



We target clinically underserved cancers

September 2022

Disclaimer

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this presentation that do not relate to matters of historical fact should be considered forward-looking statements, including statements relating to our development of AL101 and AL102, the promise and potential impact of our preclinical or clinical trial data, the timing of and plans to initiate additional clinical trials of AL101 and AL102, the timing and results of any clinical trials or readouts, the sufficiency of cash to fund operations, and the anticipated impact of COVID-19, on our business. These forward-looking statements are based on management's current expectations. The words "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "estimate," "believe," "predict," "potential" or "continue" or the negative of these terms or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: we have incurred significant losses since inception and anticipate that we will continue to incur losses for the foreseeable future. We are not currently profitable, and we may never achieve or sustain profitability; we will require additional capital to fund our operations, and if we fail to obtain necessary financing, we may not be able to complete the development and commercialization of AL101 and AL102; we have a limited operating history and no history of commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for our future viability; we are heavily dependent on the success of AL101 and AL102, our most advanced product candidates, which are still under clinical development, and if either AL101 or AL102 does not receive regulatory approval or is not successfully commercialized, our business may be harmed; due to our limited resources and access to capital, we must prioritize development of certain programs and product candidates; these decisions may prove to be wrong and may adversely affect our business; the outbreak of COVID-19, may adversely affect our business, including our clinical trials; our ability to use our net operating loss carry forwards to offset future taxable income may be subject to certain limitations; our product candidates are designed for patients with genetically defined cancers, which is a rapidly evolving area of science, and the approach we are taking to discover and develop product candidates is novel and may never lead to marketable products; we were not involved in the early development of our lead product candidates; therefore, we are dependent on third parties having accurately generated, collected and interpreted data from certain preclinical studies and clinical trials for our product candidates; enrollment and retention of patients in clinical trials is an expensive and time-consuming process and could be made more difficult or rendered impossible by multiple factors outside our control; if we do not achieve our projected development and commercialization goals in the timeframes we announce and expect, the commercialization of our product candidates may be delayed and our business will be harmed; our product candidates may cause serious adverse events or undesirable side effects, which may delay or prevent marketing approval, or, if approved, require them to be taken off the market, require them to include safety warnings or otherwise limit their sales; the market opportunities for AL101 and AL102, if approved, may be smaller than we anticipate; we may not be successful in developing, or collaborating with others to develop, diagnostic tests to identify patients with Notch-activating mutations; we have never obtained marketing approval for a product candidate and we may be unable to obtain, or may be delayed in obtaining, marketing approval for any of our product candidates; even if we obtain FDA approval for our product candidates in the United States, we may never obtain approval for or commercialize them in any other jurisdiction, which would limit our ability to realize their full market potential; we have been granted Orphan Drug Designation for AL101 for the treatment of ACC and may seek Orphan Drug Designation for other indications or product candidates, and we may be unable to maintain the benefits associated with Orphan Drug Designation, including the potential for market exclusivity, and may not receive Orphan Drug Designation for other indications or for our other product candidates; although we have received Fast Track designation for AL101, and may seek Fast Track designation for our other product candidates, such designations may not actually lead to a faster development timeline, regulatory review or approval process; we face significant competition from other biotechnology and pharmaceutical companies and our operating results will suffer if we fail to compete effectively; we are dependent on a small number of suppliers for some of the materials used to manufacture our product candidates, and on one company for the manufacture of the active pharmaceutical ingredient for each of our product candidates; and any future collaborations will be, important to our business. If we are unable to maintain our existing collaboration or enter into new collaborations, or if these collaborations are not successful, our business could be adversely affected; enacted and future healthcare legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates, if approved, and may affect the prices we may set; if we are unable to obtain, maintain, protect and enforce patent and other intellectual property protection for our technology and products or if the scope of the patent or other intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and we may not be able to compete effectively in our markets; we may engage in acquisitions or in-licensing transactions that could disrupt our business, cause dilution to our stockholders or reduce our financial resources; risks related to our operations in Israel could materially adversely impact our business, financial condition and results of operations.

These and other important factors discussed under the caption "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2020 filed with the U.S. Securities and Exchange Commission (SEC) on March 24, 2021 and our other filings with the SEC, could cause actual results to differ materially from those indicated by the forward-looking statements made in this presentation. Any such forward-looking statements represent management's estimates as of the date of this presentation. New risk factors and uncertainties may emerge from time to time, and it is not possible to predict all risk factors and uncertainties. While we may elect to update such forward-looking statements at some point in the future, except as required by law, we disclaim any obligation to do so, even if subsequent events cause our views to change. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this presentation. 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 sources to be reliable as of the date of this presentation, we have not independently verified, and we make no representation as to the adequacy, fairness, accuracy or completeness of any information obtained from third-party sources. In addition, all of the market data included in this presentation involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. Neither we nor our affiliates, advisors or representatives makes any representation as to the accuracy or completeness of the data included in this presentation or undertake to update such data after the date of this presentation. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.

Pioneers in Targeting Novel Cancer Drivers



Ayala is a clinical-stage oncology company developing and commercializing small molecule therapeutics to improve treatment outcomes in rare and aggressive cancers



Targeting key biological pathways implicated in rare and aggressive cancers through the inhibition of gamma secretase



Broad portfolio of innovative clinical-stage programs with clinical proof-of-concept demonstrated for lead candidates AL101 and AL102






Potential value enhancing milestones

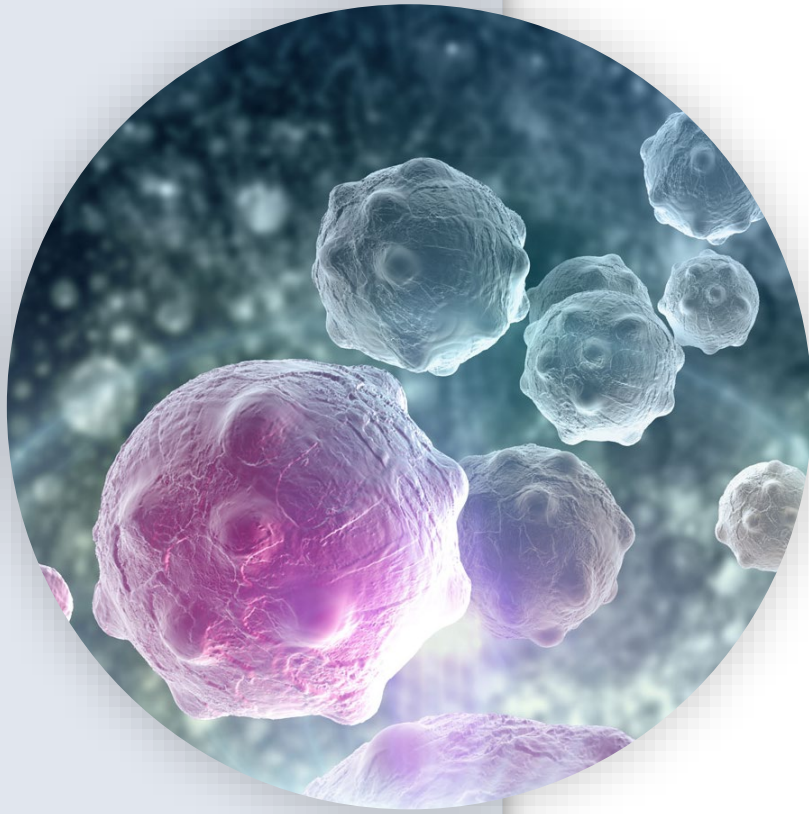
- Present long-term data from the selected dose from the RINGSIDE study with AL102 for desmoid trial (Mid 2023)
- Path for potential registration for AL101 in R/M ACC (early 2023)

