ONCOLOGY CLINICAL UPDATE
WCLC 2022

AUGUST 8, 2022

AMGEN®

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INTRODUCTION

DAVID REESE, MD

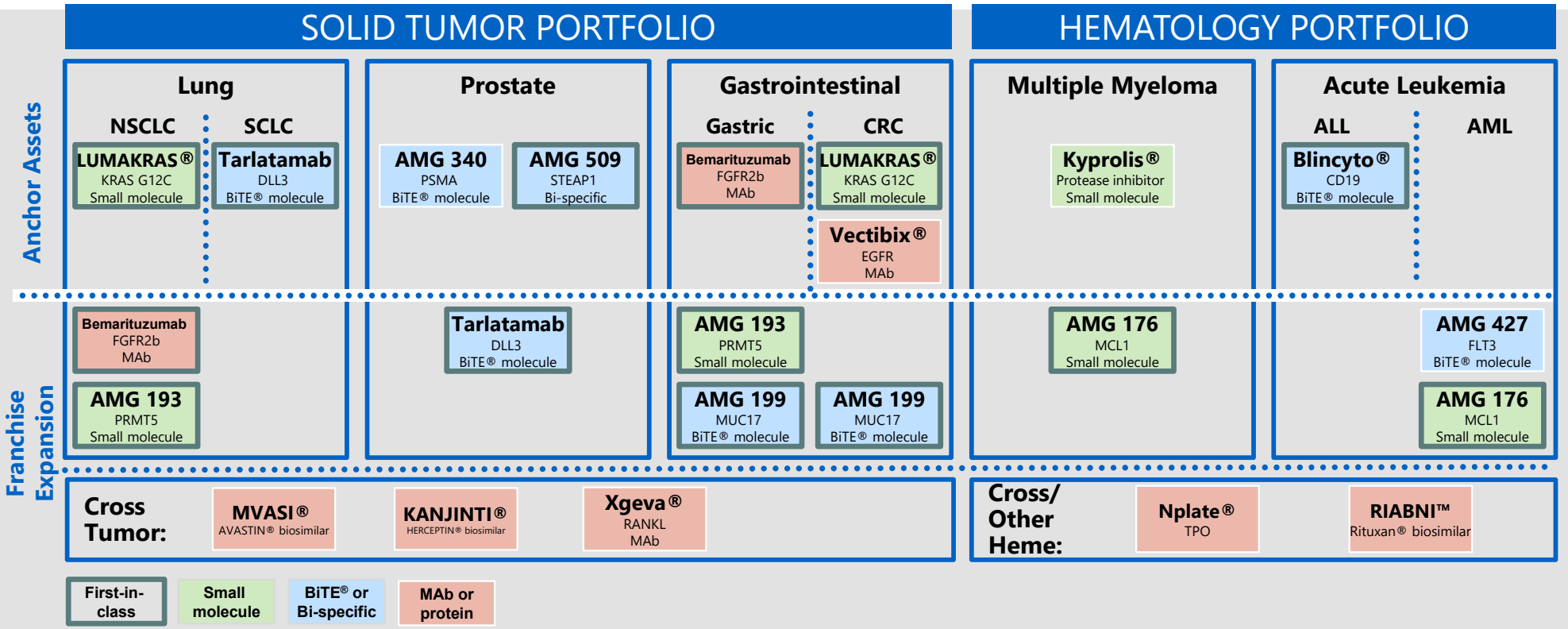
EXECUTIVE VICE PRESIDENT RESEARCH AND DEVELOPMENT

AMGEN®

Agenda

Topic	Presenter
Introduction	David Reese, M.D. – Executive Vice President, Research and Development, Amgen
LUMAKRAS® PD1 / PD-L1 and SHP2 Combination Studies	Bob Li, M.D., MPH – Memorial Sloan Kettering
Tarlatamab Dose Escalation and Expansion	Luis Paz Ares, M.D. - Hospital Universitario 12 de Octubre
Concluding Remarks	Jean-Charles Soria, M.D. – Senior Vice President Development, Amgen
Q&A	All

Broad Oncology Portfolio With Multiple First-in-class Programs



KRAS= Kirsten Rat Sarcoma; FGFR2b= fibroblast growth factor receptor 2b; BiTE®= bispecific T-cell engager; DLL3= delta-like ligand 3; PSMA= prostate-specific membrane antigen; STEAP1= Six-transmembrane epithelial antigen of prostate 1; MAb= monoclonal antibody; PRMT5= protein arginine methyltransferase 5; MUC17= Mucin 17; EGFR= epidermal growth factor receptor; MCL1= myeloid cell leukemia-1; CD19= cluster of differentiation 19; FLT3= fms-like tyrosine kinase 3; CRC= colorectal cancer; ALL= acute lymphoblastic leukemia; AML= Acute myeloid leukemia; NSCLC= non small cell lung cancer; SCLC= small cell lung cancer; RANKL= Receptor activator of nuclear factor kappa-B ligand; TPO= thrombopoietin

LUMAKRAS® COMBINATION THERAPY UPDATE

BOB LI, MD
MEMORIAL SLOAN KETTERING

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LUMAKRAS® PD1 / PD-L1 COMBINATION STUDY

CodeBreaK 100/101 Study Design

- Phase 1b multicenter, open-label studies

Key Eligibility
- Advanced *KRAS* p.G12C-mutated NSCLC
- Received (or refused) prior standard therapies
- No prior $KRAS^{G12C}$ inhibitor
- No active brain metastasis

Screening/Enrollment

Sotorasib* (oral daily) at:
- 960 mg
- 720 mg
- 360 mg
- 240 mg
- 120 mg

Sotorasib lead-in 21d or 42d then combination (N = 29)	Concurrent treatment (N = 29)
Atezolizumab 1200 mg Q3W (N = 10)	Atezolizumab 1200 mg Q3W (N = 10)
OR	*OR*
Pembrolizumab 200 mg Q3W (N = 19)	Pembrolizumab 200 mg Q3W (N = 19)

Primary endpoints: safety
Key secondary endpoints: ORR, DOR, DCR, PK

Snapshot: April 15, 2022

Here we present first data of lead-in and concurrent sotorasib with pembrolizumab or atezolizumab from CodeBreaK 100/101 with median follow-up time of 12.8 months (range: 1.6, 29.9)

*Not all doses were tested for each cohort.
KRAS = Kristen rat saccoma; NSCLC = non-small cell lung cancer; ORR = objective response rate; DOR = duration of response; DCR= disease control rate; PK= pharmacokinetics; Q3W= every 3 weeks; d= days.

Baseline Characteristics

	Total (N = 58)
Median age, years (range)	66 (29, 86)
Smoking history, n (%)*	54 (93)
Treated as first-line therapy, n (%)†	12 (21)
Prior anti-PD-(L)1, n (%)	**39 (67)**
Prior anti-PD-(L)1 as last prior line	25 (43)
ECOG performance score, n (%)	
0	11 (19)
1	47 (81)
Brain metastasis, n (%)	18 (31)
Liver metastasis, n (%)	15 (26)
PD-L1 expression, n (%)‡	
< 1%	10 (17)
1% to 49%	16 (28)
≥ 50%	21 (36)
Unknown	11 (19)

*Includes former and current smoking history. †Median (range) prior lines of therapy, 1 (0, 7). ‡Not available for all patients. ECOG= Eastern Cooperative Oncology Group; PD-L1= programmed death-ligand 1.

