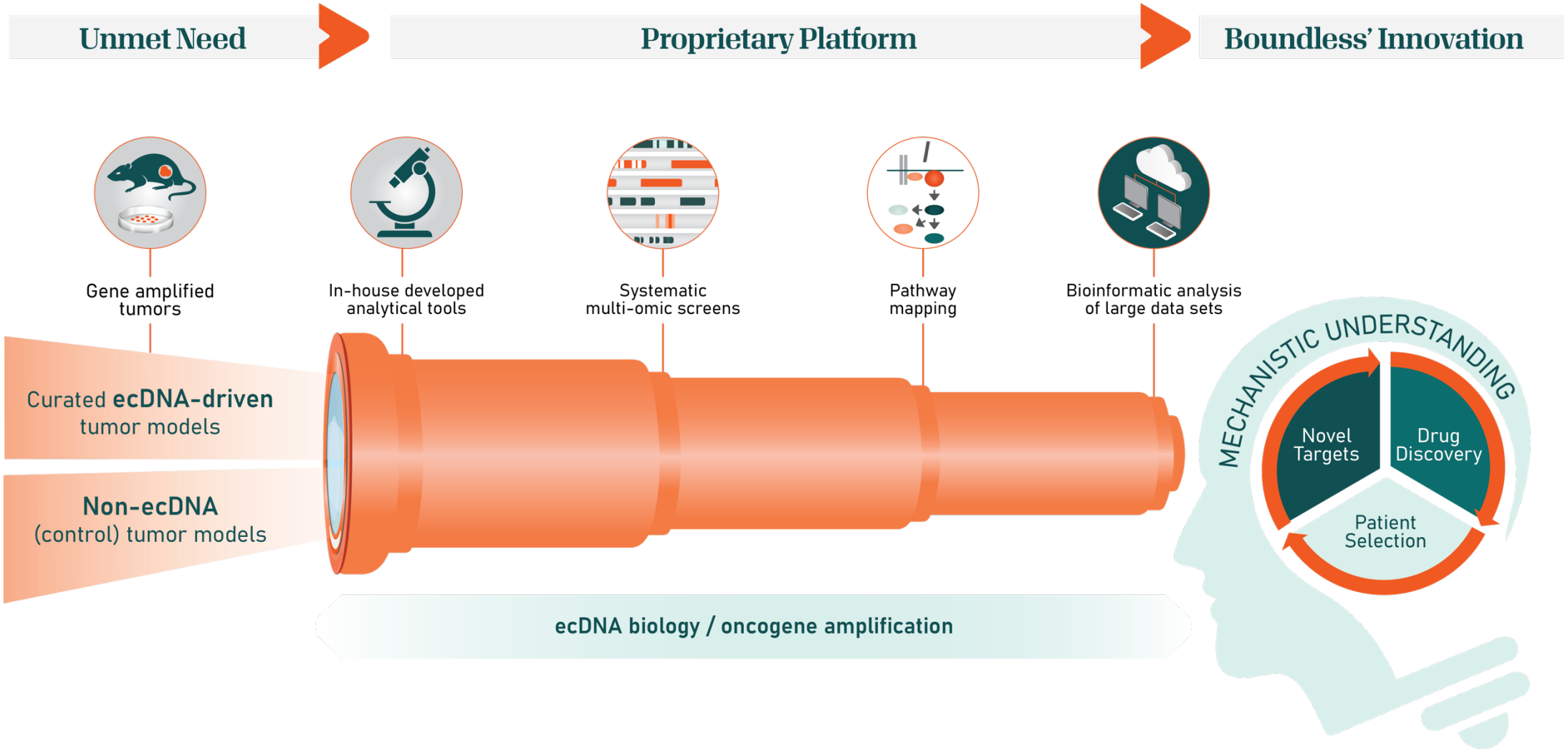


Disable ecDNA functionality =>
No more oncogene amplifications

- **Replication & transcription**
- **Assembly & repair**
- **Segregation**

Spyglass: unique platform for interrogating ecDNA-driven tumors

Proprietary target and drug candidate discovery engine



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

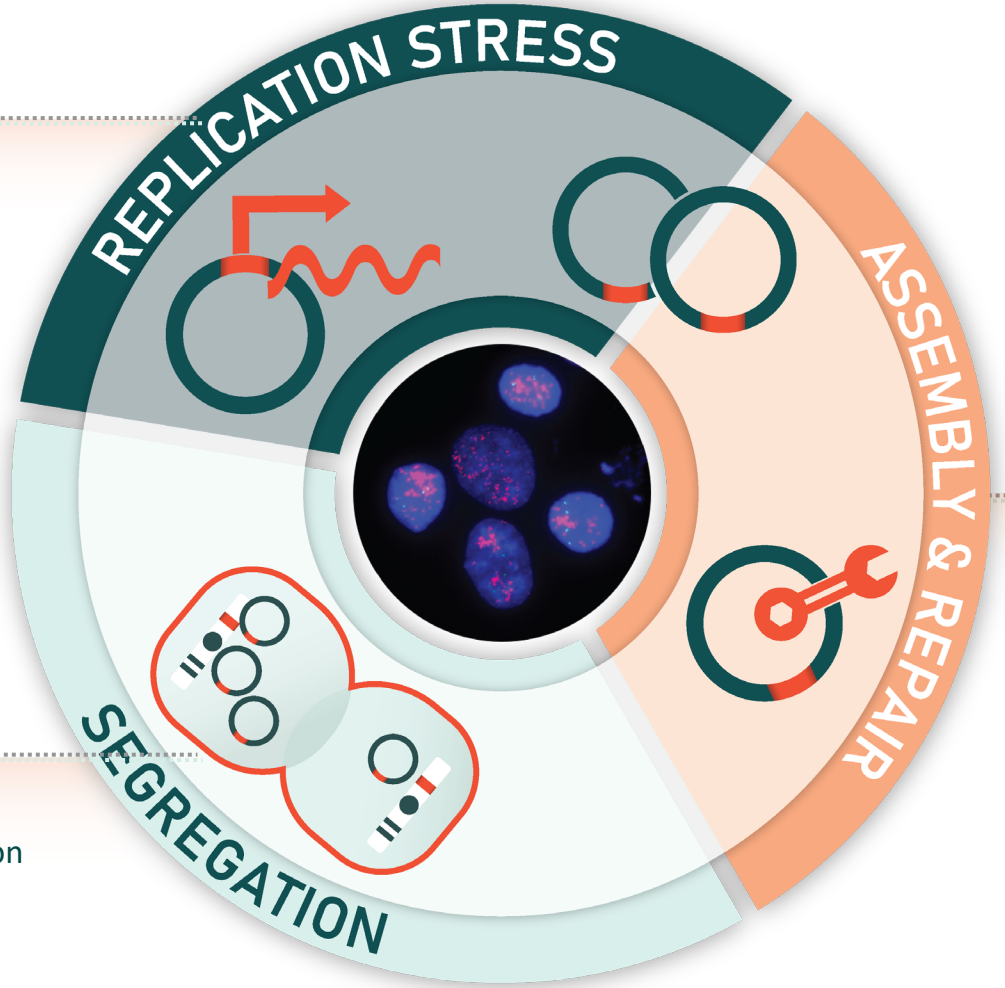
CHK1

BBI-355: PHASE 1/2 ENROLLING

Novel, oral, selective inhibitor of CHK1

BBI-098: 2nd generation CNS-penetrant CHK1i

CHK1 is master regulator of ecDNA-induced replication stress



RNR

BBI-825: PHASE 1/2

Novel, oral, selective inhibitor of RNR

RNR is a rate-limiting enzyme for assembly and repair of ecDNA

Novel kinesin

ecDTx 3: LEAD OPTIMIZATION

Kinesin required for proper segregation of ecDNA during cell division

CHK1: checkpoint kinase 1
RNR: ribonucleotide reductase

ECHO: novel investigational diagnostic test designed to detect ecDNA using routine clinical NGS data

Non-significant risk ("NSR") determination granted by FDA for use in Phase 1/2 POTENTIATE trial of BBI-355

Standard Platform

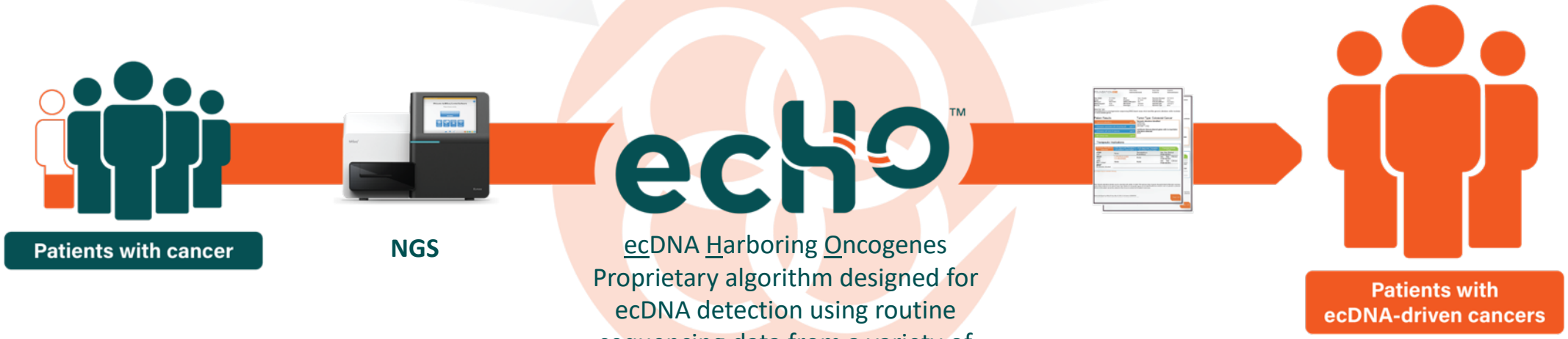
Agilent Technologies illumina

Compatible with commercial hybrid-capture NGS panel

Development Partner

SOPHiA GENETICS™

Clinical Trial Assay Development for POTENTIATE



ecDNA Harboring Oncogenes

Proprietary algorithm designed for ecDNA detection using routine sequencing data from a variety of NGS panels