Strong corporate position to execute on strategy

- Experienced management team in oncology and rare disease

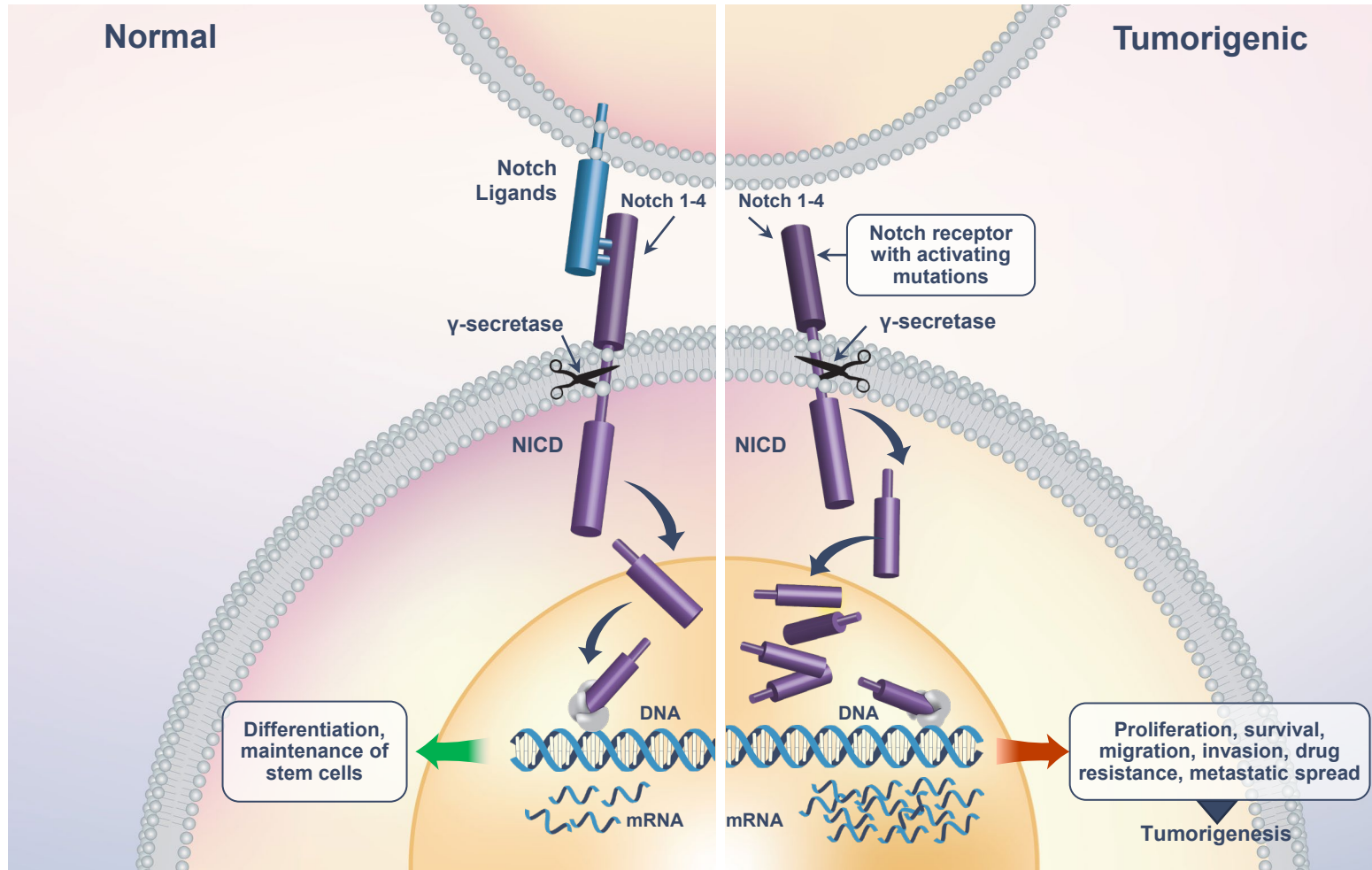
Late-Stage Pipeline Provides Multiple Opportunities for Value Creation

Indication	Product	Preclinical	Phase 1	Phase 2	Phase 3	Commercial Rights	Upcoming Milestones
Desmoid	AL102						Present long-term data from the selected dose from the RINGSIDE study (Mid 2023)
R/M ACC	AL101						Path for potential registration early 2023
R/R T-ALL	AL102						Initiate a Phase 2 trial H2-2022



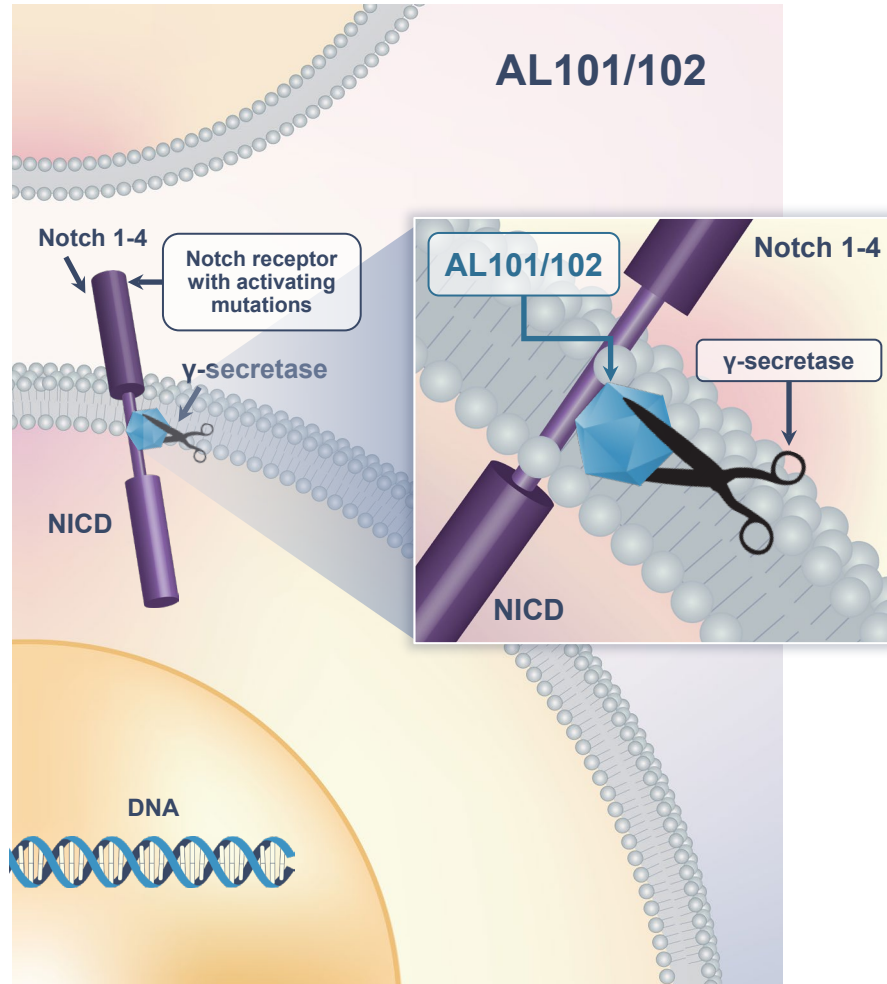
Targeting Notch Pathway Activation with Gamma Secretase Inhibitors

Notch Pathway is an Important Target for Therapeutic Anti Cancer Agents



- The Notch signaling cascade is an evolutionarily conserved pathway that has a crucial role in regulating development and homeostasis in various tissues
- Aberrant activation of the Notch pathway is implicated in multiple solid tumors and hematological cancers
- Often associated with more aggressive cancers
- In cancers, Notch is known to serve as a critical facilitator in processes such as cellular proliferation, survival, migration, invasion, drug resistance and metastatic spread
→ contributes to poorer patient prognosis

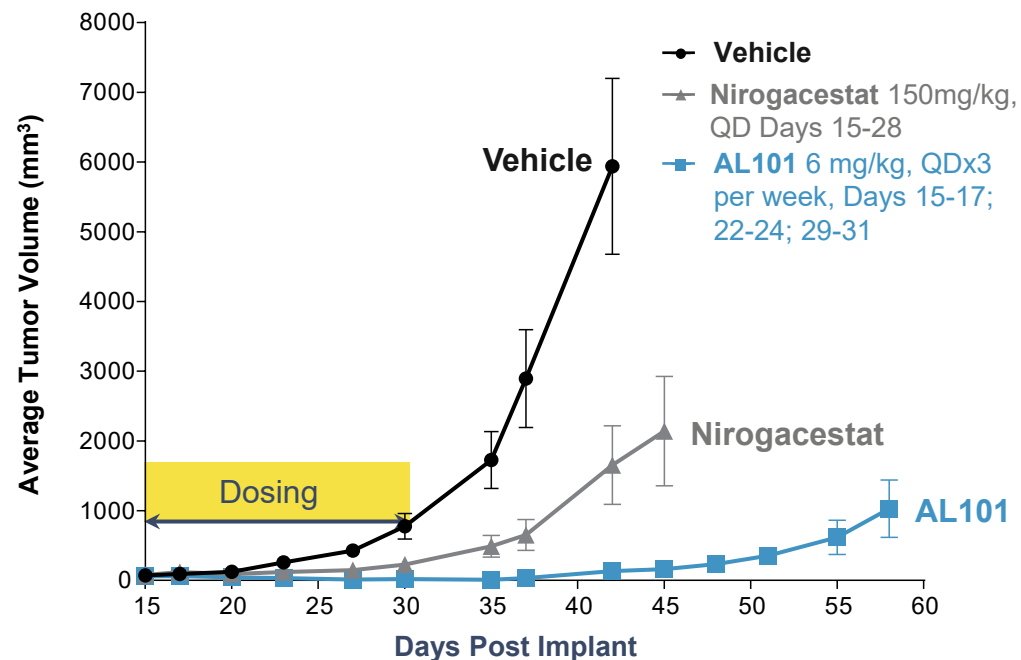
Lead Candidates AL101 and AL102 Inhibit the Notch Pathway



