Mining for Tomorrow's Cures

CLN-081 Clinical Update

December 2021

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Executive hosts of today's webinar

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Cullinan Oncology: Advancing a broad pipeline of targeted cancer therapeutics

Program (Subsidiary/Project) Modality / MOA	Discovery / Lead Optimization	IND-Enabling	Phase 1	Phase 2	Phase 3
CLN-081 (Pearl) EGFR ex20 inhibitor	**NSCLC EGFRex20**				
CLN-049 (Florentine) FLT3 x CD3 bispecific	**r / r AML**				
CLN-619 (MICA) Anti-MICA/B IgG1	**Pan cancer**				
CLN-978 (NexGem) CD19, CD3, HSA trispecific	**B-cell ALL**				
CLN-617 (Amber) IL2-IL12 fusion protein	**Pan cancer**				
Opal PD-1 x CD137L fusion protein	**Pan cancer**				
Jade TCR-based therapy targeting a novel senescence / cancer-related protein	**HPV+/ RB-**				

- **Strategy to select programs with First and/or Best in Class Potential**
- **Q4 Progress:**
  - ✓ **CLN-081 clinical update**
  - ✓ **FLT3 trial initiation**
  - ✓ **MICA trial initiation**
- **Further pipeline updates to come in early 2022**

CLN-081 Clinical update highlights

Data Summary

1 Status

- Nominated RP2D of 100mg BID

2 Efficacy

- High response rate in larger number of patients
- Durable responses and encouraging PFS

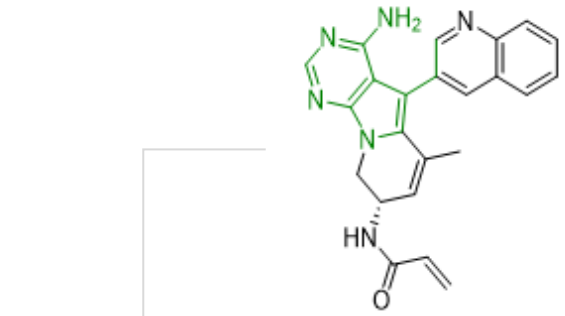
3 Safety

- Favorable safety and tolerability profile

CLN-081: A differentiated clinical profile

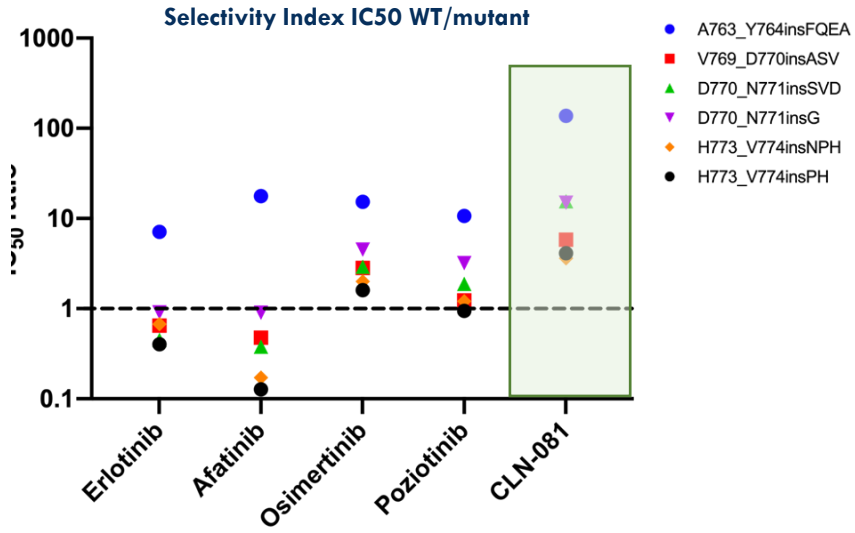
CLN-081: Selective EGFR inhibitor for NSCLC patients with exon 20 mutations