Feasibility Demonstrated

TEMPUS CARIS LIFE SCIENCES

Feasibility demonstrated using commercial NGS data files

Locally Deployed

Memorial Sloan Kettering Cancer Center

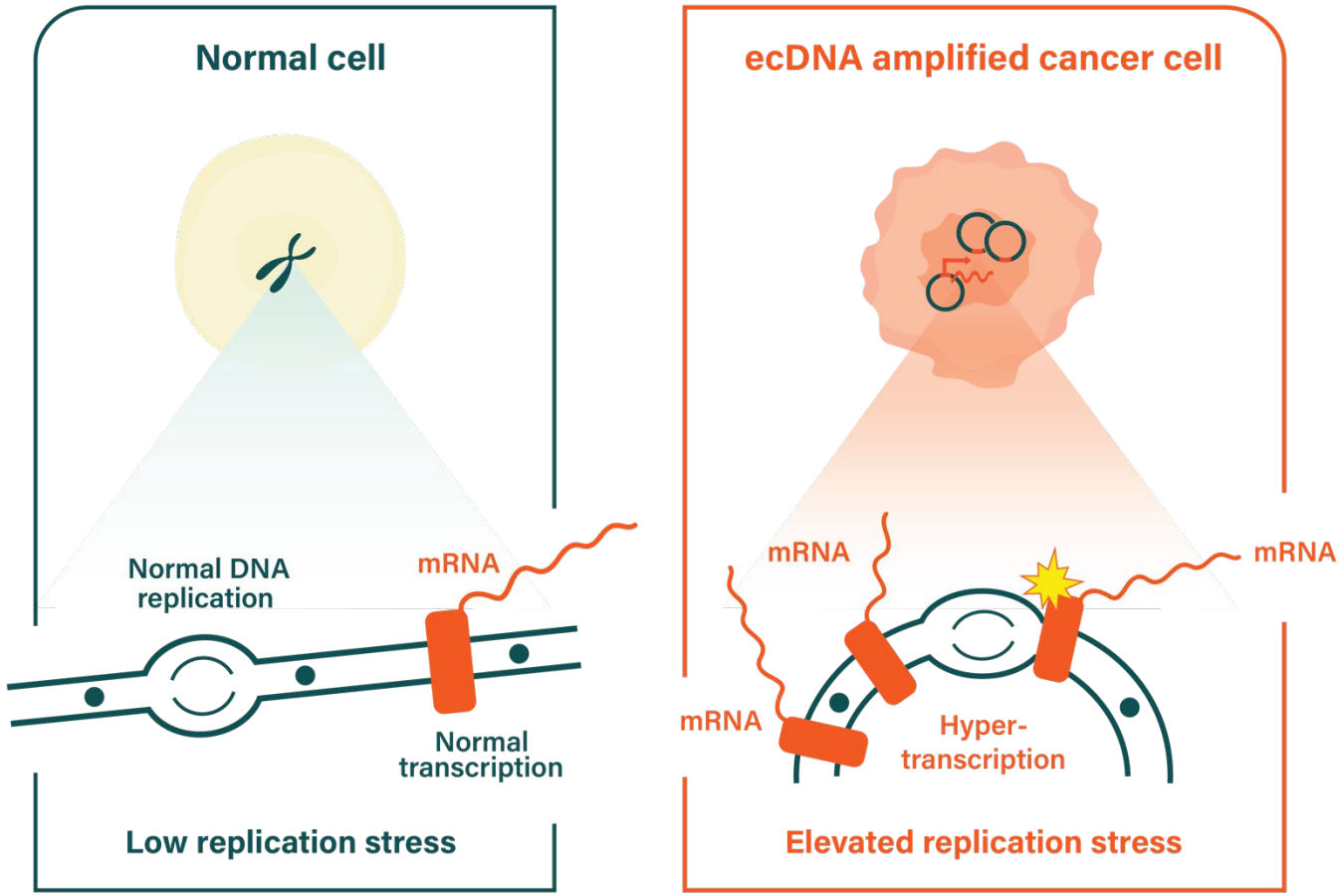
ECHO locally adopted at POTENTIATE clinical trial site for research studies

NGS: next-generation sequencing

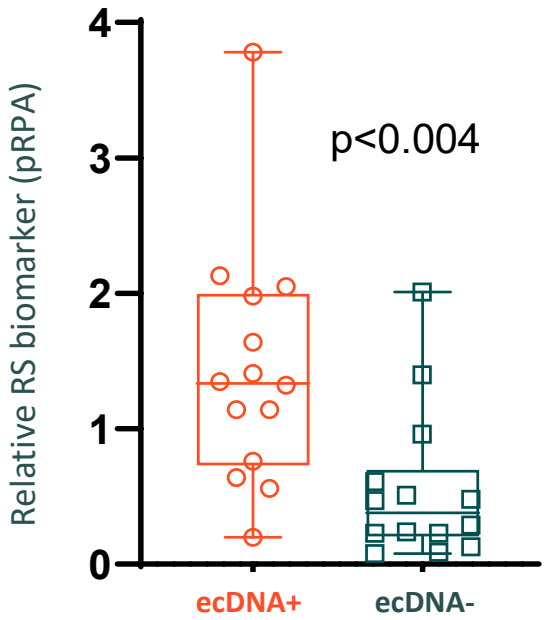
BBI-355: potentially best-in-class, oral, selective CHK1 inhibitor in Phase 1/2 POTENTIATE trial

First ecDTx; targets ecDNA-induced replication stress

ecDNA+ oncogene amplified cancer cells have significantly elevated replication stress (RS)



ecDNA amplified tumor cells display hallmarks of elevated RS



RS biomarker: phosphorylated replication protein A (pRPA)
Chowdhry et al. Cancer Res 2022.

Inhibition of checkpoint kinase 1 (CHK1) is synthetic lethal in ecDNA+ cancer cells

CHK1 is a master regulator of the RS response

High copy number amplification and rampant transcription on ecDNA results in elevated RS

Consequently, ecDNA amplified cells have significantly increased reliance on CHK1 for survival

Inhibition of CHK1 further exacerbates RS, resulting in synthetic lethality in ecDNA+ cancer cells

Elevated replication stress

Role of activated CHK1 in RS

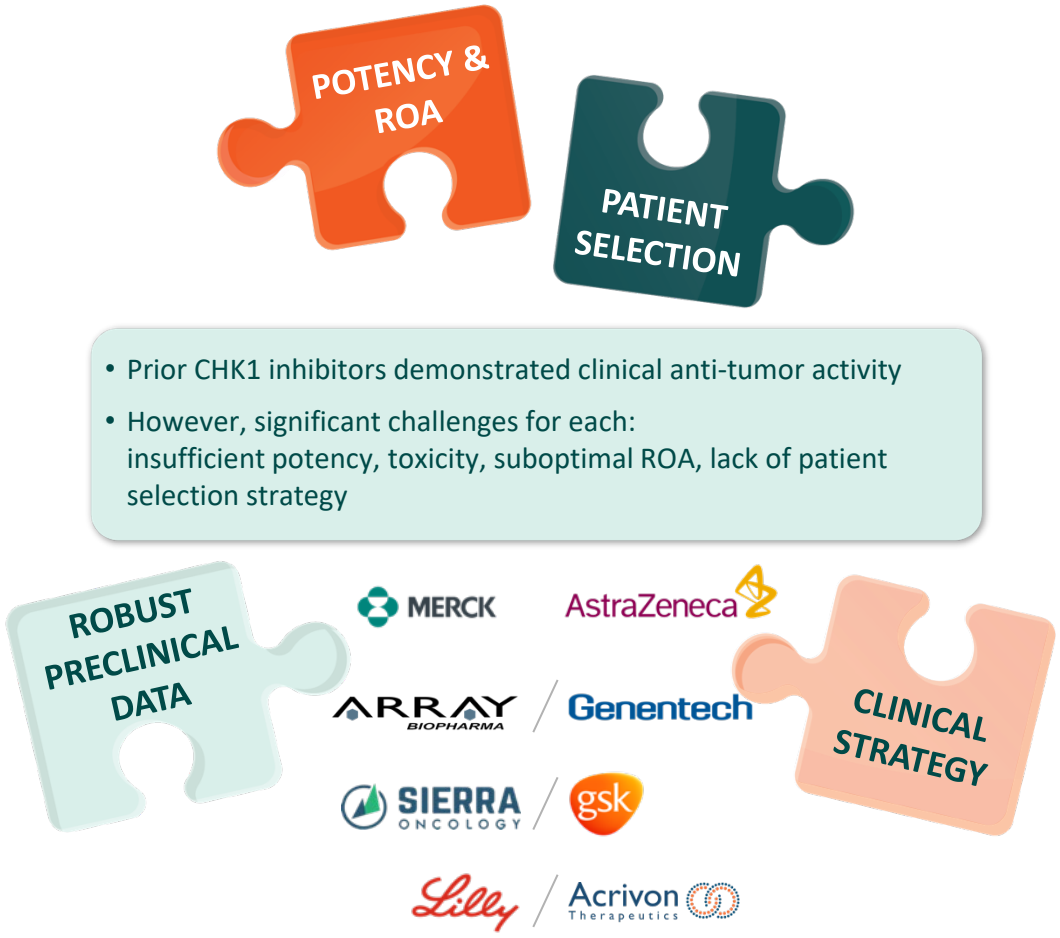
- Manage origin firing
- Stabilize stalled forks
- Pause cell cycle
- Maintain cell viability

Massive origin firing
Replication/mitotic catastrophe

Cancer cell death

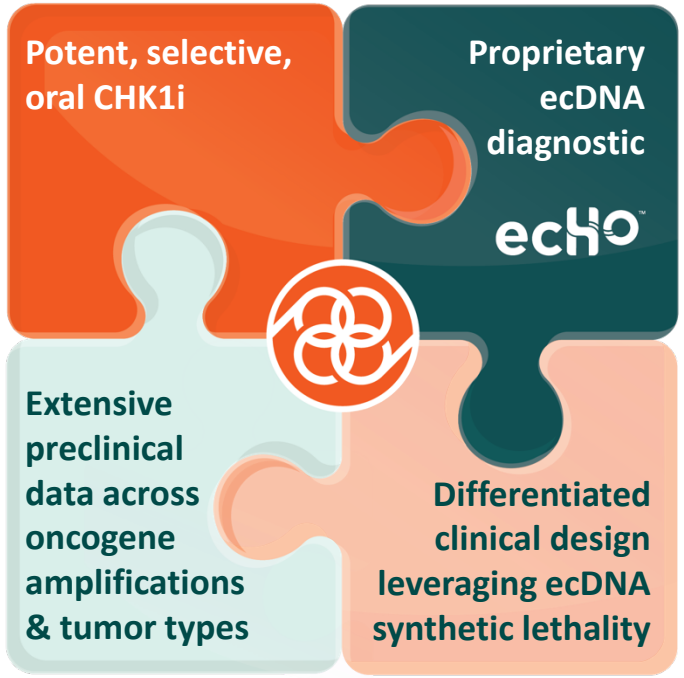
RS: replication stress

BBI-355: novel, oral, selective CHK1 inhibitor designed to disrupt ecDNA and overcome limitations of prior and existing CHK1 inhibitors



- Prior CHK1 inhibitors demonstrated clinical anti-tumor activity
- However, significant challenges for each: insufficient potency, toxicity, suboptimal ROA, lack of patient selection strategy

BBI-355 designed to target ecDNA function and unlock the potential of CHK1 inhibition in oncogene amplified cancers



ROA: route of administration

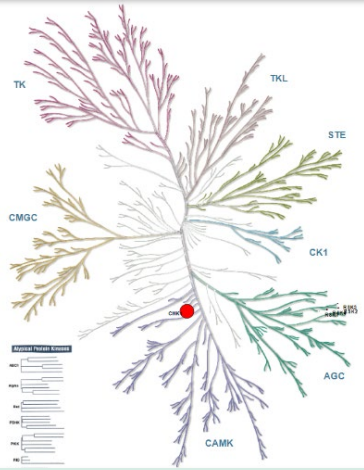
BBI-355 demonstrated single agent activity across a wide variety of oncogene amplified tumor models

BBI-355 preclinical properties

- **Potency:** 0.6 nM
- **CHK1 selectivity:** 185x CHK2
- **Oral availability:** 33% (rat)
- **CYP inhibition (uM): 1A2/2C9/2C19/2D6/3A4** >30/>30/>30/22/>30

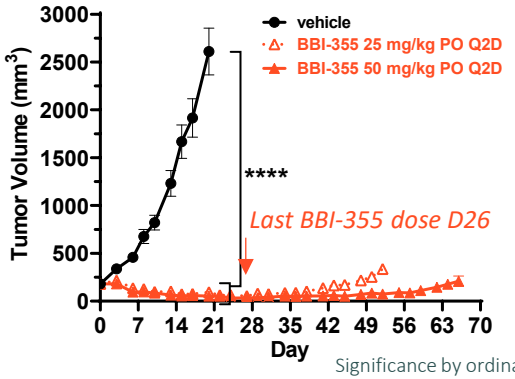
Kinases inhibited at IC_{50}<100 nM (6) with relative potencies