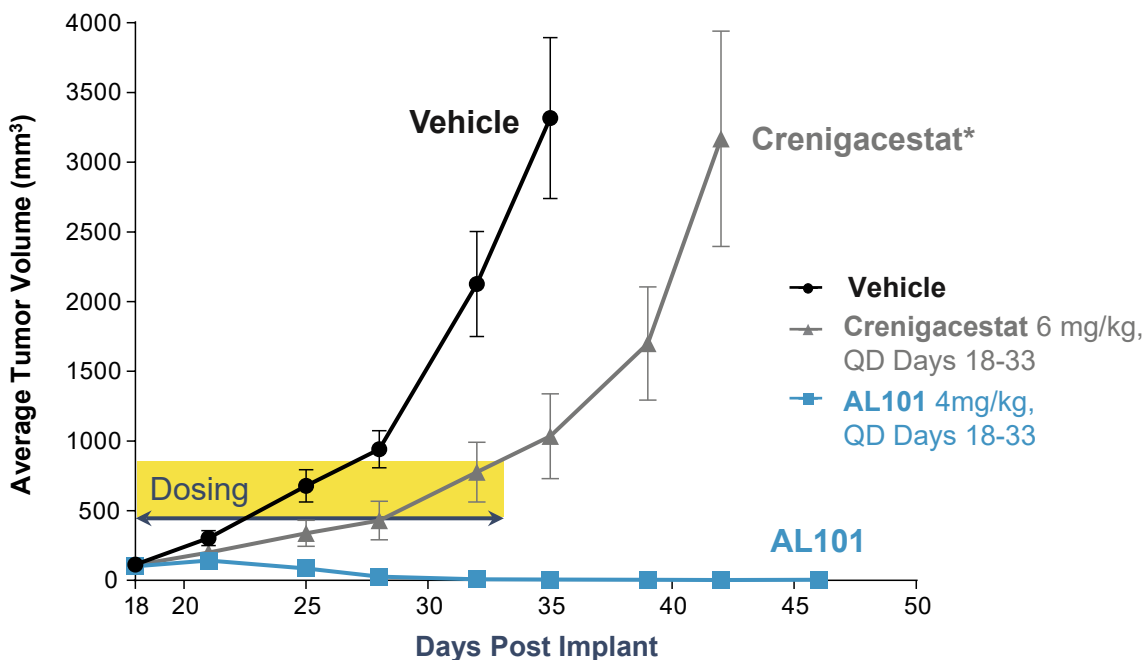
- AL101 and AL102 are potent small molecule gamma secretase inhibitors targeting the Notch pathway
- Gamma (γ) secretase enzyme is responsible for Notch activation

AL101 and AL102 Are Potent Notch Inhibitors

Effect on Tumor Growth in T-ALL Mouse Model



Tumor volume data are Mean \pm SEM for 7-8 mice per treatment arm.



*Crenigacestat is being developed by Celgene Corporation, recently acquired by BMS

Inhibition of Constitutive Notch Signaling: IC50 (nM)¹

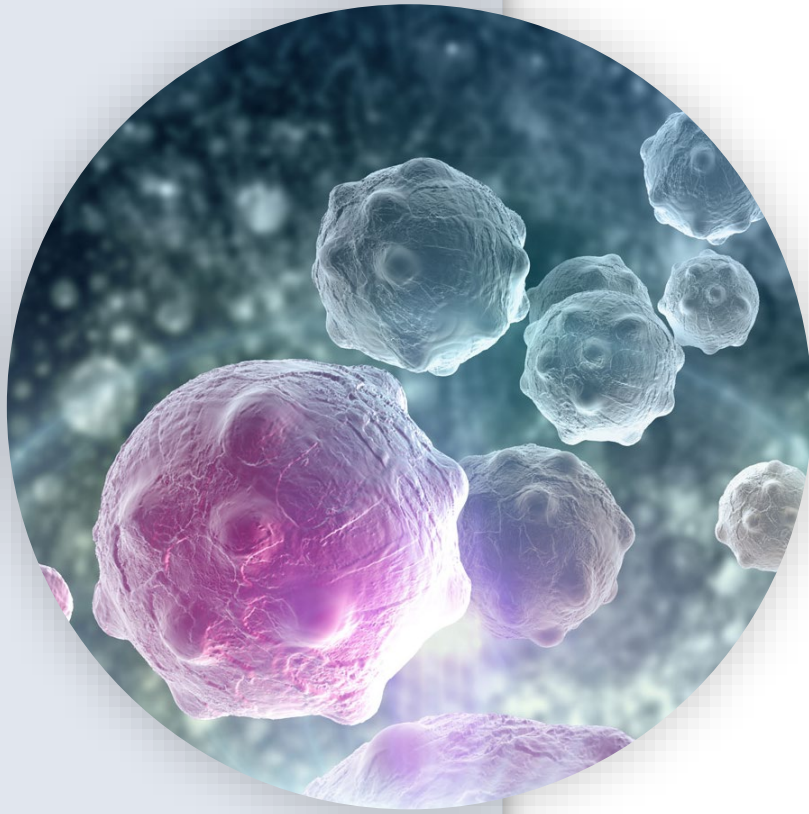
	AL101 (BMS-906024)	AL102 (BMS-986115)	Nirogacestat ² (PF-03084014)	RO-4929097 ³	MK-0752 ⁴
Notch1	1.6	6.1	13	3.8	354
Notch2	0.7	2.9	15	4.4	403
Notch3	3.4	8.1	17	22	955
Notch4	2.9	4.4	16	12	874

¹ Luciferase reporter-based assay, inhibition of constitutive Notch signaling

² Nirogacestat is being developed by SpringWorks Therapeutics, Inc.

³ RO-4929097 was developed by F. Hoffmann-La Roche Ltd. and is not under active development

⁴ MK-0752 was developed by Merck & Co., Inc. and is not under active development



AL102 – Investigational Oral, Potent and Selective
Gamma Secretase Inhibitor

Desmoid Tumors (DTs) are Rare and Aggressive Connective Tissue Tumors with Significant Unmet Need for Safe and Effective Systemic Therapies



Abrao et al., Clinics 2011



McDonald, et al., RadioGraphics 2008

DTs can aggressively infiltrate vital organs resulting in pain, loss of function and organ dysfunction with significant morbidities



