UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): June 27, 2022

RELAY THERAPEUTICS, INC.

(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-39385**	**47-3923475**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

399 Binney Street **Cambridge, Massachusetts**	**02139**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's Telephone Number, Including Area Code: (617) 370-8837

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, par value $0.001 per share	RLAY	NASDAQ Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On June 27, 2022, Relay Therapeutics, Inc. (the "Company") issued a press release, a copy of which is furnished herewith as Exhibit 99.1. The Company intends to host a virtual analyst and investor event on June 27, 2022 from 8:00 a.m. to 9:00 a.m. E.T. to discuss its anticipated registrational path for RLY-4008, a potent, selective and oral small molecule inhibitor of fibroblast growth factor receptor 2 ("FGFR2"), in cholangiocarcinoma ("CCA") and three new programs within its HR+/HER2- breast cancer franchise. The Company has made available a slide presentation to accompany the event, a copy of which is being furnished as Exhibit 99.2 to this Current Report on Form 8-K. The Company undertakes no obligation to update, supplement or amend the materials attached hereto as Exhibit 99.2.

The information in this Item 7.01, including Exhibit 99.1 and Exhibit 99.2 attached hereto, is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934 (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 8.01 Other Events.

RLY-4008 Regulatory and Clinical Data Update

On June 27, 2022, the Company announced the anticipated registrational path for RLY-4008 in CCA and the interim clinical data that was shared with the U.S. Food and Drug Administration (the "FDA") to support such path. RLY-4008 is currently being evaluated in a clinical trial in patients with advanced or metastatic FGFR2-altered solid tumors with a single arm, potentially registration-enabling cohort for pan-FGFR ("FGFRi") treatment-naïve FGFR2-fusion CCA.

The Company conducted an end-of-phase 1 meeting with the FDA to discuss next steps for the clinical development of RLY-4008. Based on discussions with the FDA, the Company has decided to move forward with a single arm trial design for FGFRi-naïve FGFR2-fusion CCA at 70 mg once daily to potentially support accelerated approval. The Company also intends to add additional supportive CCA cohorts to a New Drug Application submission, including frontline, FGFRi-experienced and FGFR2 mutation and amplification patients that could potentially facilitate a line and alteration agnostic label if the submission is approved.

The interim clinical data the Company shared with the FDA included a data cut-off of April 19, 2022 (the "Data Cut-off Date") from the dose escalation portion of the ongoing clinical trial. The interim clinical data included a safety database of 115 patients, with 58 patients treated with the once daily ("QD") dosing schedule, and 13 of these patients were FGFRi-naïve FGFR2-fusion CCA patients treated with the once daily schedule ranging from 20 mg up to 70 mg. Also, in addition to the 17 patients previously disclosed by the Company at a twice daily schedule, an additional 40 patients were evaluated with an intermittent dosing schedule, both of which have been deprioritized.

The safety analysis as of the Data Cut-off Date was consistent with the analysis from the Company's initial data disclosure for its RLY-4008 clinical trial in October 2021. Most treatment emergent adverse events were expected FGFR2 on target, low-grade, monitorable, manageable, and largely reversible. There were no observed Grade 4 or 5 adverse events. Notable off-target toxicities of hyperphosphatemia and diarrhea continued to be clinically insignificant.

The efficacy analysis from this interim clinical data on the once daily dosing schedule presented by the Company to the FDA demonstrated confirmed partial responses in 8 out of 13, or 62%, FGFRi-naïve FGFR2-fusion CCA patients across the 20 mg to 70 mg QD cohorts. There were four patients treated at the registrational trial dose of 70 mg QD as of the Data Cut-off Date, all of which had confirmed partial responses.

Breast Cancer Portfolio and New Targets

The Company also announced the following three new programs in its breast cancer franchise: a selective cyclin dependent kinase 2 ("CDK2") inhibitor, a rationally designed estrogen receptor alpha ("ERα") degrader and a selective and chemically distinct pan-mutant phosphoinostide 3-kinase alpha inhibitor, RLY-5836.

Cautionary Note Regarding Forward Looking Statements

This Current Report on Form 8-K and certain materials furnished or filed herewith contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, implied and express statements regarding the Company's strategy, business plans and focus; the progress and timing of updates on the clinical development of the programs across the Company's portfolio, including the timing of a clinical data update for RLY-4008 and the clinical initiation of the Company's CDK2 program, ERα program and RLY-5836; the expected therapeutic benefits of its programs; whether preclinical or early clinical results of the Company's product candidates will be predictive of future clinical trials; the Company's expectations

relating to its current and future interactions with the FDA, including its belief regarding a potential accelerated path to registration and label for RLY-4008; expectations regarding the Company's operating plan, use of capital, expenses, and other financial results during 2022 and in the future; and Relay Therapeutics' cash runway projection. The words "may," "might," "will," "could," "would," "should," "plan," "anticipate," "intend," "believe," "expect," "estimate," "seek," "predict," "future," "project," "potential," "continue," "target" and similar words or expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Any forward-looking statements are based on management's current expectations and beliefs, and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this in this Current Report on Form 8-K or the materials furnished or filed herewith, including, without limitation, risks associated with: the impact of the ongoing COVID-19 pandemic, changing macroeconomic conditions or uncertain geopolitical factors where the Company has operations or does business, as well as on the timing and anticipated results of its clinical trials, strategy and future operations; the delay of any current or planned clinical trials or the development of the Company's drug candidates; the risk that the results of its clinical trials may not be predictive of future results in connection with future clinical trials; the Company's ability to successfully demonstrate the safety and efficacy of its drug candidates; the timing and outcome of its planned interactions with regulatory authorities; and obtaining, maintaining and protecting its intellectual property. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in the Company's most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q, as well as any subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent the Company's views only as of today and should not be relied upon as representing its views as of any subsequent date. The Company explicitly disclaims any obligation to update any forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

Item 9.01 Financial Statements and Exhibits.

99.1	Press release issued by Relay Therapeutics, Inc. on June 27, 2022, furnished herewith.
99.2	Virtual analyst and investor event presentation, dated June 27, 2022, furnished herewith.
104	Cover Page Interactive Data File (embedded within Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

RELAY THERAPEUTICS, INC.

Date: June 27, 2022

By: /s/ Brian Adams
Brian Adams, J.D.
Chief Legal Officer

Relay Therapeutics Discloses Anticipated Registrational Path for RLY-4008 in Cholangiocarcinoma and Growing Breast Cancer Franchise at Virtual Analyst and Investor Event

End-of-phase 1 meeting with the U.S. Food and Drug Administration (FDA) resulted in alignment on the design of a single arm trial for pan-FGFR (FGFRi) treatment-naïve FGFR2-fusion cholangiocarcinoma (CCA) to potentially support accelerated approval

Interim data from the once daily (QD) dosing schedule shared with the FDA demonstrated confirmed partial responses in eight out of thirteen (62%) FGFRi-naïve FGFR2-fusion CCA patients, including all four of the patients treated at the registrational trial dose of 70 mg QD

Relay Therapeutics discloses three new programs as part of a growing HR+/HER2- breast cancer franchise: selective CDK2 inhibitor, ERα degrader, and chemically distinct pan mutant-PI3Kα (RLY-5836)

Relay Therapeutics continues to expect its current cash, cash equivalents and investments will be sufficient to fund its current operating plan into 2025

Cambridge, MA – June 27, 2022 – Relay Therapeutics, Inc. (Nasdaq: RLAY) a clinical-stage precision medicine company transforming the drug discovery process by combining leading-edge computational and experimental technologies, will announce today the anticipated registrational path for RLY-4008 and three new programs within a growing HR+/HER2- breast cancer franchise at a virtual analyst and investor event from 8:00 a.m. to 9:00 a.m. ET.

“2022 has proven to be an extremely productive year so far for Relay Therapeutics and we’re looking forward to sharing updates across our portfolio today,” said Sanjiv Patel, M.D., Relay Therapeutics’ president and chief executive officer. “We are excited to be announcing the anticipated registrational path for RLY-4008 and the maturation of the data to support that pathway. In addition, building on the foundation of our PI3Kα franchise, we will outline a broad commitment to developing comprehensive treatment options for breast cancer patients. We believe our platform and approach have the potential to address some of the hardest-to-treat diseases and are excited to do just that in the coming years.”

RLY-4008 Regulatory and Clinical Data Update

Relay Therapeutics conducted an end-of-phase 1 meeting with the FDA to discuss next steps for the clinical development of RLY-4008. Based on discussions with the FDA, the Company has decided to move forward with a single arm trial design for FGFRi-naïve FGFR2-fusion CCA at 70 mg once daily to potentially support accelerated approval. The Company also intends to add additional supportive CCA cohorts to an NDA submission, including frontline, FGFRi-experienced and FGFR2 mutation and amplification patients that could potentially facilitate a line and alteration agnostic label if the submission is approved.

The interim data shared with the FDA included a data cut-off of April 19, 2022, from the dose escalation portion of the ongoing study. The interim data included a safety database of 115 patients, with 58 patients treated with the once daily (QD) dosing schedule, and 13 of these patients were FGFRi-naïve FGFR2-fusion CCA patients treated with the once daily schedule ranging from 20 mg up to 70 mg. Also, in addition to the 17 patients previously disclosed at a twice daily (BID) schedule, an additional 40 patients were evaluated with an intermittent dosing schedule, both of which have been deprioritized.

The safety analysis as of the April 19, 2022 cut-off date was consistent with the analysis from the initial October 2021 data disclosure. Most treatment emergent adverse events were expected FGFR2 on target, low-grade, monitorable, manageable, and largely reversible. There were no observed Grade 4 or 5 adverse events. Notable off-target toxicities of hyperphosphatemia and diarrhea continued to be clinically insignificant.

The efficacy analysis from this interim data on the once daily dosing schedule presented to the FDA demonstrated confirmed partial responses in eight out of thirteen (62%) FGFRi-naïve FGFR2-fusion CCA patients across the 20 mg to 70 mg QD cohorts. There were four patients treated at the registrational trial dose of 70 mg QD as of the April 19, 2022 cut-off date, all of which had confirmed partial responses.

An update from the FGFRi-naïve FGFR2-fusion CCA patients treated at 70 mg QD across dose escalation and expansion is expected to be presented at a medical meeting in the second half of 2022. The entirety of the dose escalation data is expected to be presented at a medical meeting or published by the end of the first half of 2023. Lastly, initial data from the non-CCA expansion cohorts is expected to be presented in 2023.

Breast Cancer Portfolio and New Targets

Relay Therapeutics today disclosed three new programs from a growing breast cancer franchise including a selective CDK2 inhibitor, a rationally designed ERα degrader, and a chemically distinct pan-mutant selective PI3Kα inhibitor (RLY-5836).

- CDK2 is a common cause of resistance to the over 50,000 patients a year in the U.S. on CDK4/6 inhibitors and potentially an important PI3Kα combination partner. Relay Therapeutics progressed from first compound synthesized to an advanced CDK2 lead compound with robust selectivity over other CDK family members in less than a year. This program is expected to enter the clinic in Q4 2023 or Q1 2024.
- Leveraging the Dynamo™ platform, Relay Therapeutics has been able to move from the traditional empirical design of bi-functional degraders to rationally designed molecules. The company expects to nominate an ERα degrader development candidate in 2023.
- As a demonstration of Relay Therapeutics' commitment to PI3Kα mutant inhibition, the Company has designed a selective and chemically distinct pan-mutant PI3Kα inhibitor, RLY-5836. RLY-5836 is expected to be ready to enter the clinic in 2023.

Conference Call Information

Relay Therapeutics will host a live webcast and conference call today beginning at 8:00 am E.T. The virtual analyst and investor event will be webcast live and may be accessed through Relay Therapeutics' website under Events in the News & Events section through the following link: https://ir.relaytx.com/news-events/events-presentations. An archived replay of the webcast will be available following the event.

About RLY-4008

RLY-4008 is a potent, selective and oral small molecule inhibitor of FGFR2, a receptor tyrosine kinase that is frequently altered in certain cancers. FGFR2 is one of four members of the FGFR family, a set of closely related proteins with highly similar protein sequences and properties. Preclinically, RLY-4008 demonstrated FGFR2-dependent killing in cancer cell lines and induced regression in *in vivo* models, while minimal inhibition of other targets was observed, including other members of the FGFR family. In addition, RLY-4008 demonstrated strong activity against known clinical on-target resistance mutations in cellular and *in vivo* preclinical models. RLY-4008 is currently being evaluated in a clinical trial in patients with advanced or metastatic FGFR2-altered solid tumors with a single arm, potentially registration-enabling cohort for pan-FGFR ("FGFRi") treatment-naïve FGFR2-fusion CCA. To learn more about the clinical trial of RLY-4008, please visit here.

About Relay Therapeutics

Relay Therapeutics (Nasdaq: RLAY) is a clinical-stage precision medicines company transforming the drug discovery process by combining leading-edge computational and experimental technologies with the goal of bringing life-changing therapies to patients. As the first of a new breed of biotech created at the intersection of disparate technologies, Relay Therapeutics aims to push the boundaries of what is possible in drug discovery. Its Dynamo™ platform integrates an array of leading-edge computational and experimental approaches designed to drug protein targets that have previously been intractable. Relay Therapeutics' initial focus is on enhancing small molecule therapeutic discovery in targeted oncology and genetic disease indications. For more information, please visit www.relaytx.com or follow us on Twitter.