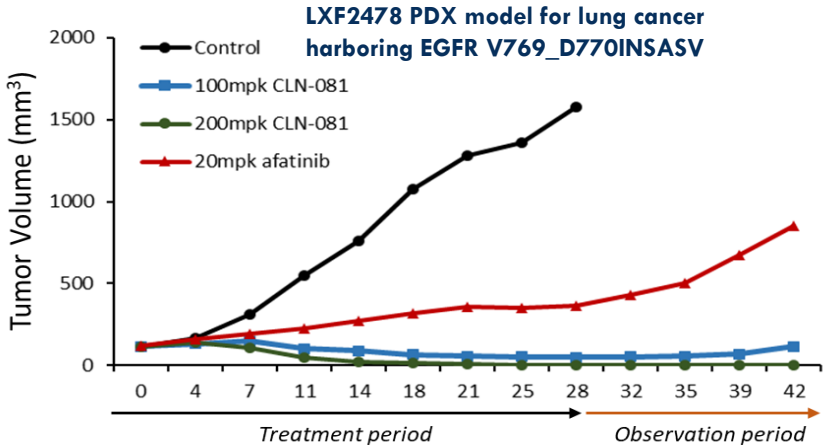
CLN-081: Unique design properties



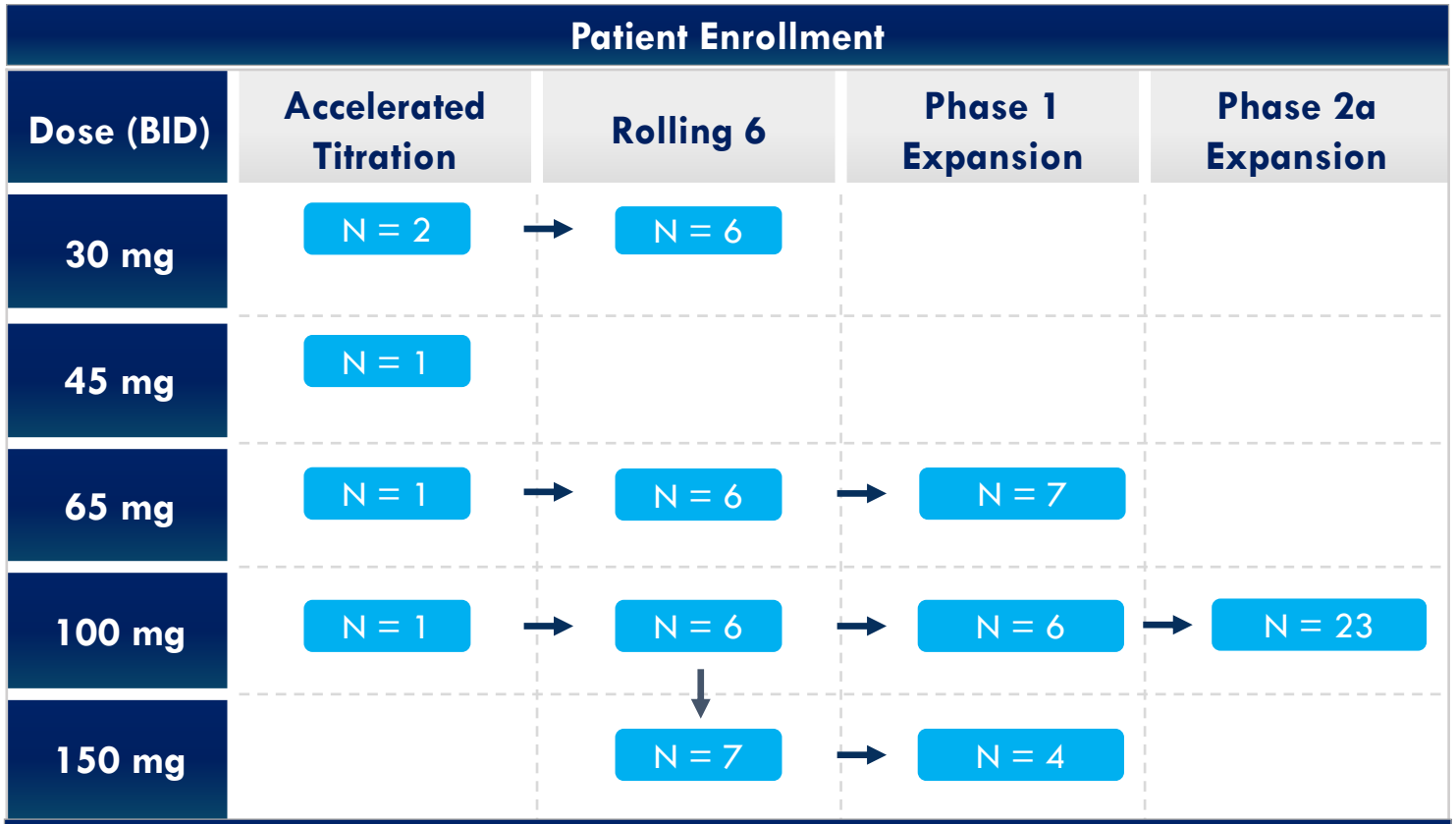
- Distinct chemical scaffold
- HER2-sparing
- High selectivity to mutant vs WT EGFR