Kate



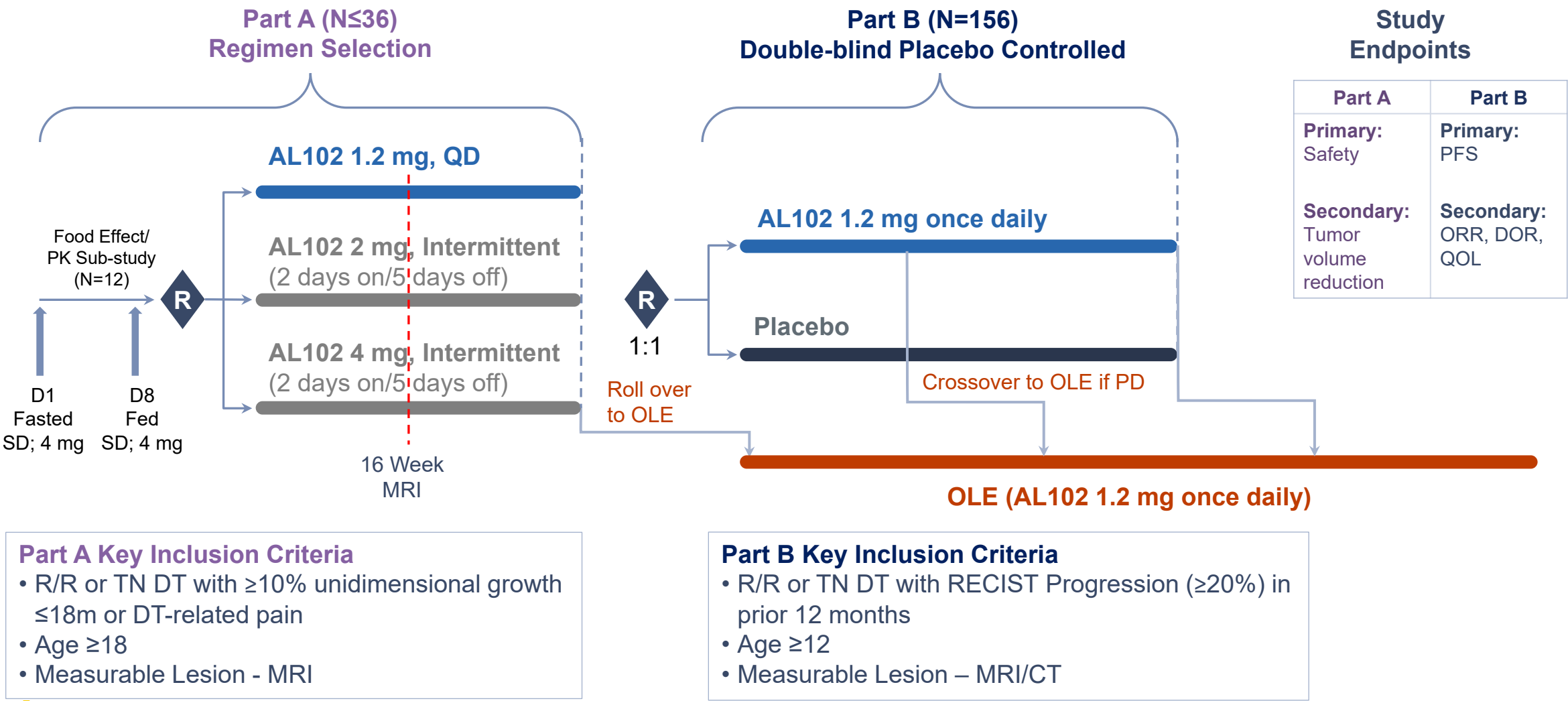
Ashley

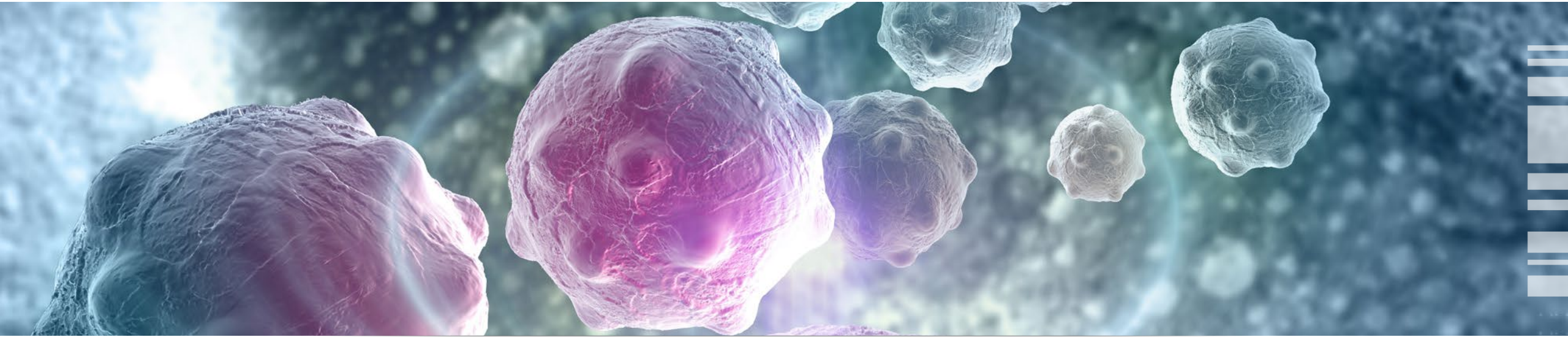
- People living with DTs like Kate and Ashley, have difficult journey with limited options
- Research indicates that the main impact on individuals living with DTs is pain, social isolation, changes to education and employment, insomnia, anxiety, and depression¹

- Annual incidence of ~1,700 in the US²
- No approved drug and no standard of care for systemic therapies in progressing DT
- 6,600 - 8,000 patients actively receiving treatment in the US in any given year³
- Recurrence rate after surgery is up to 77%⁴

RINGSIDE: Pivotal Phase 2/3 Trial Evaluating AL102 in Desmoid Tumors

Part A completed; Part B initiated

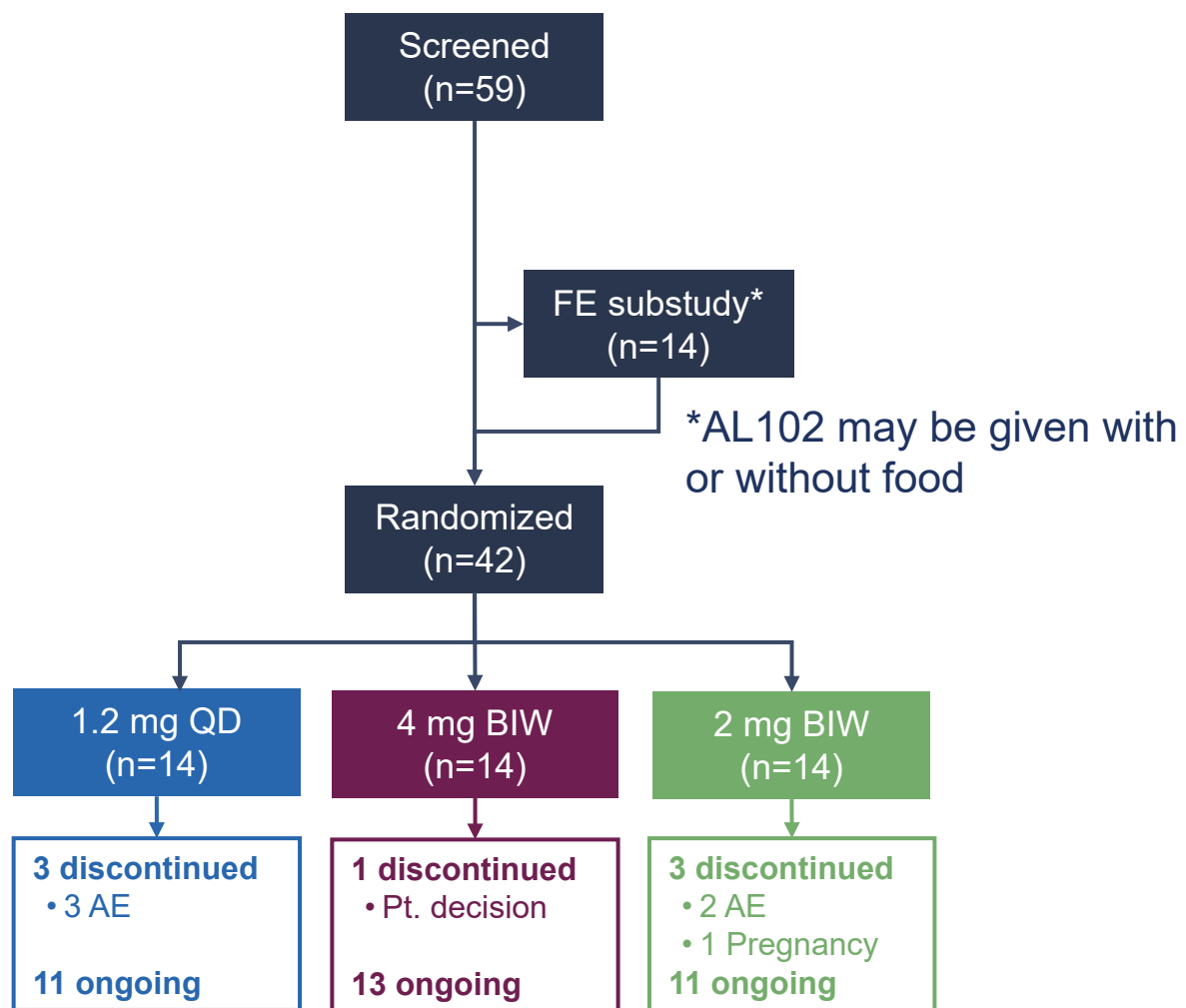




Interim Results Part A Phase 2/3
ESMO 2022



Part A Disposition, Demographics, and Baseline Characteristics



Baseline characteristics were generally balanced across treatment groups

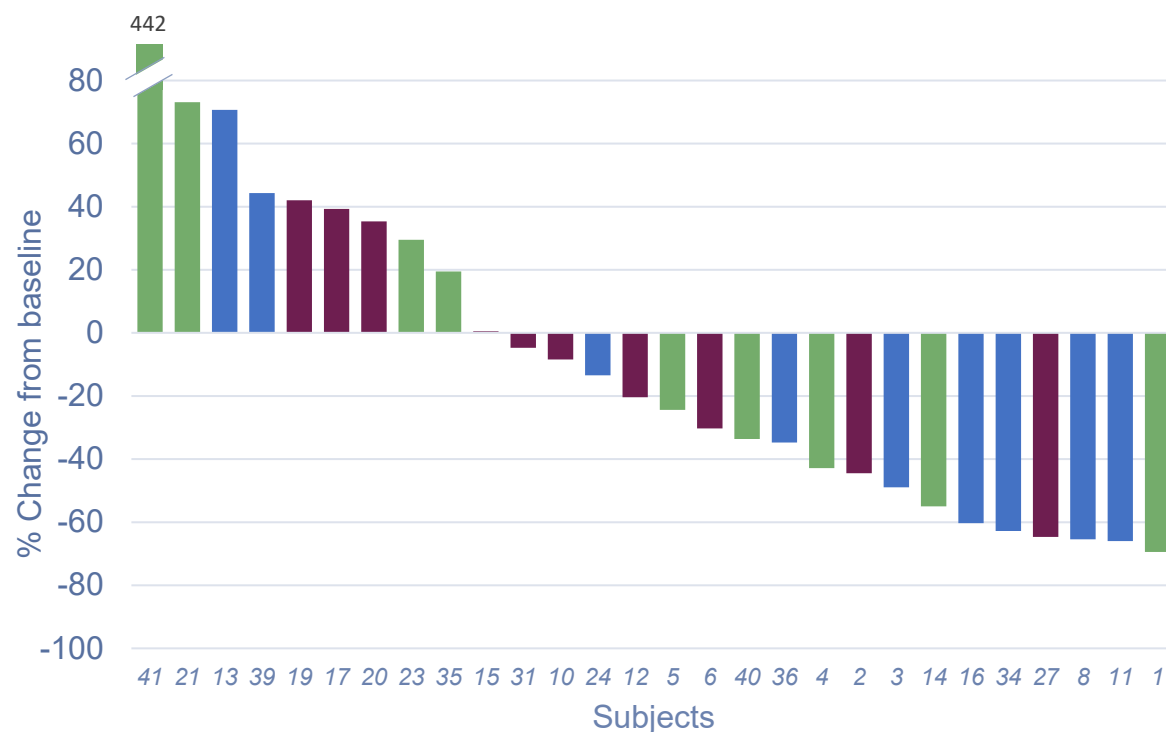
	Total (N=42)
Age (years), median (range)	38.5 (19,72)
Gender – female n (%)	31 (74)
Location of tumor at diagnosis, n (%)	
Intra Abdominal	11 (26)
Other	31 (74)
Prior DT therapies, n (%)	29 (69)
Prior DT surgeries performed, n (%)	20 (48)
Prior DT radiation therapies, n (%)	4 (10)
Prior therapy treatment type, n (%)	
Chemotherapy	23 (55)
Hormonal Therapy	8 (19)
Targeted Small Molecule	7 (17)
Weeks on study, mean (range)	>23 (4,40)