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impact of the ongoing COVID-19 pandemic, changing macroeconomic conditions or uncertain geopolitical factors where Relay Therapeutics has operations or does business, as well as on the timing and anticipated results of its clinical trials, strategy and future operations; the delay of any current or planned clinical trials or the development of Relay Therapeutics' drug candidates; the risk that the results of its clinical trials may not be predictive of future results in connection with future clinical trials; Relay Therapeutics' ability to successfully demonstrate the safety and efficacy of its drug candidates; the timing and outcome of its planned interactions with regulatory authorities; and obtaining, maintaining and protecting its intellectual property. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in Relay Therapeutics' most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q, as well as any subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent Relay Therapeutics' views only as of today and should not be relied upon as representing its views as of any subsequent date. Relay Therapeutics explicitly disclaims any obligation to update any forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

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Exhibit 99.2

RELAY®
THERAPEUTICS

Analyst & Investor Event

June 27, 2022

Disclaimer

This presentation contains forward-looking statements and information about our current and future prospects and our operations and financial results, which are based on currently available information. All statements other than statements of historical facts contained in this presentation, including statements regarding our strategy, future financial condition, future operations, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "design," "due," "estimate," "expect," "goal," "intend," "may," "objective," "opportunity," "plan," "predict," "positioned," "potential," "seek," "should," "target," "will," "would" and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. These forward-looking statements include express or implied statements about the initiation, timing, progress and results of our current and future clinical trials and current and future preclinical studies of our product candidates; the timing of disclosures regarding our pipeline and additional clinical data for RLY-4008 and initial clinical data for RLY-2608; the potential therapeutic benefits of our product candidates, including potential efficacy and tolerability, and combination potential of our product candidates; whether preliminary results from our preclinical or clinical trials will be predictive of the final results of the trials or any future clinical trials of our product candidates; the possibility that unconfirmed results from these trials will not be confirmed by additional data as the clinical trials progress; the competitive landscape and market opportunities for our product candidates; the expected strategic benefits under our collaborations; our ability to successfully establish or maintain collaborations or strategic relationships for our product candidates; expectations regarding current and future interactions with the U.S. Food and Drug Administration (FDA); our ability to manufacture our product candidates in conformity with the FDA's requirements; the capabilities and development of our Dynamo™ platform; our financial performance; the effect of the COVID-19 pandemic, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations, including but not limited to our preclinical studies and future clinical trials; our plans to develop, manufacture and commercialize our current product candidates and any future product candidates; and the implementation of our business model and operating plans as well as the strategic plans for our business, current product candidates and any future product candidates.

Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make due to a number of risks and uncertainties. These and other risks, uncertainties and important factors are described in the section entitled "Risk Factors" in our most recent Annual Report on Form 10-K or most recent Quarterly Report on Form 10-Q, as well as any subsequent filings with the Securities and Exchange Commission. Any forward-looking statements represent our views only as of the date of this presentation and we undertake no obligation to update or revise any forward-looking statements, whether as a result of new information, the occurrence of certain events or otherwise. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and our own internal estimates and research. While we believe these third-party studies, publications, surveys and other data to be reliable as of the date of this presentation, we have not independently verified, and make no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, no independent source has evaluated the reasonableness or accuracy of our internal estimates or research and no reliance should be made on any information or statements made in this presentation relating to or based on such internal estimates and research.

This presentation contains trademarks, trade names and service marks of other companies, which are the property of their respective owners.

Relay Tx – Patient-Driven & Execution Focused

New Breed of Biotech

Clear Focus

Validated Targets	Therapeutic Areas	Modalities
Innovators	Oncology	Small molecules
Challengers	Genetic diseases	Degraders

Validated Approach

Clinical

- FGFR2 *RLY-4008*
- PI3Kα^{PAN} *RLY-2608*
- SHP2 *RLY-1971*

Pre-clinical

- PI3Kα^{PAN} *RLY-5836*
- Selective CDK2
- ERα Degrader

Execution-Focused

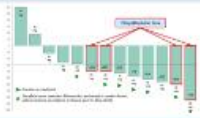
2022 Commitments & Disclosures to be Made Today

RLY-4008 (FGFR2)	RLY-2608 (PI3Kα^{PAN})	RLY-1971 (SHP2)	Next target in pipeline
Expansion cohorts open Additional data update in 2H 2022	Clinical trial initiated	GDC-6036 (KRAS G12C) combination trial initiated in July 2021	Selective CDK2 inhibitor
+ Regulatory & data update	+ RLY-5836 -PI3Kα^{PAN}		+ ERα degrader
+ Pivotal cohort commenced			

Previously disclosed | To be disclosed today | + Additional disclosure today

Agenda

1. RLY-4008 Regulatory Update



2. Breast Cancer Portfolio

3. Overview of Dynamo™ Platform

4. Future Guidance and Q&A

RLY-4008: FGFR2 Selective Inhibitor – Alignment on Registrational Trial Design

Extensive Dose Finding Completed

Dose Escalation (Opened Sep 2020) → **Dose Expansion** (Opened Dec 2021) → **Pivotal Expansion** (Commenced)

- Dose Escalation: Twice-daily, intermittent, & once daily schedules explored
- Dose Expansion: 70 mg QD ongoing
- Pivotal Expansion: 70 mg QD selected

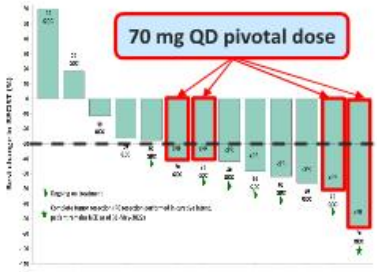
70 mg QD selected

Pivotal Study Aligned with FDA

- *Pivotal Expansion*: *FGFR2*-fusion+ cholangiocarcinoma (CCA) without prior FGFRi (n=100)
- *Supportive cohorts*:
  - FGFR2-fusion+ CCA with prior FGFRi (n=50)
  - FGFR2-fusion+ CCA with no prior treatment (n=20)
  - FGFR2 amps/mut CCA (n=20)

Encouraging Efficacy

FGFR2-fusion+ cholangiocarcinoma (CCA) without prior FGFRi



Project Optimus shaped trial design

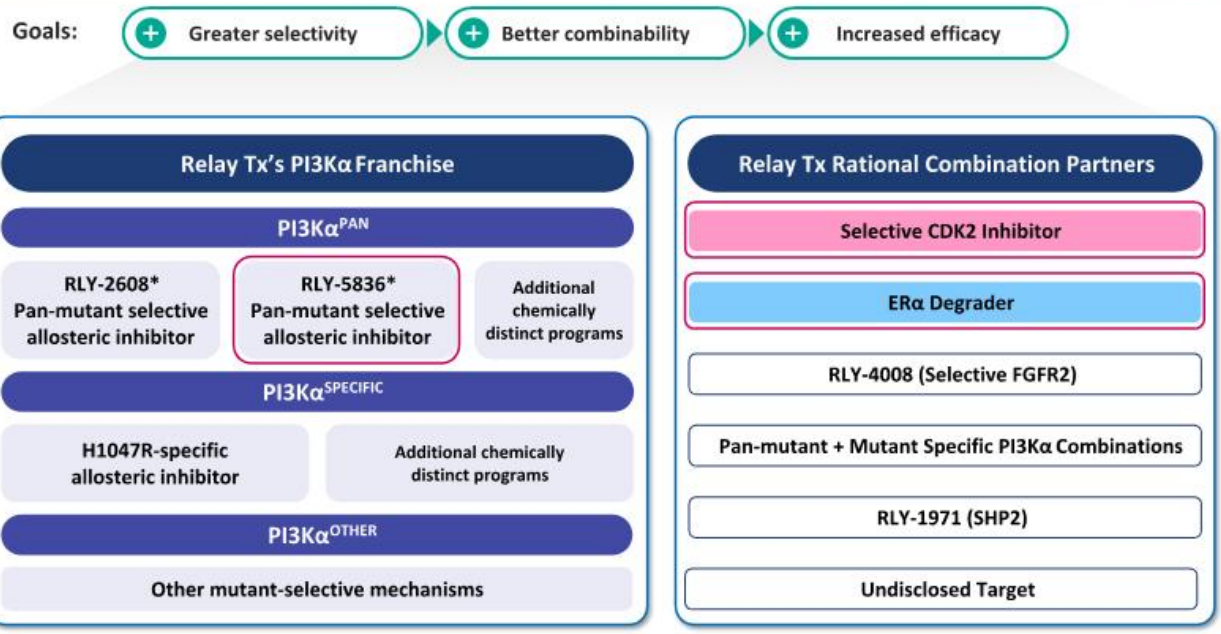
Alignment with FDA on single arm, trial design for FGFRi-naïve FGFR2-fusion CCA to potentially support accelerated approval

Potential for RLY-4008 as an important treatment option for patients

Preliminary data as of 19-April-2022

2

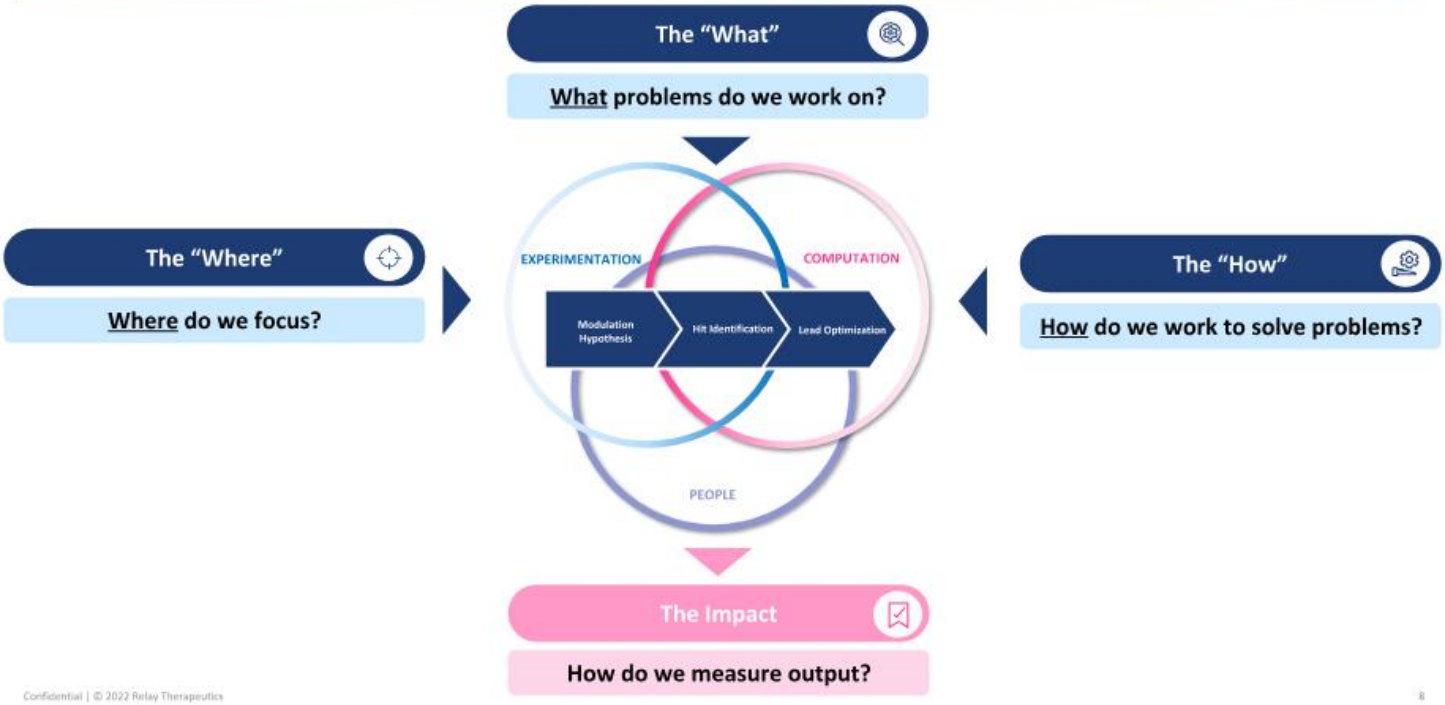
Relay Tx's Emerging Breast Cancer Franchise



*Covers H1047X, E542X, E545X hot spots

New programs disclosed today

Relay Tx – Understanding Next Generation Drug Discovery: 4 Questions



Relay Tx – Capital, Team & Execution Focus to Deliver on Anticipated Milestones

RELAY THERAPEUTICS

Breast Cancer Franchise

RLY-2608 (PI3Kα^{PAN})

Initial data in 1H 2023

Selective CDK2

Clinical start in Q4 2023 or Q1 2024

ERα Degrader

Development candidate nomination in 2023

Tumor Agnostic

RLY-4008 (Selective FGFR2)

Additional data updates in 2H 2022 & 2023

RLY-1971 (SHP2)

Atezolizumab combo trial to be initiated in 2H 2022

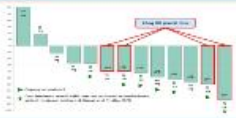
$898M

Cash, cash equivalents and investments as of the end of Q1 2022

Current cash, cash equivalents and investments are expected to be sufficient to fund current operating plan into 2025