Select CLN-081 pre-clinical data





CLN-081 Phase 1/2a trial design



Geographic Footprint						
Location	US	Netherlands	Singapore	Hong Kong	Taiwan	China
# of Sites	9	1	2	1	1	IND approved

- 36 patients enrolled in Phase 1/2a at 100 mg BID
- Expanded enrollment at 150 mg BID stopped after 11 patients based on clinical profile
- Dose of 100 mg BID nominated as RP2D

Zai Lab has licensed CLN-081 for Greater China.

Clinical data cutoff as of 1 Dec 2021

Heavily pretreated patient population including prior EGFR TKI or immunotherapy

Select Baseline Characteristics	
Characteristic	**All patients (n=73)**
Median age (range)	64 (36-82)
Number of prior systemic anticancer regimens	
1 (%)	22 (30%)
2 (%)	32 (44%)
≥3 (%)	16 (22%)
Median (range)	2 (0-9)
Prior EGFR TKI (non-Ex20)	27 (37%)
Prior pozio and/or mobo (%)	4 (5%)
Prior checkpoint inhibitor therapy (%)	39 (53%)
Brain mets at baseline (%)	28 (38%)

- Heavily pretreated population
- Over 65% of patients with 2 or more prior lines of treatment
- Prior EGFR TKI treatment in 37% of patients
- Over 50% of patients treated previously with checkpoint inhibitor

Differentiated safety and tolerability profile of CLN-081 at proposed RP2D

Dose (BID)	100 mg	150 mg	Overall
Safety Population (n, %)	39	11	73
Grade 1 TRAE of interest			
Skin Rash	21 (54)	4 (36)	38 (52)
Diarrhea	10 (26)	1 (9)	14 (19)
Elevated ALT / AST	2 (5)	1 (9)	6 (8)
Anemia	3 (8)	--	5 (7)
Grade 2 TRAE of interest			
Skin Rash	7 (18)	1 (9)	14 (19)
Diarrhea	3 (8)	1 (9)	4 (5)
Elevated ALT / AST	2 (5)	--	2 (3)
Anemia	1 (3)	--	2 (3)
Grade 3 TRAE of interest			
Skin Rash	--	1 (9)	1 (1)
Diarrhea	--	2 (18)	2 (3)
Elevated ALT / AST	2 (5)	2 (18)	6 (8)
Anemia	1 (3)	2 (18)	5 (7)
Treatment Related Dose Reduction	5 (13)	3 (27)	10 (14)
Treatment Related Dose Discontinuation	1 (3)	2 (18)	5 (7)

100 mg BID nominated as RP2D

At 100 mg BID (N=39):

- **No Gr ≥3 rash/diarrhea**
- **Rash/diarrhea 3:1 Gr 1:2 ratio**
- **No systematic GI prophylaxis**
- **One pt with G3 pneumonitis***