N, number of patients with data; BIW, twice weekly: 2 days on, 5 days off; QD, once daily; Data Cut Jul 14, 2022

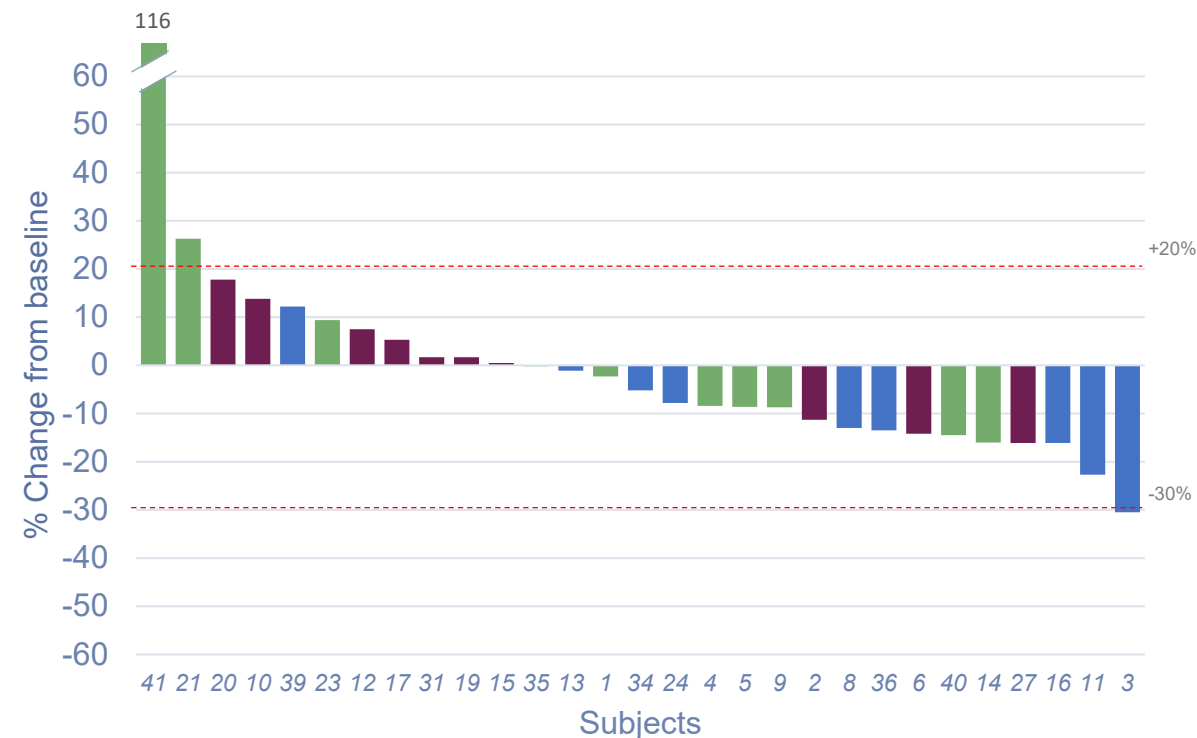
Rapid Activity Observed Across all Doses at Week 16

- Activity observed in all dose arms
- PR (central) observed at 16 weeks (confirmed 28 weeks)

Week 16 Volume Change from Baseline (N=28)



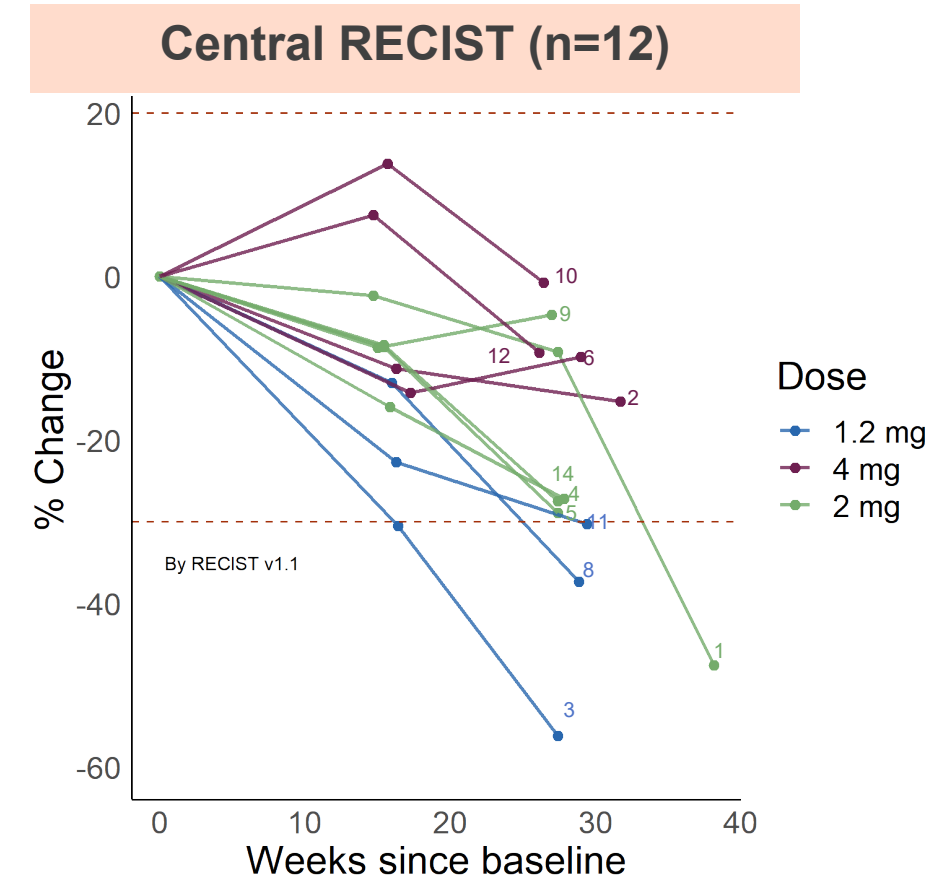
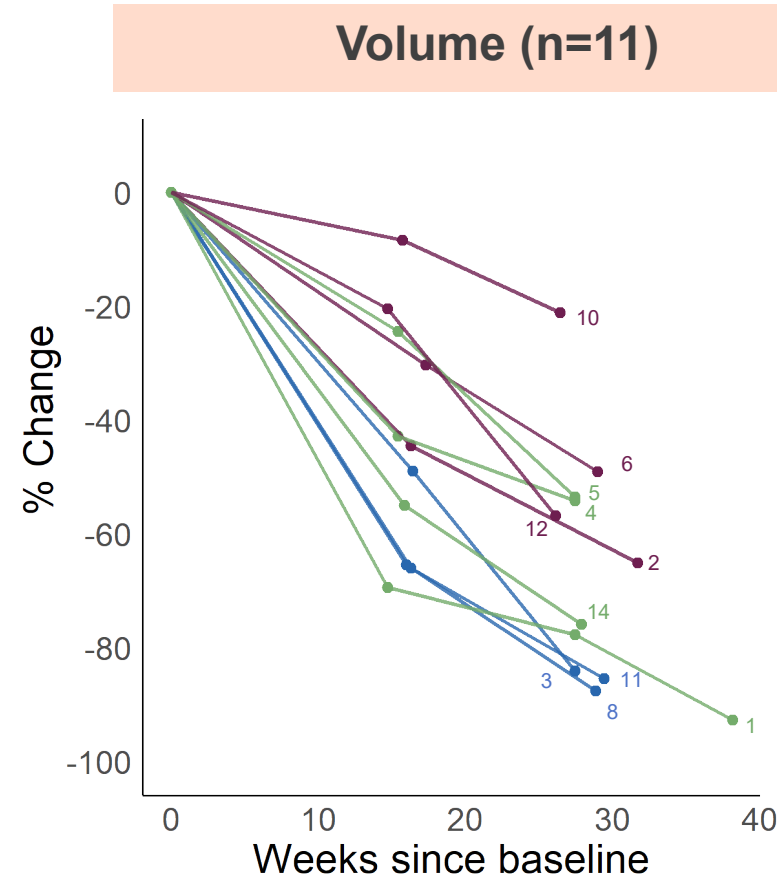
Week 16 Central RECIST % Change from Baseline (n=29)