Agenda

1. RLY-4008 Regulatory Update



2. Breast Cancer Portfolio

3. Overview of Dynamo™ Platform

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RLY-4008 – Context: October 2021 Clinical Data Disclosure - Dose Escalation

Dose Escalation
(Opened September 2020)

Bayesian Optimal Interval Escalation (BOIN) design

Unresectable or metastatic solid tumors

FGFR2-alterations per local assessment (tumor tissue or blood)

Both FGFRi-naïve & FGFRi-treated allowed

Once & twice daily schedules explored across 6 different doses

October 2021 Disclosure

Data from 2021 AACR-NCI-EORTC Molecule Targets Presentation (October 2021, n = 49 patients)

RLY-4008 Data

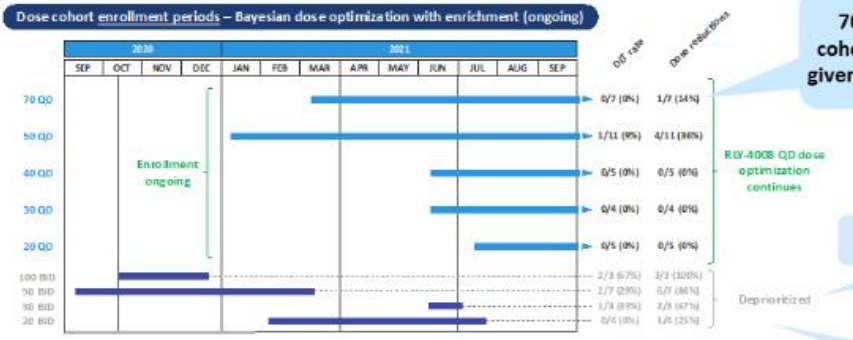
- **Execution** → 49 patients (through October 2021)
- **Selectivity** → No significant hyperphosphatemia (FGFR1) or diarrhea (FGFR4) observed to-date
- **Safety and Tolerability** → Robust inhibition of FGFR2 with promising initial tolerability data
- **Early Efficacy** → 3 out of 6 fusion+ CCA FGFRi naïve patients with confirmed PRs

Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference

RLY-4008 - Dose Escalation
BID Schedule De-Prioritized & 70 mg QD Selected For Expansion Cohorts

Data from 2021 AACR-NCI-EORTC Molecular Targets Presentation (October 2021)

FGFR2 – RLY-4008 FIH Study: Parallel Bayesian Dose Optimization Ongoing



70 mg QD selected for expansion cohorts with goal to optimize efficacy given sustained 95% target engagement

BID schedule de-prioritized

In addition, intermittent dose schedule explored and deprioritized

Doses at ≥40mg resulted in 90%+ target inhibition

RLY-4008– Continued Clinical Execution

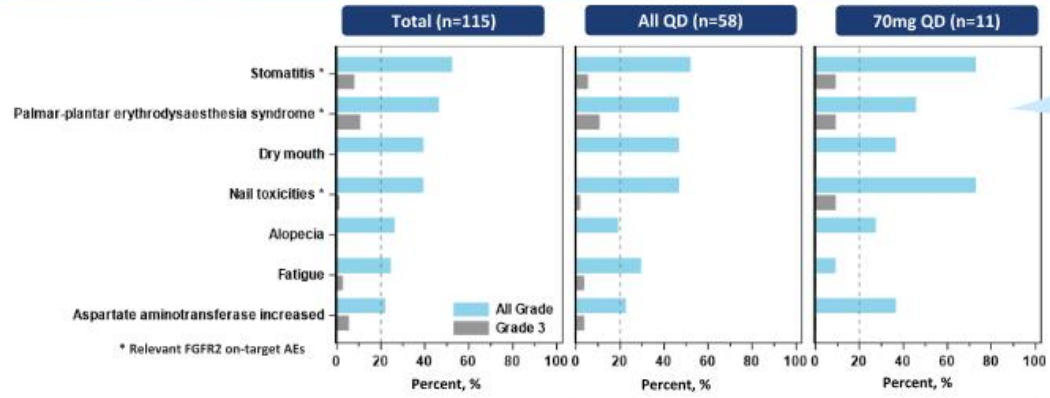
	Presentation at EORTC NCI AACR in Oct 2021 (as of 9 Sept 2021)	Relay Tx Analyst and Investor Event in June 2022 (as of 19 April 2022)		
	Total	Total	QD (once daily)	70 mg QD
Total Patients Dosed	49	115	58	11
Cholangiocarcinoma (CCA) Patients				
FGFRi pre-treated				
Fusion	25	49	25	1
Other FGFR2 alteration	3	6	2	1
FGFRi naïve				
Fusion	7*	24	13	4
Other FGFR2 alteration	5	11	6	2
Non-Cholangiocarcinoma				
Fusion	0	7	2	1
Mutation	6	13	7	1
Amplification	1	3	2	0
Other FGFR2 driven tumor	2	2	1	1
Countries Open	1	11		
Sites	11	35		

*6 evaluable

Continued robust clinical execution since the October disclosure

RLY-4008 – Treatment Emergent Adverse Events (TEAEs) Profile

TEAEs ≥20%



Most TEAEs are expected FGFR2-on target, low grade, monitorable, manageable and largely reversible

Median time on treatment (wks)	16	18	16
Dose modification due to related TEAEs			
Dose interruption (%)	38	38	55
Dose reduction (%)	21	19	36
Dose discontinuation (%)	0	0	0

70 mg QD actual dose intensity of 65 mg/day

No drug related dose discontinuation

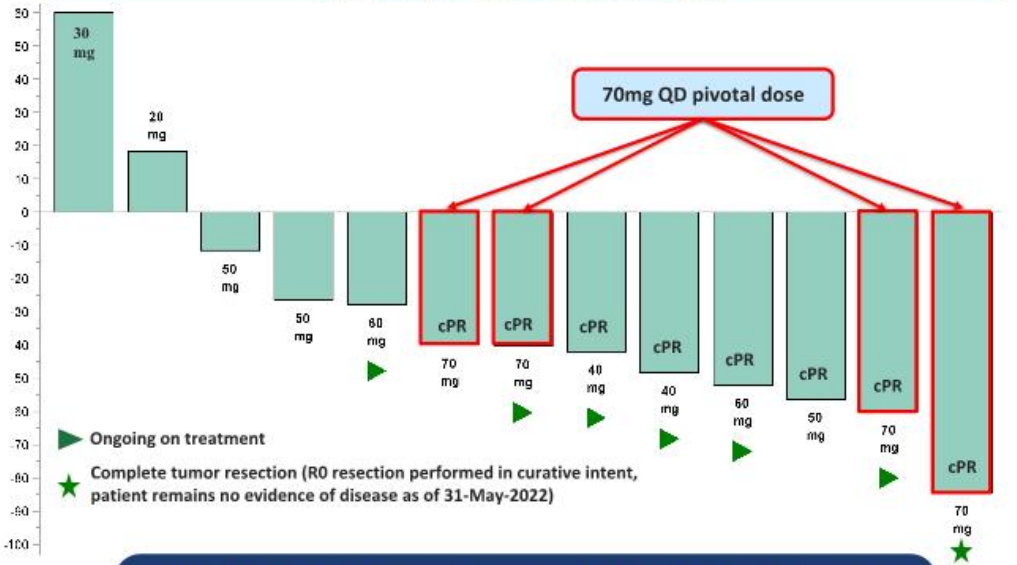
Clinically insignificant off-target hyperphosphatemia (14%, all Gr 1-2) and diarrhea (10%, all Gr 1-2) allow for optimization of FGFR2 inhibition

Note: Treatment-emergent adverse events (TEAEs) ≥ 20% in total population

Preliminary data as of 19-April-2022

RLY-4008 – Radiographic Tumor Regression Data Continue to Show Promise for FGFRi-Naïve Cholangiocarcinoma QD Patients

Best RECIST Change (%) from Baseline Based on Investigator Evaluated Response for FGFRi-Naïve Cholangiocarcinoma Patients



Approved Pan-FGFR inhibitors demonstrate 23-36% ORR in this population

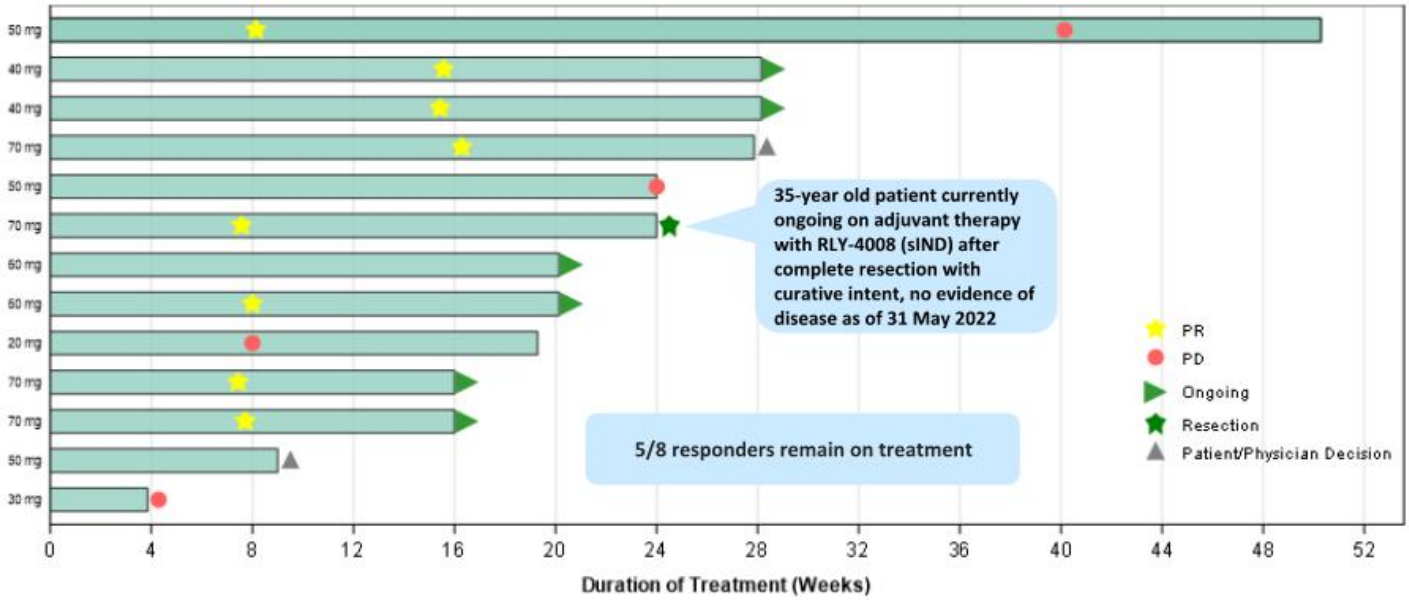
In October 2021 disclosure:
- 3 out of 6 fusion+ CCA FGFRi naïve patients with confirmed PRs

In June 2022 disclosure:
- 8/13 pts with confirmed PRs, 6 pts ongoing (**62%** ORR) across all once daily doses

cPR = confirmed partial response; ORR = overall response rate

Preliminary data as of 19-April-2022

RLY-4008 – Time on Treatment for FGFRi-Naïve Cholangiocarcinoma QD Patients

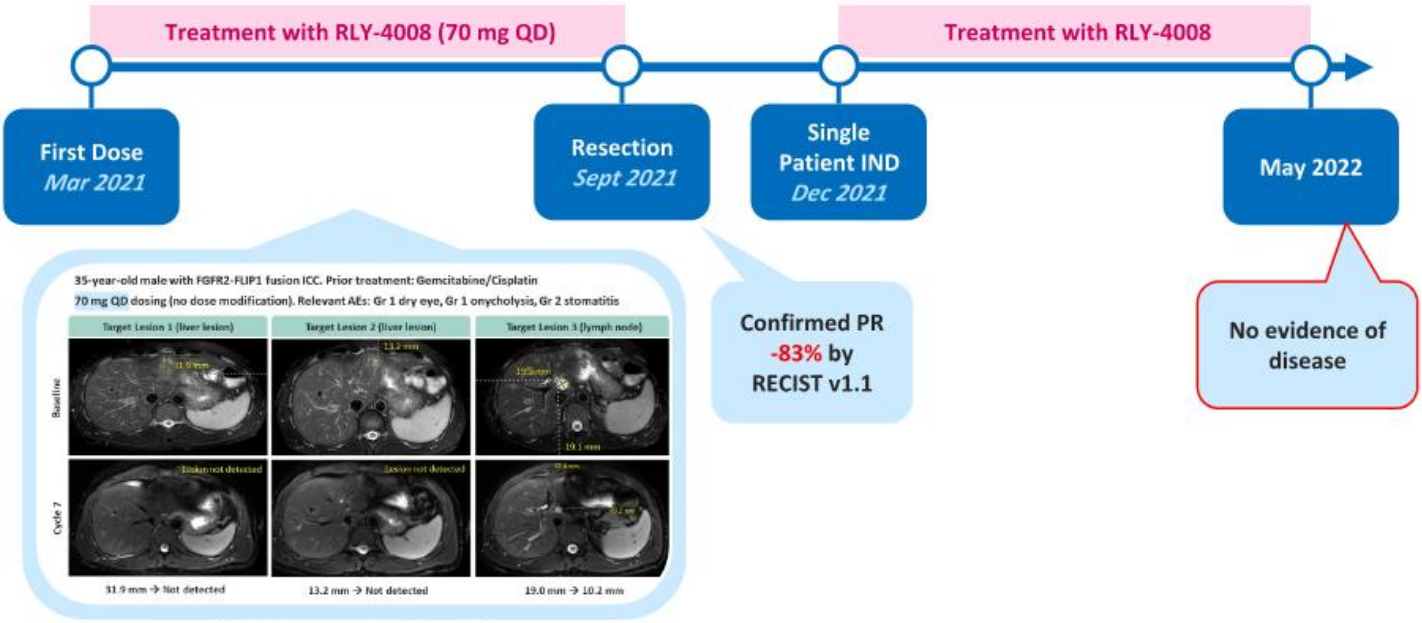


Note: All PRs in this cohort have been confirmed.