Safety by Dose: Pembrolizumab Concurrent

TRAE*, n (%)	Sotorasib 120 mg (N = 5)		Sotorasib 360 mg (N = 8)		Sotorasib 720 mg (N = 2)		Sotorasib 960 mg (N = 4)	
	Any	≥3	Any	≥3	Any	≥3	Any	≥3
Any grade TRAE	**5 (100)**	**4 (80)**	**7 (88)**	**6 (75)**	**2 (100)**	**2 (100)**	**3 (75)**	**3 (75)**
ALT increased	2 (40)	1 (20)	3 (38)	1 (13)	2 (100)	2 (100)	3 (75)	3 (75)
AST increased	2 (40)	2 (40)	3 (38)	0	2 (100)	2 (100)	3 (75)	1 (25)
Hepatotoxicity	**2 (40)**	**2 (40)**	**3 (38)**	**2 (25)**	**2 (100)**	**2 (100)**	**3 (75)**	**3 (75)**

- **Higher rate of TRAEs than with either monotherapy[1–3], with no fatal TRAEs**
- **At lower doses of sotorasib, there was a trend towards less liver enzyme elevations, although sample sizes were limited**
- **Given the safety data for this combination, sotorasib lead-in was explored**

Hepatotoxicity included ALT increased, AST increased, immune-mediated hepatitis, ALP increased, bilirubin increased, and GGT increased; also included hepatic enzyme increased for sotorasib + pembrolizumab lead-in; liver function test increased, drug-induced liver injury, and transaminases increased for sotorasib + atezolizumab *Any grade TRAE or grade ≥ 3 TRAE occurring in ≥ 1 patient in any dose cohort.

ALT= alanine aminotransferase; ALP= alkaline phosphatase; AST= aspartate aminotransferase; GGT= gamma-glutamyltransferase; TRAE= treatment related adverse event; ALT= Alanine transaminase; AST= Aspartate transaminase

1. Hong DS, et al. N Eng J Med. 2020;383:1207-1217.; 2. Mok TSK, et al. Lancet. 2019;393:1819-1830; 3. Herbst RS, et al, N Engl J Med. 2020; 383:1328-1329.

Safety Summary: Lead-in versus Concurrent

	Sotorasib + Atezolizumab Lead-In (N = 10)	Sotorasib + Atezolizumab Concurrent (N = 10)	Sotorasib + Pembrolizumab Lead-In (N = 19)	Sotorasib + Pembrolizumab Concurrent (N = 19)
TRAE, any grade	10 (100)	9 (90)	15 (79)	17 (89)
Grade 3	3 (30)	5 (50)	10 (53)	14 (74)
Grade 4*	0	1 (10)	0	1 (5)
TRAE leading to sotorasib and/or IO discontinuation	1 (10)	5 (50)	6 (32)	10 (53)
Median duration of sotorasib, months (min, max)	6.5 (1, 18)	4.4 (1, 14)	2.8 (1, 15)	4.9 (2, 30)
Median duration of combination, months (min, max)‡	1.5 (0, 18)	2.5 (1, 14)	0.7 (1, 15)	2.3 (1, 9)
Hepatotoxicity grade ≥ 3, median onset, days (range)	**50 (28, 93)**	**67 (36, 147)**	**73 (45, 127)**	**51 (29, 190)**

- **Lead-in had lower incidence of Grade 3-4 TRAEs and TRAEs leading to discontinuation than concurrent**
- **Grade 3-4 hepatotoxicity first occurrence was outside DLT window† in 88% of patients; 97% of events resolved with corticosteroids, treatment modification, and/or discontinuation**
- **The incidence of hepatotoxicity TRAEs was similar in IO-naïve versus IO-pretreated patients**

Hepatotoxicity included ALT increased, AST increased, ALP increased, bilirubin increased, GGT increased; also hepatitis, liver function test increased, drug-induced liver injury, transaminases increased for sotorasib+atezolizumab; also hepatic enzyme increased, immune-mediated hepatitis for sotorasib lead-in+pembrolizumab; also autoimmune hepatitis for sotorasib+pembrolizumab concurrent.

*Grade 4 TRAEs were ALT increased (n = 1; related to sotorasib and atezolizumab), and AST increased (n = 1; related to sotorasib).

‡Duration of combination calculated for patients receiving both sotorasib and IO; one patient in a lead-in cohort did not receive IO and not included

†DLT window was 21 days following initiation of combination treatment. IO= immune-oncology; TRAE= treatment related adverse event; DLT= dose-limiting toxicity

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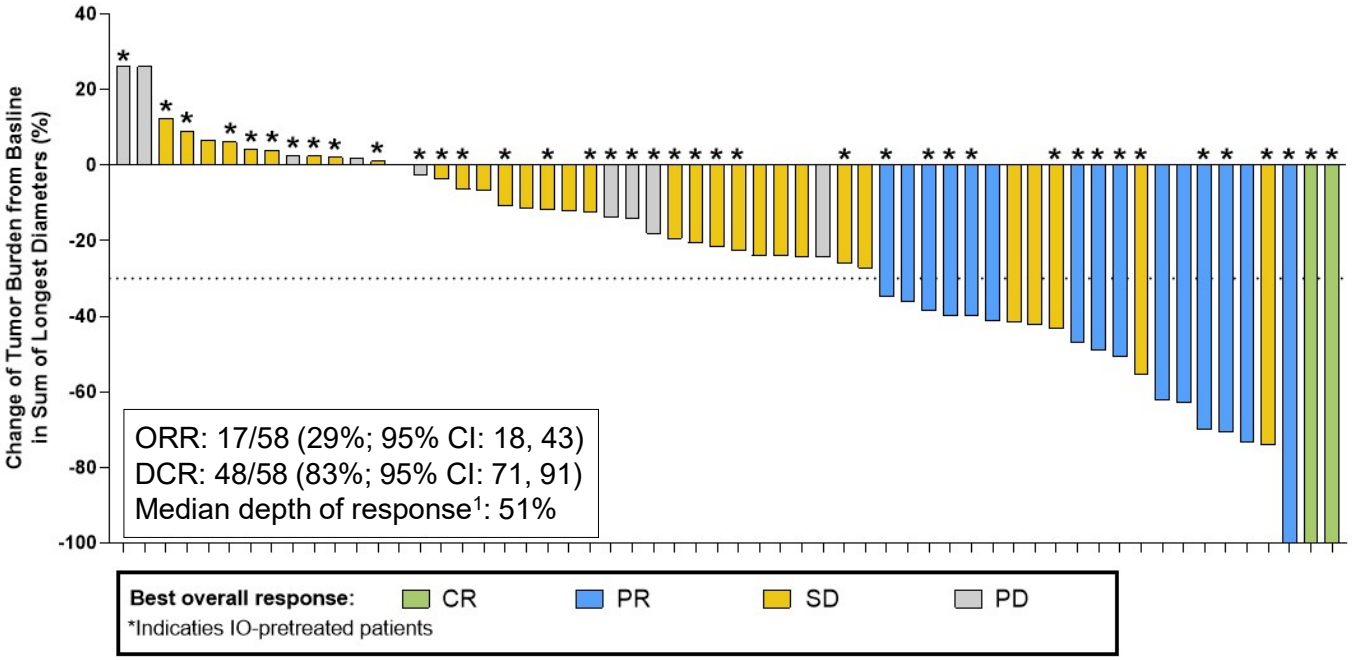
Safety for Sotorasib Lead-in + Pembrolizumab

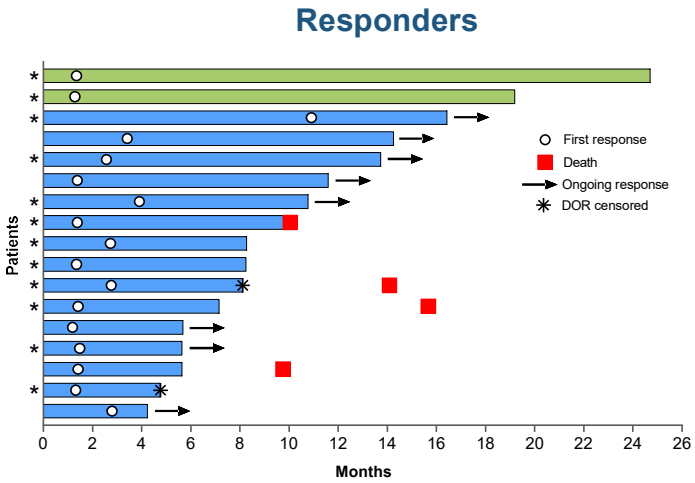
TRAE*, n (%)	Sotorasib 120 mg (N = 3)		Sotorasib 240 mg (N = 5)		Sotorasib 360 mg (N = 11)	
	Any	Grade ≥ 3	Any	Grade ≥ 3	Any	Grade ≥ 3
All TRAEs	**3 (100)**	**3 (100)**	**3 (60)**	**1 (20)**	**9 (82)**	**6 (55)**
ALT increased	2 (67)	2 (67)	1 (20)	1 (20)	6 (55)	3 (27)
AST increased	2 (67)	2 (67)	1 (20)	1 (20)	6 (55)	2 (18)
ALP increased	2 (67)	0	0	0	3 (27)	2 (18)
Diarrhea	1 (33)	0	1 (20)	0	6 (55)	1 (9)
Arthralgia	1 (33)	0	0	0	2 (18)	0
Nausea	0	0	0	0	4 (36)	0
Fatigue	0	0	0	0	4 (36)	0
Hypokalemia	0	0	0	0	3 (27)	2 (18)
Decreased appetite	0	0	0	0	3 (27)	0
Headache	0	0	0	0	2 (18)	0
Hepatotoxicity	**2 (67)**	**2 (67)**	**2 (40)**	**1 (20)**	**6 (55)**	**5 (45)**

