RELAY®
THERAPEUTICS

Post-ESMO Conference Call Presentation

September 2022

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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 and 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.

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Relay Tx – New Breed of Biotech

EXPERIMENTATION

Deep structural understanding

Chemical biology insights

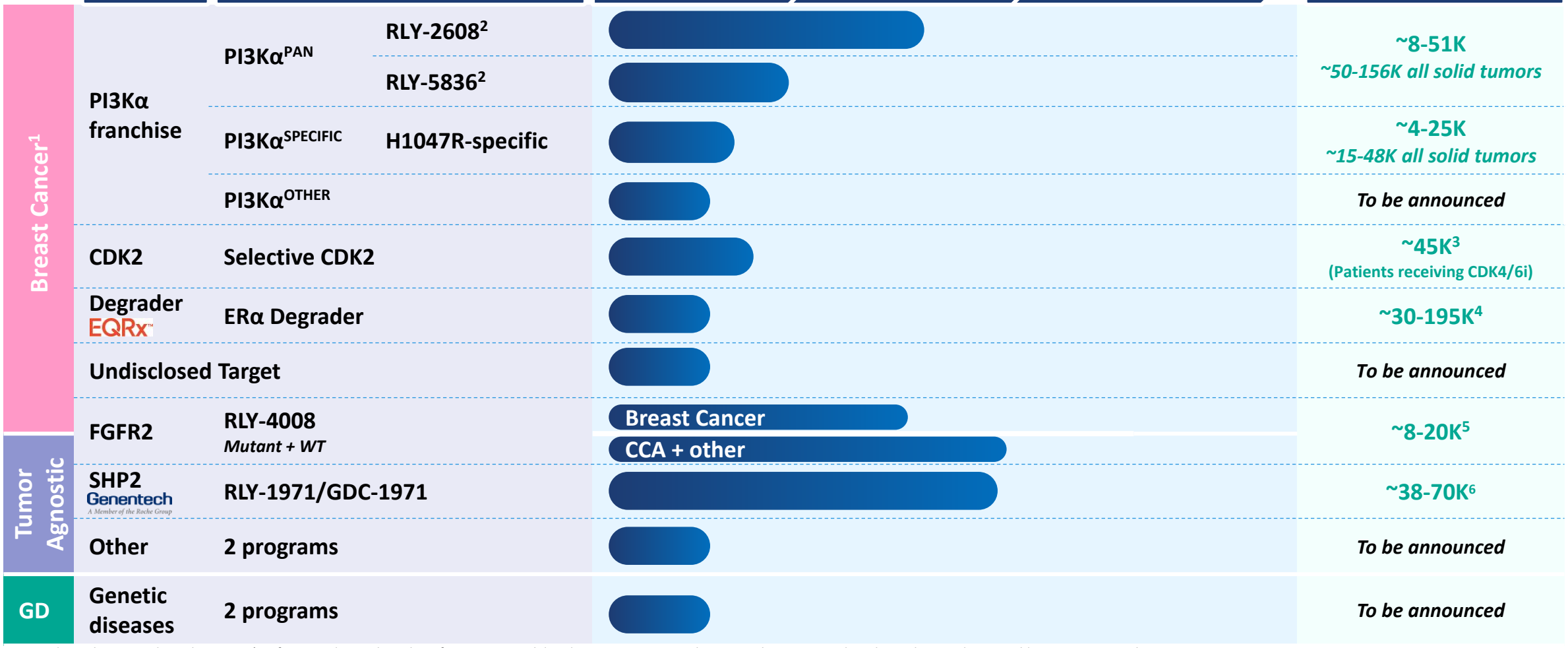
Physics-based simulations

AI / ML

COMPUTATION

PEOPLE

Relay Tx – Extensive Precision Medicine Focused Pipeline



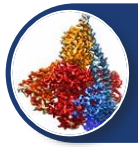
Note: Unless otherwise indicated, patient #'s refer to total annual number of US patients with late-line cancers compared to comprehensive annual incidence that may be amenable to treatment with our programs

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 – Anticipated Milestones

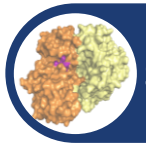
Breast Cancer Franchise

RLY-2608 (PI3Kα^{PAN})



Initial data in 1H 2023

Selective CDK2



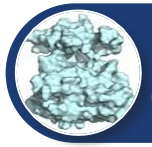
Clinical start in 4Q 2023 or 1Q 2024

ERα Degrader

Development candidate nomination in 2023

Tumor Agnostic

RLY-4008 (Selective FGFR2)

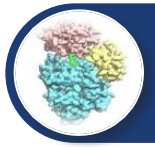


✓ Additional data update in 2H 2022

Full dose escalation data in 1H 2023

Non-CCA expansion cohorts data in 2023

GDC-1971 (RLY-1971, SHP2)



✓ Atezolizumab combo trial initiated

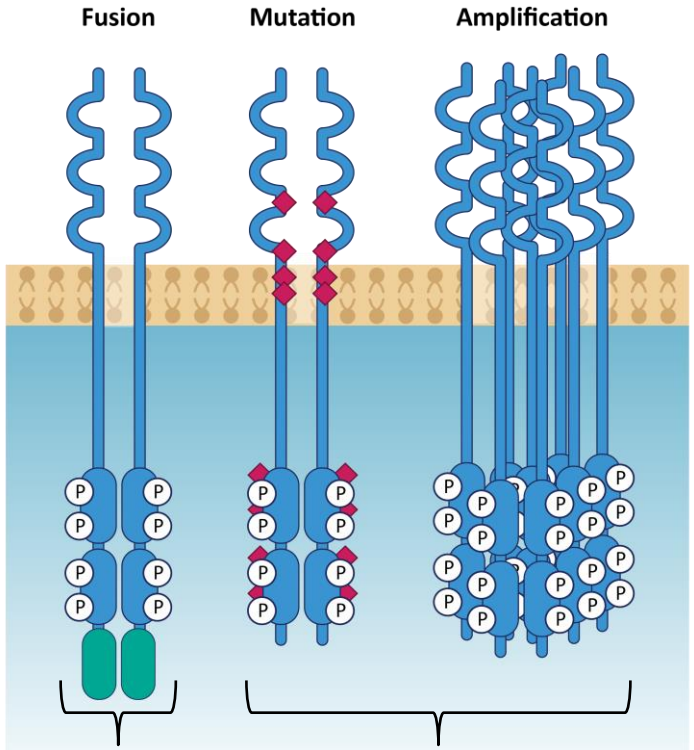
✓ Disclosed today

\+ New guidance issued today

\+ Pivotal cohort full enrollment in 2H 2023

FGFR2 – Validated Target Present in Several Tumor Types

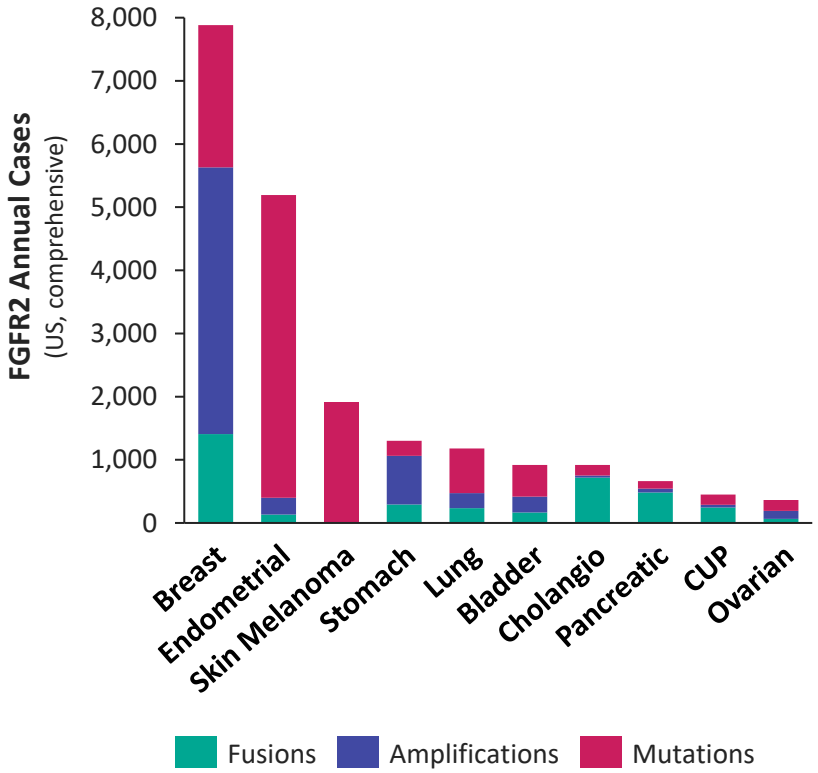
Three classes of driver alterations in FGFR2