1.2 mg QD 4 mg BIW 2 mg BIW

Early and Rapid Activity Across All Doses with Deepening of Tumor Shrinkage Over Time

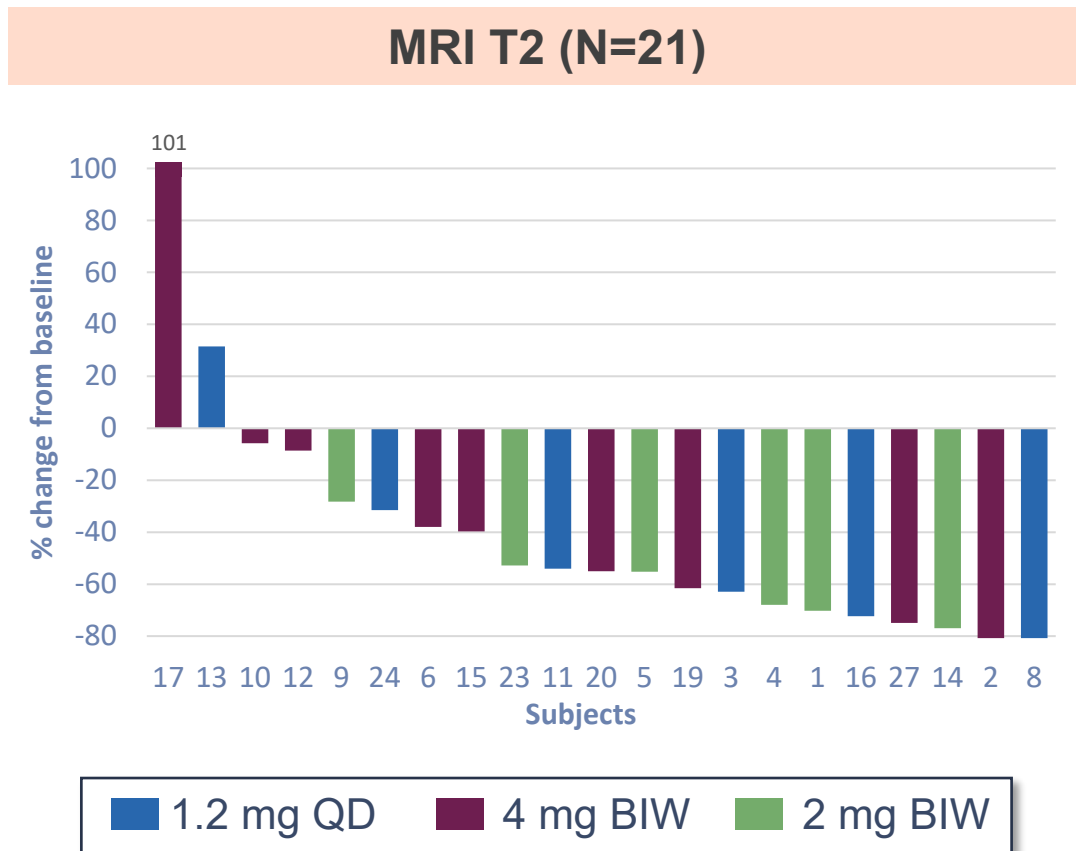
- 12 subjects had at least 2 MRI analyses on Dose
- 4 central PRs: 1 at week 16 confirmed at week 28, 2 at week 28, 1 at week 40



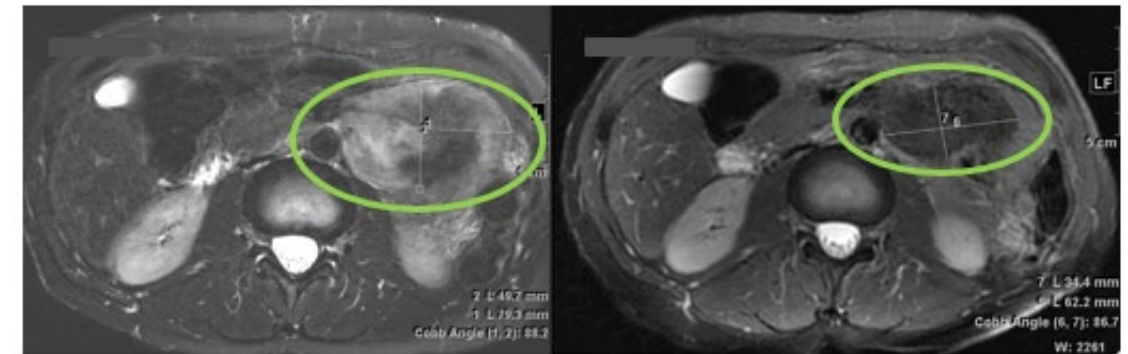
BIW, twice weekly, QD, once daily; Data cut: Jul 14, 2022

T2 Changes Reflect Decrease in Cellularity

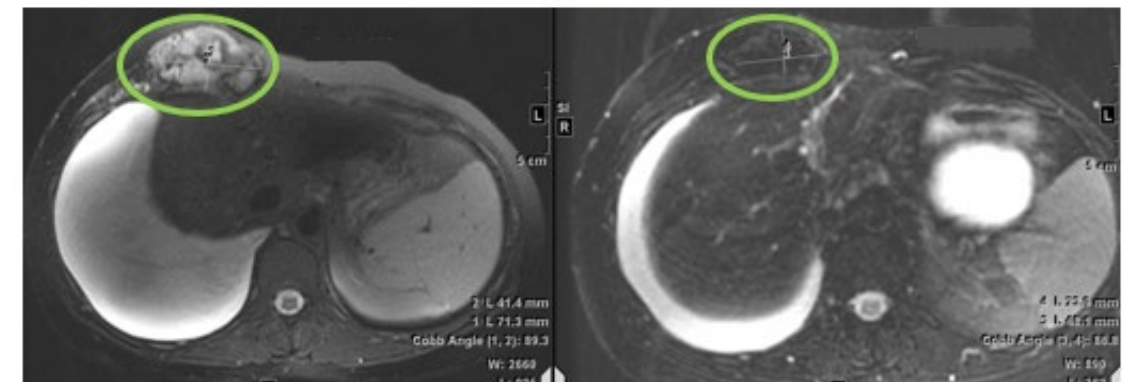
- Reduction of T2 intensity in 19 of 21 subjects at Week 16
- Reduction of T2 intensity and size in 2 subjects at Week 28



Subject #11*



Subject #2



Baseline

Week 28

Treatment-related AEs in ≥20% of Subjects

New investigational drug AL102 has a safety profile consistent with GSI

- AL102 was generally well tolerated with a manageable safety profile in all dose arms
- Most AEs were grade 1-2
- Grade 3 AEs were uncommon
- No grade 4 or 5 AEs
- 4 SAEs in 3 patients were assessed as unrelated to AL102 by the investigator
- AEs causing discontinuation included diarrhea, stomatitis, ALT elevation and rash
- AEs were consistent with mechanism of action of GSIs

Treatment-related AEs in ≥20% of Subjects

		1.2 mg QD (n=14)		4 mg BIW (n=14)		2 mg BIW (n=14)	
System Organ Class	Preferred Term	Any Grade	Grade 3	Any Grade	Grade 3	Any Grade	Grade 3
Gastrointestinal disorders	Diarrhoea	11 (79)	1 (7)	8 (57)	1 (7)	7 (50)	-
	Nausea	5 (36)	-	5 (36)	-	3 (21)	-
	Dry mouth	5 (36)	-	5 (36)	-	-	-
	Stomatitis	6 (43)	1 (7)	2 (14)	-	-	-
General disorders	Fatigue	5 (36)	-	5 (36)	-	5 (36)	-
Investigations	AST Increased	2 (14)	-	3 (21)	-	1 (7)	-
Metabolism and nutrition	Hypophosphataemia	4 (29)	-	1 (7)	-	2 (14)	-
Reproductive system	Amenorrhoea	1 (7)	-	3 (21)	-	-	-
Skin and subcutaneous tissue	Alopecia	5 (36)	-	3 (21)	-	1 (7)	-
	Dry skin	6 (43)	-	3 (21)	-	-	-
	Pruritus	6 (43)	-	2 (14)	-	-	-
	Rash maculo-popular	4 (29)	-	1 (7)	-	1 (7)	-
	Rash	-	-	3 (21)	-	2 (14)	1 (7)
	Dermatitis acneiform	4 (29)	-	-	-	1 (7)	-
	Hair colour changes	3 (21)	-	1 (7)	-	-	-