Overall safety data from lead-in and concurrent cohorts support lower dose sotorasib and lead-in administration for better tolerability

*Any grade TRAE or grade ≥ 3 TRAE occurring in ≥ 1 patient in any dose cohort.
TRAE= treatment related adverse event; ALT= Alanine transaminase; AST= Aspartate transaminase; ALP= Alkaline Phosphatase.

Efficacy

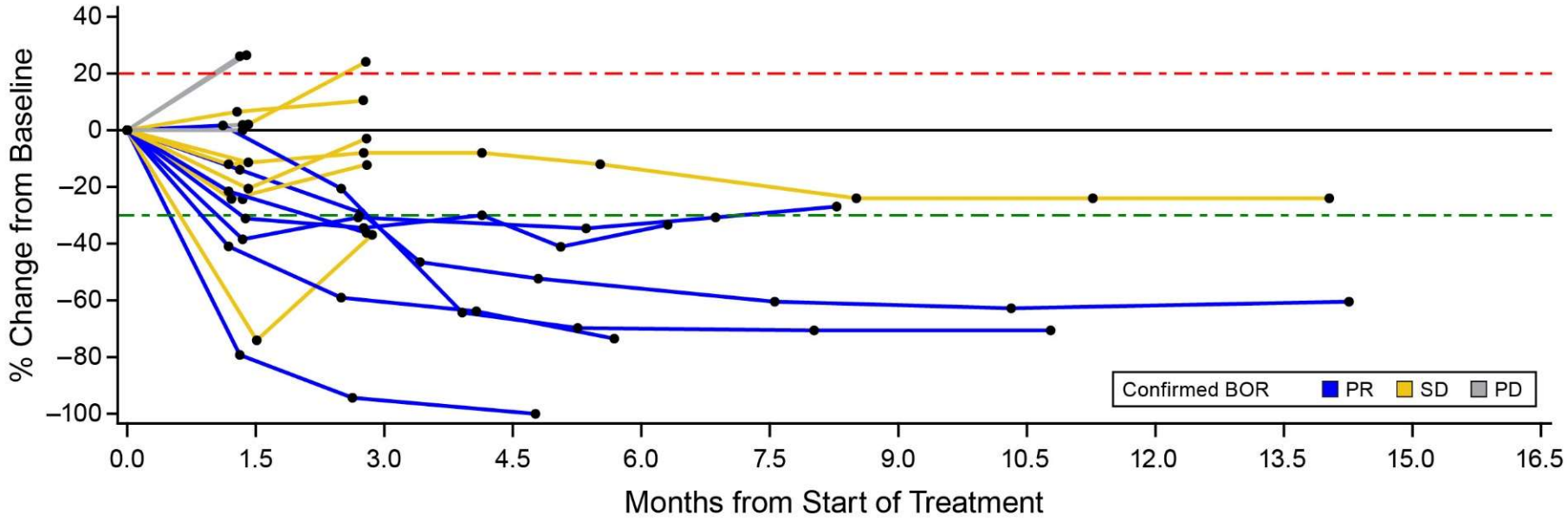




- **Deep and durable responses were observed for this combination across all cohorts, including at low doses**
- **Among the 17 responders, median duration of response was 17.9 months (95% CI: 5.6, NE)**
- **Response was similar in IO-naïve and IO-pretreated patients**

[1]Median depth of response among responders. CR= complete response; PD= progressive disease; PR= partial response; SD= stable disease; ORR= objective response rate; DCR= disease control rate; IO= immune-oncology.

Efficacy for Sotorasib Lead-In + Pembrolizumab



- **Durable clinical benefit observed with sotorasib lead-in + pembrolizumab, with deep responses**
- **In the 7 patients with confirmed response, 3 remain on combination treatment at data cutoff**

BOR= best overall response; PD= progressive disease; PR= partial response; SD= stable disease

Conclusions

- **In mostly IO-pretreated patients, sotorasib with atezolizumab or pembrolizumab led to a higher incidence of grade 3-4 TRAEs than observed with monotherapy[1–3]**
  - In sotorasib + pembrolizumab concurrent cohorts, lower sotorasib doses trended toward less hepatotoxicity and fewer grade ≥3 events
  - Sotorasib lead-in had lower rates of grade 3-4 TRAEs and TRAEs leading to discontinuation compared with concurrent administration
  - 88% of Grade 3-4 hepatotoxicity occurring outside DLT window and resolving with corticosteroids, treatment modification, and/or discontinuation
- **Lead-in cohorts demonstrated durable clinical activity and depth of response**
- **Among the 17 responders, median duration of response was 17.9 months (95% CI: 5.6, NE)**

Low dose sotorasib as lead-in followed by combination with pembrolizumab will be further studied in 1L patients with advanced NSCLC to assess benefit-risk

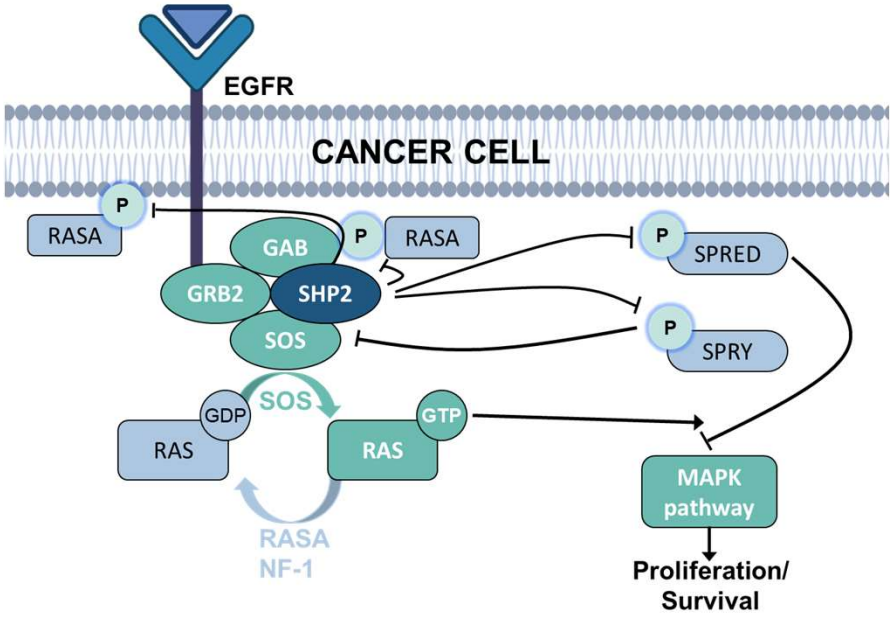
TRAE= treatment related adverse event; IO= immune-oncology; DLT= dose-limiting toxicity; 1L= first line.

1. Hong DS, et al. N Eng J Med. 2020;383:1207-1217; 2. Mok TSK, et al. Lancet. 2019;393:1819-1830; 3. Herbst RS, et al, N Engl J Med. 2020; 383:1328-1329.