CHK1 only kinase with substantial inhibition <50 nM



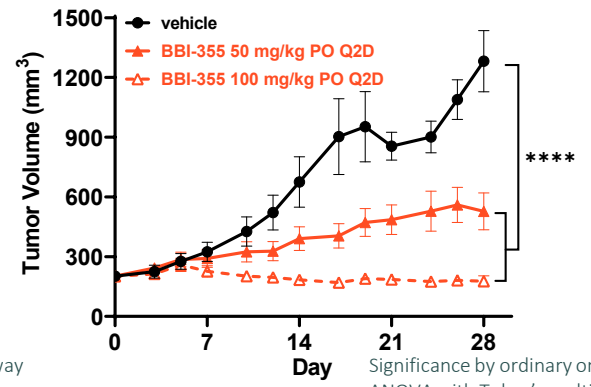
- **Orally administered BBI-355 demonstrated single agent activity across multiple CDX and PDX models**
- **Dose-dependent anti-tumor activity, including durable tumor regressions, observed at levels well-tolerated *in vivo***

MYCN^{amp} neuroblastoma CDX



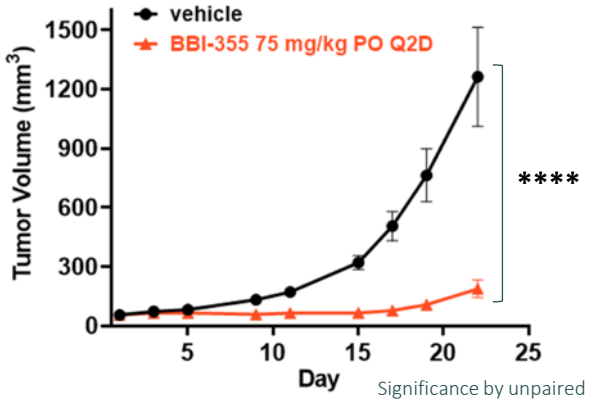
Significance by ordinary one-way ANOVA with Tukey's multiple comparisons; ****p<0.0001

FGFR2^{amp} gastric cancer PDX



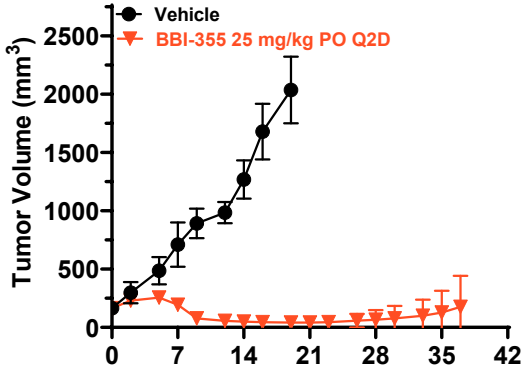
Significance by ordinary one-way ANOVA with Tukey's multiple comparisons; ****p<0.0001

CDK4^{amp} osteosarcoma CDX



Significance by unpaired t-test; ****p = 0.0006

MYC^{amp} SCLC PDX



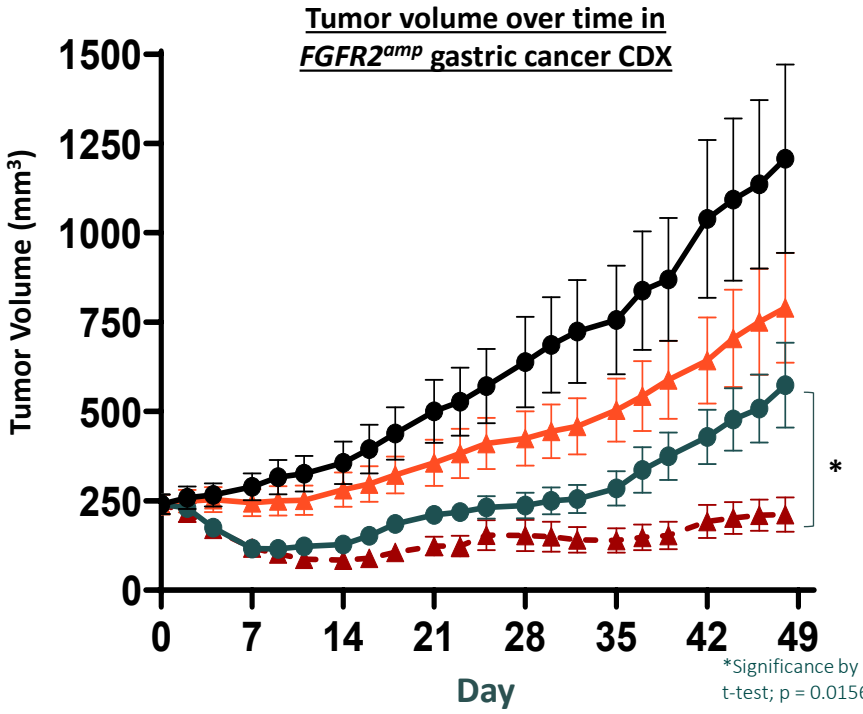
Significance by unpaired t-test; ***p<0.001

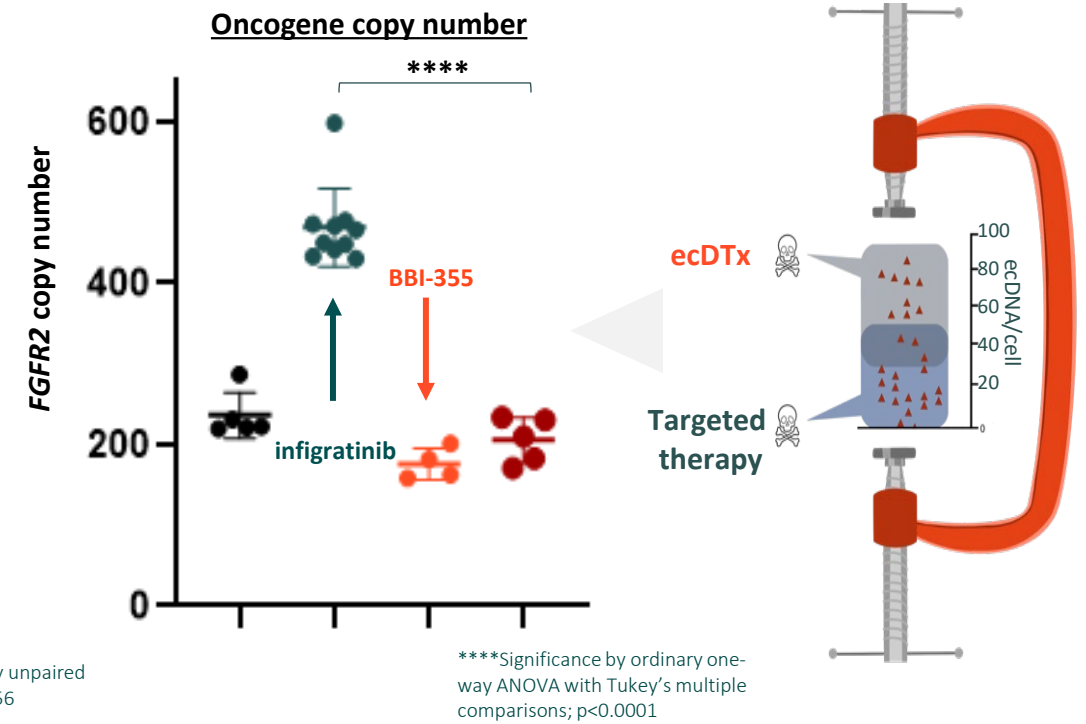
BBI-355 dosed for duration unless indicated

BOUNDLESS BIO

CDX: cell-line derived xenograft model
NSCLC: non-small cell lung cancer
PDX: patient-derived xenograft model

BBI-355 demonstrated synergistic combination activity in preclinical models of cancer indications in which single agent targeted therapies have not proven effective in the clinic





Therapy Enhanced Synthetic Lethality

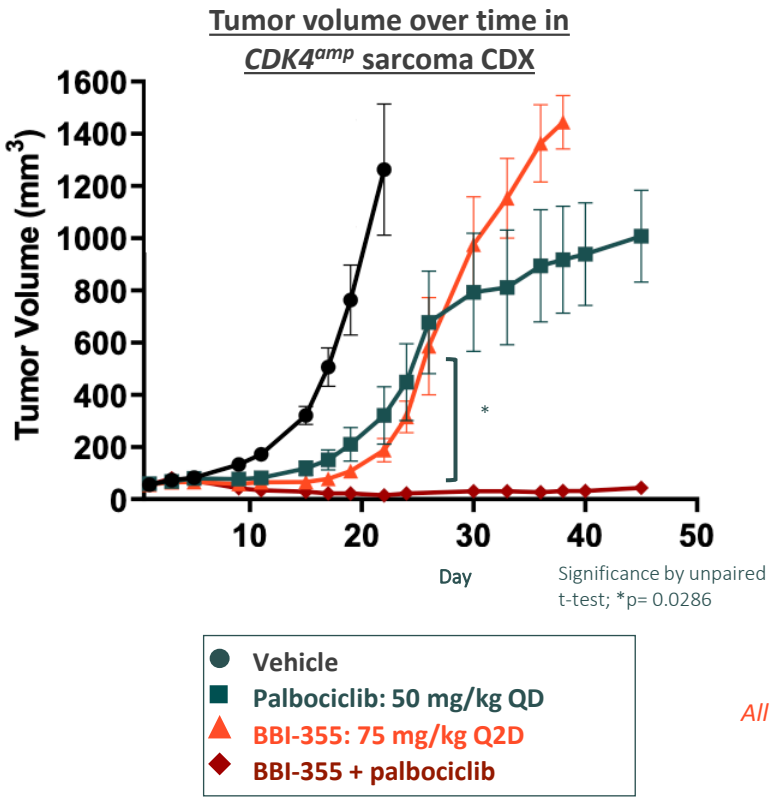
- Targeted therapy kills low copy number cells, driving population toward ecDNA-reliant high copy number cells
- ecDTx kills ecDNA-reliant high copy number cells
- Together, all oncogene amplified cells are killed

- FGFR2 inhibition with infigratinib resulted in minimal, transient anti-tumor activity, consistent with clinical experience
- When combined with BBI-355, extended synergistic tumor regression observed

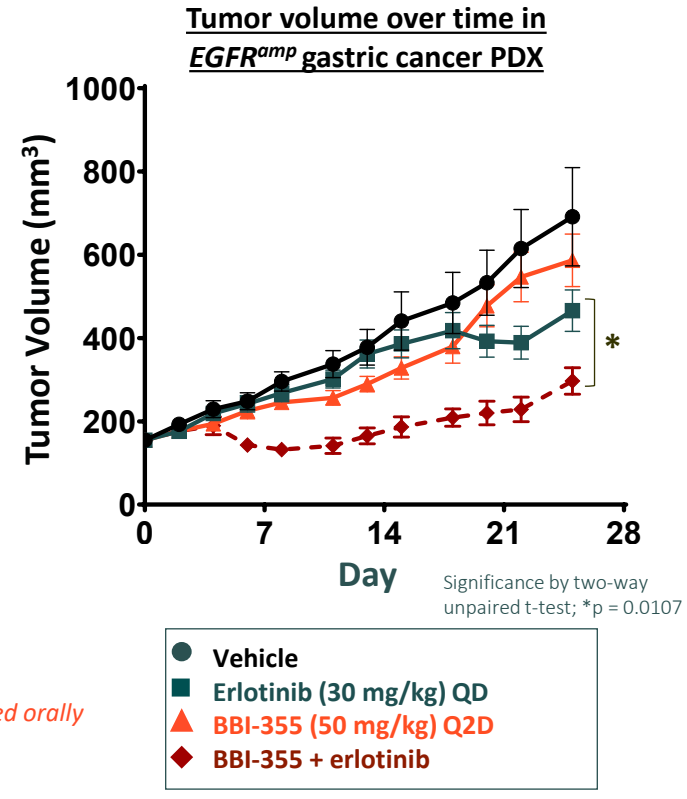
CDX: cell-line derived xenograft model

BBI-355 demonstrated *in vivo* proof of concept in multiple additional oncogene addicted xenograft models