~3K-5K patients in the US per year[1]

~5K-15K patients in the US per year[1]

FGFR2 alterations are observed across multiple tumor types[2]



FGFR2-altered cancers remain a high unmet medical need

Current FDA Accelerated Approvals for FGFR2-Altered Cancers

Tumor Type	FGFR2 Fusion & Rearrangement	FGFR2 Oncogenic Mutation	FGFR2 Amplification
FGFRi-naïve Cholangio-carcinoma	23-36% ORR Pemigatinib Infigratinib	No FDA-approved targeted therapy	
FGFRi-resistant Cholangio-carcinoma			
Other FGFR2-altered solid tumors			

Sources: Image adapted from Babina IS, Turner NC. Nat Rev Cancer 2017;17: 318-332; FoundationInsights® database, using 8 copies as the threshold for amplification, and including only mutations with known or likely functional significance; SEER and ACS databases
1. Patient #'s refer to total annual number of US patients with late-line cancers vs. comprehensive annual incidence that may be amenable to treatment with our programs; 2. Cholangio, cholangiocarcinoma; CUP, carcinoma unknown primary

FGFR2 – Selective Inhibitor Required to Address Large Unmet Medical Need

Second Line:
FGFRi Treatment Naïve Precedent

FGFRi treatment naïve patient population

Compound	Company	Stage	FGFR2 Selective	Response Rate	Dosing Schedule	% of Patients with Hyperphosphatemia[1]	% of Patients with Diarrhea	% of Patients Discontinued or Dose Reduced
Pemigatinib	Incyte	Approved[3]	No	36% (ICC)	2 weeks on, 1 week off	94%	47%	23%
Infigratinib	QED therapeutics	Approved[3]	No	23% (ICC)	3 weeks on, 1 week off	90%	24%	75%
Futibatinib	TAIHO ONCOLOGY, INC.	Phase 2/3	No	42% (ICC)	Once daily dosing	91%	~28%	56%
Erdafitinib	janssen	Approved[3]	No	32% (Urothelial Carcinoma)	Personalized dosing based on phosphate levels[2]	76%	47%	66%

[1] As defined by increased serum phosphate; except for infigratinib which is not specified
[2] Initial dose (8 mg QD) adjusted to 9 mg QD only in absence of hyperphosphatemia
[3] Currently have accelerated approval

High toxicity limits efficacy of non-selective FGFR inhibitors

Late-Line:
Retreating with Chemo Precedent

Regimen	Trial	Stage	Population	Response Rate	Progression-Free Survival *(median)*	Overall Survival *(median)*	% Deaths Due to Chemo	% of Patients Discontinued or Dose Reduced
FOLFOX Chemotherapy	ABC-06	Phase 3	All Comers, 2L	3% (ICC)	3.3 months (ICC)	5.7 months (ICC)	4%	74%

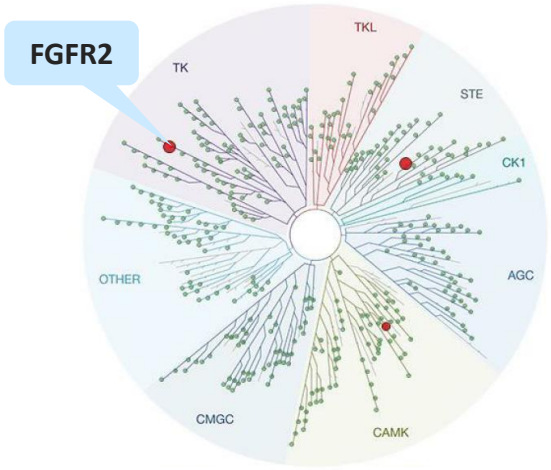
Late-line treatment with chemotherapy can be highly toxic and only results in incremental efficacy

A selective inhibitor of FGFR2 with broad activity against acquired resistance mutations is necessary to address significant unmet need in patients with FGFR2-altered tumors

Sources: Pemigatinib – Prescribing information; Infigratinib – Prescribing information; Futibatinib/TAS-120 – AACR 2021 (diarrhea %s approximated from presentation); Erdafitinib – Prescribing information; FOLFOX – ABC-06 Publication in Lancet Oncology 2021

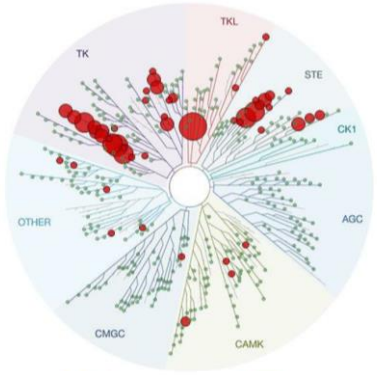
RLY-4008 – A Highly Selective and Irreversible FGFR2 Inhibitor

RLY-4008

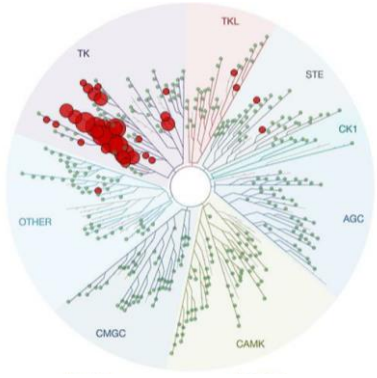


Pan-FGFR Inhibitors

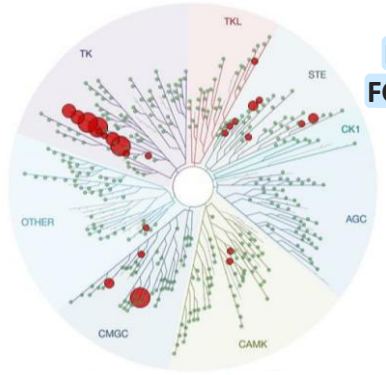
AZD4547



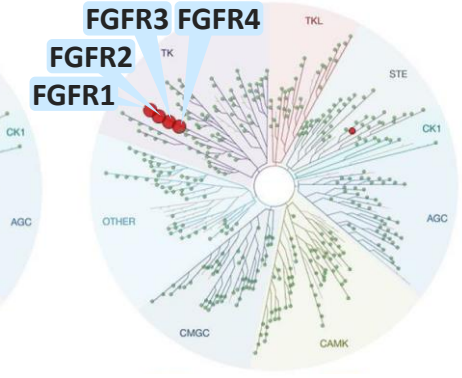
Erdafitinib



Pemigatinib

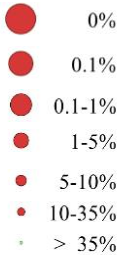


Futibatinib



Percent Control

Percent Control



Note: Single experiment that tested each compound run at 500nM against 468 targets in the absence of ATP and without preincubation
Source: KINOMEscan™ by Eurofins DiscoverX

RLY-4008 – Summary of Sept 2022 Interim Data Disclosure at ESMO

Favorable Interim Safety Profile

- Favorable Tolerability & Safety profile across 195 patients
- Highly Selective with no clinically significant off-target tox

Initial Efficacy Observed in Fusion+ CCA FGFRi-Naïve Patients

RLY-4008

88% ORR

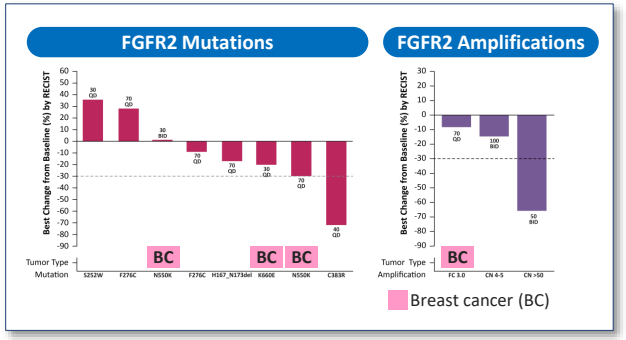
15 of 17 pt at pivotal dose (70 mg QD)[1]

63% ORR (24 of 38 pt)
fusion+ CCA FGFRi-naïve patients across all doses[2]

Approved pan-FGFRi

23-36% ORR[3]

Potential Outside of CCA



Early signs of activity in non-CCA patients, including breast cancer
(presented at Oct 2021 Triple Meeting)

CCA = Cholangiocarcinoma; ORR = Overall Response Rate; QD = once daily dosing; PR = partial response

1. ORR from interim data disclosure: 15 PRs at 70 mg QD: 14 confirmed PRs, 1 unconfirmed PR in an ongoing patient (confirmed ORR = 82%); 2. ORR from interim data disclosure: 24 PRs across all doses: 22 confirmed PRs, 2 unconfirmed PR (confirmed ORR = 58%); 3. Referenced approved pan-FGFRi are Pemigatinib and Infigratinib; ORR based on prescribing information. These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.