LUMAKRAS® SHP2 COMBINATION STUDY

Preclinical rationale and putative mechanisms of resistance support the combination of sotorasib with a SHP2 inhibitor

- Genomic alterations in the RTK pathway have been identified as a putative mechanism of resistance to sotorasib[1]
- In mouse xenograft models, combining sotorasib with a SHP2 inhibitor (SHP2i) impaired RTK signaling to RAS and enhanced anti-tumor efficacy[2,3]



This study evaluated the safety and efficacy of sotorasib combined with RMC-4630, a small molecule SHP2i with a focus on patients with NSCLC

KRAS= Kirsten rat sarcoma; NSCLC= non-small cell lung cancer; RAS= rat sarcoma virus; RTK= receptor tyrosine kinase; SHP2i= Src homology region 2 domain-containing phosphatase-2 inhibitor.

1. Li BT, et al. J Clin Oncol. 2022;50(36 suppl):Abstract #360490. **2**. Rex K, et al. Cancer Res. 2021;81(13 suppl):Abstract #1057. **3.** Smith JAM, et al. Cancer Res. 2020;80(16 suppl):Abstract #1943.

Study Design: Sotorasib + SHP2 Inhibitor (RMC-4630)

- Phase 1b multicenter, open-label study (NCT04185883); data cutoff: April 11, 2022

Screening/Enrollment

Key eligibility criteria*
- Locally advanced or metastatic *KRAS* p.G12C solid tumors
- Prior anti-PD(L)1 and/or platinum-based chemo and targeted therapy (NSCLC)
- Allowed prior $KRAS^{G12C}$ inhibitor

PART 1: Dose Exploration (N = 27)

Sotorasib (960 mg PO daily) + RMC-4630 (PO) at:

- 200 mg at days 1 and 2 Q7D
- 140 mg at days 1 and 2 Q7D
- 100 mg starting dose at days 1 and 2 or days 1 and 4 Q7D

Primary endpoints: Safety
- Dose-limiting toxicities
- TRAEs and TEAEs
- Changes in vital signs, ECGs, and clinical laboratory tests

Secondary endpoints
- Pharmacokinetics
- ORR, DOR, TTR, PFS, DCR, duration of stable disease per RECIST v1.1, OS

*Prior systemic therapy for advanced/metastatic disease (other tumor types).
KRAS= Kristen rat sarcoma; NSCLC= non-small cell lung cancer; DCR, disease control rate; DOR, duration of response; ECG, electrocardiogram; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PO, per oral; Q7D, every 7 days; RECIST, Response Evaluation Criteria in Solid Tumors; TEAE, Treatment-emergent adverse event; TRAE, treatment-related adverse event; TTR, time to response.

Baseline Characteristics

	NSCLC (N=11)	Total (all tumors)* (N=27)
Median age, years (range)	64 (51–78)	63 (43–78)
Male, n (%)	4 (36)	15 (56)
Smoking history, n (%)†	11 (100)	19 (70)
ECOG performance score, n (%)		
0	10 (90)	5 (19)
1‡	0	20 (74)
Brain metastasis, n (%)	7 (64)	13 (48)
Liver metastasis, n (%)	3 (27)	11 (41)
Median lines of prior therapies, n (range)	**3 (1–6)**	**3 (1–6)**
Prior $KRAS^{G12C}$ inhibitor, n (%)§	**5 (45)**	**11 (41)**
Prior anti-PD-(L)1, n (%)	10 (91)	15 (56)

*Total cohort includes patients with NSCLC (n = 11; 41%), colorectal cancer (n = 9; 33%), and other solid tumors (n = 7; 26%).
†Includes former and current smoking history.
‡One patient with NSCLC had a change in Eastern Cooperative Oncology Group performance score from 1 to 2 during screening, and one patient with missing entry.
§Includes 8 patients treated with sotorasib and 3 patients treated with adagrasib. KRAS= Kristen rat sarcoma; PD-L!= programed death ligand 1; NSCLC= non-small cell lung cancer

Most Common Treatment-Related Adverse Events

Variable, n (%)	Sotorasib + RMC-4630 (N = 27)*					
	Sotorasib 960 mg + RMC-4630 100 mg (N = 6)		Sotorasib 960 mg + RMC-4630 140 mg (N = 10)		Sotorasib 960 mg + RMC-4630 200 mg (N = 11)	
	All Grades	Grade 3	All Grades	Grade 3	All Grades	Grade 3
Total TRAE	**6 (100)**	**1 (17)**	**4 (40)**	**1 (10)**	**7 (64)**	**4 (36)**
Edema†	2 (33)	0	0	0	6 (55)	0
Diarrhea	1 (17)	0	1 (10)	0	5 (45)	2 (18)
Dry mouth	0	0	2 (20)	0	1 (9)	0
Fatigue	0	0	0	0	3 (27)	0
AST increased	2 (33)	1 (17)	0	0	0	0
ALT increase	2 (33)	0	0	0	0	0
Ascites	0	0	1 (10)	1(10)	0	0
TRAE leading to sotorasib dose modification**	1 (17)		1 (10)		3 (27)	
TRAE leading to RMC-4630 dose modification**	2 (33)		1 (10)		4 (36)	

TRAEs consistent with known safety profile of sotorasib and RMC-4630
Edemas (peripheral and facial) were most common TRAE; all were Grade 1 or 2, and none led to discontinuation

*Related to either study drug across all doses. Includes TRAEs with >10% patient incidence across all grades and all grade ≥ 3 TRAEs; no Grade 4 or 5 TRAEs were reported. **Patients dose reduced or interrupted both drugs for increased ALT, diarrhea, pleural effusion, colitis, fatigue (1 each); sotorasib only for diarrhea, increased AST, dry mouth, dyspnea (1 each); RMC-4630 only for peripheral edema, ascites, hypertension, constipation, liver function test increased (1 each)
†Includes general, peripheral, periorbital, and facial edema; TRAE= treatment related adverse event; ALT= Alanine transaminase; AST= Aspartate transaminase

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Efficacy*

Response assessed by investigator	NSCLC	
	All enrolled (N = 11)	$KRAS^{G12C}$ inhibitor-naïve (N = 6)
ORR, % (95% CI)	**27 (6, 61)**	**50 (12, 88)**
Best overall response, n (%)		
Partial response	3 (27)	3 (50)
Stable disease	4 (36)	3 (50)
Progressive disease	4 (36)	0
Disease control rate, n (%)	**7 (64)**	**6 (100)**

Other tumor types: 8 CRC (5 SD; 3 PD); 1 ovarian cancer (PR with an 81% reduction in tumor burden); 1 pancreatic adenocarcinoma (SD), and 2 other solid tumors (1 SD, 1 NE).

- **Disease control in 7 of 11 patients with NSCLC and in all patients who were $KRAS^{G12C}$ i-naïve**
- **Promising early efficacy observed in patients with NSCLC who were $KRAS^{G12C}$ i-naïve**
- **Two of 3 patients with PR had an ongoing response at data cutoff**

*Efficacy is summarized only for evaluable patients who were treated and had the opportunity for at least 1 post-baseline scan.
CRC= colorectal cancer; NE= non-evaluable; PD= progressive disease; PR= partial response; SD= stable disease; NSCLC= non-small cell lung cancer; KRAS= Kristen rat sarcoma

Conclusions

- **Preclinical rationale and putative mechanisms of resistance support the combination of sotorasib with a SHP2 inhibitor**
- **Sotorasib plus a SHP2 inhibitor, RMC-4630 appears safe and well-tolerated in *KRAS* p.G12C-mutated solid tumors**
  - No Grade 4 or fatal TRAEs and few TRAE-related discontinuations
- **Promising and durable clinical activity observed, most notably in KRAS^{G12C} inhibitor-naïve NSCLC**

Phase 2 study underway (NCT05054725) to further define efficacy and safety of this combination in KRAS^{G12C} inhibitor-naïve patients with mNSCLC
(WCLC 2022 e-poster #EP08.02-111)

SHP2= Src homology region 2 domain-containing phosphatase-2; KRAS= Kristen rat sarcoma; NSCLC= non-small cell lung cancer