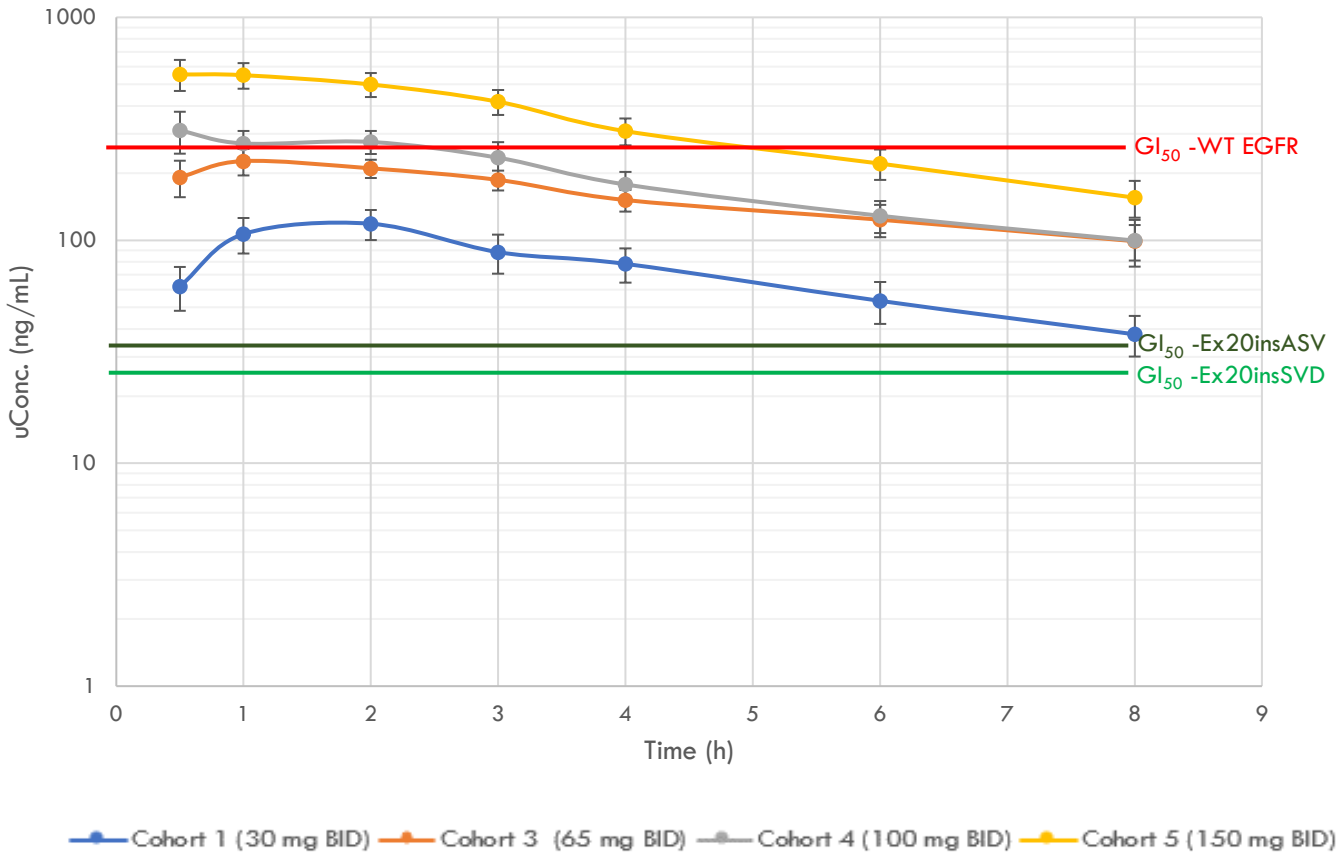
At 150 mg BID (N=11):