Data cut-off: August 01, 2022; efficacy analysis includes patients with measurable disease who had opportunity for ≥2 tumor assessments or discontinued treatment with <2 tumor assessments

RLY-4008 – ReFocus Trial Design

Part 1: Dose Escalation

Unresectable or metastatic solid tumors

FGFR2 alterations per local assessment

Both FGFRi-naïve & FGFRi-treated allowed

RLY-4008
RP2D:
70 mg QD

Part 2: Dose Expansion

Cholangiocarcinoma (CCA)

Pivotal cohort

FGFR2-fusion+ CCA without prior FGFRi *(N=100)*

Pivotal supportive

FGFR2-fusion+ CCA with prior FGFRi *(N=50)*

FGFR2-fusion+ CCA with no prior treatment *(N=20)*

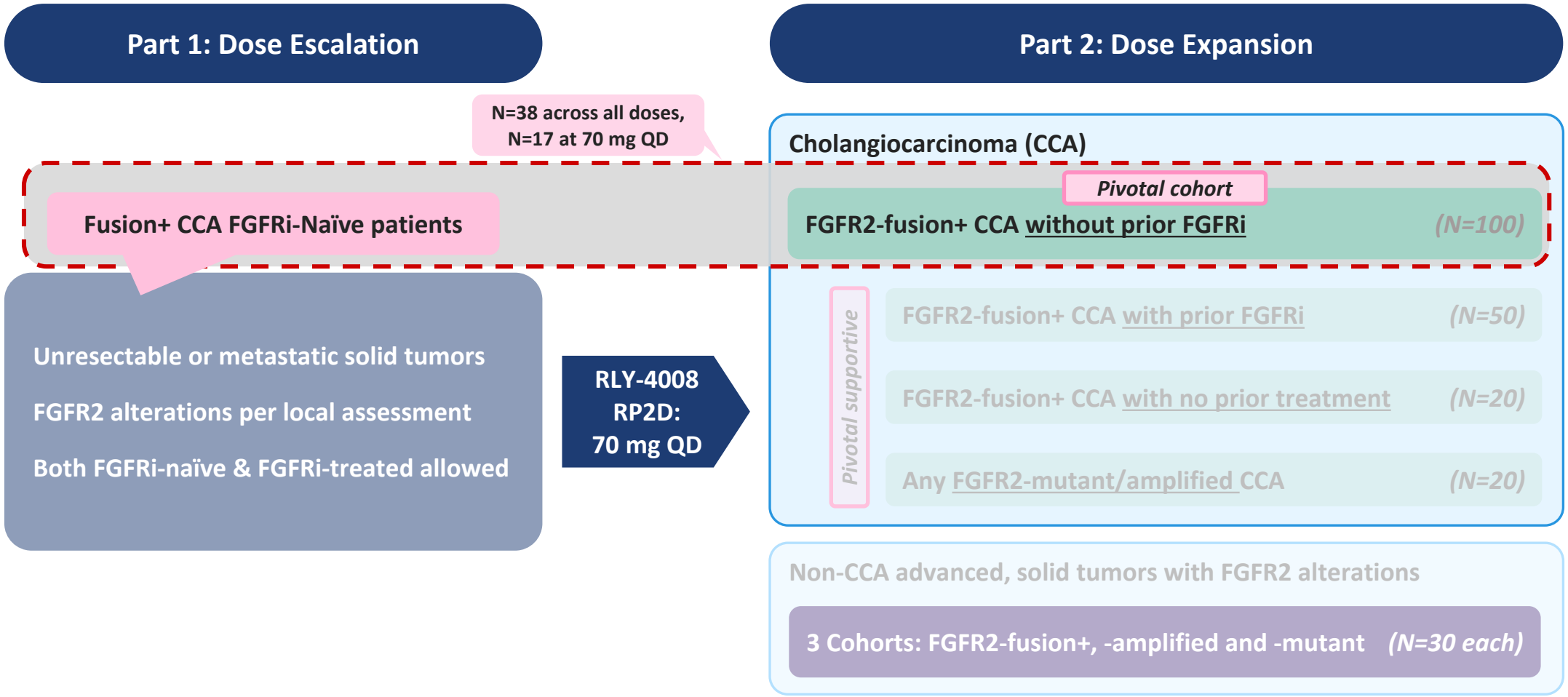
Any FGFR2-mutant/amplified CCA *(N=20)*

Non-CCA advanced, solid tumors with FGFR2 alterations

3 Cohorts: FGFR2-fusion+, -amplified and -mutant *(N=30 each)*

Data cut-off: August 01, 2022; efficacy analysis includes patients with measurable disease who had opportunity for ≥2 tumor assessments or discontinued treatment with <2 tumor assessments

RLY-4008 – Continued Robust Activity Observed in FGFRi-Naïve CCA Patients



Interim Efficacy Data from Sept 2022 ESMO Disclosure Includes 38 Fusion+ CCA FGFRi-Naïve QD Patients (17 at 70 mg QD)

Data cut-off: August 01, 2022; efficacy analysis includes patients with measurable disease who had opportunity for ≥2 tumor assessments or discontinued treatment with <2 tumor assessments

RLY-4008 – Patient Characteristics

Parameter	Fusion+ CCA FGFRi-Naïve[1]		Total (N=195)[2]
	70 mg QD (N=17)	All doses (N=38)	
Age (years), median (range)	57 (36-81)	58 (33-81)	59 (23-87)
Female, %	59%	58%	62%
Race, %			
White / Asian / Black / Unknown	41% / 24% / 0% / 35%	58% / 21% / 3% / 18%	63% / 15% / 4% / 18%
ECOG PS[3], %			
0	53%	50%	38%
1	47%	50%	58%
2	0%	0%	3%
Prior lines of systemic therapy, %			
0	0%	0%	2%
1	41%	47%	20%
2	47%	32%	29%
3+	12%	21%	49%
Baseline sum of target lesions (RECIST 1.1, mm), median (range)	57 (10-157)	63 (10-216)	79 (10-274)