TARLATAMAB UPDATE

LUIS PAZ ARES, MD

HOSPITAL UNIVERSITARIO 12 DE OCTUBRE

AMGEN®

Small Cell Lung Cancer Is One Of The Most Aggressive Solid Tumors

- **Incidence**[1-2,6]
  - 15% of lung cancer cases, >330,000 new cases worldwide annually
  - Strongly associated with smoking
  - 70% of patients have extensive-stage disease at diagnosis[3-6]
- **Poor prognosis**
  - Extensive-stage disease 5-year survival rate of <3%[7]
- **Limited survival benefit**
  - ~12-13 months mOS in 1L[8,9]
  - ~8.5 months mOS in 2L[10]
  - ~5 months mOS in 3L+[11]
- **~70K 1L & relapse addressable patients across major markets***

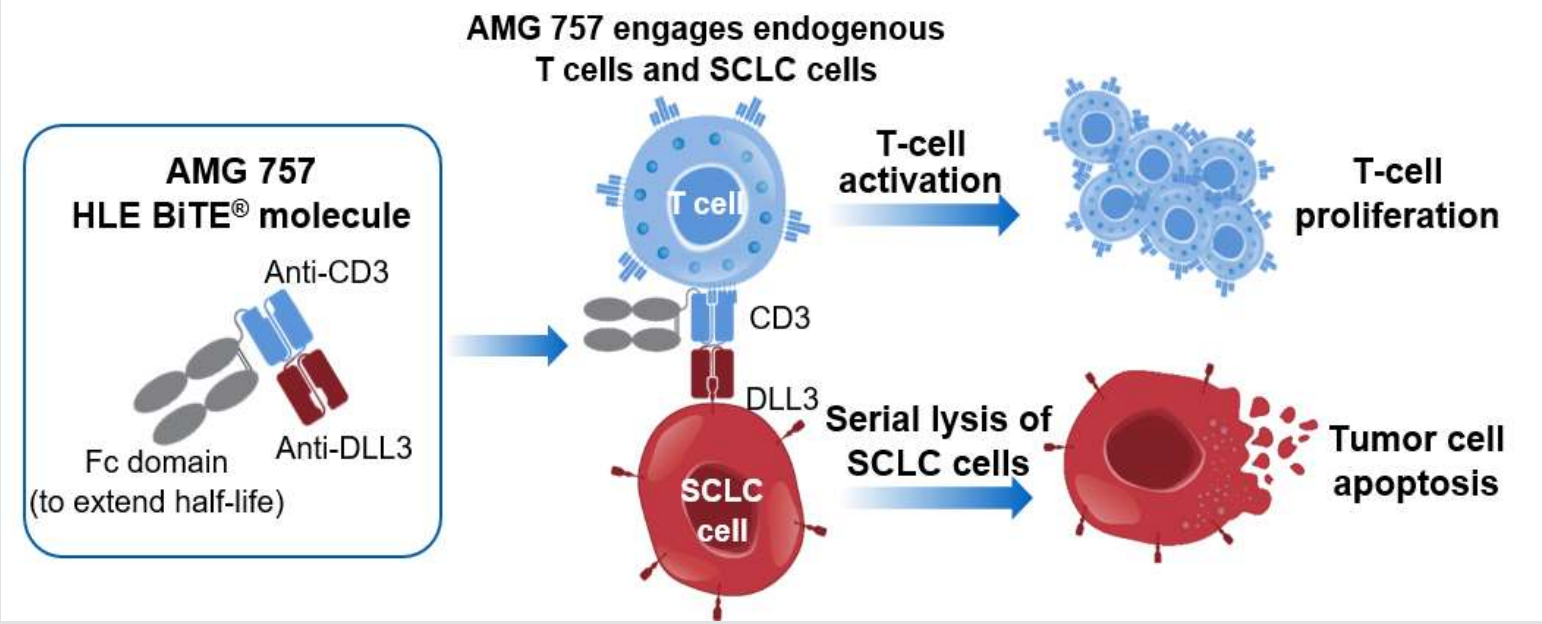
1. National Institutes of Health. https://www.cancer.gov/types/lung/hp/small-cell-lung-treatment-pdq. Accessed August 25, 2021. **2.** IARC. Global Cancer Observatory: Cancer Today. https://gco.iarc.fr/today/data/factsheets/populations/900-world-fact-sheets.pdf. Accessed March 25, 2022. **3.** Oronsky B, et al. *Neoplasia*. 2017;19:991-1002. **4**. Ellis PM, et al. *J Thorac Dis*. 2011;3:183-188.**5.** Huber RM, et al. *Breathe*. 2012;8:315-330. **6.** Demedts IK, et al. *Eur Respir J*. 2010;35:202-215. **7.** Pavan et al. Journal for ImmunoTherapy of Cancer (2019) 7:205. **8.** Horn L. et al. N Engl J Med 2018;379:2220-9. **9**. Paz-Ares L. et al. Lancet 2019; 394: 1929–39. **10.** Reck M, Vicente D, Ciuleanu T, et al. Efficacy and safety of nivolumab (nivo) monotherapy versus chemotherapy (chemo) in recurrent small cell lung cancer (SCLC): results from Checkmate 331. Presented at: ESMO Immuno-oncology Congress 2018; 13 to 16 December 2018; Geneva, Switzerland. **11.** Coutinho AD, Shah M, Lunacsek OE, Eaddy M, Willey JP. Real-world treatment patterns and outcomes of patients with small cell lung cancer progressing after 2 lines of therapy. Lung Cancer. 2019;127:53-58.

mOS= median overall survival; 1L= first-line

*Major markets: US, Germany, France, Japan (Amgen internal data)

Tarlatamab Is a First-In-Class HLE BiTE® Molecule Targeting DLL3

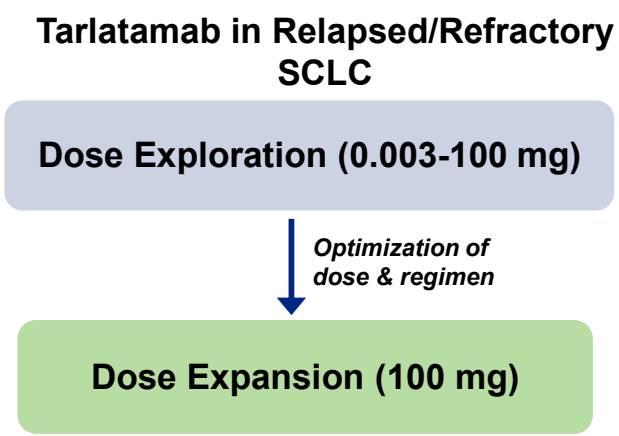
- **BiTE® molecules engage a patient's own T cells to attack and eradicate cancer cells[1–3]**



1.Stieglmaier J, et al. Expert Opin Biol Ther. 2015;15:1093–9;
2. Einsele H, et al. Cancer. 2020;126:3192–201;
3. Bargou R, et al. Science. 2008;321:974-977. 4.

BiTE®= bispecific T-cell engager; CD= cluster of differentiation; Fc= fragment crystallizable; HLE= half-life extended; DLL3= delta-like ligand 3; SCLC= small cell lung cancer

First-in-Human Study of Tarlatamab



Primary Objectives	▪ Evaluate safety and tolerability in SCLC ▪ Determine MTD or RP2D
Secondary Objectives	▪ Characterize PK ▪ Evaluate preliminary antitumor activity
Exploratory Objectives	▪ Evaluate immunogenicity of tarlatamab ▪ Assess biomarker expression

- **Study design** – open-label, multi-center study of tarlatamab with dose escalation ranging from 0.003 mg to 100 mg and dose expansion at 100 mg administered by IV infusion every 2 weeks, with/without step dose
- Data cutoff of 15 June 2022, median follow-up time of 8.5 months (range, 0.2–30.7)
- **Disease assessment** – Antitumor activity assessed using modified RECIST 1.1 every 8 ± 1 weeks

IV= intravenous; MTD= maximum tolerated dose; PK= pharmacokinetics; RP2D= recommended phase 2 dose; SCLC= small cell lung cancer; RECIST= Response Evaluation Criteria in Solid Tumors.