- **Expanded enrollment discontinued after 11 patients**
- **G3: diarrhea (2), rash (1), pneumonitis (1)**, Transaminitis (1); G4 Transaminitis (1)**
- **Increased dose reduction and/or discontinuation**

*Patient reported as G3 drug-related pneumonitis (confounded by recent treatment with CPI, concurrent hydropneumothorax in contralateral lung)
**Patient reported as G3 drug-related pneumonitis (confounded by concurrent pneumocystis infection, had stopped CLN-081 3 weeks prior to event)

PK profile consistent with clinical safety profile

Average Unbound Plasma Concentration over Time



- **CLN-081 PK well-behaved to date**
- **Sustained PK exposure over GI50 for ex20ins EGFR for 8h post dose**
- **Limited time of exposure over GI50 for WT EGFR at doses ≤ 100 mg BID**
- **Consistent with clinical safety profile at 100 mg versus 150 mg BID dose**

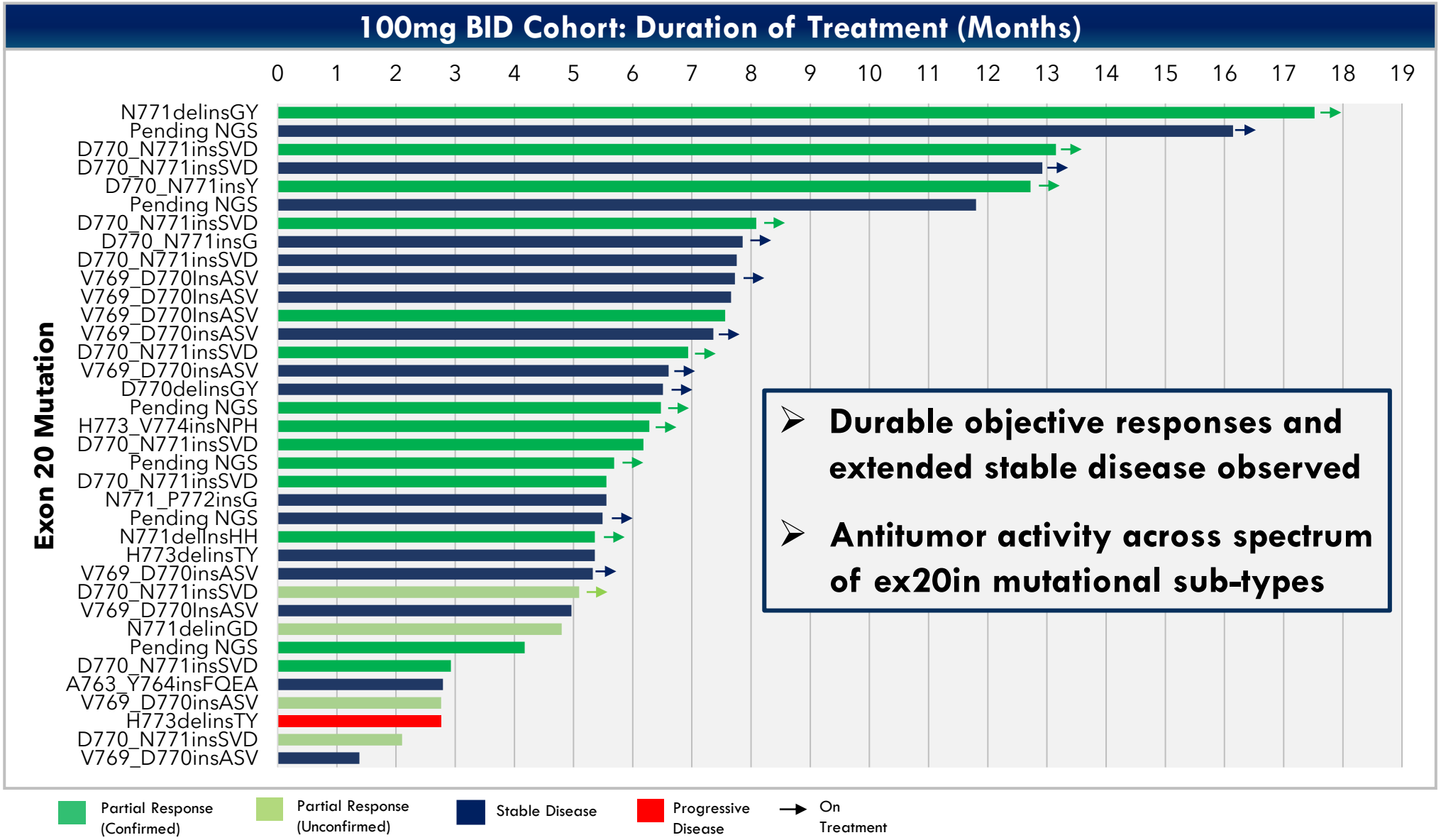
Data from Phase 1 patients. Uses standard error of the mean.