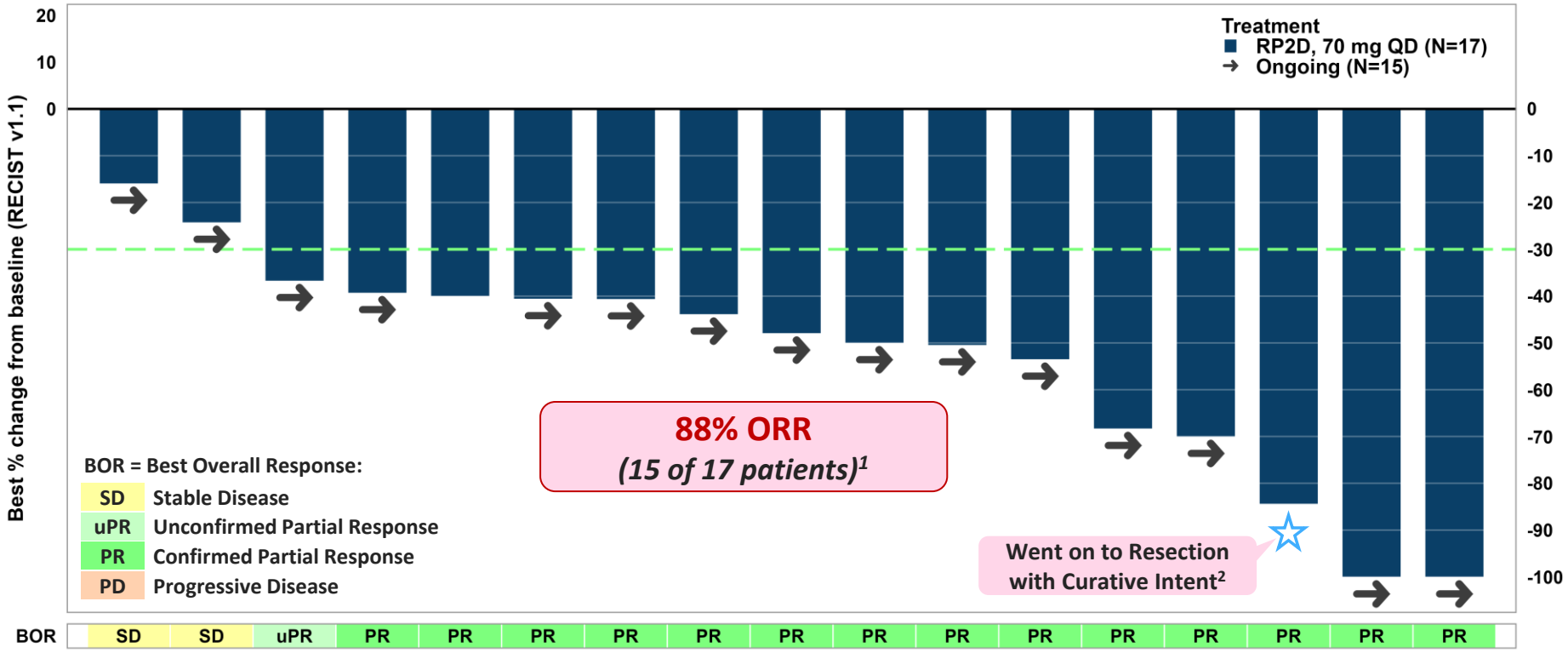
1. Efficacy analysis includes patients with previously treated, FGFR2i-naïve CCA treated at the RP2D. Patients with measurable disease who had opportunity for ≥2 tumor assessments to confirm response or discontinued treatment with <2 tumor assessments
2. Patients in safety population who received ≥1 dose of RLY-4008 at any dose level
3. ECOG PS = Eastern Cooperative Oncology Group Performance Scale

Data cut-off: August 01, 2022; efficacy analysis includes patients with measurable disease who had opportunity for ≥2 tumor assessments or discontinued treatment with <2 tumor assessments

RLY-4008 – Interim Response Data

FGFRi-Naïve Fusion+ CCA Patients at Pivotal Dose (70 mg QD)

Best RECIST Change (%) from Baseline Based on Investigator Evaluated Response for Fusion+ CCA FGFRi-Naïve Patients at 70 mg QD (N=17)



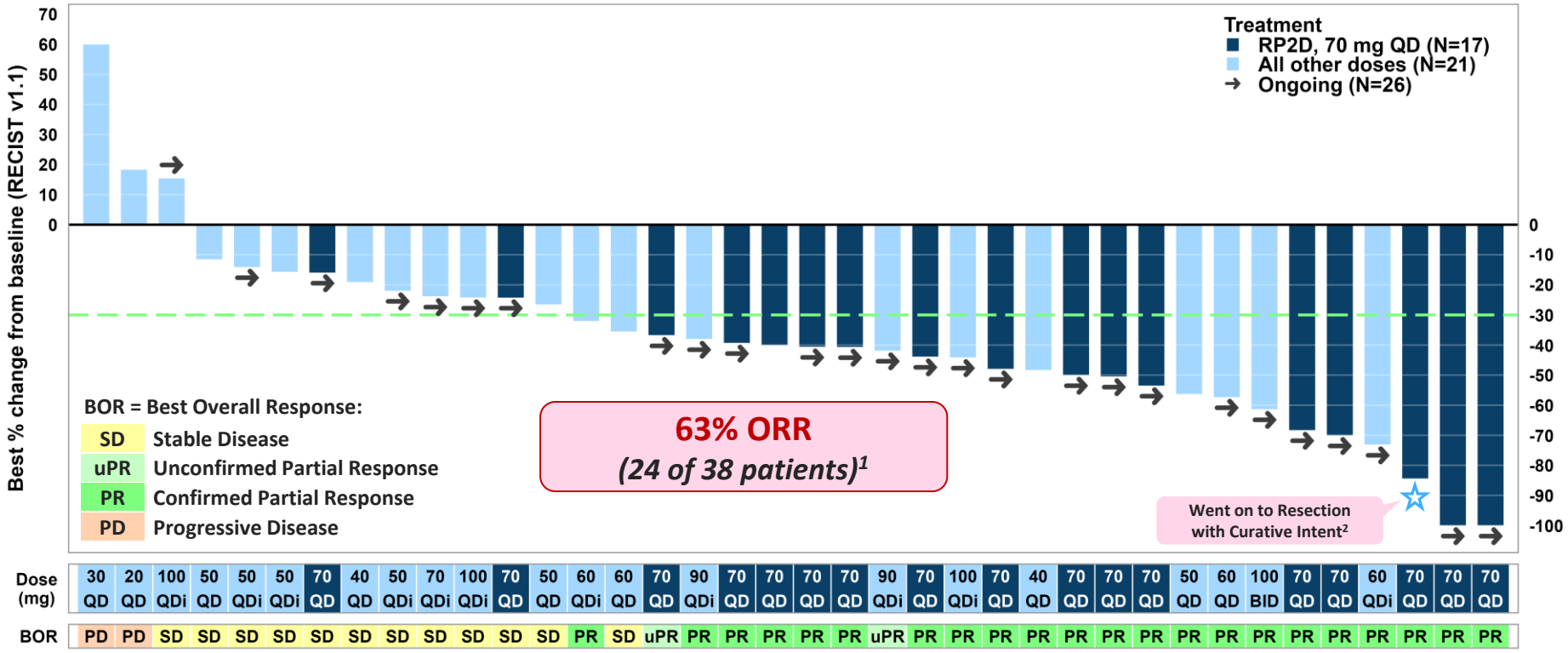
Approved Pan-FGFR Inhibitors Demonstrate 23-36% ORR in This Population[3]

1. Confirmed ORR = 82%: 14 confirmed PRs, 1 unconfirmed PR in an ongoing patient; 2. Complete tumor resection: R0 resection performed in curative intent, patient remains no evidence of disease as of 31 May 2022;
3. Referenced approved pan-FGFRi are Pemigatinib and Infigratinib; ORR based on prescribing information. These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.
Data cut-off: August 01, 2022; efficacy analysis includes patients with measurable disease who had opportunity for ≥2 tumor assessments or discontinued treatment with <2 tumor assessments

RLY-4008 – Interim Response Data

FGFRi-Naïve Fusion+ CCA Patients Across All Doses

Best RECIST Change (%) from Baseline Based on Investigator Evaluated Response for Fusion+ CCA FGFRi-Naïve Patients Across All Doses (N=38)