Key Eligibility Criteria & Patient Characteristics

Inclusion Criteria

- Histologically/cytologically confirmed SCLC
  - Progressed/recurred following ≥ 1 platinum-based chemotherapy (including a PD-L1 inhibitor, if standard of care)
- ECOG performance status: 0–2
- ≥ 2 measurable lesion(s)

Exclusion Criteria

- Untreated or symptomatic brain metastases
- Prior anti-cancer therapy within 28 days
- Immunodeficiency or systemic steroid use
- Interstitial lung disease

Baseline Characteristic	All Patients (N = 106)
Median age, years (range)	64 (32–80)
Current/former smoker, n (%)	13 (12) / 81 (76)
ECOG performance status: 0–1, n (%)	105 (99)
Prior lines of therapy, n (%)	
1	30 (28)
2	44 (42)
≥ 3	32 (30)
Median (range)	2 (1–6)
Prior anti-PD-(L)1 treatment, n (%)	52 (49)
Extensive stage disease at initial diagnosis, n (%)	99 (93)
Prior brain / liver metastases, n (%)	29 (27) / 54 (51)

ECOG= Eastern Cooperative Oncology Group; PD-1= programmed death-1; PD-L1= programmed death-ligand 1; SCLC= small cell lung cancer.

Treatment-Related Adverse Events and Events of Interest Summary

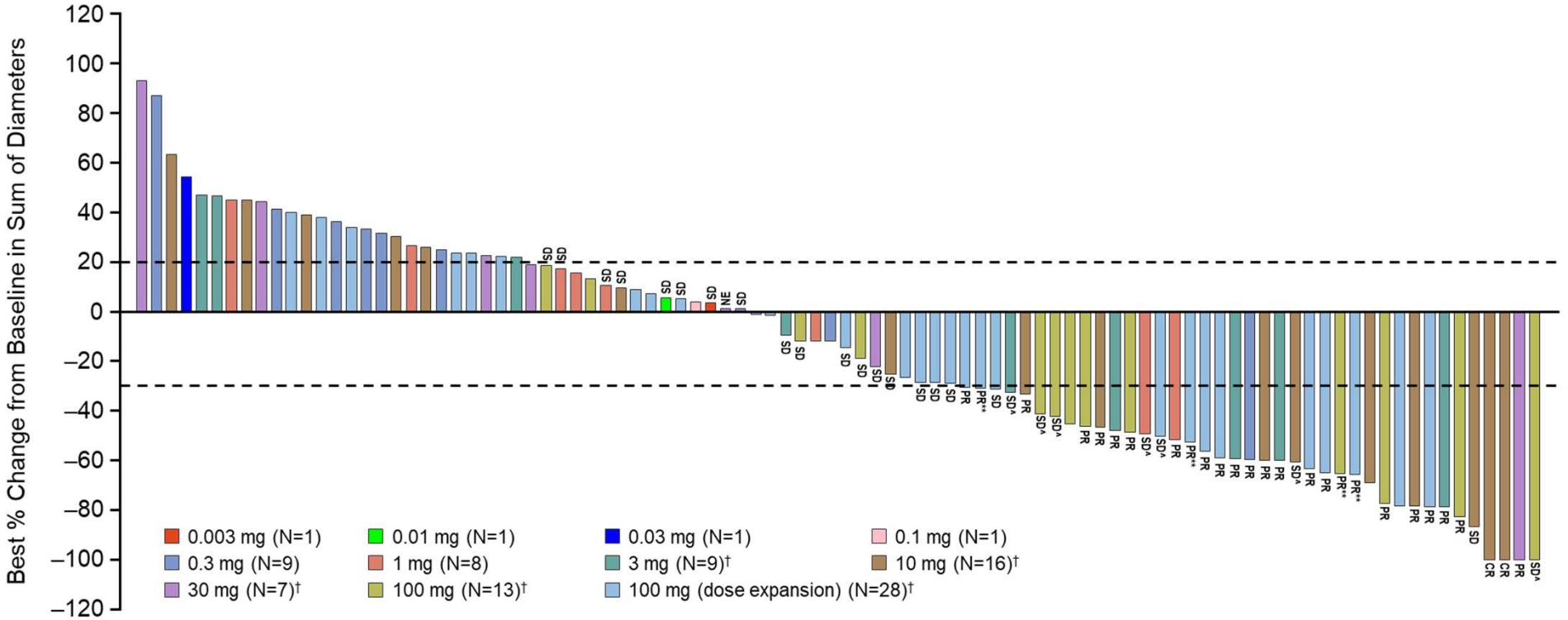
Treatment-related AEs (by preferred term)	Patients (N = 106)	
	All Grades, n (%)	Grade ≥ 3, n (%)*
Any treatment-related AE	97 (92)	33 (31)
CRS	56 (53)	1 (1)
Neurologic events	53 (50)	7 (7)
Neutropenia	17 (16)	10 (9)

- **CRS AEs (Lee, 2014) were mostly grade 1, occurred in cycle 1 and rarely recurred in subsequent cycles, and were generally manageable with steroids, IV fluids, and anti-pyretics (8/106 patients [8%] required tocilizumab for CRS); no grade 4/5 CRS**
- **Treatment-related neurologic events (NEs) were predominantly grade 1 and either dysgeusia or headache**
- **TRAEs occurring in ≥15% patients (% all Grades/Grade ≥3) were CRS (53/1), Pyrexia (38/2), Dysgeusia (23/0), Fatigue (22/3) and Nausea (20/0)**

Tarlatamab showed a manageable safety profile across evaluated doses

*Includes one patient with grade 5 pneumonitis; AE= adverse event; CRS= cytokine release syndrome; TRAE= treatment-related adverse event.

Tarlatamab Induces Response in Previously Treated SCLC

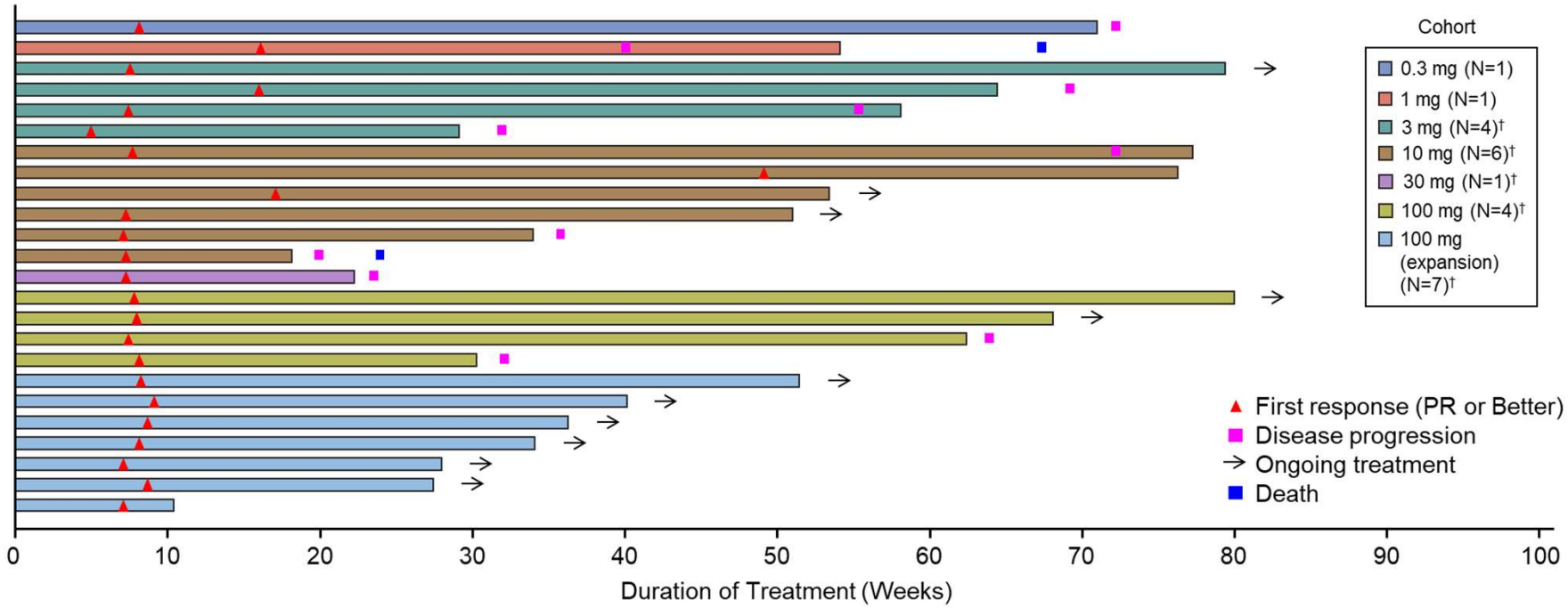


Confirmed ORR, 23% (2 CRs, 22 PRs); 37% of patients with tumor shrinkage ≥ 30%
52% disease control rate