PR = partial response; PD = progressive disease

Preliminary data as of 19-April-2022 [16]

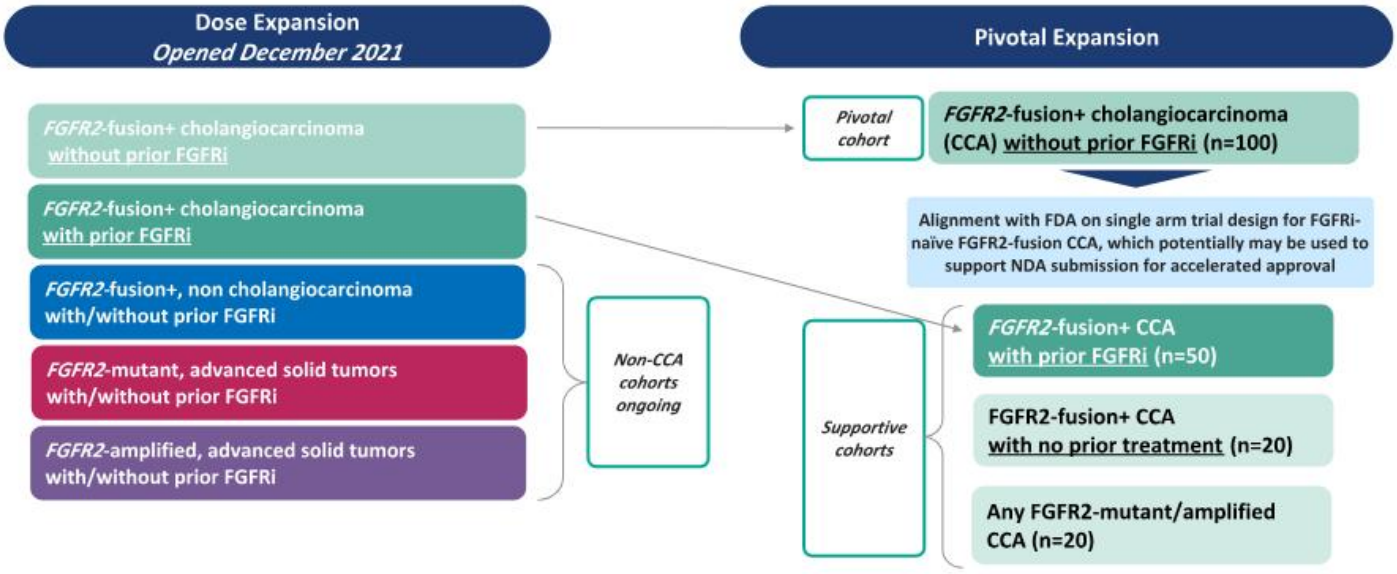
RLY-4008 - Patient with Near Complete Regression of FGFR2-Fusion, FGFRi-Naïve CCA Underwent Resection with No Evidence of Disease as of May 2022



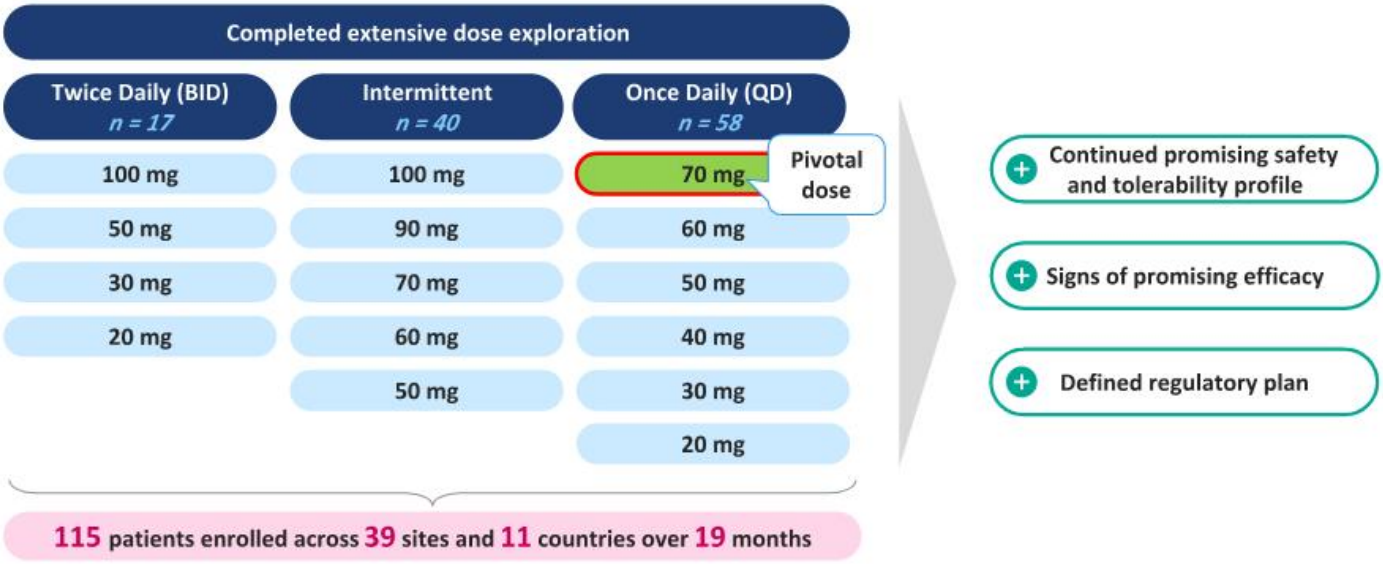
Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference
Courtesy: Dr. V. Sahoi (U Michigan)

Preliminary data as of May 2022

RLY-4008 – Pivotal Study Design



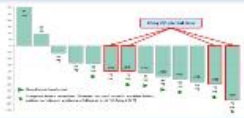
RLY-4008 – Exemplary Clinical Execution



QD: once daily, Intermittent: 3 wks on – 1 wk off, BID: twice daily

Agenda

1. RLY-4008 Regulatory Update

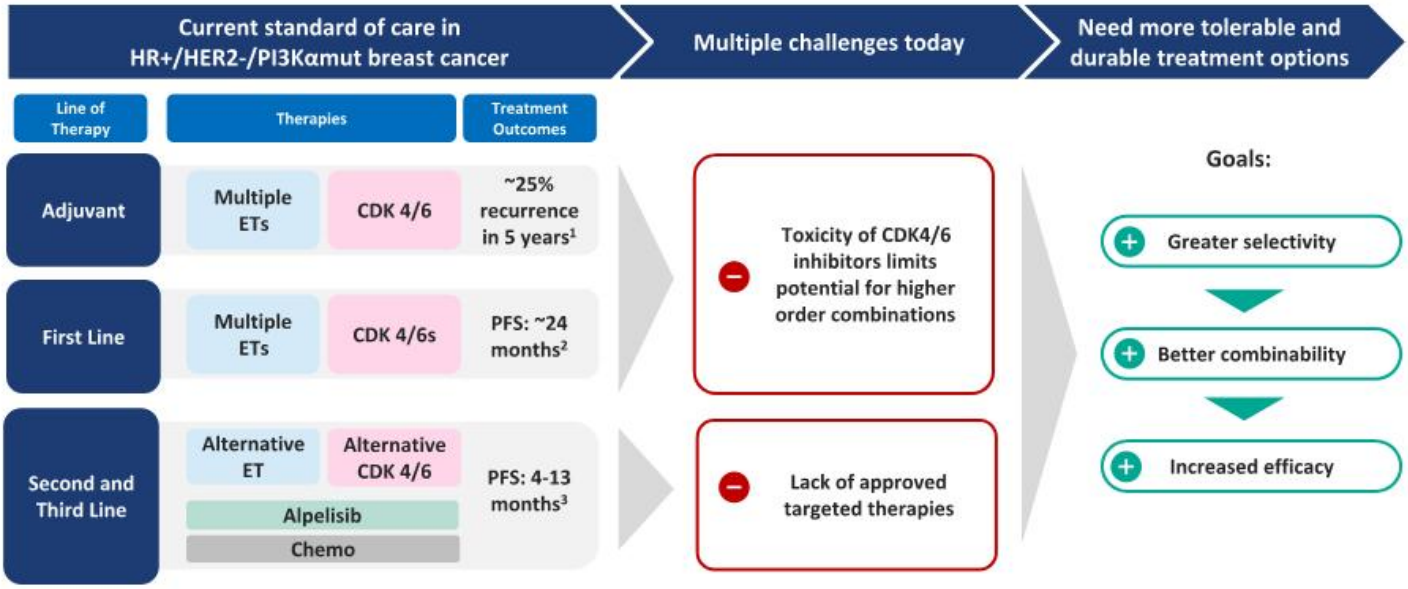


2. Breast Cancer Portfolio

3. Overview of Dynamo™ Platform

4. Future Guidance and Q&A

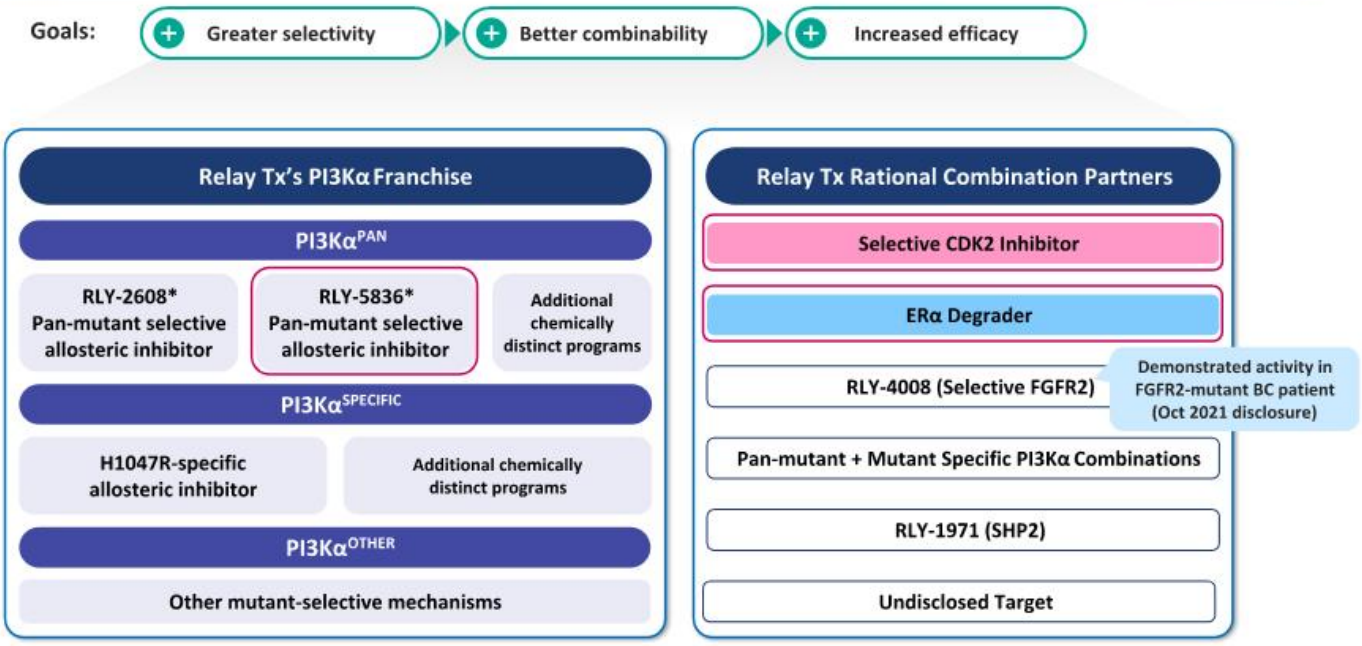
Breast Cancer – Challenges with Current Treatment Landscape