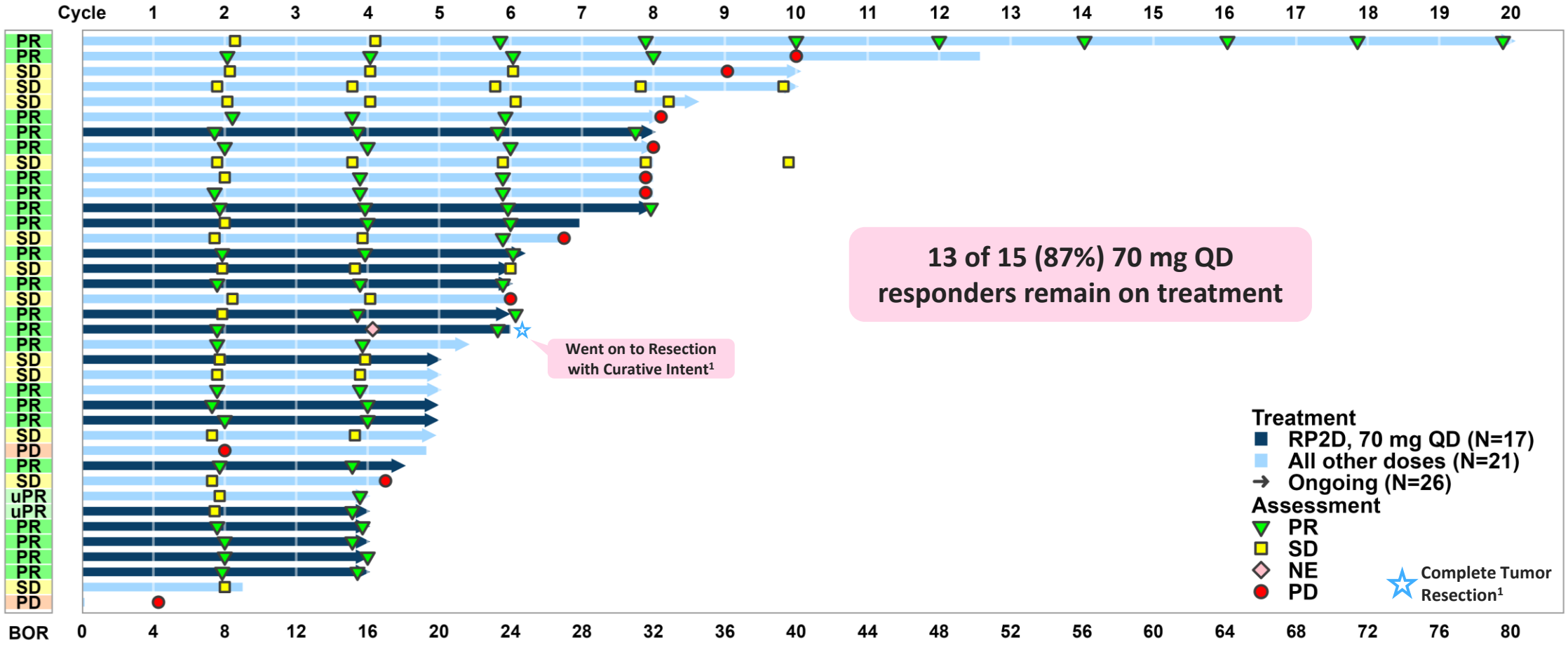
92% of Patients With Tumor Reduction Across All Dose Levels, Majority of Patients With Partial Response per RECIST 1.1

QDi = once daily dosing on an intermittent schedule (3 weeks on drug, 1 week off); BID = twice daily dosing

1. Confirmed ORR = 58%: 22 confirmed PRs, 2 unconfirmed PR
2. Complete tumor resection: R0 resection performed in curative intent, patient remains no evidence of disease as of 31 May 2022

Data cut-off: August 01, 2022; efficacy analysis includes patients with measurable disease who had opportunity for ≥2 tumor assessments or discontinued treatment with <2 tumor assessments

RLY-4008 – Time on Treatment for Fusion+ CCA FGFRi-Naïve Patients (All Doses)



BOR = Best Overall Response:

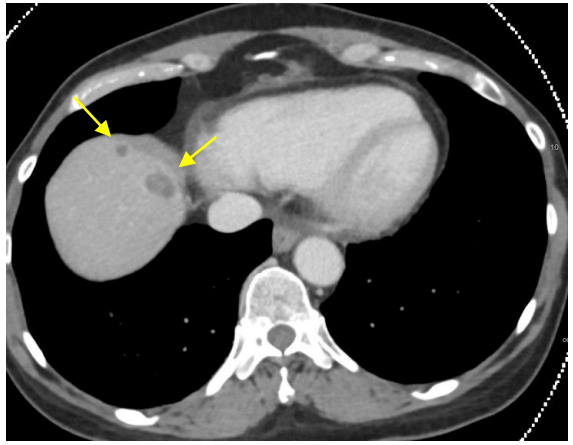
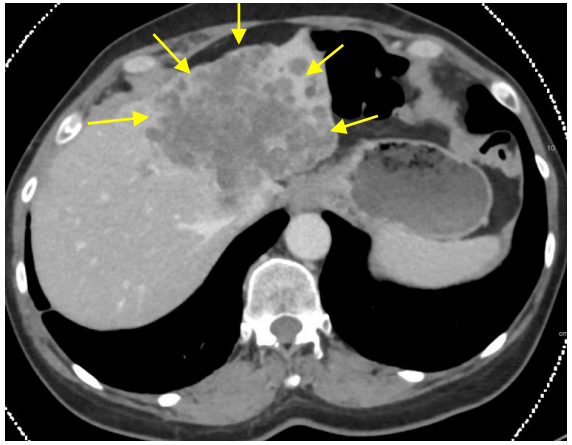
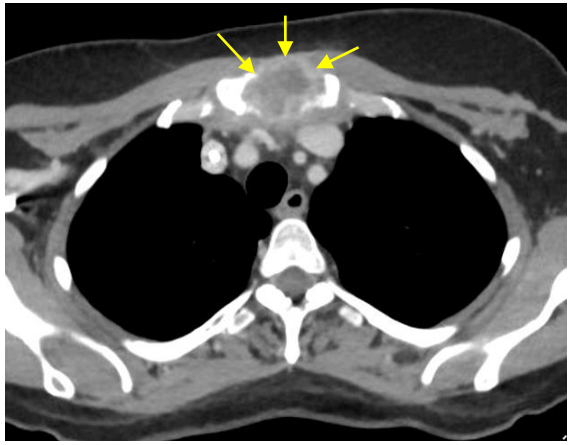
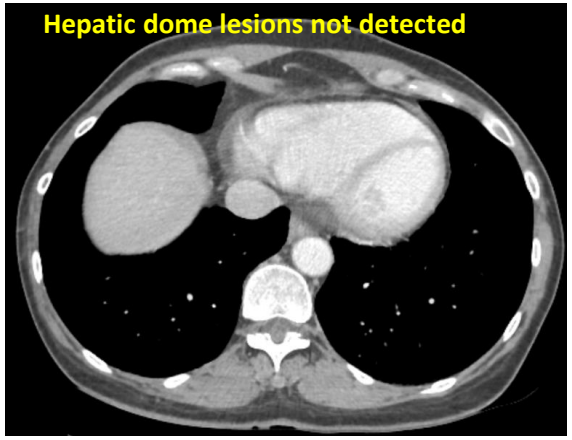
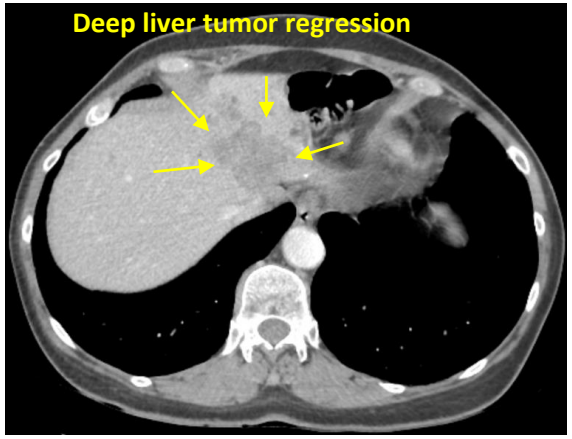
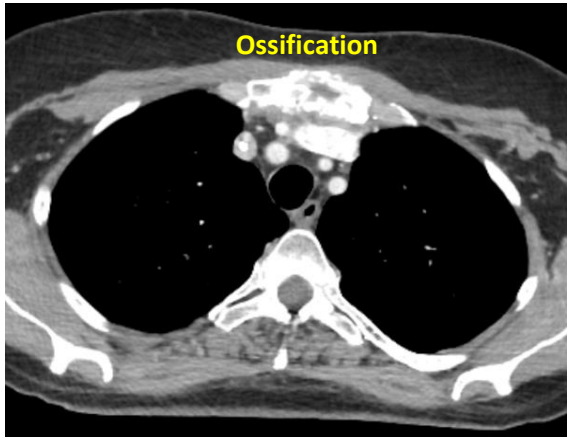
SD	Stable Disease
uPR	Unconfirmed Partial Response
PR	Confirmed Partial Response
PD	Progressive Disease

- **Median duration of exposure: 5.5 months (range: <0.1 to 18.5 months)**
- **Median time to response: 1.8 months**
- **12/38 (32%) Discontinued - 1 resection with curative intent, 8 PD, 1 AE, 2 withdrawal of consent**

1. Complete tumor resection: R0 resection performed in curative intent, patient remains no evidence of disease as of 31 May 2022

Data cut-off: August 01, 2022; efficacy analysis includes patients with measurable disease who had opportunity for ≥2 tumor assessments or discontinued treatment with <2 tumor assessments