† Indicates step dosing with 1 mg run-in dose. Plot includes patients who received ≥ 1 dose of tarlatamab, had at least 9 weeks follow-up after first dose of tarlatamab, and had sum of diameters available in post-baseline assessments. Unlabeled bars include confirmed and unconfirmed PD. CR= complete response; NE= not evaluable; ORR= objective response rate; PR= partial response; SD= stable disease.
PR** indicates patients had an initial PR and still have potential for future confirmative scans; SD^ indicates patients had an initial response but did not have confirmation of response on the subsequent scan; SCLC= small cell lung cancer.

Tarlatamab Delivers Durable Responses in Previously Treated SCLC

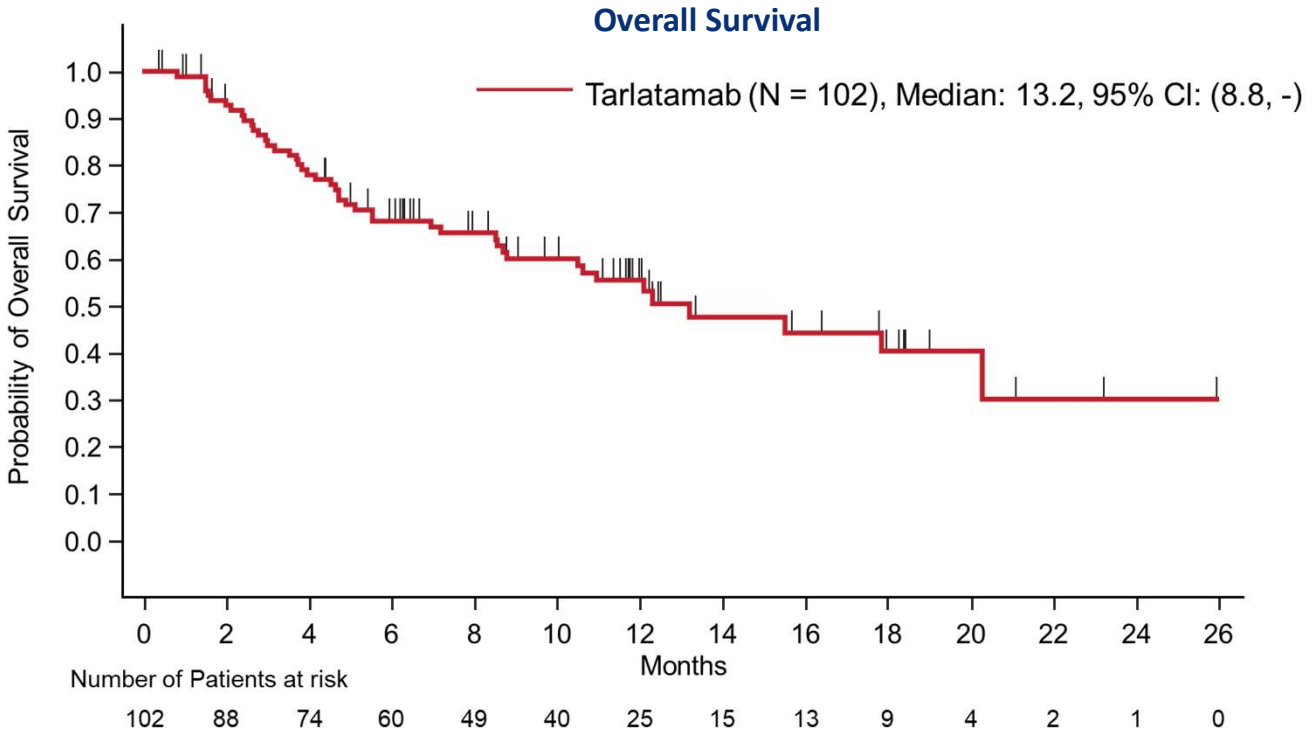
Duration of Response in Confirmed Responders (n=24)



- **Median duration of response was <u>13.0 months</u> (95% CI: 6.2, 14.9)***
  - 11 responders had treatment ongoing as of data cutoff, including 2 complete responders
  - Median time to response was 1.8 months (range: 1.2–7.4)

Bar graph includes all patients with confirmed response (n = 24), with each bar representing 1 patient. *The interim time to event analysis set used in the duration of response analysis includes subjects whose data cut-off date is at least 6 months after first dose date (N=23). † Indicates step dosing with 1 mg run-in dose.
SCLC= small-cell lung cancer; PR= partial response; CI= confidence interval

Survival with Tarlatamab in Previously Treated SCLC



Median overall survival of 13.2 months (95% CI: 8.8, -)

*Survival analysis population (N=102) included subjects who received their first dose on or prior to 16Dec2021 to allow at least 6 months of follow-up to allow sufficient data maturity before data cutoff. CI, confidence interval; OS, overall survival; SCLC= small-cell lung cancer; CI- confidence interval

Tarlatamab Conclusions

- **First DLL3-targeted immune therapy to undergo clinical evaluation**
- **Promising antitumor activity with remarkable response durability**
  - Confirmed ORR of 23% and median DOR of 13 months
  - Median OS of 13.2 months
- **Acceptable safety profile**
- **Potentially registrational Phase 2 study is underway in 2L+ SCLC patients**

DLL-3= delta-like ligand 3; ORR= objective response rate; DOR= duration of response; OS= overall survival; 2L= second-line; SCLC= small-cell lung cancer; CI- confidence interval

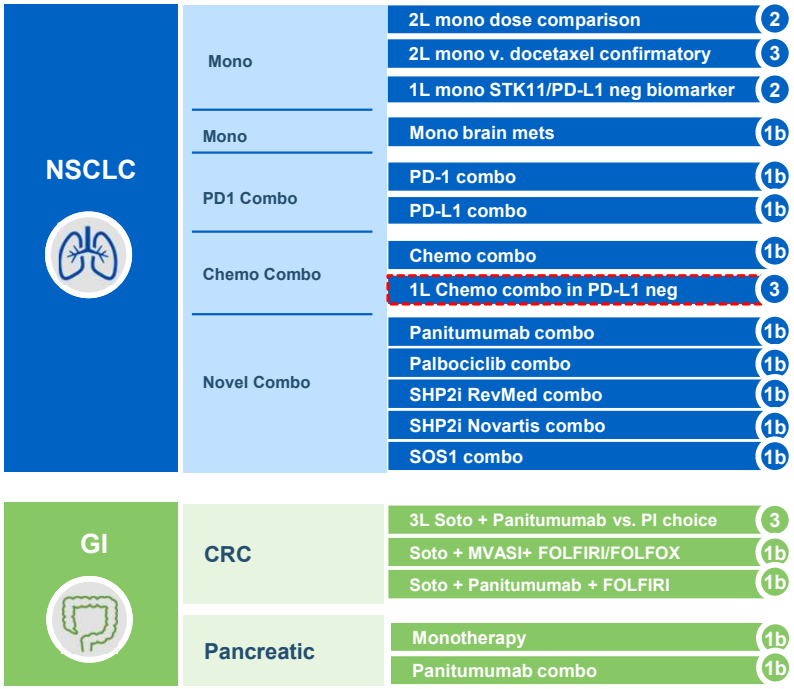
CONCLUDING REMARKS

JEAN-CHARLES SORIA, MD

SENIOR VICE PRESIDENT GLOBAL DEVELOPMENT ONCOLOGY

AMGEN®

Investigating LUMAKRAS® in multiple combinations, different tumor types, and earlier lines of therapy