Data cut: Jul 14, 2022. AE, adverse event, N, number of patients with data; BIW, twice weekly; QD, once daily

a. Data on in the table is showed as number of subjects (%)

b. Subjects are counted once at the highest grade per preferred term

Conclusions Based on Interim Results from RINGSIDE Part A

- AL102 was generally well tolerated with a manageable safety profile in all investigated arms
 - Safety is consistent with the MOA and the GSI class of drug
- Efficacy was demonstrated across all arms
 - Consistent across measures (Volume, Central/Local RECIST and T2, T1)
 - Responses are seen within 16 weeks and are maintained and deepen over time
 - First PR seen at 16 weeks and 3 additional PRs over the follow up period
- RINGSIDE Part A results support the initiation of Part B and Open Label Extension

Strong Engagement with Desmoid/Sarcoma Advocacy Groups

- Strong relationships with DTRF and SPAEN, the two largest patient advocacy groups in the US and EU
- Actively collaborating with advocate groups and physician societies globally



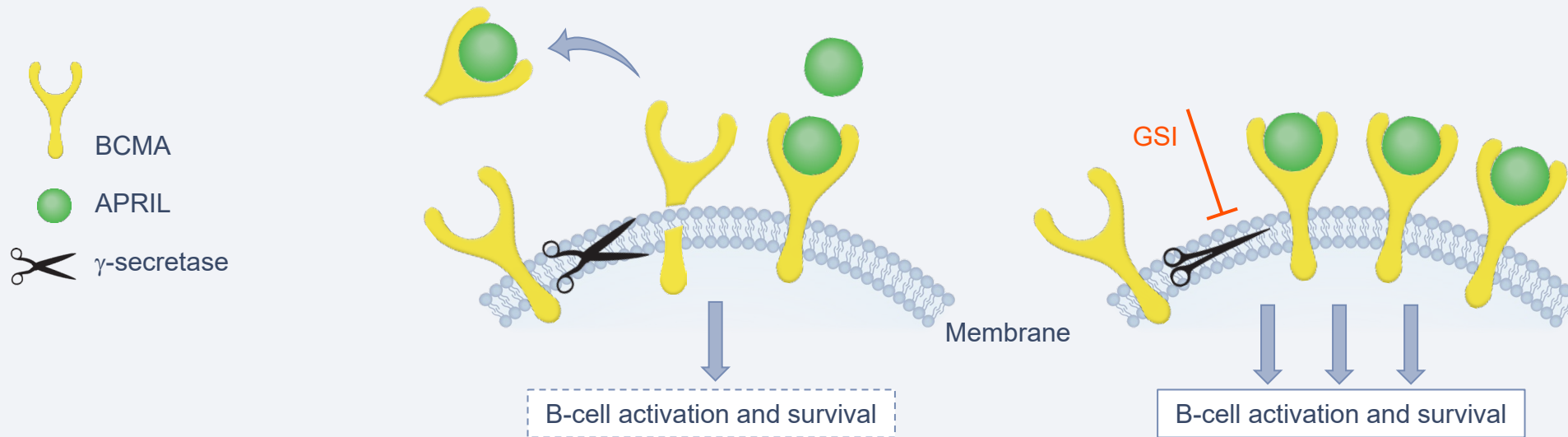
AL102 Has Potential to Enhance Anti-BCMA Efficacy in Multiple Myeloma

Multiple Myeloma:

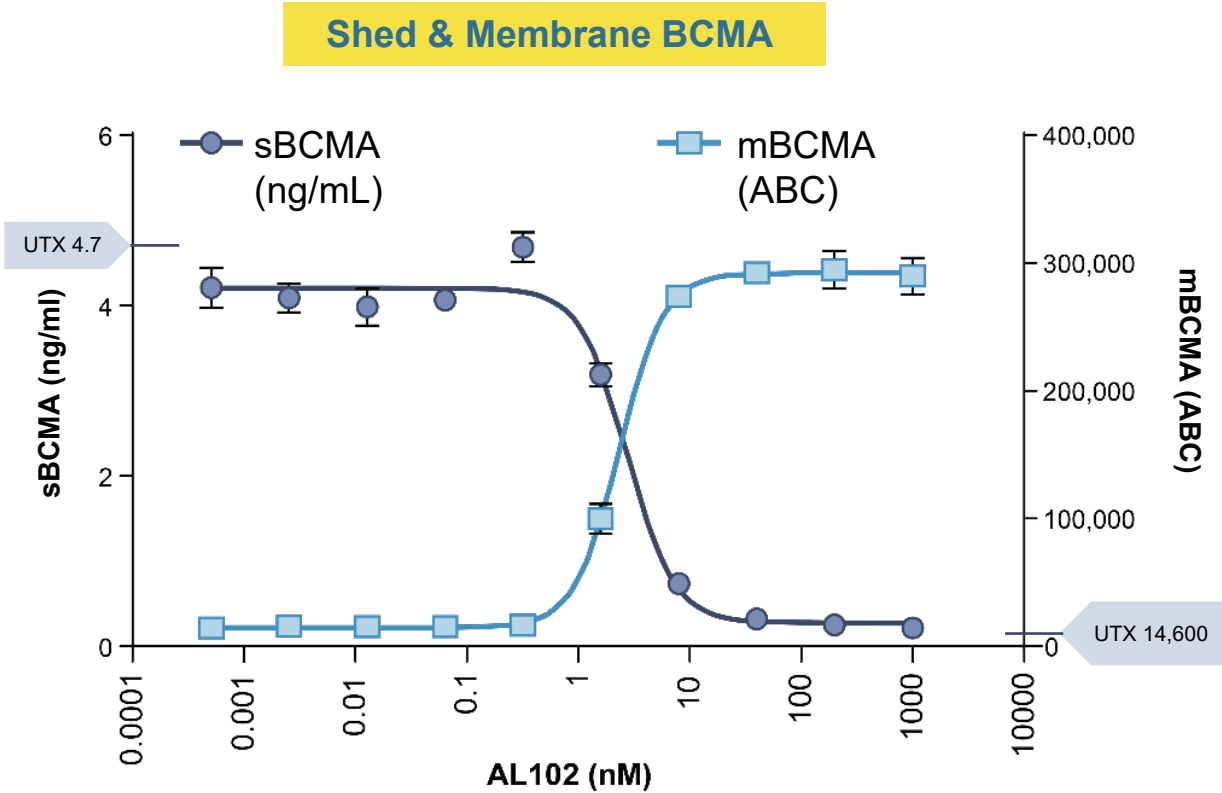
- MM is the second most common blood cancer in the US
- MM is still considered incurable, and relapse remains nearly inevitable for the majority of patients
- US incidence of ~26,500 new patients in the relapsed/refractory setting
- Anti-BCMA class emerging as promising therapeutic option for MM, estimated sales of >\$6 billion by 2027

AL102 has the potential to enhance anti-BCMA therapies by:

- Increasing BCMA levels on MM cells
- Decreasing circulating soluble BCMA
- Reducing sequester of anti-BCMA therapy by soluble BCMA