Encouraging response rate in expanded cohort at RP2D

Response	100 mg BID (n=36), RP2D	150 mg BID (n=11)	Overall (n=70)
Best Response, n (%)			
PR (Confirmed)	14 (39)	3 (27)	25 (36)
PR (Pending)	1 (3)	--	1 (1)
PR (Unconfirmed)	3 (8)	2 (18)	7 (10)
Stable Disease (SD)	17 (47)	5 (45)	34 (49)
Progressive Disease (PD)	1 (3)	1 (9)	3 (4)

- Stable disease or PR observed in 35/36 (97%) of patients at RP2D

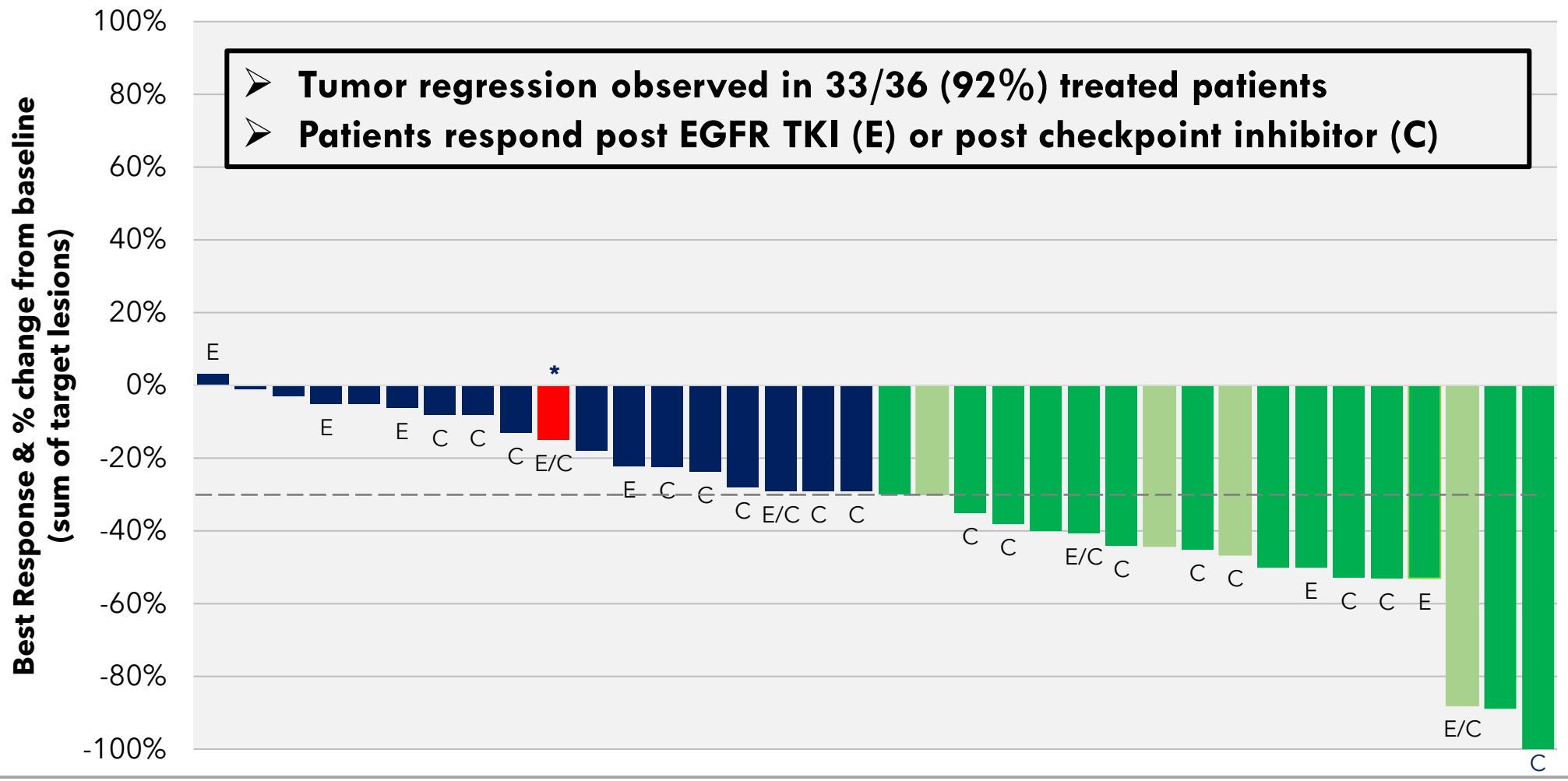
Durable objective responses and extended stable disease in patients treated at 100 mg BID