RLY-4008 – Patient Treated at 70 mg QD Resulted in 68% Tumor Regression

	Liver lesions	Liver lesions	Bone lesion
Baseline			
Cycle 5			

56-year-old Female With FGFR2-PLETHA4 Rearrangement ICC. Refractory to Gemcitabine/Cisplatin; Treated at 70 mg QD Dosing, Demonstrated Confirmed Partial Response per RECIST (-68%); Ongoing in Response

RLY-4008 – Interim Safety Data from ESMO Disclosure Includes 195 Patients

Included in safety data for ESMO disclosure (N=195)

Part 1: Dose Escalation

Unresectable or metastatic solid tumors

FGFR2 alterations per local assessment

Both FGFRi-naïve & FGFRi-treated allowed

RLY-4008
RP2D:
70 mg QD

Part 2: Dose Expansion

Cholangiocarcinoma (CCA)

Pivotal cohort

FGFR2-fusion+ CCA without prior FGFRi *(N=100)*

Pivotal supportive

FGFR2-fusion+ CCA with prior FGFRi *(N=50)*

FGFR2-fusion+ CCA with no prior treatment *(N=20)*

Any FGFR2-mutant/amplified CCA *(N=20)*

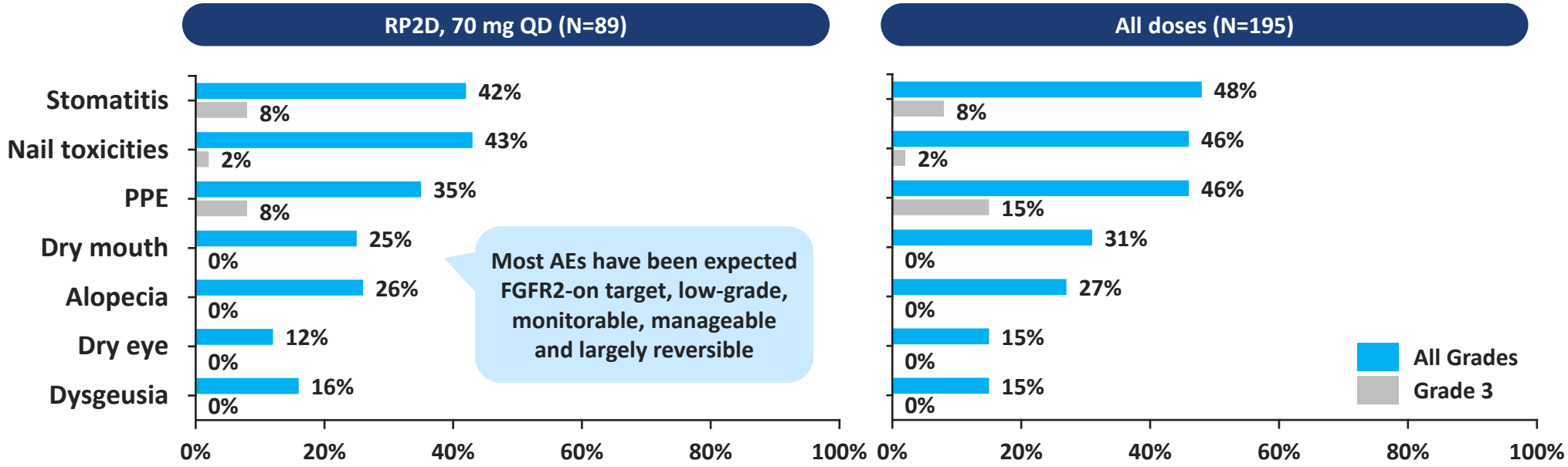
Non-CCA advanced, solid tumors with FGFR2 alterations

3 Cohorts: FGFR2-fusion+, -amplified and -mutant *(N=30 each)*

Data cut-off: August 01, 2022; efficacy analysis includes patients with measurable disease who had opportunity for ≥2 tumor assessments or discontinued treatment with <2 tumor assessments

RLY-4008 – Treatment-Related Adverse Events (TRAEs) Interim Profile

TRAEs ≥ 15%



TRAE Dose Modification	RP2D, 70 mg QD (N=89)	All Doses (N=195)
Dose interruption (%)	42%	47%
Dose reduction (%)	27%	33%
Dose discontinuation (%)	1%	1%*

Doses at ≥40 mg QD result in 90%+ target inhibition

Clinically Insignificant Off-Target Hyperphosphatemia (12%, all Gr 1-2) and Diarrhea (4%, all Gr 1-2) Allow for Optimization of FGFR2 Inhibition

* 1 hypersensitivity, 1 retinal pigment epithelial detachment, both resolved

Data cut-off: August 01, 2022; efficacy analysis includes patients with measurable disease who had opportunity for ≥2 tumor assessments or discontinued treatment with <2 tumor assessments

RLY-4008 – Additional Disclosures Expected in 2023

Part 1: Dose Escalation

Entire dose escalation to be disclosed in 1H23

Unresectable or metastatic solid tumors

FGFR2 alterations per local assessment

Both FGFRi-naïve & FGFRi-treated allowed

RLY-4008 RP2D: 70 mg QD

Last full update: October 2021 at Triple Meeting

Part 2: Dose Expansion

Cholangiocarcinoma (CCA)

Pivotal cohort

FGFR2-fusion+ CCA without prior FGFRi *(N=100)*

Pivotal supportive

FGFR2-fusion+ CCA with prior FGFRi *(N=50)*

FGFR2-fusion+ CCA with no prior treatment *(N=20)*

Any FGFR2-mutant/amplified CCA *(N=20)*

Non-CCA advanced, solid tumors with FGFR2 alterations

3 Cohorts: FGFR2-fusion+, -amplified and -mutant *(N=30 each)*

Non-CCA data to be disclosed in 2023

An initial look at efficacy data for other cohorts included in Oct 2021 Triple Meeting update

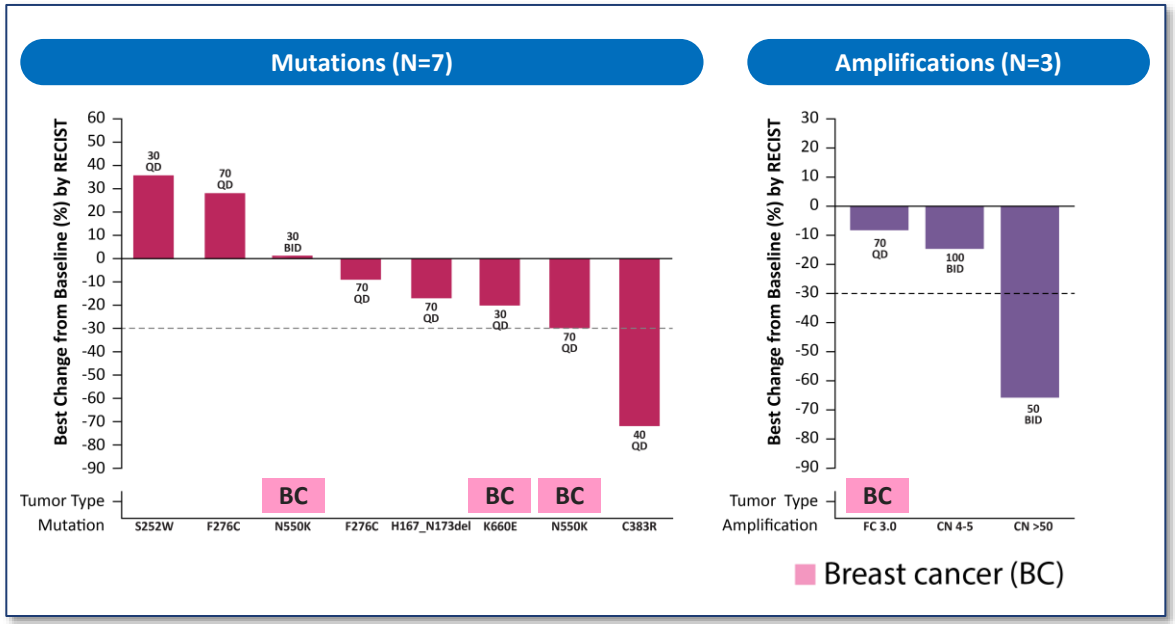
Data cut-off: August 01, 2022; efficacy analysis includes patients with measurable disease who had opportunity for ≥2 tumor assessments or discontinued treatment with <2 tumor assessments