Oncogene amplified sarcoma and gastric cancer; synergistic activity in combination with targeted therapy



All drugs administered orally

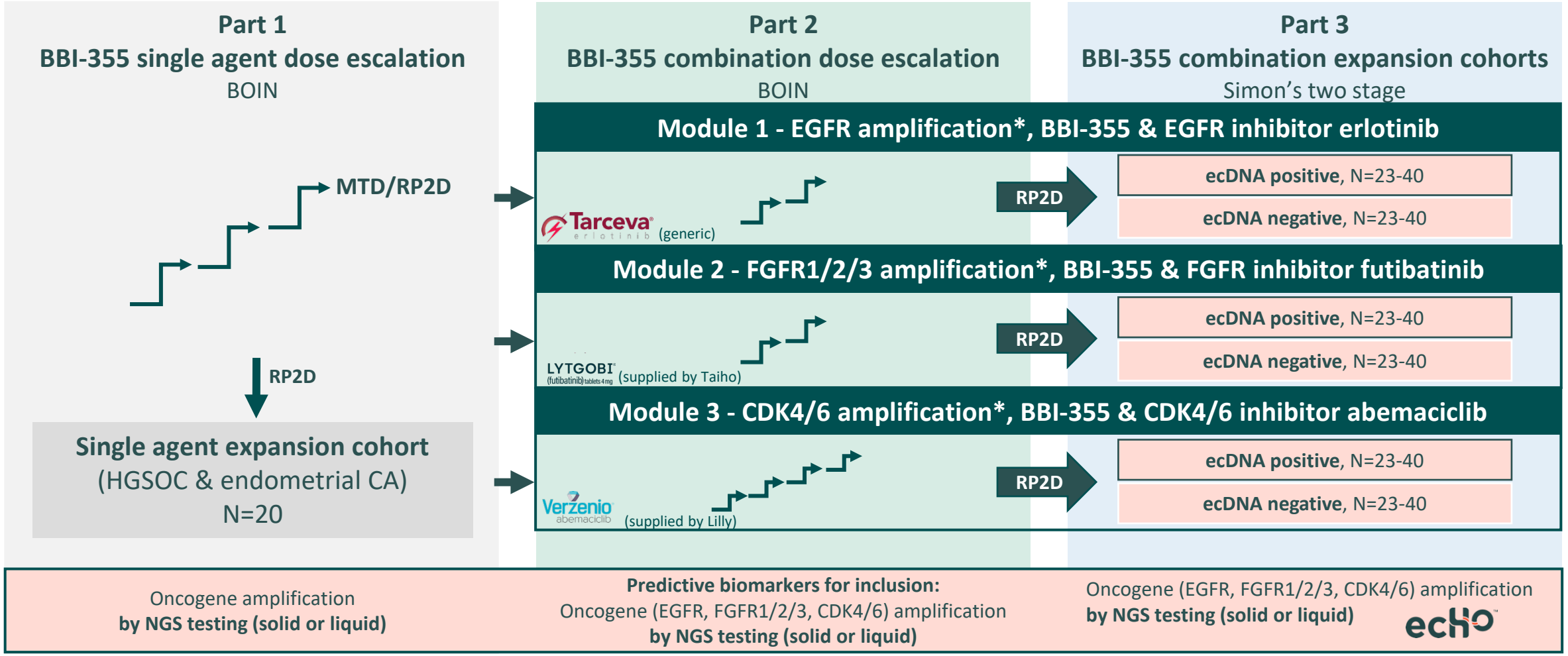


Combination of BBI-355 with targeted therapy *in vivo* resulted in:

- **Deeper tumor regressions**
- **Longer duration of response**

CDX: cell-line derived xenograft model
PDX: patient-derived xenograft model

Phase 1/2 study of BBI-355 designed to drive to clinical proof of concept in multiple solid tumor settings



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

BOUNDLESS BIO

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

*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)

Preliminary human pharmacokinetic (PK) data of BBI-355 showed dose-proportionality and achieved exposures in the predicted therapeutically active range at 60 mg PO Q2D, which is a tolerated dose level

Dose Escalation

80 mg Q2D*

120 mg 2ON/5OFF**

60 mg Q2D

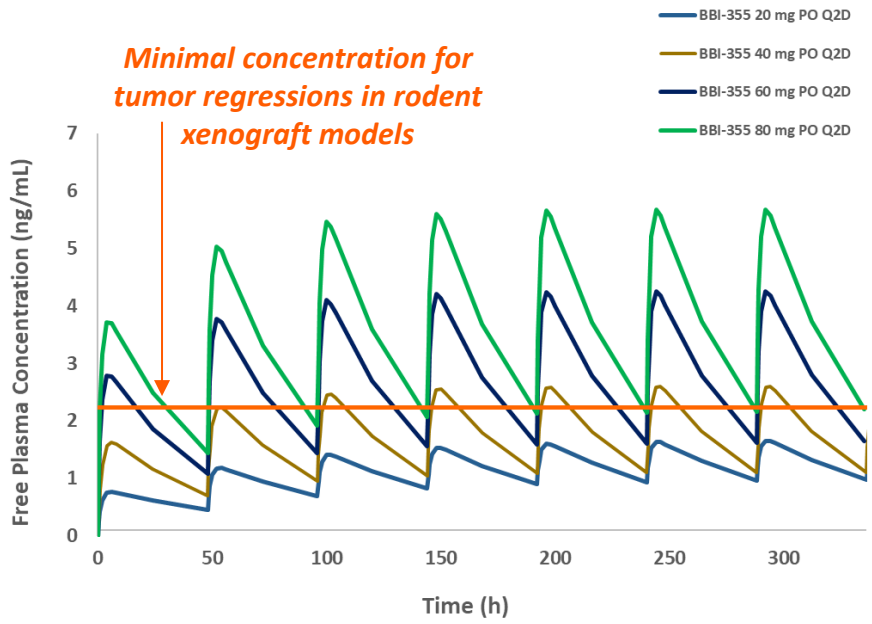
80 mg 2ON/5OFF+

40 mg Q2D

20 mg Q2D

Multiple dosing regimens evaluated

Preliminary Q2D PK Profiles



- BBI-355 demonstrated good oral bioavailability in human subjects
- Average C_{max} and AUC showed dose proportionality from 20 to 80 mg Q2D
- Average $T_{1/2}$: ~40h, leading to drug accumulation of ~2 to 3-fold
- Moderate inter-subject variability observed

*Dose limiting toxicities (DLTs) in 2 of 4 subjects (i.e., neutrophil count decreased, platelet count decreased)
**DLTs in 3 of 3 subjects (i.e., neutrophil count decreased, platelet count decreased)
+DLT in 1 of 5 subjects (i.e., neutrophil count decreased)

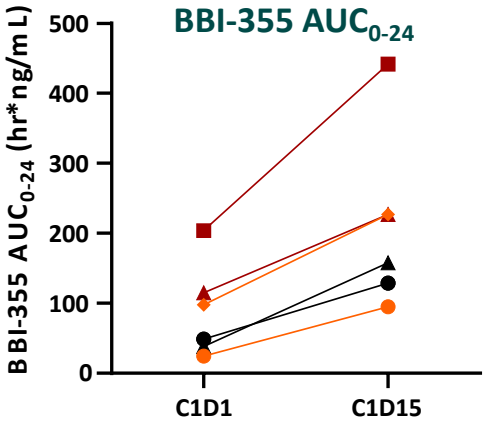
AUC: area under the curve
PO: oral

Q2D: every two days
2ON/5OFF: two days on drug and 5 days off drug

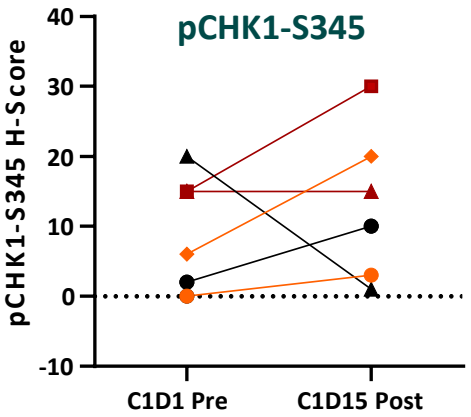
Evidence of BBI-355 pharmacodynamic activity observed in clinical samples across dose levels

pCHK1-S345 induction in skin and tumor biopsies

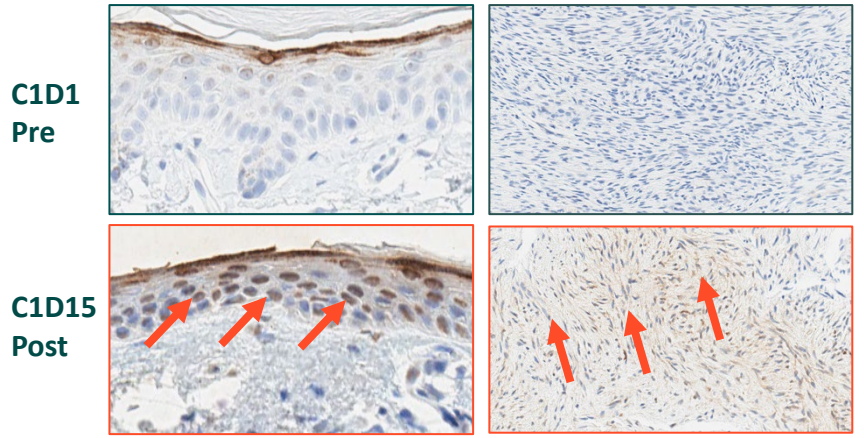
PK from day 1 and day 15



PD biomarker data from paired skin biopsies
Day 1 pre-dose and day 15 post-dose



Representative examples
(skin and tumor biopsy)