- **Durable objective responses and extended stable disease observed**
- **Antitumor activity across spectrum of ex20in mutational sub-types**

Tumor regression observed in majority of patients treated at 100 mg BID

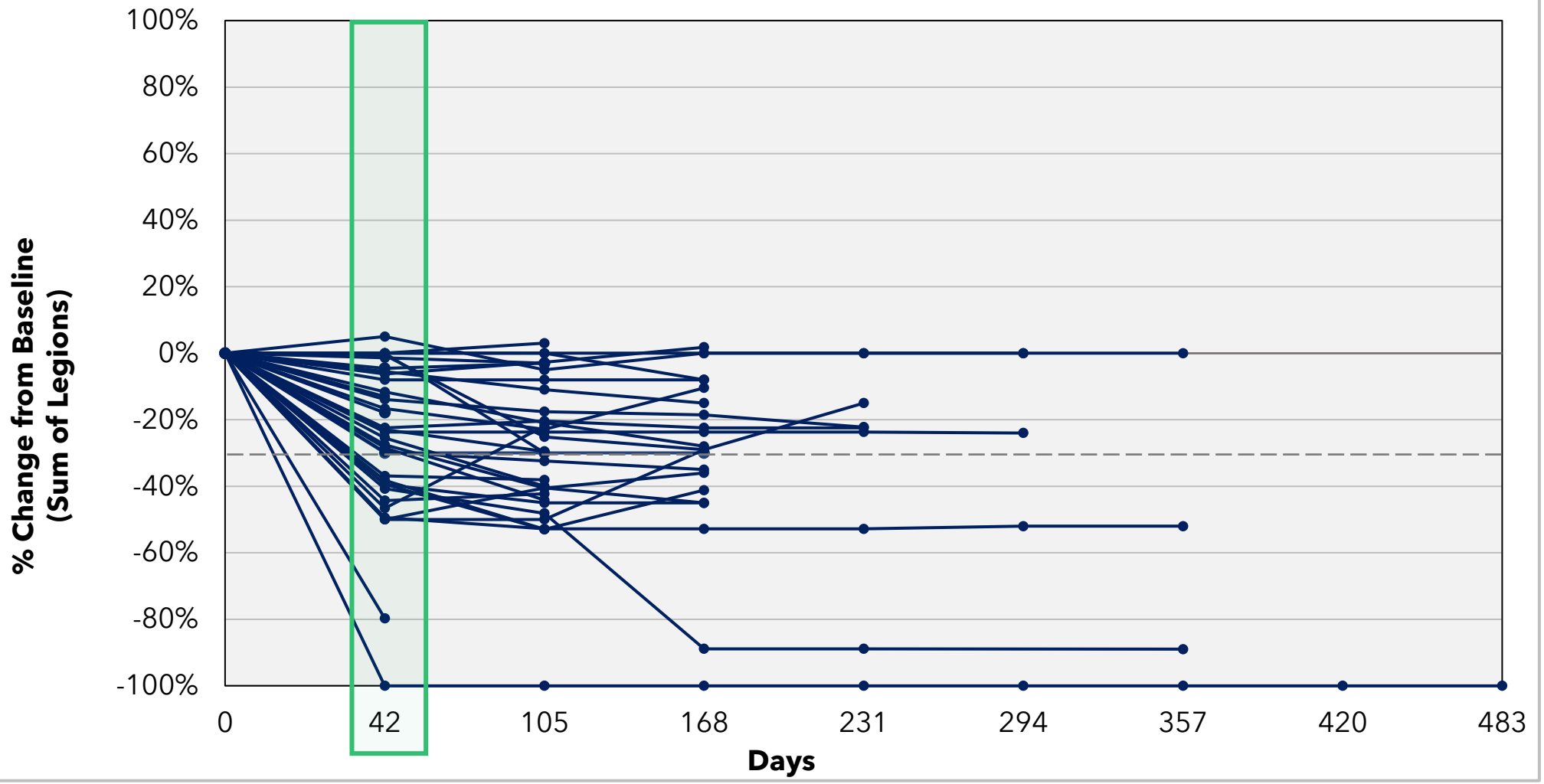
100mg BID Cohort: % Δ from Baseline in Target Lesions