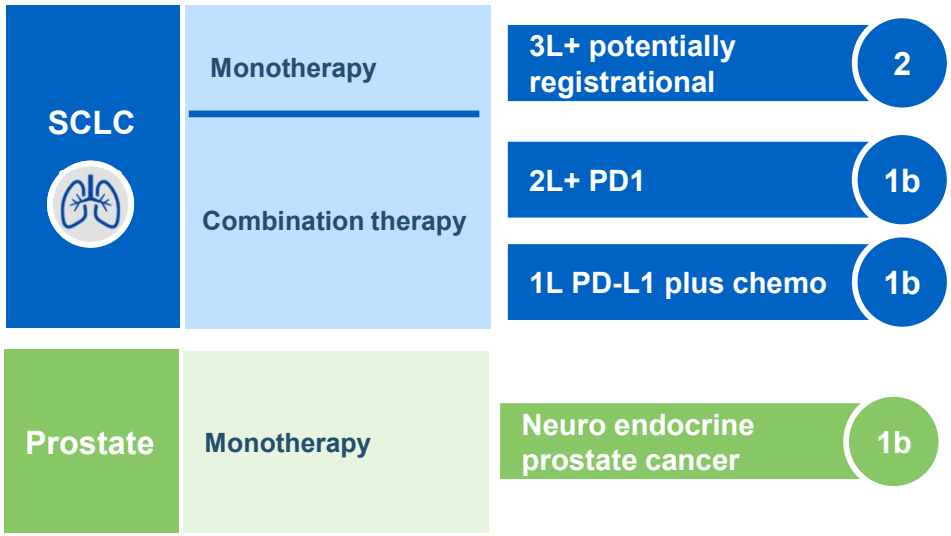
- Largest and broadest clinical program
- Pursuing NSCLC, CRC, and pancreatic cancers
- Exploring 10+ combinations
- Multiple potential paths to first-line NSCLC

Planned

Does not included deprioritized cohorts MEK +/- panitumumab, EGFR (afatinib), mTORi (everolimus), Chemo Docetaxel and Carbo/Pac

Mono= monotherapy; combo= combination therapy; mets= metastasis; STK11= serine/threonine kinase 11; chemo= chemotherapy; SHP2i= Src homology region 2-containing protein tyrosine phosphatase 2 inhibitor; RevMed= Revolution Medicines; SOS1= son of sevenless 1; Soto= sotorasib; PI= principle investigator; FOLFIRI= Folinic acid, fluorouracil and irinotecan; GI= gastrointestinal; NSCLC= non small cell lung cancer; CRC= colorectal cancer; 1L= first line; 2L= second line; 3L= third line; PD1= programmed cell death protein 1; FOLFOX= fluorouracil, leukovorin, and oxaliplatin; mTORi = mammalian target of rapamycin inhibitor; MEK= mitogen-activated protein kinase kinase; EGFR= epidermal growth factor receptor

Tarlatamab has transformative potential in SCLC and other tumor types



SCLC Patients have:

- Poor prognosis[7]
- Limited survival benefit[8-11]
- ~70K 1L & relapse addressable patients*

In 3L+ SCLC Tarlatamab demonstrated:

- Confirmed ORR of 23%
- Median DOR of 13 months
- Median OS of 13.2 months

7. Pavan et al. Journal for ImmunoTherapy of Cancer (2019) 7:205. **8.** Horn L. et al. N Engl J Med 2018;379:2220-9. **9**. Paz-Ares L. et al. Lancet 2019; 394: 1929–39. **10.** Reck M, Vicente D, Ciuleanu T, et al. Efficacy and safety of nivolumab (nivo) monotherapy versus chemotherapy (chemo) in recurrent small cell lung cancer (SCLC): results from Checkmate 331. Presented at: ESMO Immuno-oncology Congress 2018; 13 to 16 December 2018; Geneva, Switzerland. **11.** Coutinho AD, Shah M, Lunacsek OE, Eaddy M, Willey JP. Real-world treatment patterns and outcomes of patients with small cell lung cancer progressing after 2 lines of therapy. Lung Cancer. 2019;127:53-58.

1L= first-line; 2L= second-line; 3L= third-line; ORR= objective response rate; DOR= duration of response; OS= overall survival; SCLC= small-cell lung cancer; PD-L1= programmed death ligand 1; PD1= programmed death protein 1

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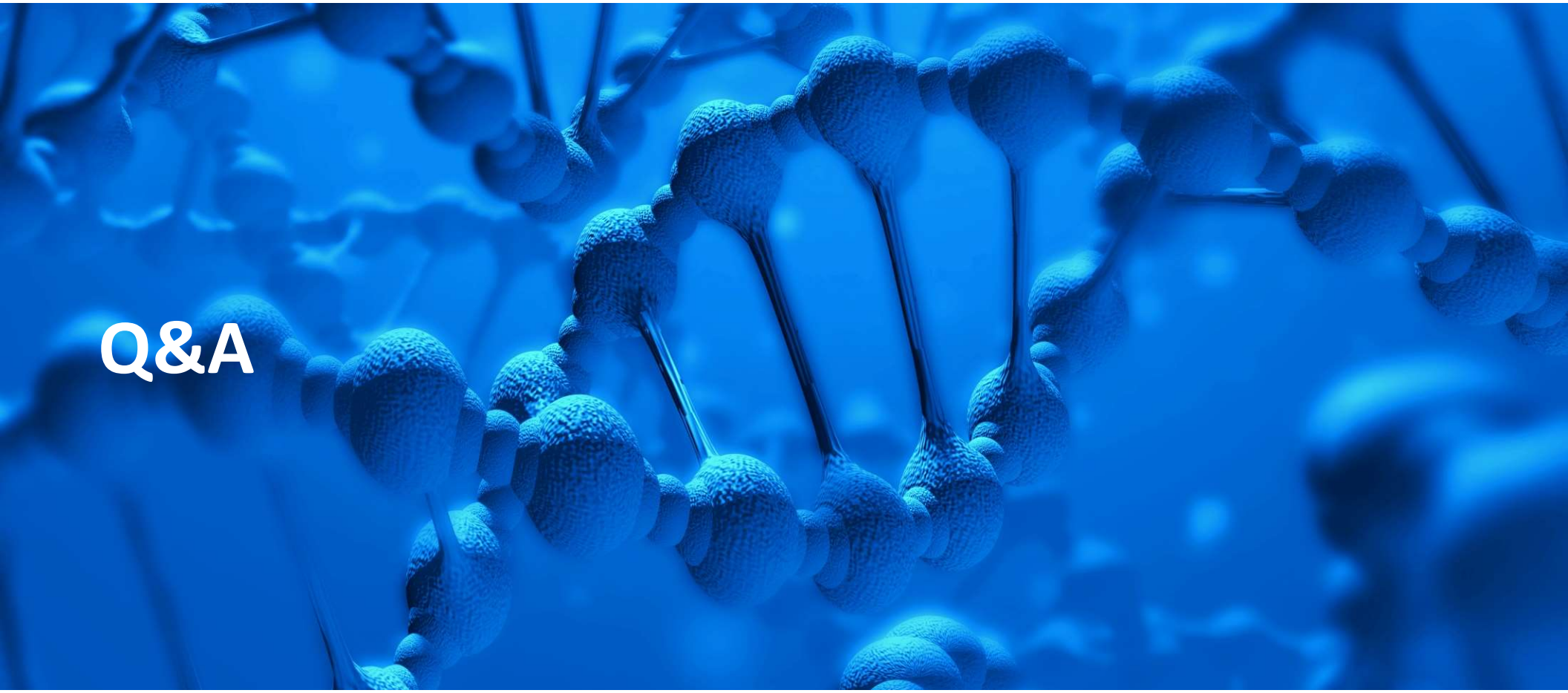
Q&A