ET - Endocrine Therapy

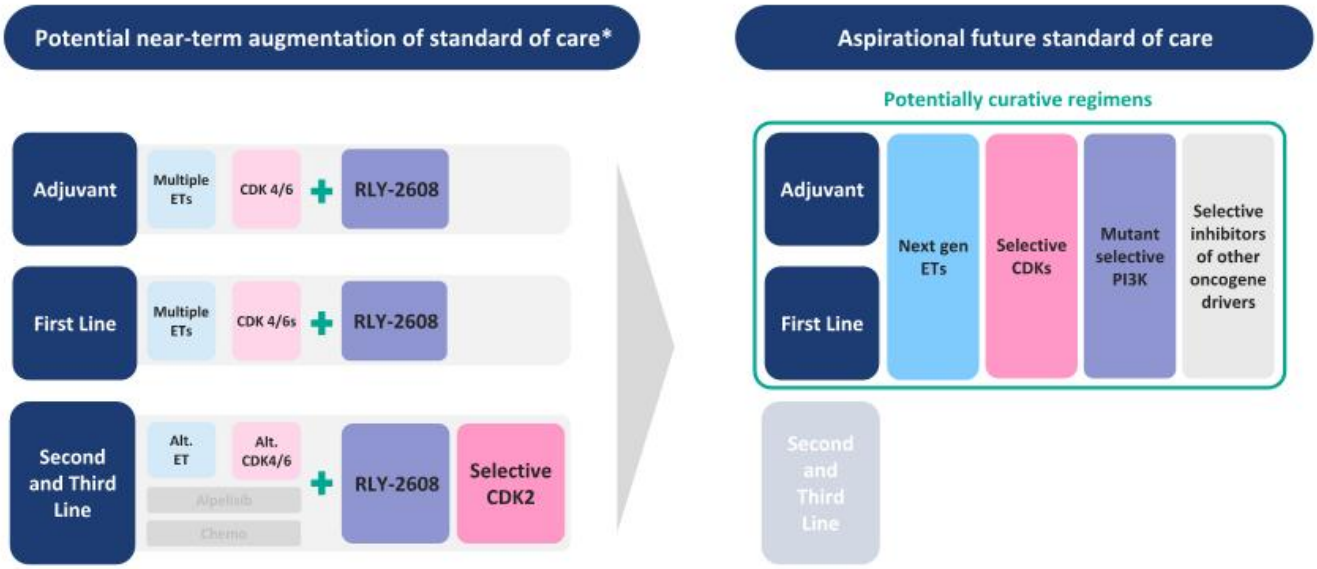
[1]Adjuvant treatment outcome sources: SEER; van de Velde 2011 Lancet 377:321; Morden 2017 J Clin Oncol 35:2507; Jakesz 2005 Lancet 366:455; Margolese 2016 Lancet 387:849; Blok 2017 J Natl Cancer Inst 1:110; Anastrozole; Davies 2013 Lancet 381:805. [2]First Line treatment outcome sources: ESMO 2022 169P; PALOMA-2; Hortobagyi 2016 N Engl J Med 375:1738; Hortobagyi 2018 Ann Oncol 29:1541; Goetz 2017 J Clin Oncol35:3638; Johnston 2019 NPJ Breast Cancer 5:5. [3]Second and third line treatment outcome sources: Andre 2021 Ann Oncol 32:208; Rugo 2021 Lancet 22:489; Turner 2021 Oncologist; ASCO 2022 #1005.

Relay Tx's Emerging Breast Cancer Franchise



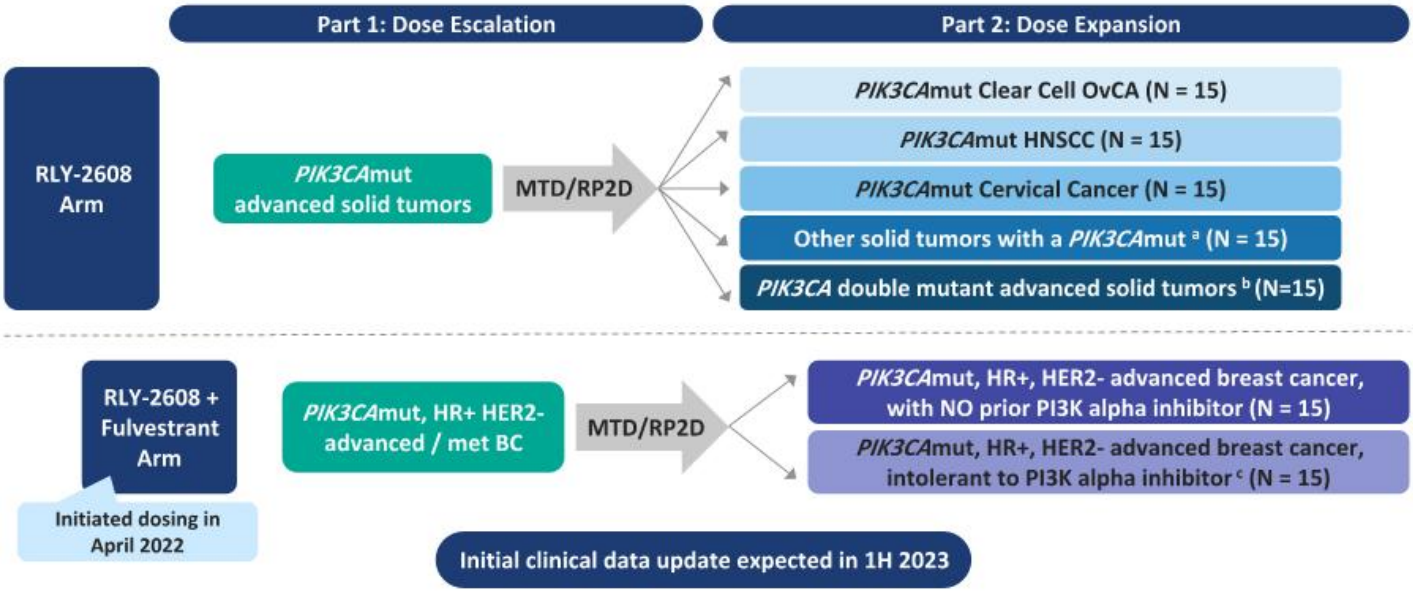
*Covers H1047X, E542X, E545X hot spots

Seeking to Transform the Breast Cancer Treatment Paradigm



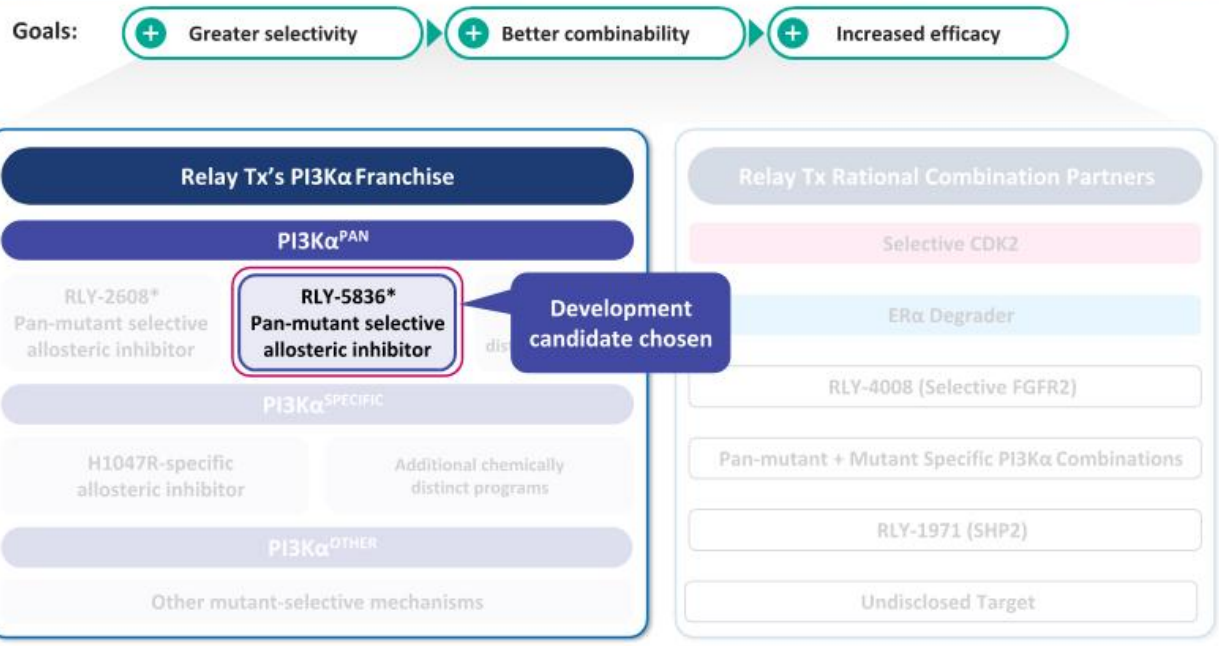
*If approved

PI3Kα – RLY-2608 Trial Design



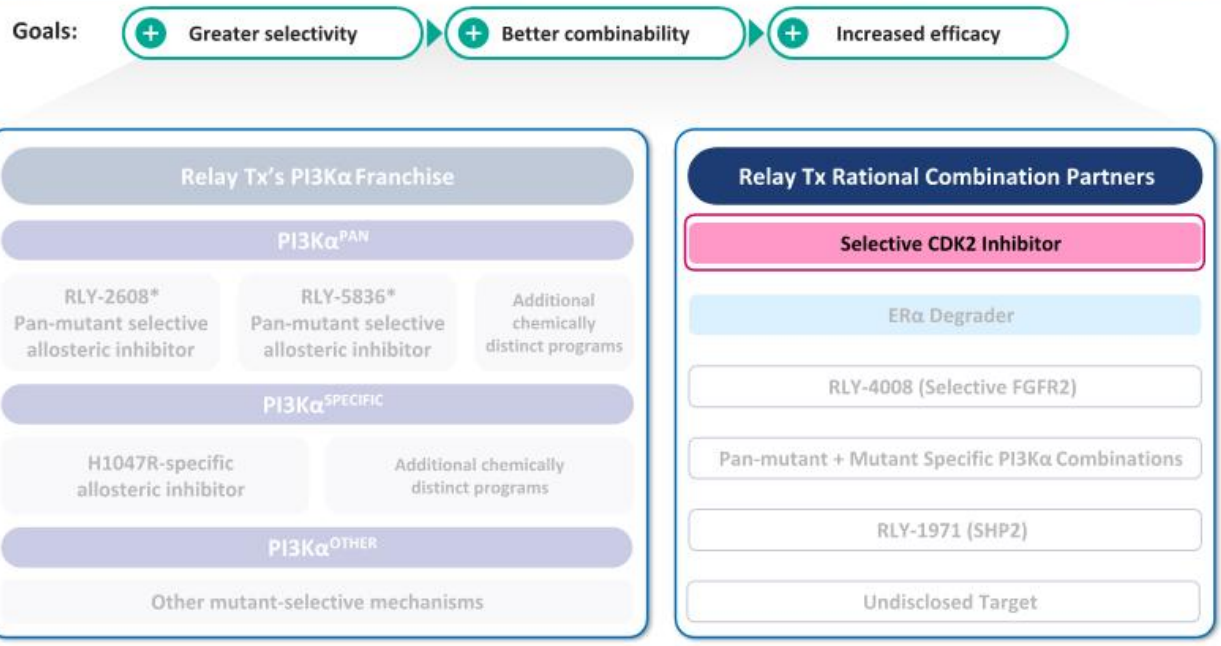
a. Excludes PIK3CAmut clear cell OvCA (ovarian cancer), HNSCC (head & neck squamous cell carcinoma), and Cervical cancer patients; b. Double mutation defined as one major PIK3CA mutation (E542X, E545X, H1047X) + ≥1 additional PI3KCA mutation per local assessment; c. Intolerance to PI3K alpha inhibitors is defined as treatment discontinuation due to treatment-related AE (e.g., hyperglycemia, rash, diarrhea, stomatitis) other than severe hypersensitivity reaction and/or life-threatening reactions, such as anaphylaxis and Stevens-Johnson syndrome. MTD = maximum tolerated dose; RP2D = recommended phase 2 dose

Relay Tx's Emerging Breast Cancer Franchise



*Covers H1047X, E542X, E545X hot spots

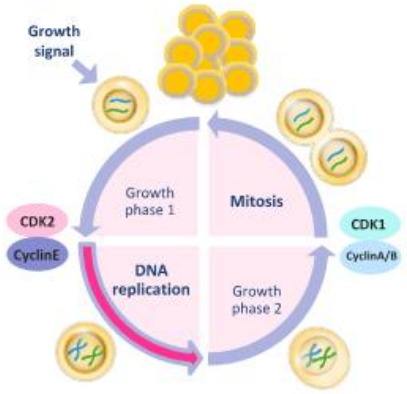
Relay Tx's Emerging Breast Cancer Franchise



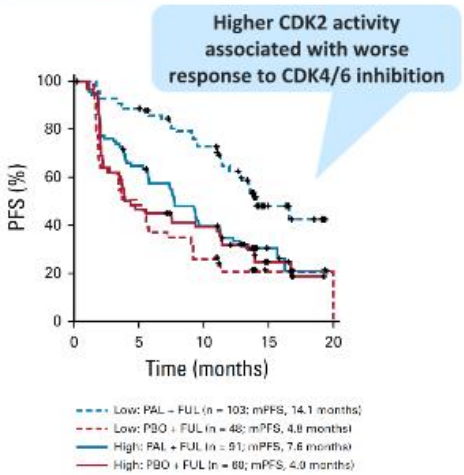
*Covers H1047X, E542X, E545X hot spots

CDK2 – A Validated Target in ER+ Breast Cancer

Cyclin E activates CDK2 to drive cancer



Clinical data demonstrate the importance of CDK2 in ER+ breast cancer



Turner, N.C., *et al.* JCO 2019

~45K patients receiving CDK4/6 inhibitors in the US

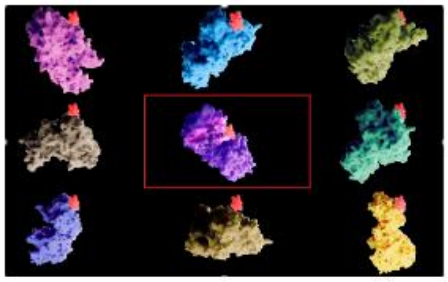
Patients receiving adjuvant CDK 4/6i	~23K
Patients receiving 1L CDK 4/6i	~18K
Patients receiving 2L CDK 4/6i	~5K