40 mg Q2D (Skin)
005-01-0009

40 mg Q2D (Tumor)
002-01-0008

20 mg Q2D
- 002-01-0005
- 002-01-0007

40 mg Q2D
- 002-01-0008
- 005-01-0009

80 mg Q2D
- 001-01-0015
- 004-01-0016

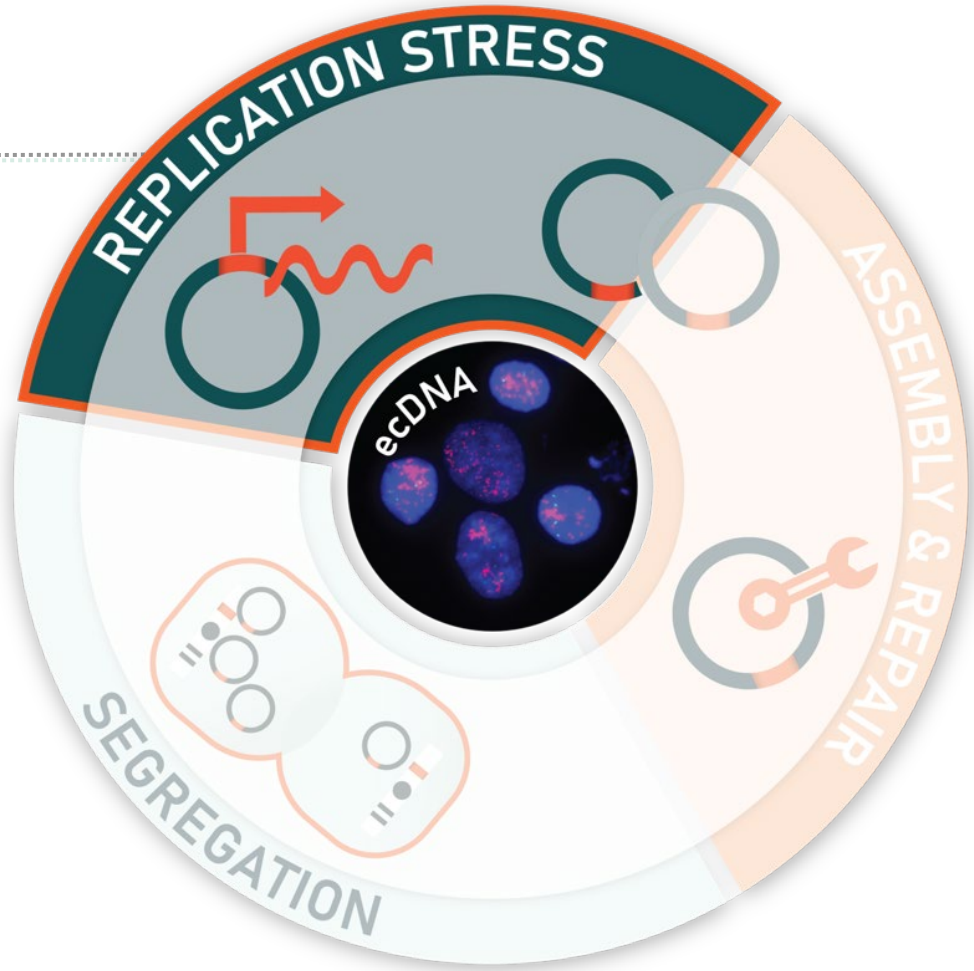
C1D1: cohort 1 day 1
C1D15: cohort 1 day 15
H-Score: histochemical scoring

BBI-355 summary: the first ecDTx in clinical development for oncogene amplified cancer

CHK1: checkpoint kinase 1

BBI-355: PHASE 1/2

- BBI-355 is a potentially **best-in-class, oral, selective** CHK1 inhibitor in development to address the **unmet medical needs** of patients with oncogene amplified cancer
- **Currently no cancer therapy** has been approved for patients with *EGFR*, *FGFR*, or *CDK4/6* amplifications, a large segment of cancer patients
- The **POTENTIATE** trial's modular design (NCT05827614) enables multiple avenues for expansion opportunities across diverse oncogene amplifications and tumor types
- Initial human PK data shows dose-proportionality with exposures in the predicted therapeutically active range
- Preliminary clinical data of BBI-355 as a single agent and in combination with EGFR or FGFR inhibitors in 2H 2025

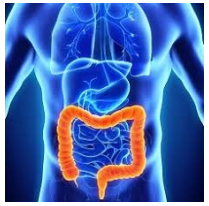
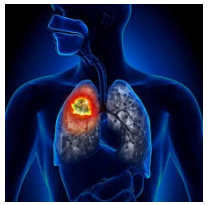


BBI-825: first-in-class, oral, selective RNR inhibitor in Phase 1/2 STARMAP trial

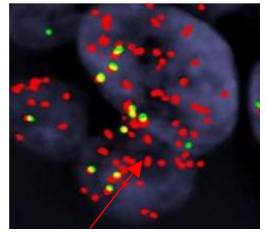
Second ecDTx; targets ecDNA assembly & repair

Oncogene amplifications, often on ecDNA, are a frequent mechanism of clinical resistance to multiple therapeutic modalities

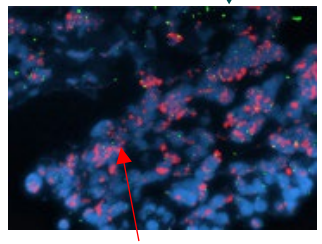
Tissue images from clinical specimens suggest resistance amplifications are frequently ecDNA-mediated

CANCER	INITIAL ONCOGENE DRIVER	CLINICAL THERAPY	ONCOGENE AMPLIFICATION DRIVING RECURRENCE
CRC 	*EGFR*^{mut} *BRAF*^{V600E} *KRAS*^{G12C}	Anti-EGFR mAbs BRAF^{V600E}, KRAS^{G12C} inhibitors	***KRAS*** ***MET*** ***BRAF*** ***EGFR***
NSCLC 	*ALK*^{fusion} *EGFR*^{mut} *ROS1*^{fusion} *KRAS*^{G12C}	ALK, EGFR, ROS1, KRAS^{G12C} inhibitors Anti-EGFR mAbs	***KRAS*** ***ERBB2*** ***MET***

- Misale 2012 Nature
- Bardelli 2013 Canc Disc
- Yaeger 2017 Canc Res
- Awad 2021 NEJM
- Tan 2023 Clin Can Res
- Sacher 2023 NEJM

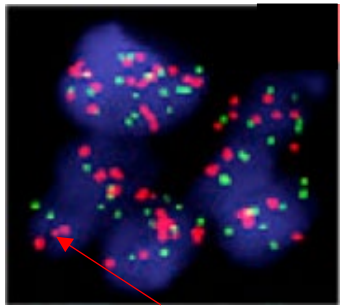


BRAF (on ecDNA)



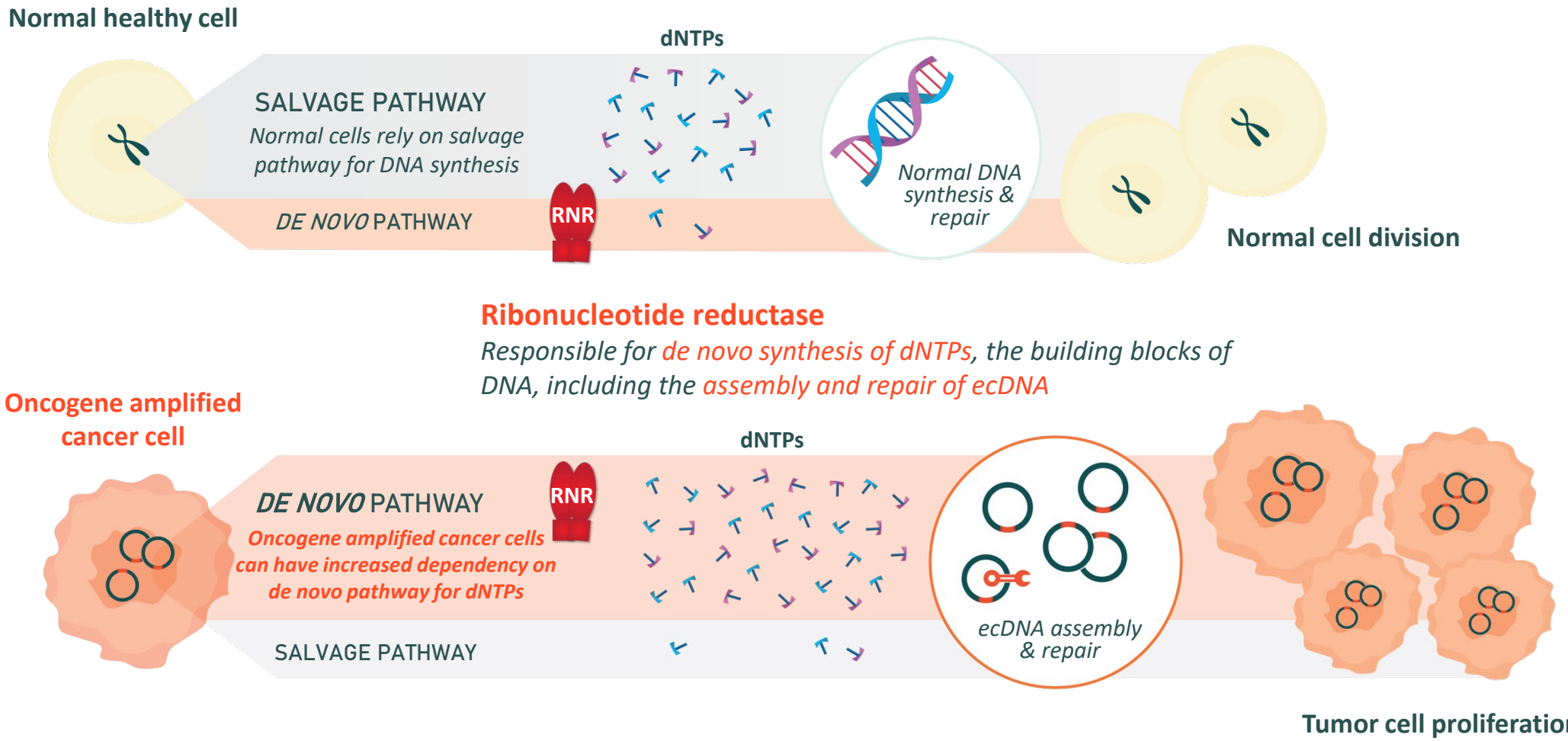
KRAS (on ecDNA)

- Wang 2019 J Hem Onc
- Takezawa 2012 Canc Disc
- Dagogo-Jack 2020 Clin Canc Res
- Schoenfeld 2020 Clin Canc Res
- Roper 2020 Cell Reports Med
- Priest 2023 npj Prec Onc
- Park 2024 Eur J of Can



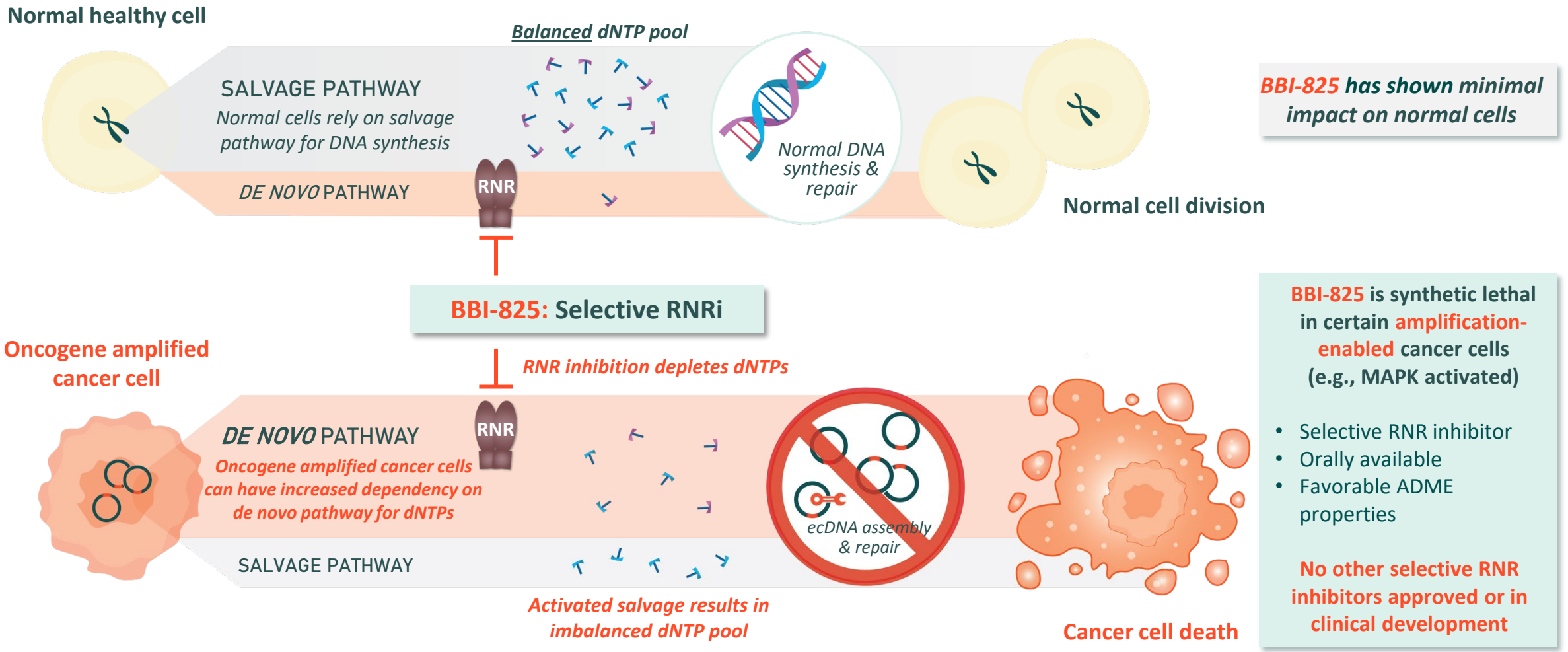
MET (on ecDNA)