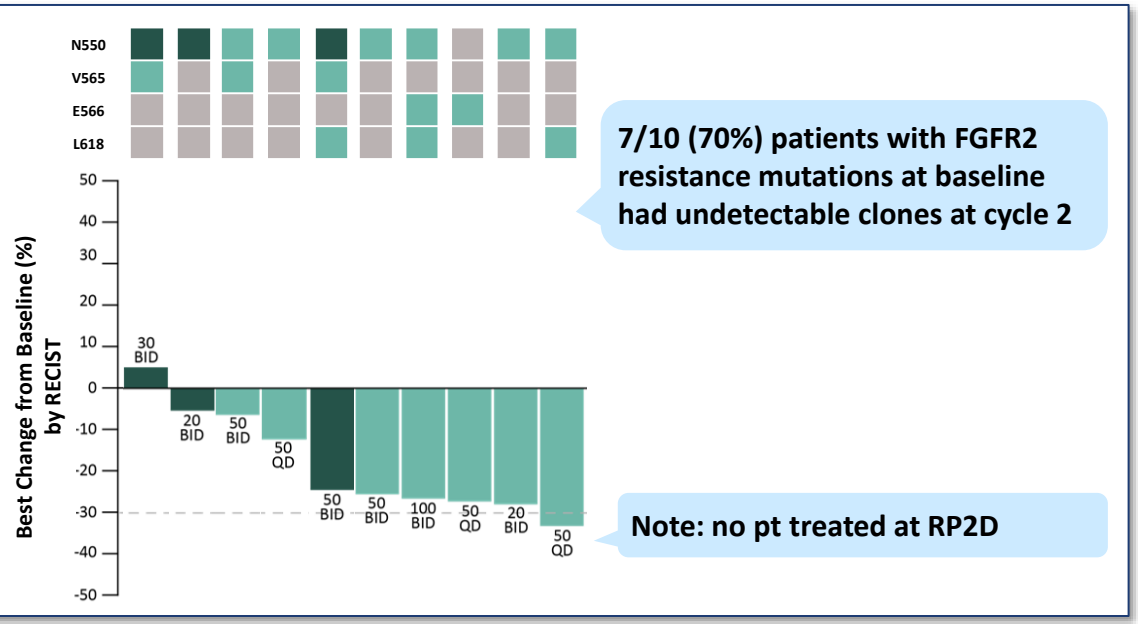
RLY-4008 – Observations from October 2021 Initial Clinical Data Disclosure

October 2021:
Presented at Triple Meeting *(data as of 09 September 2021)*

Tumor regression also observed across FGFR2 mutations (N=7) and amplifications (N=3)

Demonstrated activity against resistance mutations in pan-FGFRi-resistant cholangiocarcinoma (N=10)





Entire Dose Escalation Data Expected to be Disclosed in 1H 2023

RLY-4008 – Summary of ESMO Disclosure and Anticipated Milestones

Favorable Interim Safety Profile

- Favorable Tolerability & Safety profile across 195 patients
- Highly Selective with no clinically significant off-target tox

Initial Efficacy Observed in Fusion+ CCA FGFRi-Naïve Patients

RLY-4008

88% ORR

15 of 17 pt at pivotal dose (70 mg QD) [1]

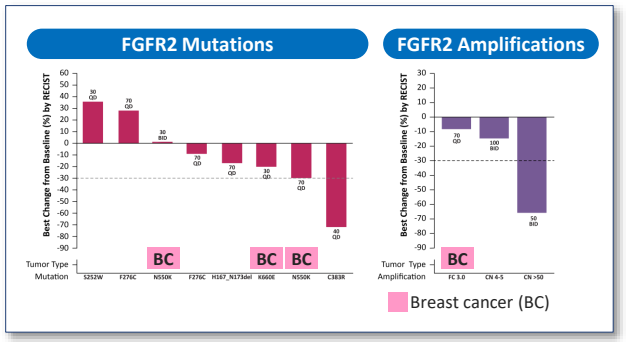
63% ORR (24 of 38 pt)

fusion+ CCA FGFRi naïve patients across all doses[2]

Approved pan-FGFRi

23-36% ORR[3]

Potential Outside of CCA



Early signs of activity in non-CCA patients, including breast cancer
(presented at Oct 2021 Triple Meeting)

1H 2023:
Full dose escalation data

2H 2023:
Pivotal cohort full enrollment

2023:
Non-CCA expansion cohorts

CCA = Cholangiocarcinoma; ORR = Overall Response Rate; QD = once daily dosing; PR = partial response

1. ORR from interim data disclosure: 15 PRs at 70 mg QD: 14 confirmed PRs, 1 unconfirmed PR in an ongoing patient (confirmed ORR = 82%); 2. ORR from interim data disclosure: 24 PRs across all doses: 22 confirmed PRs, 2 unconfirmed PR (confirmed ORR = 58%); 3. Referenced approved pan-FGFRi are Pemigatinib and Infigratinib; ORR based on prescribing information. These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.

Data cut-off: August 01, 2022; efficacy analysis includes patients with measurable disease who had opportunity for ≥2 tumor assessments or discontinued treatment with <2 tumor assessments

Relay Tx's Emerging Breast Cancer Franchise Addresses Large Opportunity

Goals: Greater selectivity → Better combinability → Increased efficacy

Relay Tx's PI3Kα Franchise

PI3Kα^{PAN}

- RLY-2608* Pan-mutant selective allosteric inhibitor
- RLY-5836* Pan-mutant selective allosteric inhibitor
- Additional chemically distinct programs

PI3Kα^{SPECIFIC}

- H1047R-specific allosteric inhibitor
- Additional chemically distinct programs

PI3Kα^{OTHER}

- Other mutant-selective mechanisms

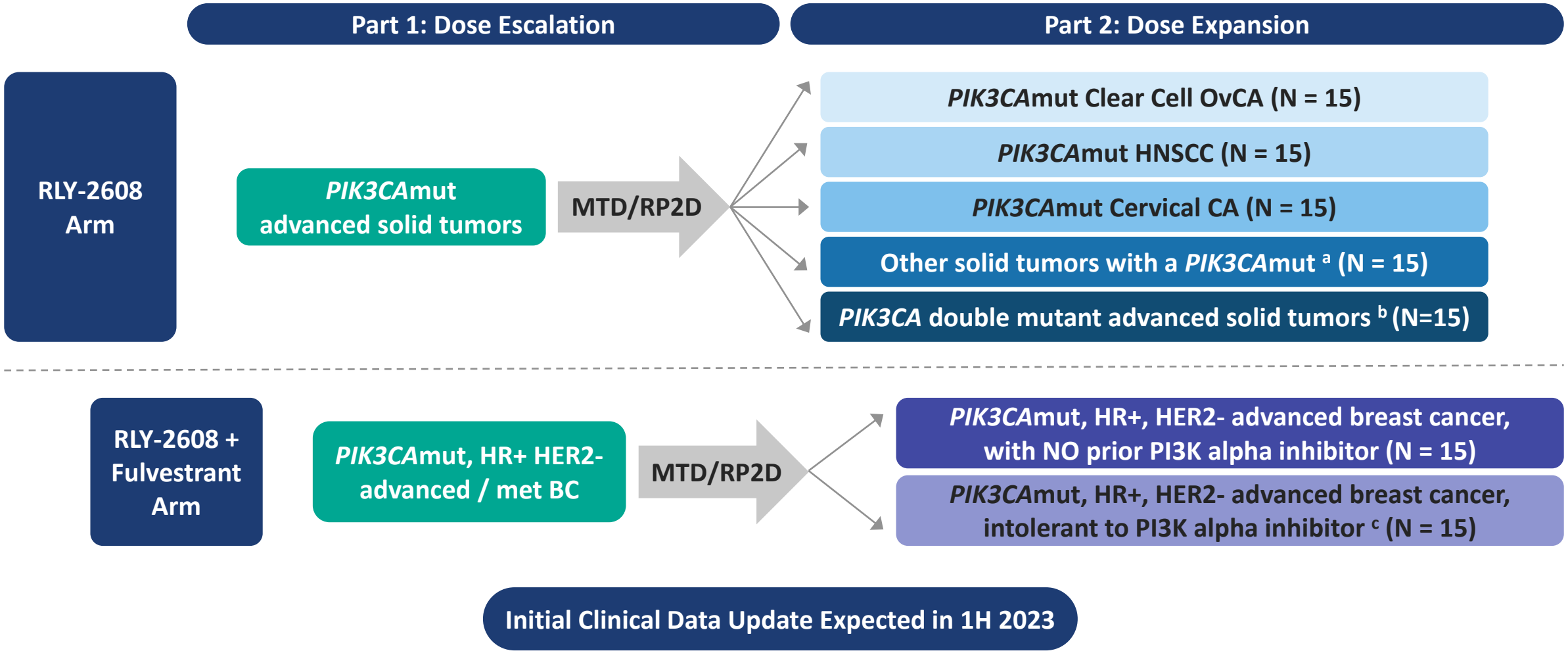
Relay Tx Rational Combination Partners

- Selective CDK2 Inhibitor
- ERα Degrader
- RLY-4008 (Selective FGFR2)
- Pan-mutant + Mutant Specific PI3Kα Combinations
- GDC-1971 (SHP2)
- Undisclosed Target

Demonstrated activity in FGFR2-mutant BC patient (Oct 2021 disclosure, data update in 2023)

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

PI3Kα – RLY-2608 Trial Design



Initial Clinical Data Update Expected in 1H 2023

a. Excludes PIK3CAmut clear cell OvCA, HNSCC, 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.