Source: Foundation Medicine Insights; SEER 2022; Decision Resources Group Breast Cancer Market Forecast, Feb 2022 (above corresponds to 2023 forecasted patient numbers); Scheidemann, 2021; Li, 2020

CDK2 – Relay Tx Unlocking Insights Into the Drivers of CDK2 Selectivity

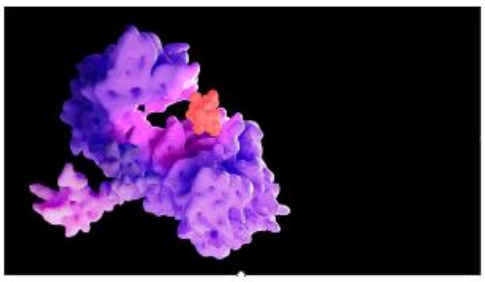
Traditional approach

Non-selective CDK inhibitors

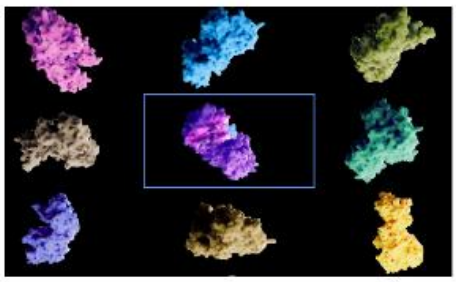


Relay Tx Approach

Motion-based insights into drivers of CDK2 selectivity…



…leveraged to design highly selective CDK2 inhibitors



CDK2 – Computational Modeling Designed to Enable Breakthrough Speed

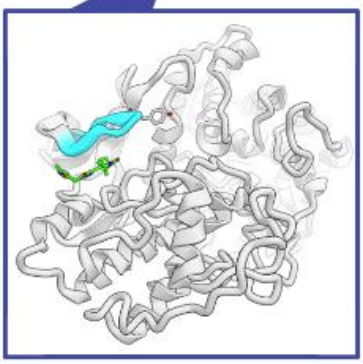
Collect MD frames
500 frames / MD
1000's of MDs

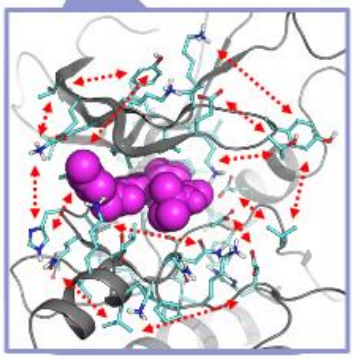
Extract features
~50,000 distances / frame

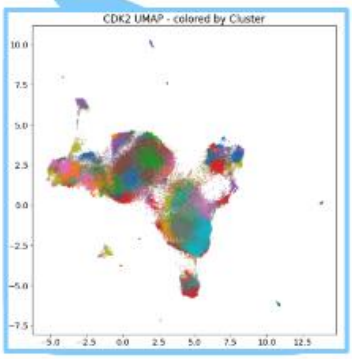
Cluster frames
100 clusters / CDK

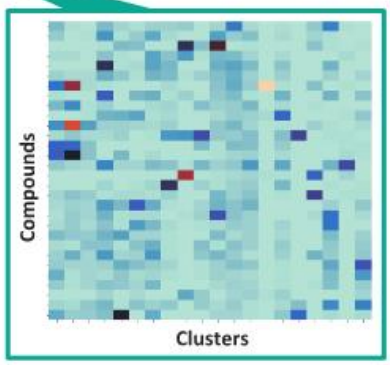
Assign cluster populations
200 cl. pops / ligand

Predict selectivity









First compound synthesized to identification of a lead compound in <1 year

CDK2 – Relay Tx's CDK2 Inhibitors Observed to be Highly Selective and Demonstrated Combination Potential with RLY-2608 in Breast Cancer

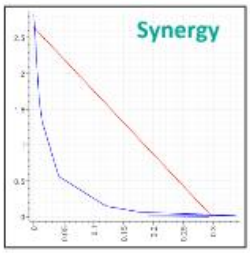
RTX-1 and RTX-2 achieved exquisite selectivity for a CDK2 inhibitor

		RTX-1	RTX-2
Biochemical Potency	CDK2/CycE IC_{50} (μM)	0.002	0.004
Biochemical Selectivity (fold over)	CDK1/CycB	300x	94x
	CDK4/CycD1	810x	270x
	CDK6/CycD3	830x	280x
	CDK9/CycT1	7900x	2400x
	GSK3β	59000x	68000x

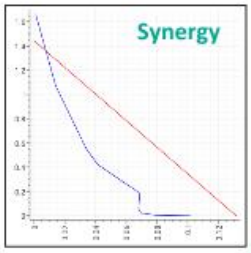
RTX-2 was synergistic with RLY-2608(PI3Kα^{PAN}) in HR+ *PIK3CA*-mut breast cancer resistant to CDK4/6 inhibitors

RTX-2 (CDK2 inhibitor) + RLY-2608 (PI3Kαinhibitor)

CDK4/6i Sensitive



CDK4/6i Resistant



Clinical start expected in Q4 2023 or Q1 2024

Relay Tx's Emerging Breast Cancer Franchise

*Covers H1047X, E542X, E545X hot spots

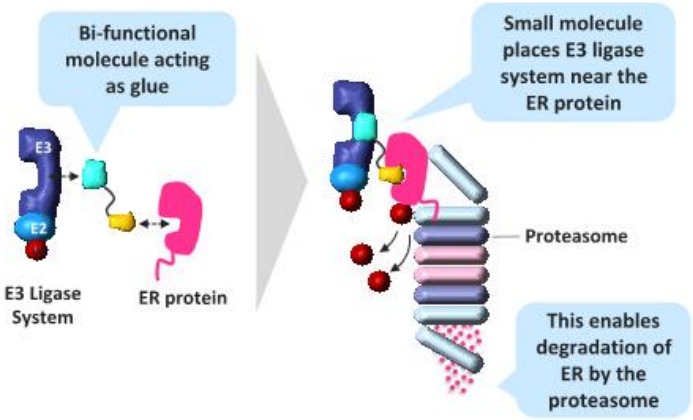
ERα Degrader – Endocrine Therapy is Central in the Treatment of HR+/HER2- Breast Cancer

Endocrine therapies are currently used in every line of therapy in HR+/HER2- Breast Cancer

Line of Therapy	Endocrine Tx
Adjuvant	Use of Endocrine Therapies
First Line	
Second Line +	

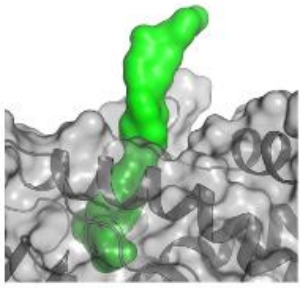
In-house ERα Degrader would further strengthen Relay Tx's Breast Cancer franchise

Enabling degradation of the estrogen receptor (ER) protein



ERα Degrader – Rational Design of Targeted Protein Degraders

Traditional Approach

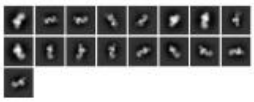


Relay Tx Approach

Multiple experimental tools deployed….

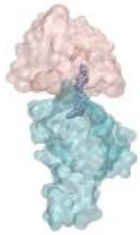
X-ray Crystallography

Cryo-EM



Binary complex HDX-MS

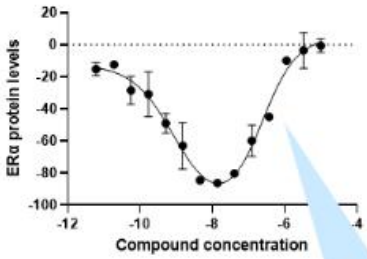
…to inform long-time scale MD models



Conformational models enable effective triage of degrader design ideas

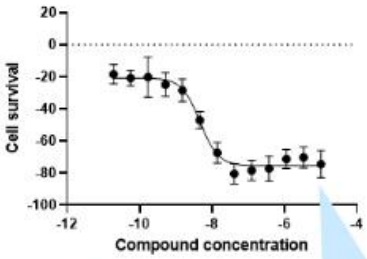
ERα Degrader – Relay Tx has Rapidly Obtained Potent Degraders of ERα

Protein degradation*



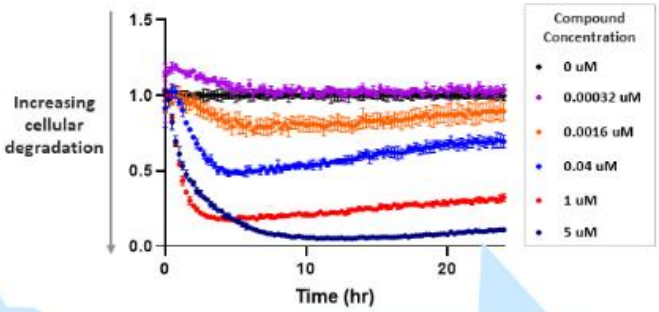
Hook effect characteristic of degraders observed with Relay Tx compound