Ribonucleotide reductase (RNR) is the rate-limiting enzyme in the *de novo* synthesis of dNTPs, which are essential for the assembly and repair of ecDNA



dNTPs: deoxyribonucleotide triphosphates

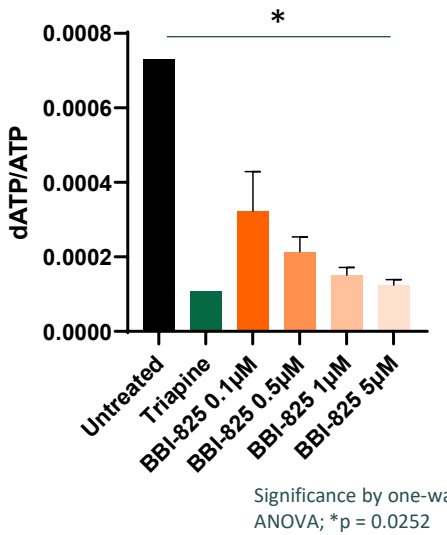
BBI-825 is a novel, oral, selective RNR inhibitor designed to disrupt the assembly and repair of ecDNA



ADME: absorption, distribution, metabolism, and excretion
dNTPs: deoxyribonucleotide triphosphates

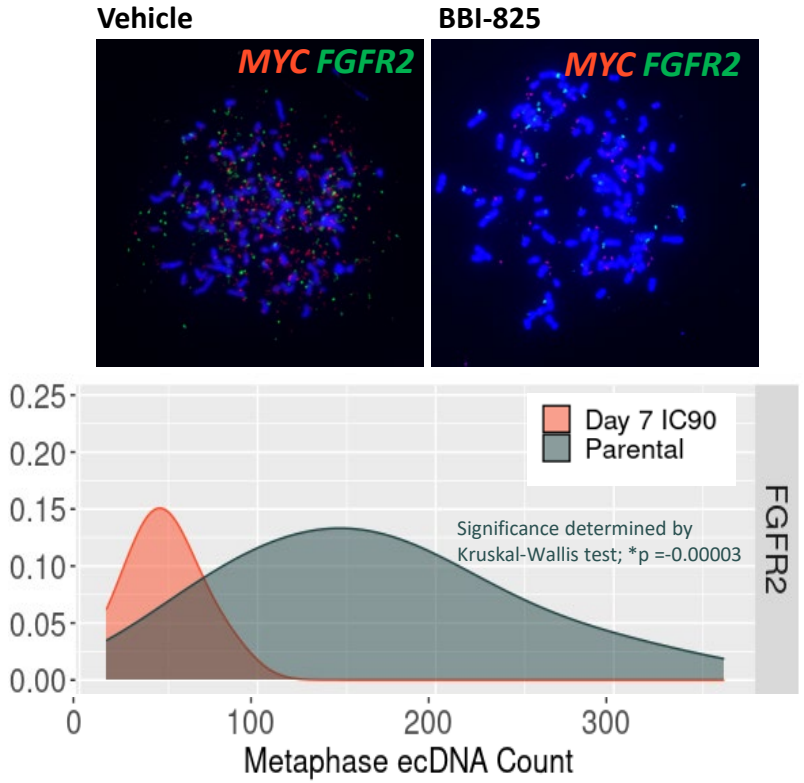
BBI-825 resulted in dNTP depletion, reduced ecDNA, and cytotoxicity in ecDNA amplified cancer cells

Reduction in dNTP Levels

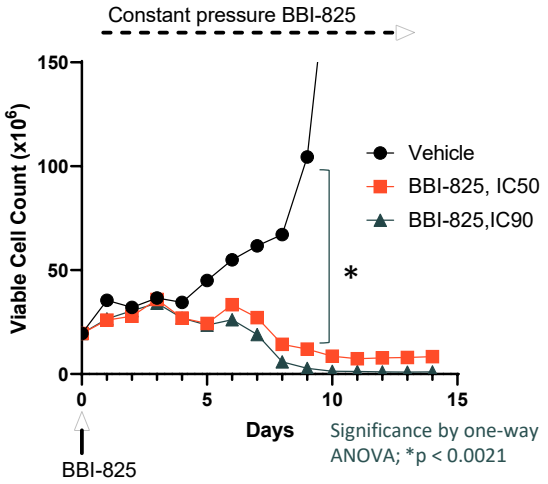


Significance by one-way ANOVA; *p = 0.0252

Reduction in ecDNA Levels



Cytotoxicity to ecDNA amplified cancer cells



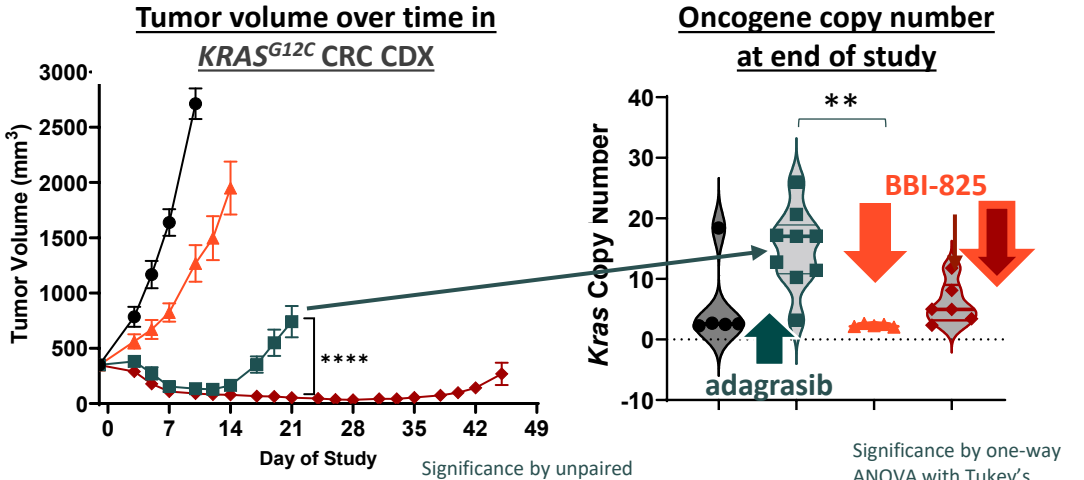
Significance by one-way ANOVA; *p < 0.0021

In *MYC* and *FGFR2* amplified ecDNA+ GI cancer cells, treatment with BBI-825 resulted in depletion of dNTPs and reduced ecDNA levels, leading to tumor cell death

dNTPs: deoxyribonucleotide triphosphates
GI: gastrointestinal

BBI-825 demonstrated synthetic lethality in combination with KRAS^{G12C} inhibition in *KRAS^{G12C}*-addicted syngeneic colorectal cancer xenograft, both preventing and treating resistance post-emergence

Combination of BBI-825 with adagrasib prevented resistance to KRAS^{G12C} inhibition, resulting in durable tumor regressions



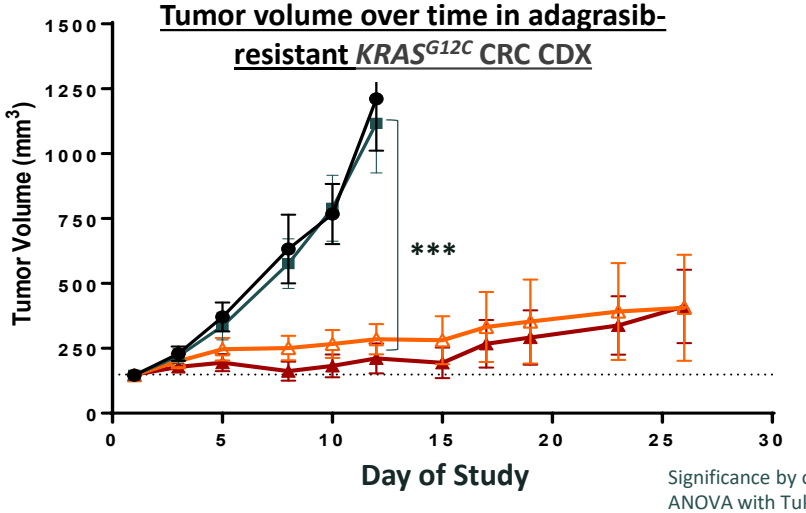
Significance by unpaired t-test; ****p < 0.0001

Significance by one-way ANOVA with Tukey's multiple comparison test; ** p < 0.01

- Vehicle
- Adagrasib: 50 mg/kg QD
- BBI-825: 50 mg/kg Q2D
- Combo: BBI-825 + adagrasib

KRAS^{G12C}–mutated CRC CDX model

Single-agent BBI-825 treated resistance post-KRAS^{G12C} inhibition, resulting in significant anti-tumor activity



Significance by ordinary one-way ANOVA with Tukey's multiple comparisons; ***p < 0.001

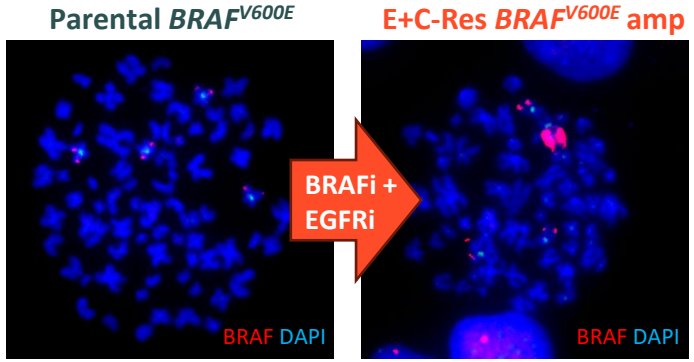
- Vehicle
- Adagrasib: 50 mg/kg QD
- BBI-825: 50 mg/kg Q2D
- Combo: BBI-825 + adagrasib

KRAS^{G12C}–mutated CRC CDX model that has become resistant to adagrasib via amplifications on ecDNA

CDX: cell line-derived xenograft model
CRC: colorectal cancer

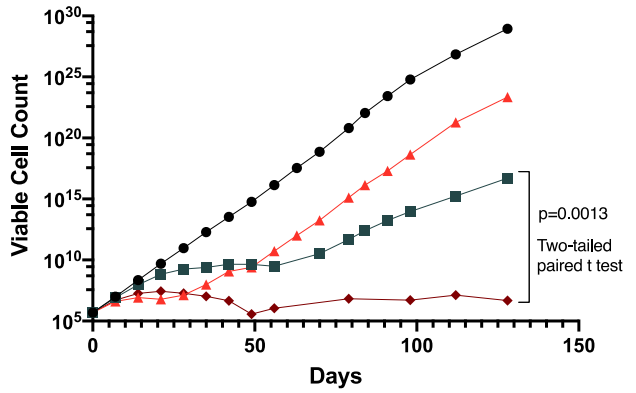
BBI-825 overcame amplification-based resistance to BRAFi + EGFRi treatment of *BRAF*^{V600E} CRC cells *in vitro*