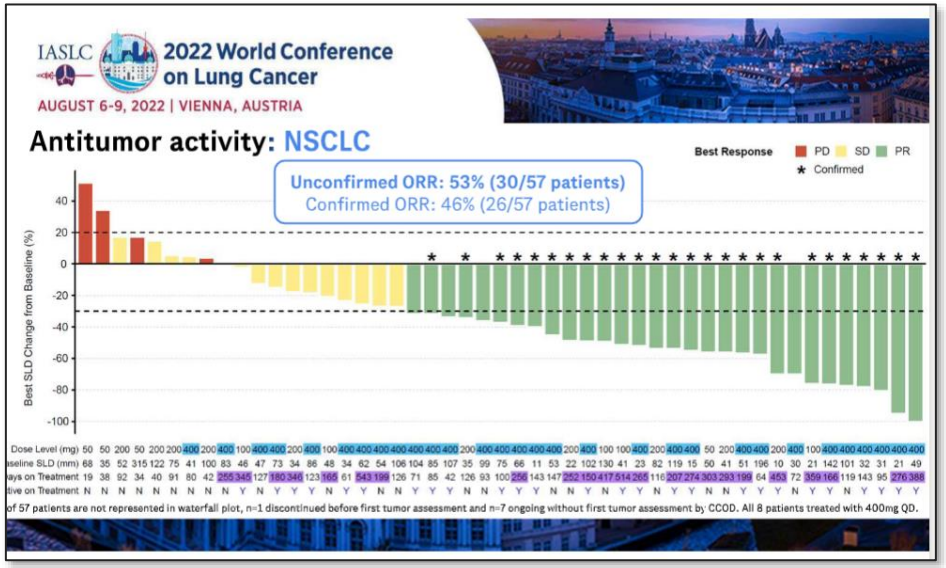
SHP2 – Genentech Global Collaboration for GDC-1971 (Formerly RLY-1971)

Two ongoing trials with GDC-1971:

GDC-1971
+
GDC-6036 (KRAS G12Ci)
initiated July 2021

GDC-1971
+
Atezolizumab (PD-L1 Ab)
initiated August 2022

Clinical Update for GDC-6036 Monotherapy at World Lung 2022 (Ph1)



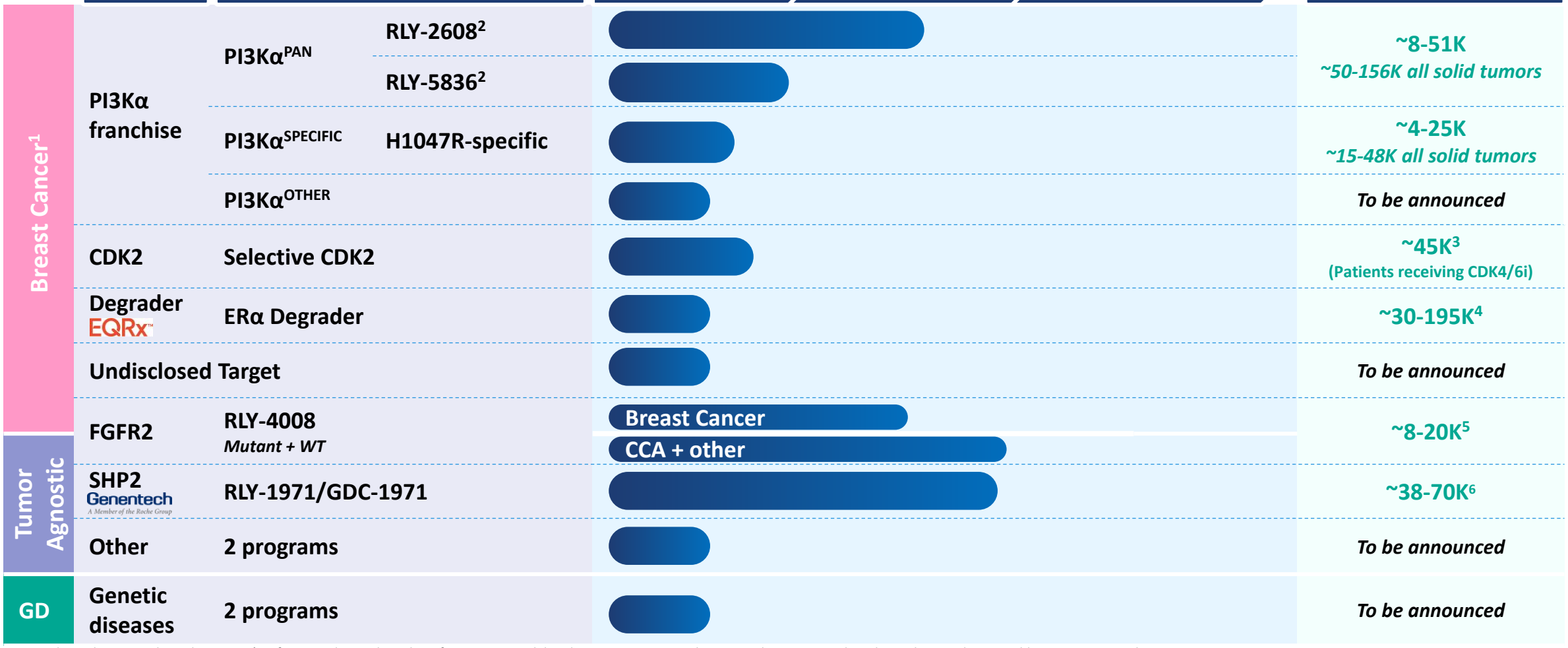
Unconfirmed ORR: 53% (30/57 patients)
Confirmed ORR: 46% (26/57 patients)

Collaboration Provides Meaningful Economics to Relay Tx*

* As of June 30, 2022: $95 million in upfront & milestone payments received, plus an opt-in option for 50/50 profit share and up to $700M in potential additional total milestones, low-to-mid teen royalties on global net sales plus eligible to receive additional royalties upon approval of GDC-1971 and GDC-6036 in combination

Source: World Lung 2022 #OA03.04

Relay Tx – Extensive Precision Medicine Focused Pipeline



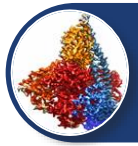
Note: Unless otherwise indicated, patient #'s refer to total annual number of US patients with late-line cancers compared to comprehensive annual incidence that may be amenable to treatment with our programs

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

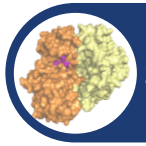
Breast Cancer Franchise

RLY-2608 (PI3Kα^{PAN})



Initial data in 1H 2023

Selective CDK2



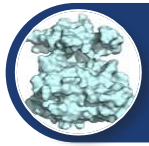
Clinical start in 4Q 2023 or 1Q 2024

ERα Degrader

Development candidate nomination in 2023

Tumor Agnostic

RLY-4008 (Selective FGFR2)



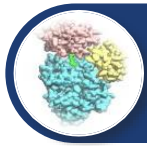
✓ Additional data update in 2H 2022

Full dose escalation data in 1H 2023

Non-CCA expansion cohorts data in 2023

\+ Pivotal cohort full enrollment in 2H 2023

GDC-1971 (RLY-1971, SHP2)



✓ Atezolizumab combo trial initiated

$838M

Cash, cash equivalents and investments as of the end of 2Q 2022

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

✓ Disclosed today

\+ New guidance issued today