Cellular proliferation*



Relay Tx compound potently inhibits cellular proliferation

Cellular degradation kinetics

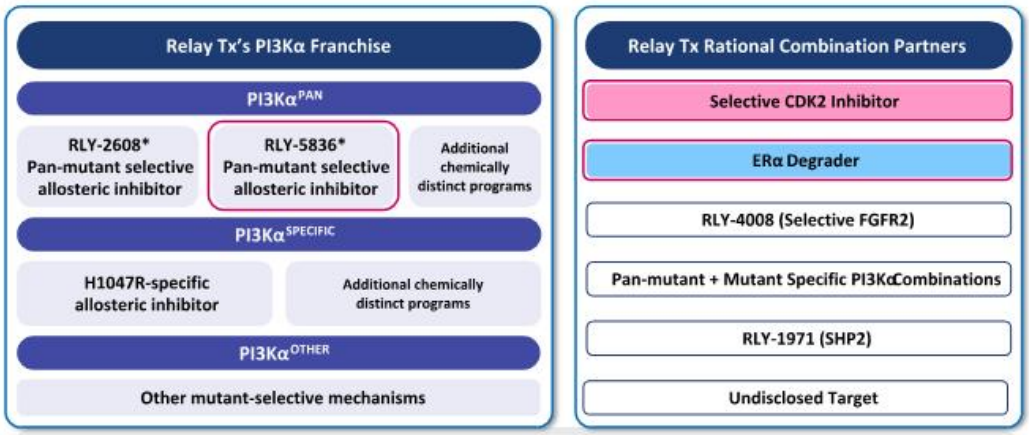


Increasing compound concentration yields faster and deeper protein degradation

Development candidate nomination expected in 2023

*MCF7-ERα -HiBiT cells

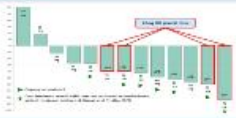
Large Breast Cancer Patient Population



~195K patients diagnosed annually in the US with HR+, HER2- breast cancer

Agenda

1. RLY-4008 Regulatory Update

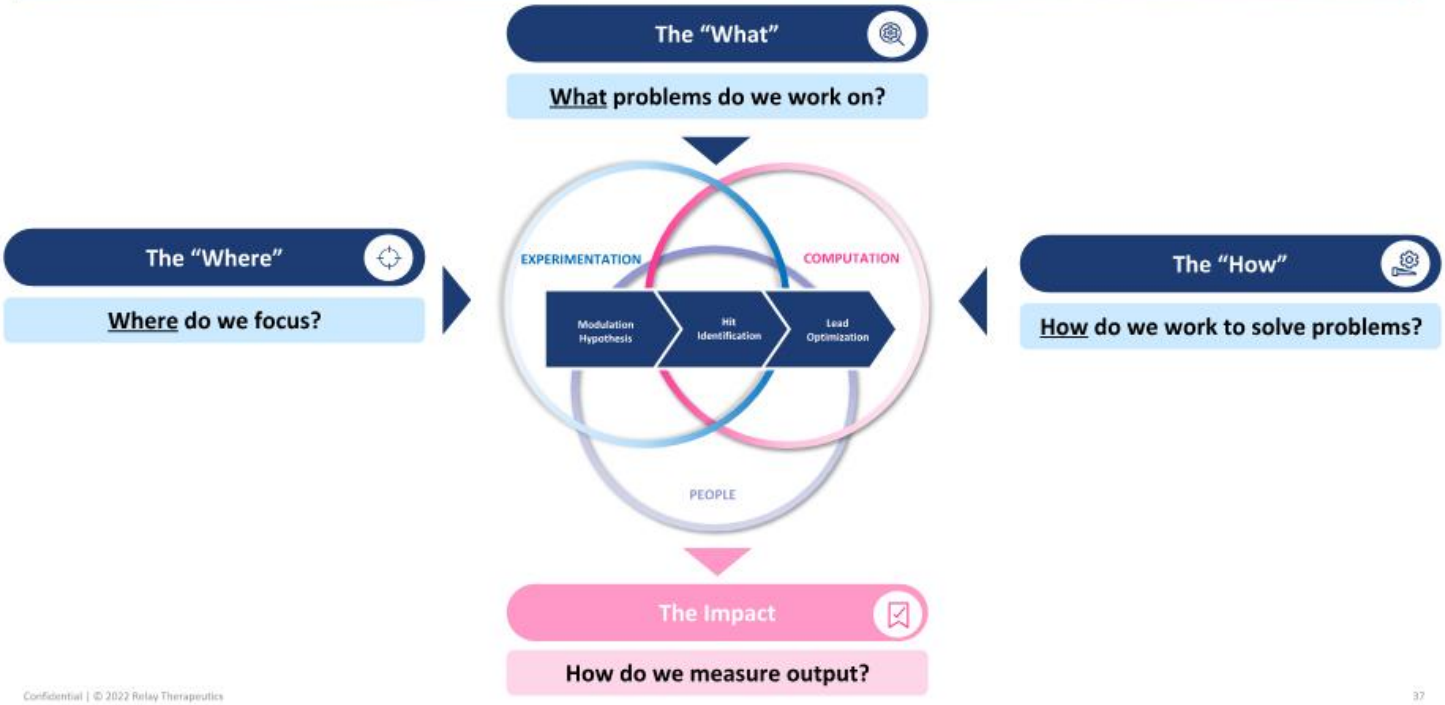


2. Breast Cancer Portfolio

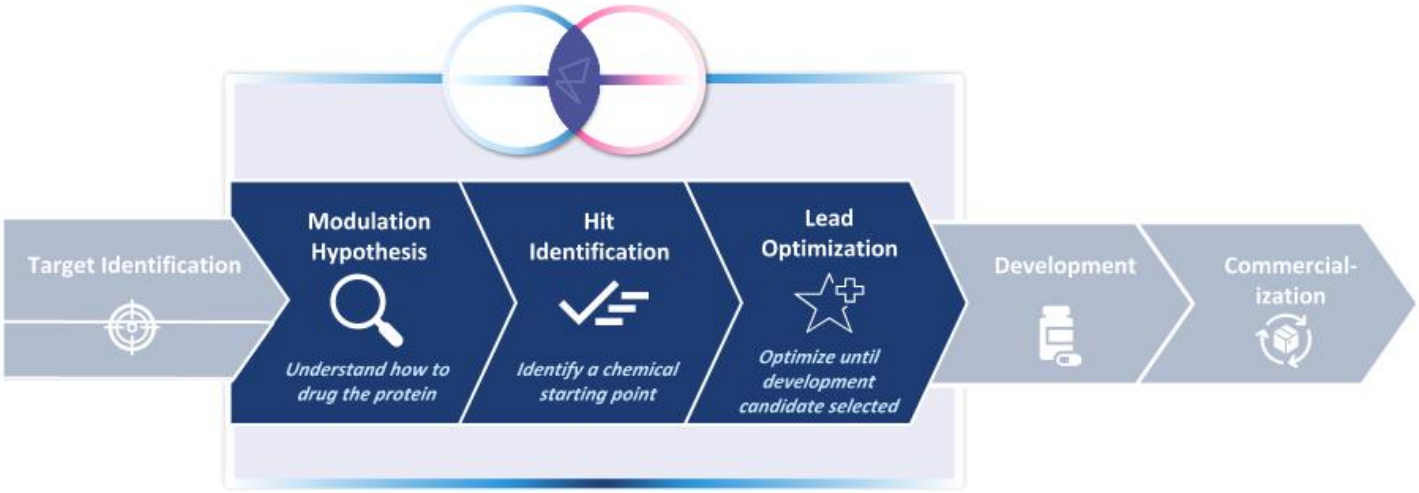
3. Overview of Dynamo™ Platform

4. Future Guidance and Q&A

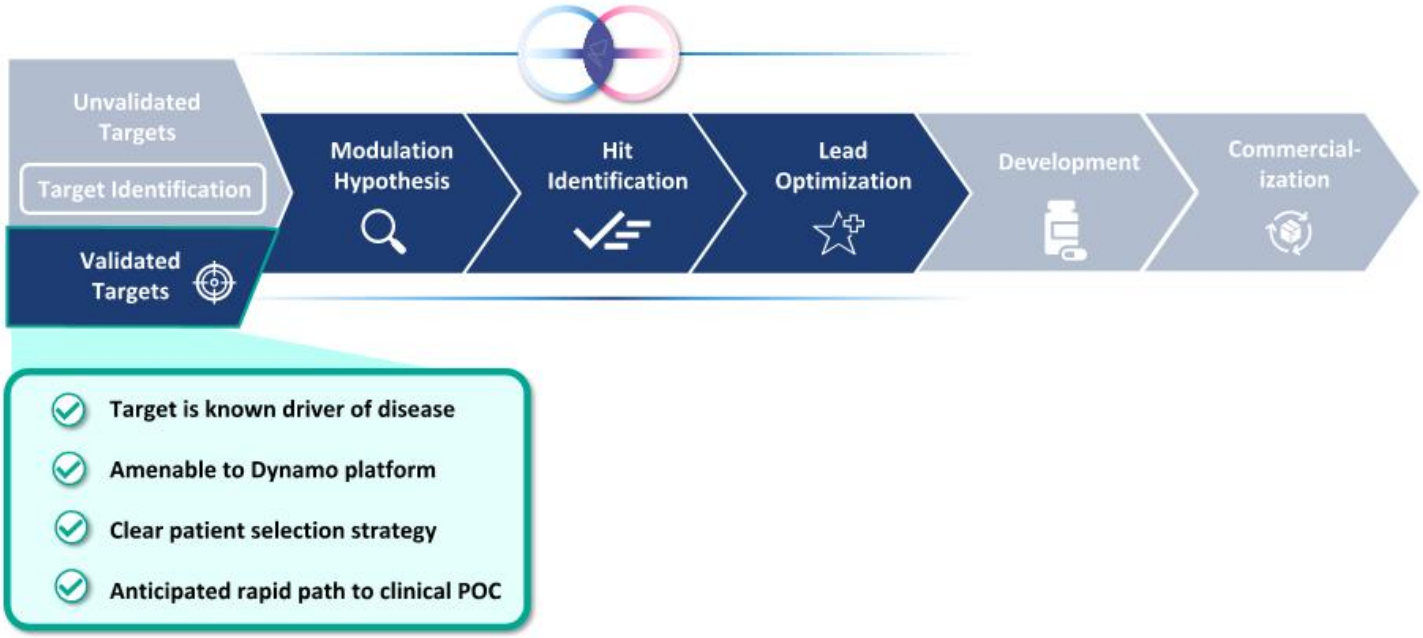
Relay Tx – Understanding Next Generation Drug Discovery: 4 Questions



Relay Tx – Where We Focus Our Dynamo™ Platform Today

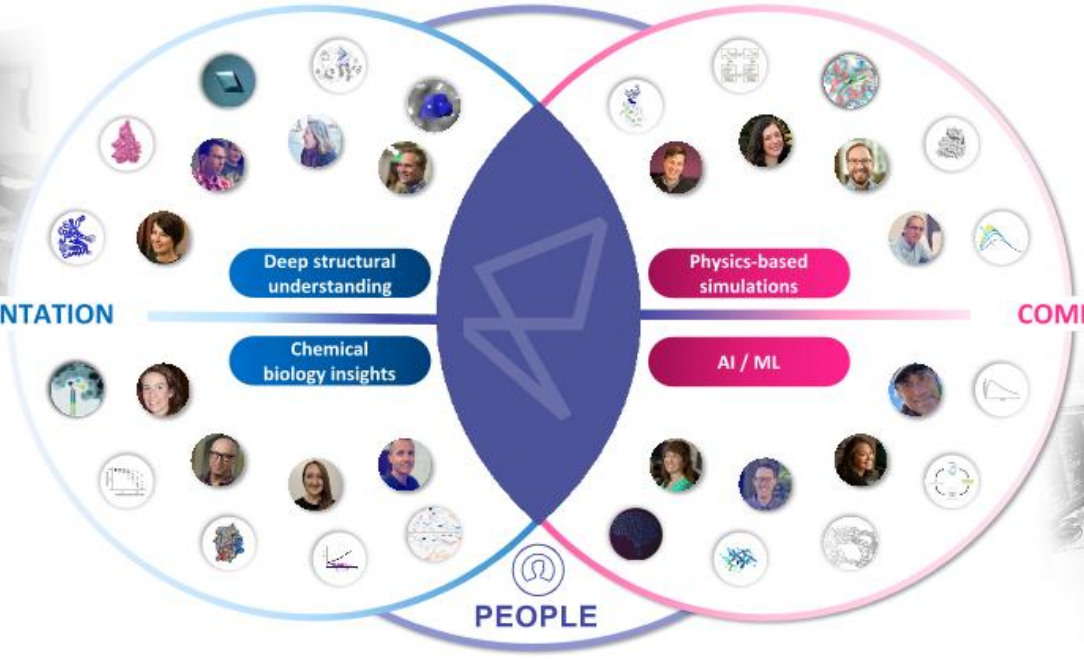


Relay Tx – What Problems We Tackle

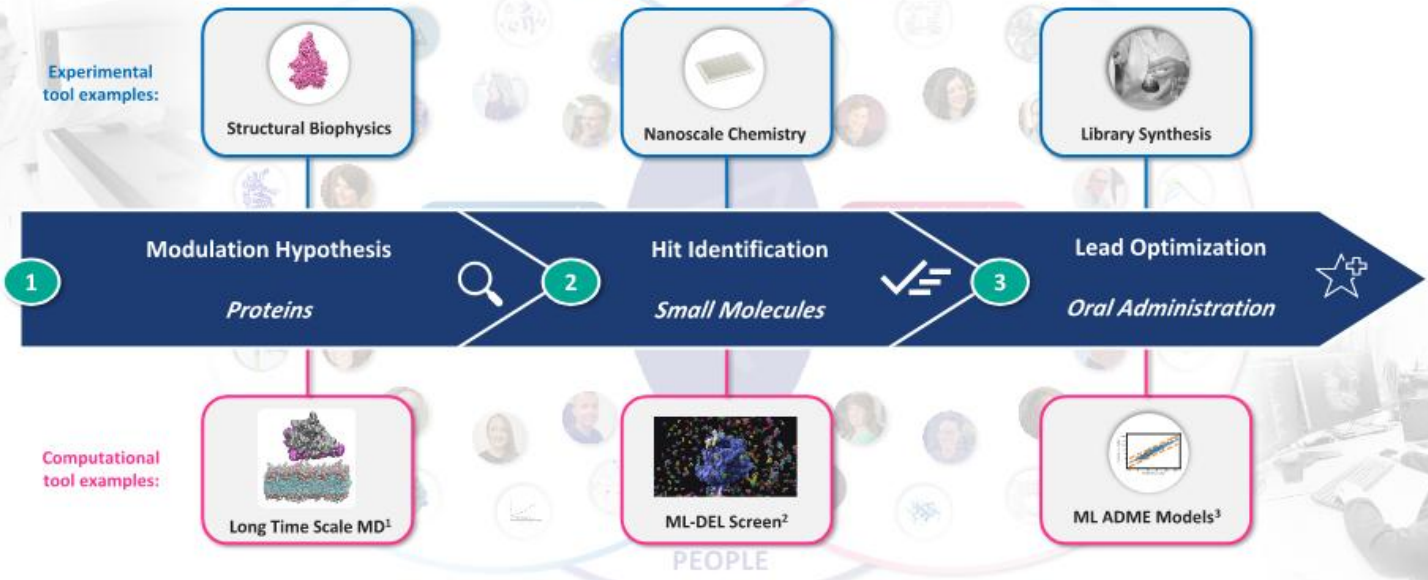


- Target is known driver of disease
- Amenable to Dynamo platform
- Clear patient selection strategy
- Anticipated rapid path to clinical POC

Relay Tx – How Our Team Solves Problems – The Dynamo™ Platform



Relay Tx – How Our Team Solves Problems – Our 3-Step Drug Discovery Process

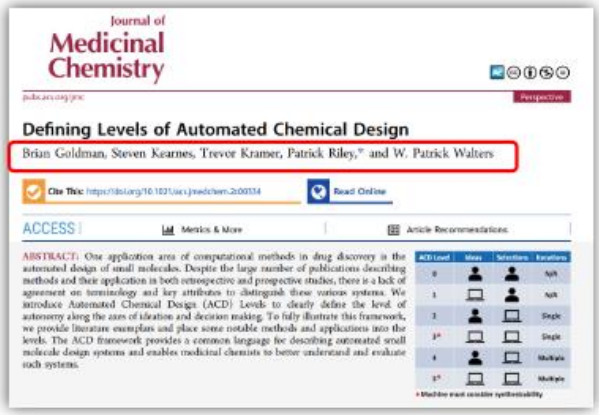


[1]MD - molecular dynamics. [2]ML-DEL - machine-learning DNA-encoded small-molecule libraries. [3]ML ADME - machine learning adsorption, distribution, metabolism and excretion.