** PD due to progression of non-target lesions.*

CLN-081 acts rapidly: Tumor regression in 86% of 100mg BID patients at first assessment

100mg BID Cohort: Change from baseline (sum of target lesions)



First on-treatment scan

Durability profile building for patients treated at RP2D

Phase 1 Patients at 100 mg BID (n = 13)	
*Duration of Response, Median	>15 months
*Progression Free Survival, Median	12 months
**Disease Control Rate	92%

* Based upon Kaplan-Meier estimates
** Disease control rate (DCR): % of patients with stable disease ≥6 months or any PR

- **Follow-up on Phase 1 patients at 100 mg BID shows encouraging response duration, progression-free survival and disease control rates.**
- **Follow-up ongoing in Phase 2a patients at 100 mg BID.**

Disease control rates in patients treated at 100 mg BID based on baseline CNS status

Phase 1 Patients at 100 mg BID*	
Disease Control Rate (DCR)**, All (N=13)	92%
➢ CNS Disease History at Baseline (N=4)	100%
➢ No CNS Disease History at Baseline (N=9)	89%

* Patients with stable, treated brain metastases included; active, untreated brain metastases excluded

** Disease control rate (DCR): % of patients with stable disease ≥6 months or any PR

- **Disease control rates comparable, irrespective of CNS disease status at baseline in patients treated at 100 mg BID**
- **Examples of patients with reductions in CNS lesions have been noted**

CLN-081 Conclusions and next steps

Summary

- Updated data at the proposed RP2D of 100 mg BID, reaffirms differentiated clinical profile for CLN-081 (an oral TKI)

Efficacy

- High response rate maintained with expanded patient numbers at RP2D
- Durable responses and encouraging PFS
- Antitumor activity across a spectrum of EGFR ex20ins mutational sub-types, and in patients who progress on other EGFR ex20ins TKI

Safety

- Differentiated safety and tolerability profile with reduced rate of all-grade diarrhea, and no grade 3 diarrhea or rash to date at RP2D
- Reduced rates of dose reduction/discontinuation

Next Steps

- Move rapidly toward a potentially pivotal 2L trial, and expand clinical development to the 1L setting
- Regulatory update planned in Q1 2022

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Q&A

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