Amplification-mediated resistance in *BRAF*^{V600E} CRC

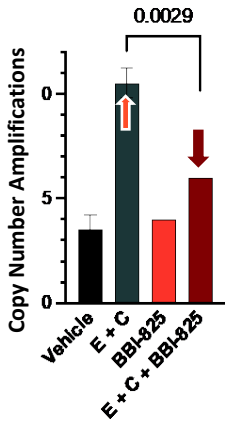


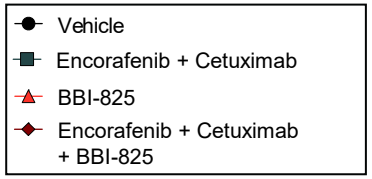
- ***BRAF*^{V600E} mutant CRC cell lines developed rapid resistance to encorafenib + cetuximab via oncogene amplification**
- **Combination with BBI-825 prevented resistance and led to cancer cell death**
- **Additional *BRAF*^{V600E} melanoma and endometrial cancer models also demonstrated BBI-825 synergy with standard of care**

Cancer cell cytotoxicity over time in *BRAF*^{V600E} CRC WiDr cells

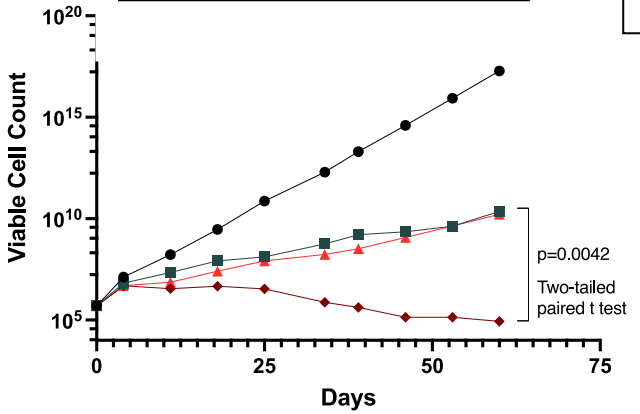


BRAF



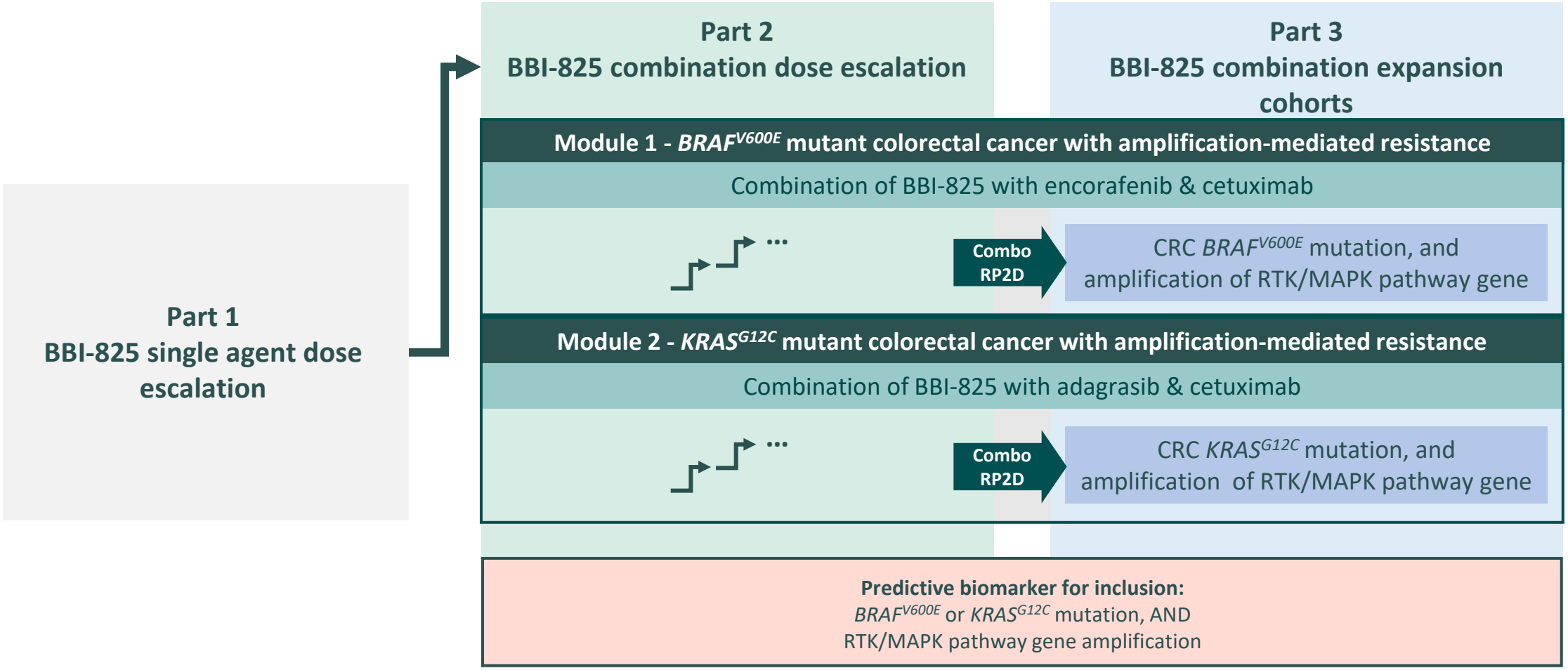


Cancer cell cytotoxicity over time in *BRAF*^{V600E} CRC COLO201 cells



E: encorafenib
C: cetuximab
CRC: colorectal cancer

Phase 1/2 study of BBI-825 evaluates prevention and treatment of amplification-mediated resistance to RTK/MAPK pathway inhibitors

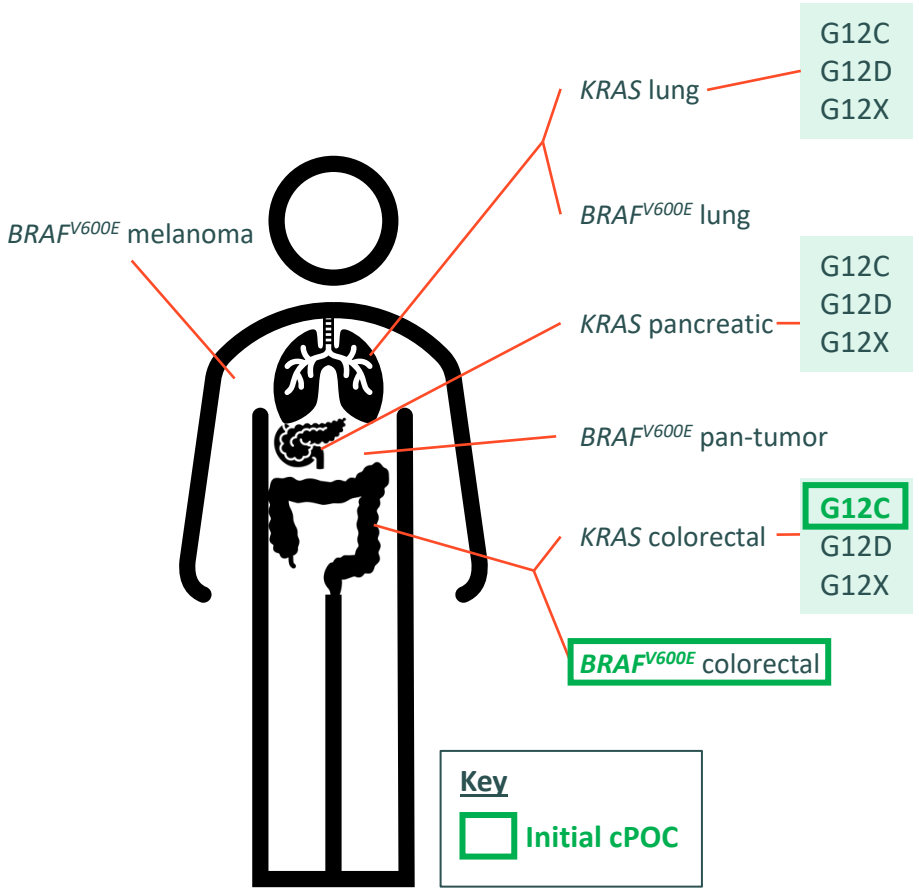


"**STARMAP**": Study Treating Acquired Resistance; MAPK Amplifications

CRC: Colorectal cancer
MAPK: Mitogen-activated protein kinases
RP2D: Recommended Phase 2 Dose
RTK: Receptor tyrosine kinase

MAPK-pathway amplification-mediated acquired resistance

Initial clinical proof of concept (cPOC) and total addressable market (TAM)



KRAS^{G12C} and BRAF^{V600E} Inhibitors	Resistance Mechanisms	Next Line/ Combo
KRAS^{G12C} Inhibitors (+/-EGFRi) Krazati™ (adagrasib) Lumakras™ (sotorasib) Divarasib…	2nd-site *KRAS*/*BRAF* mutations	2nd-gen inh SHP2i SOS1i
	"Bypass mechanisms"	I/O Chemo Other
KRAS^{G12X} Inhibitors MRTX1133 RMC-9805, -5127…	MAPK-pathway amplifications	**BBI-825**
BRAF^{V600E} Inhibitors (+/-MEKi/EGFRi) Braftovi™ (encorafenib) Tafinlar™ (dabrafenib) Zelboraf™ (vemurafenib)		

% of patients clinically observed to develop amplifications upon resistance

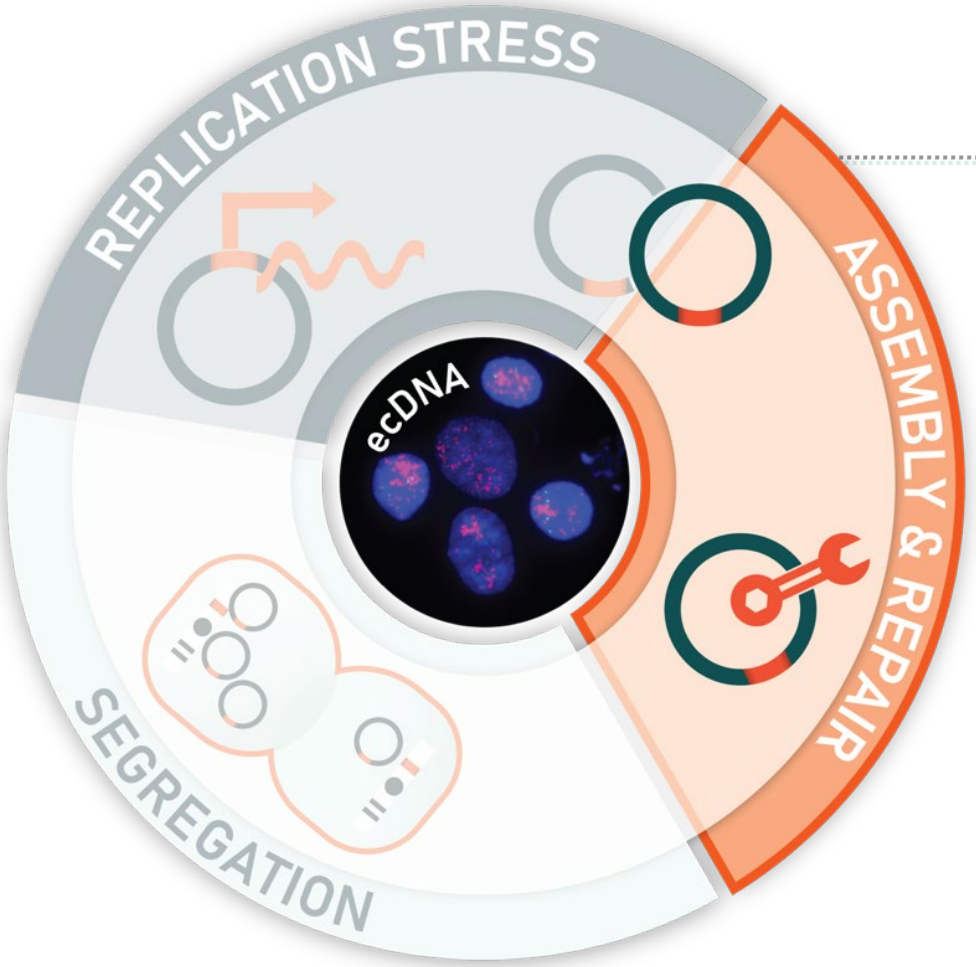
G12C CRC (**35%** Yaeger 2024)
G12C CRC (**58%** Yaeger 2023)
G12C CRC (**80%** Desai 2023)
***G12C* PDAC** (**32%** Dilly 2024)
***G12C* NSCLC** (**24%** Awad 2021)
***G12C* Pan-Tumor** (**63%** Sacher 2023)