Relay Tx – How Our Team Solves Problems – Using Industry-Leading Expertise

RELAY THERAPEUTICS

We believe the Relay Tx Team is leading the field of Automated Chemical Design (ACD)



Journal of Medicinal Chemistry

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Perspective

Defining Levels of Automated Chemical Design

Brian Goldman, Steven Kearnes, Trevor Kramer, Patrick Riley,* and W. Patrick Walters

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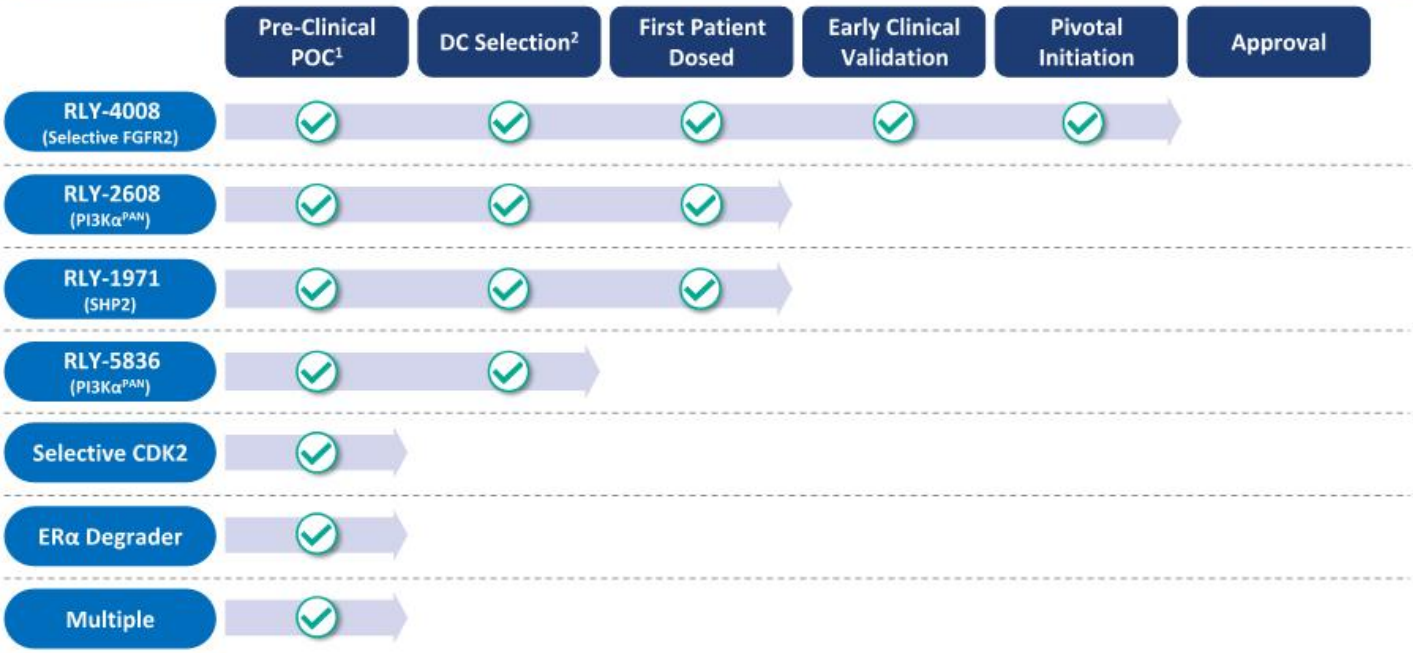
ABSTRACT: One application area of computational methods in drug discovery is the automated design of small molecules. Despite the large number of publications describing methods and their application in both retrospective and prospective studies, there is a lack of agreement on terminology and key attributes to distinguish these various systems. We introduce Automated Chemical Design (ACD) Levels to clearly define the level of autonomy along the axes of ideation and decision making. To fully illustrate this framework, we provide literature exemplars and place some notable methods and applications into the levels. The ACD framework provides a common language for describing automated small molecule design systems and enables medicinal chemists to better understand and evaluate such systems.

ACD Framework describes automated small molecule design systems

ACD Level	Ideas	Selections	Iterations
0	👤	👤	N/A
1	💻	👤	N/A
2	👤	💻	Single
3*	💻	💻	Single
4	👤	💻	Multiple
5*	💻	💻	Multiple

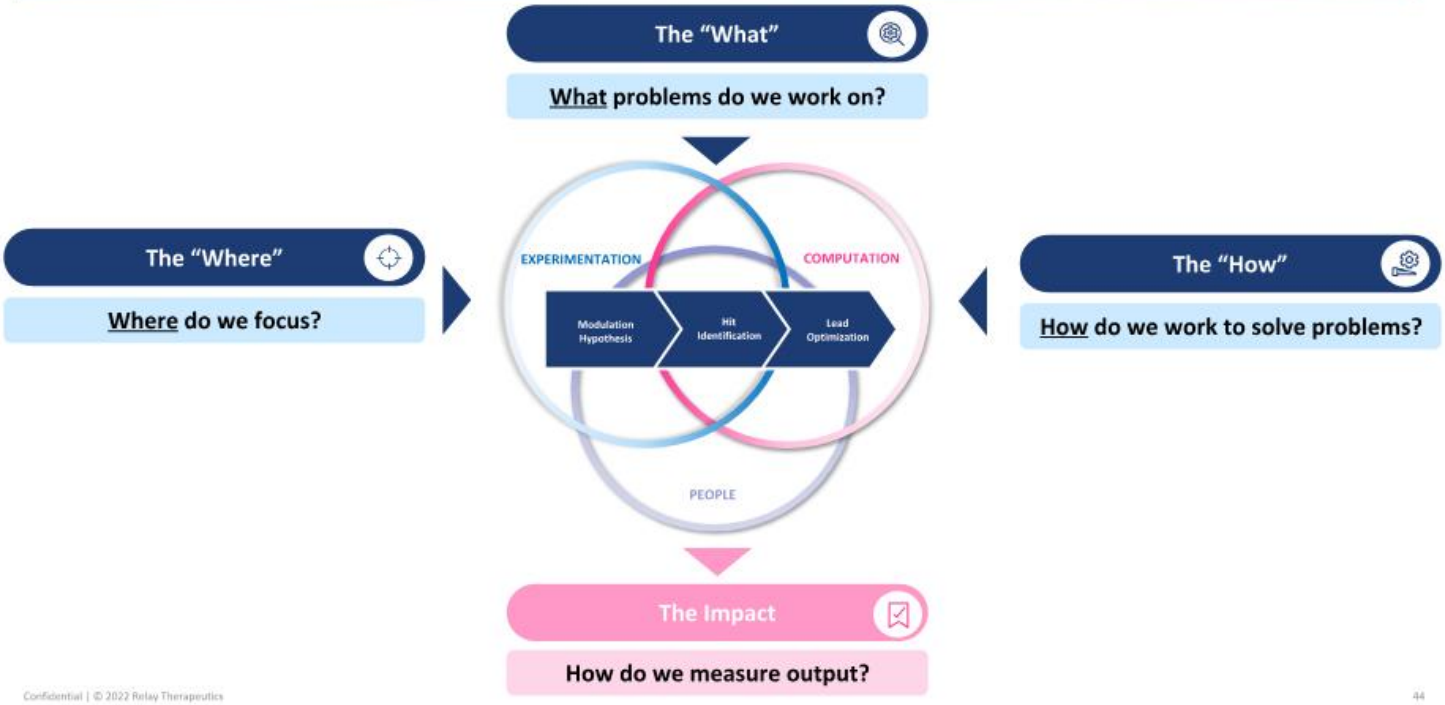
*Machine must consider synthesizability

Relay Tx – Measuring our Impact



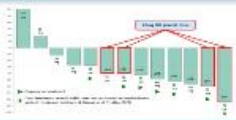
[1]POC - proof-of-concept. [2]DC - development candidate.

Relay Tx – Understanding Next Generation Drug Discovery: 4 Questions



Agenda

1. RLY-4008 Regulatory Update



2. Breast Cancer Portfolio

3. Overview of Dynamo™ Platform

4. Future Guidance and Q&A

2022 Milestones – Proven Execution Focus

RLY-4008 (FGFR2)

- Expansion cohorts open
- Additional data update in 2H 2022
- Regulatory & data update
- Pivotal cohort commenced

RLY-2608 (PI3Kα^{PAN})

- Clinical trial initiated
- RLY-5836 -PI3Kα^{PAN}

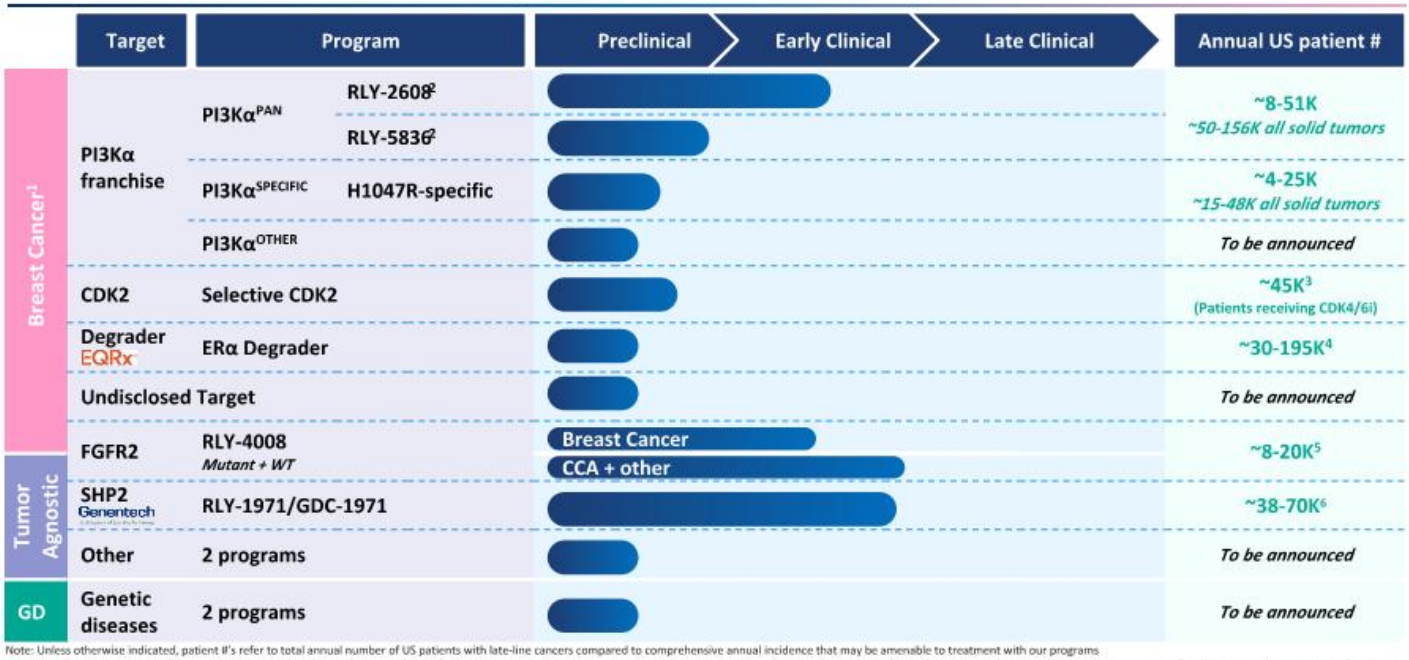
RLY-1971 (SHP2)

- GDC-6036 (KRAS G12C) combination trial initiated in July 2021

Next target in pipeline

- Selective CDK2
- ERα Degrader

Relay Tx – Extensive Precision Medicine Focused Pipeline



Note: Unless otherwise indicated, patient #'s refer to total annual number of US patients with late-line cancers compared to comprehensive annual incidence that may be amenable to treatment with our programs
1. Unless otherwise indicated, all breast cancer patient numbers refer to HR+/HER2- breast cancer tumors 2. RLY-2608 covers H1047X, E542X, E545X hot spots 3. ~45k HR+/HER2- breast cancer patients expected to receive CDK 4/6 inhibitors in adjuvant setting, first-line setting, and second-line setting in 2023, per Decision Resources Breast Cancer Market Forecast, report dated February 2022 4. HR+/HER2- US late-line breast cancer patients compared to HR+/HER2- US incident breast cancer patients 5. FGFR2 altered late-line solid tumors compared to comprehensive annual FGFR2 altered incident solid tumors 6. SHP2 combo only includes KRAS G12C in lung and CRC, EGFR mutations in lung, and ALK fusions in lung

Relay Tx – Capital, Team & Execution Focus to Deliver on Anticipated Milestones

RELAY THERAPEUTICS

Breast Cancer Franchise

RLY-2608 (PI3Kα^{PAN})

Initial data in 1H 2023

Selective CDK2

Clinical start in Q4 2023 or Q1 2024

ERα Degrader

Development candidate nomination in 2023

Tumor Agnostic

RLY-4008 (Selective FGFR2)

Additional data updates in 2H 2022 & 2023

RLY-1971 (SHP2)

Atezolizumab combo trial to be initiated in 2H 2022

$898M

Cash, cash equivalents and investments as of the end of Q1 2022

Current cash, cash equivalents and investments are sufficient to fund current operating plan into 2025

Q&A