V600E CRC (**44%** Tan 2023)
V600E CRC (**24-38%** Kopetz 2024)
***V600E* melanoma** (**45%** Dharanipragada 2023)

While we seek to demonstrate initial POC in *KRAS^{G12C}* and *BRAF^{V600E}* CRC, BBI-825's TAM may be pan-tumor and pan-RAS

CRC: colorectal cancer
NSCLC: non-small cell lung cancer
cPOC: clinical proof of concept

BBI-825 summary: the second ecDTx in clinical development for cancer with resistance gene amplifications



RNR: ribonucleotide reductase

BBI-825: PHASE 1/2

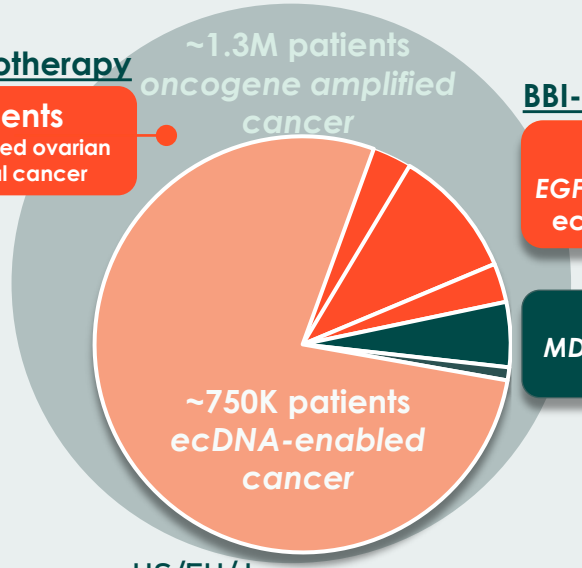
- BBI-825 is a **first-in-class, oral, selective** RNR inhibitor in development to address **patient populations** with MAPK-pathway activated cancer
- **Rapid resistance in multiple tumor types** is a limitation of current targeted therapies, presumably due to **amplification** of resistance genes
- Preclinically, BBI-825 demonstrated **significant tumor growth inhibition**, including regressions, in MAPK pathway-activated tumor models
- **STARMAP** trial modular design (NCT06299761) enables multiple avenues for expansion opportunities across pan-tumor and pan-RAS and activated cancers
- Preliminary pharmacokinetic data from Part 1 showed a lack of dose-proportional exposure; **BBI-825** STARMAP trial will not advance at this time

Boundless Bio: leading a new area of cancer biology and targeting a large unmet need

Seeking to address oncogene amplification market by targeting oncogene agnostic nodes of ecDNA biology

BBI-355 Monotherapy

~65k patients
Oncogene amplified ovarian and endometrial cancer

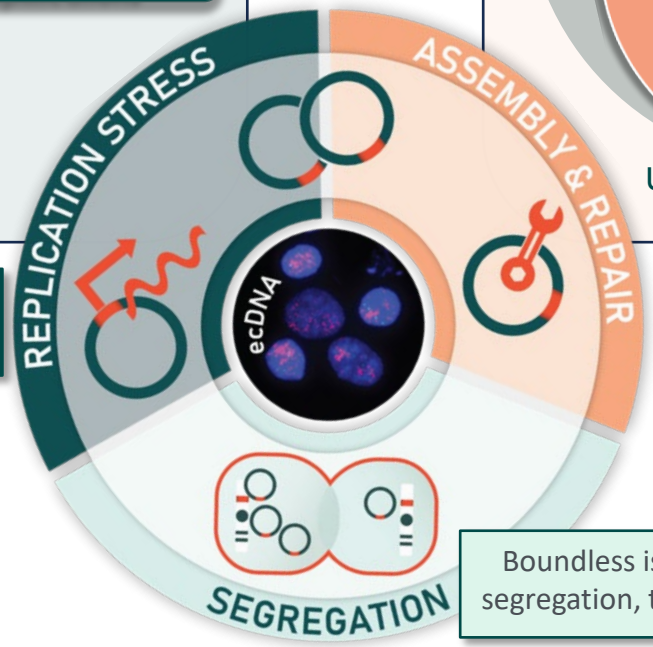


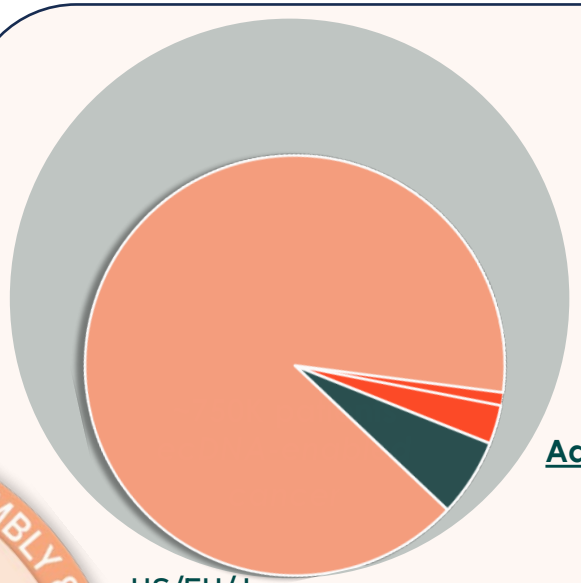
US/EU/Japan per year

BBI-355 Combinations

~80k patients[1]
EGFR, FGFR, and CDK4/6 ecDNA amplifications

~30k patients
MDM2 and MET ecDNA amplifications





US/EU/Japan per year

BBI-825 Combinations

~18k patients[2]
$KRAS^{G12C}$ and $BRAF^{V600E}$ metastatic CRC

~30k patients
$KRAS^{G12D/V/A/R}$ metastatic CRC

BBI-825 Combinations for Add'l Cancer Types (non-CRC)

~335k patients
Other metastatic KRAS and BRAF mutant solid tumors

BBI-355 targets ecDNA induced replication stress
Potential to treat ~175k new patients per year

BBI-825 targets ecDNA assembly & repair
Potential to treat >380k new patients per year

Boundless is targeting additional nodes of biology, including ecDNA segregation, to further unlock oncogene amplified patient populations

1: # of new patients per year in US/EU/Japan with *EGFR*, *FGFR*, *CDK4/6* amplifications on ecDNA are estimated to be 15K, 50K, 15K, respectively

2: # of new CRC patients per year in US/EU/Japan with $KRAS^{G12C}$ and $BRAF^{V600E}$ are estimated to be 5K and 13K, respectively

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

Dedicated to Oncogene Amplified Cancers by targeting a 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 is the leading ecDNA company
- **Spyglass**: ecDNA-focused discovery engine
- **ecDTx**: multiple clinical-stage programs with robust preclinical data
- **ECHO**: diagnostic designed to identify ecDNA+ cancers using routine NGS assays

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; IP life through at least 2041-2044
- Approximately $167M in cash and equivalents*, provides expected runway into 2027

Multiple Value Drivers

ecDTx	Target	ecDNA Node	Anticipated Milestones
BBI-355	CHK1	Replication Stress	2H 2025: Initial clinical POC from Phase 1/2 POTENTIATE trial
BBI-825	RNR	Assembly & Repair	STARMAP study will not advance at this time
ecDTx 3	Kinesin	Segregation	Mid-2025: Development Candidate; 1H 2026: Submit IND

*Total pro forma cash, cash equivalents, and short-term investments

Boundless Bio: a breakthrough biotech company leading the next wave of innovation in cancer treatment

CANCER TREATMENT BREAKTHROUGHS

1940s CHEMOTHERAPY

1990-2000s TARGETED THERAPY

2010s IMMUNOTHERAPY

2020s-2030s
ecDNA-DIRECTED THERAPIES (ecDTx)

Each prior wave of therapeutic innovation has been unable to address a critical population:

PATIENTS WITH ONCOGENE AMPLIFIED CANCERS

FIERCE Biotech Fierce 15 HONOREE 2023

BIOTECH BREAKTHROUGH AWARD 2022 OVERALL BIOPHARMA COMPANY OF THE YEAR

BOUNDLESS BIO

Unbound by convention, bound to save lives

www.boundlessbio.com
@BoundlessBio

Bibliography of recent reviews and publications covering ecDNA—active hyperlinks

2024	**Paul Mischel, Howard Chang**	*Nature*: Enhancing transcription-replication conflict targets ecDNA-positive cancers
2024	**Howard Chang, Paul Mischel, Charles Swanton**	*Nature*: Origins and impact of extrachromosomal DNA
2024	**Vineet Bafna, Roel Verhaak**	Nature Genetics: Mapping extrachromosomal DNA amplifications during cancer progression
2024	**Paul Mischel, Howard Chang**	*Nature Reviews Cancer*: Extrachromosomal DNA in cancer
2023	**Paul Mischel, Vineet Bafna, Howard Chang, Roel Verhaak**	*Nature*: Extrachromosomal DNA in the cancerous transformation of Barrett's oesophagus
2022	**Vineet Bafna, Paul Mischel**	*Annual Reviews*: Extrachromosomal DNA in Cancer
2022	**Paul Mischel, Howard Chang**	*Nature Structural and Molecular Biology*: Gene regulation on extrachromosomal DNA
2022	**Rene Medema (Netherlands Cancer Inst.)**	*Chromosoma*: Life of double minutes: generation, maintenance, and elimination
2022	**Vineet Bafna, Howard Chang, Paul Mischel**	*Annual Reviews*: Extrachromosomal DNA: An Emerging Hallmark in Human Cancer
2020	**Anton Henssen, Howard Chang, Paul Mischel, Vineet Bafna, Roel Verhaak**	*Nature Genetics*: Extrachromosomal DNA is associated with oncogene amplification and poor outcome across multiple cancers
2020	**Paul Mischel, Charles Swanton (Crick Inst.)**	*Annals of Oncology*: Extrachromosomal DNA—relieving heredity constraints, accelerating tumour evolution
2020	**Christopher Ott (Mass Gen)**	*Cancer Cell*: Circles with a Point: New Insights into Oncogenic Extrachromosomal DNA
2019	**Roel Verhaak, Vineet Bafna, Paul Mischel**	*Nature Reviews*: Extrachromosomal oncogene amplification in tumour pathogenesis and evolution