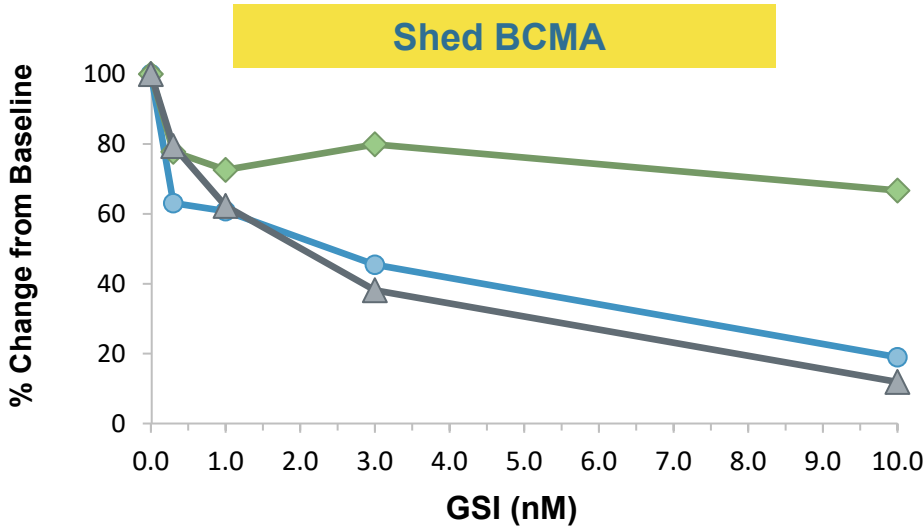
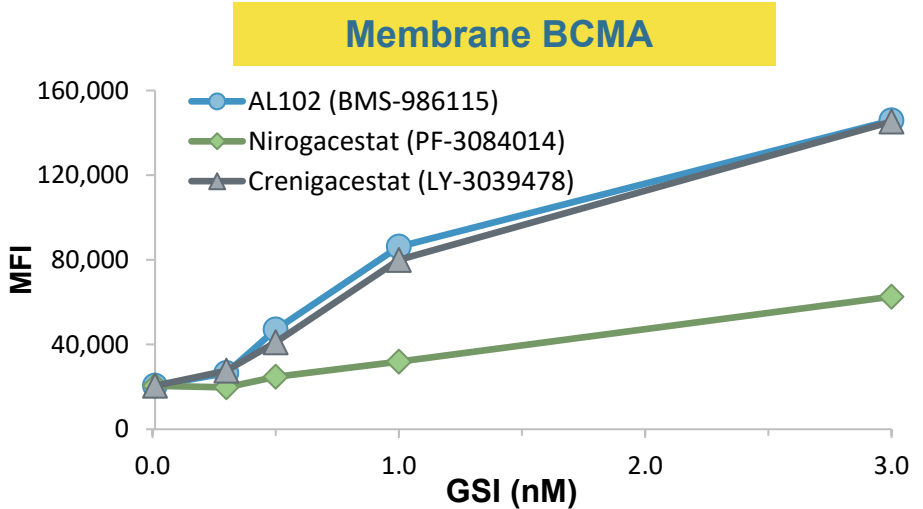


AL102 Increased Membrane BCMA and Reduced Shed BCMA and in MM Cell Lines

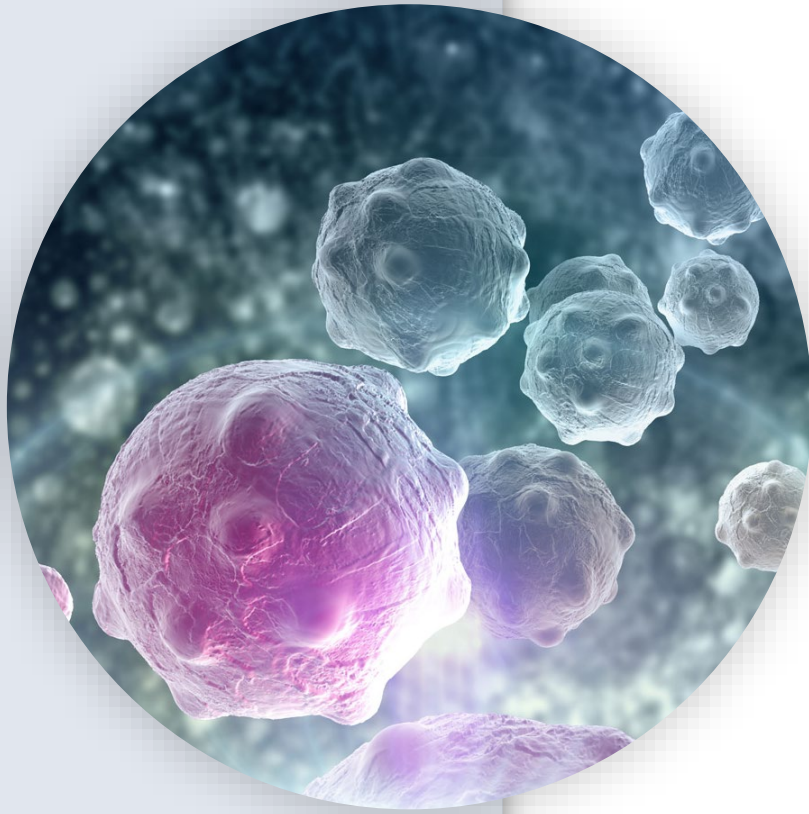


sBCMA drops below LLoQ and mBCMA increases ~20 fold

	sBCMA (ng/mL)	mBCMA (ABC)
EC50	2.787	2.341



20-fold increase in the levels of cell surface BCMA



AL101 – Investigational Targeted
Therapy for Notch Activation

AL101 for Potential Treatment of R/M Adenoid Cystic Carcinoma (ACC)

ACC is a rare malignancy of secretory glands



ACC

- Mainly salivary gland tumors, but also in eye, trachea, breast, and lungs
- Tend to grow around nerves, spread quickly and are tough to remove surgically



Patient Population

- Annual US incidence ~3,400¹
- R/M ACC ~1,700
- Notch-activating mutations 20%²



Unmet Need

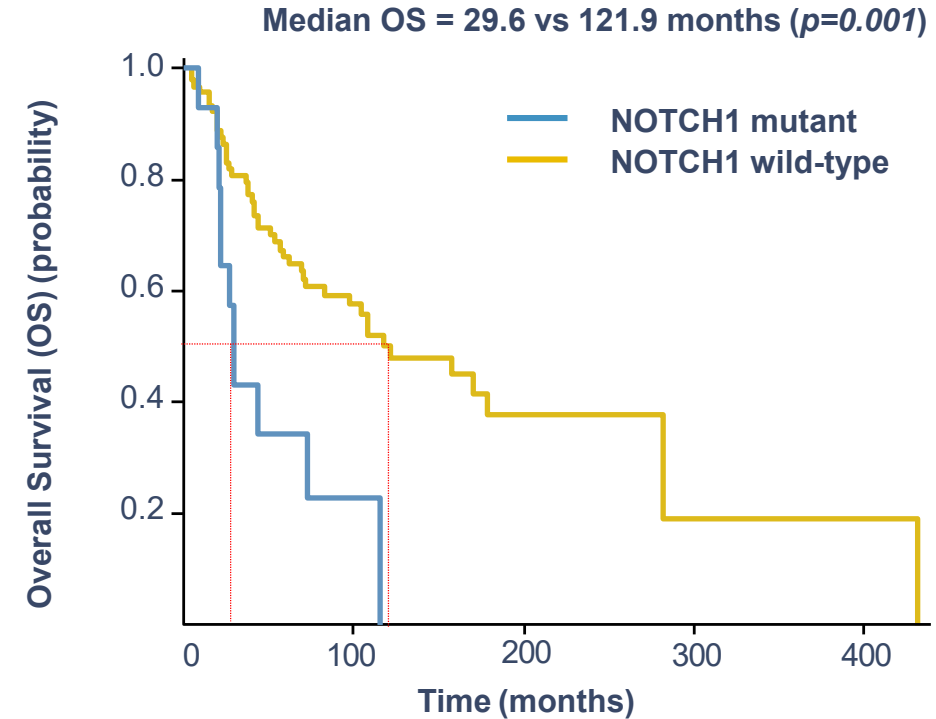
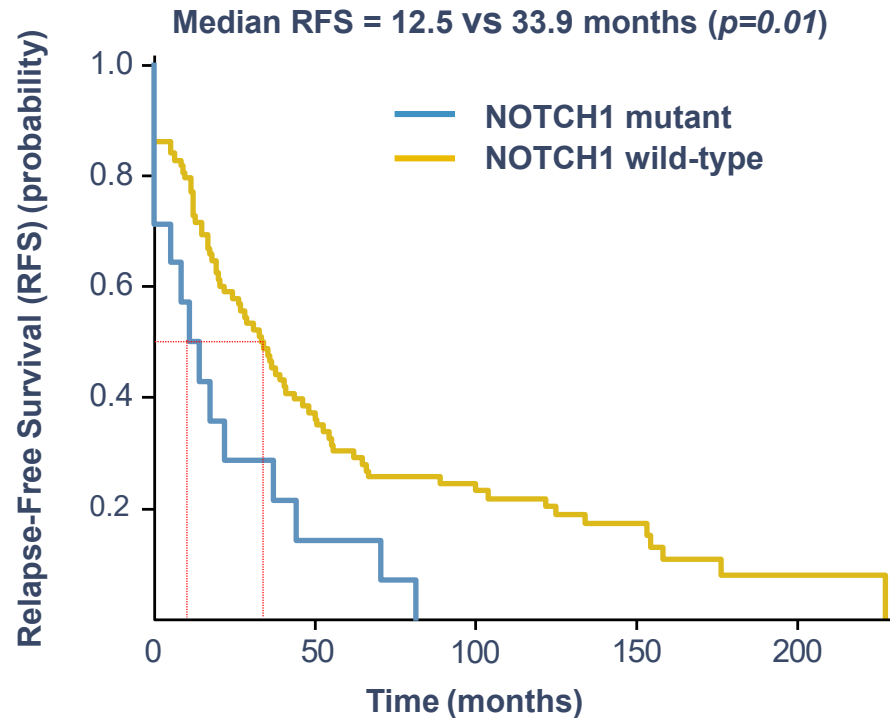
- No FDA approved therapy, limited treatment options
- SOC surgery and radiation in early disease and chemo or lenvatinib for advanced disease



AL101 Opportunity

- 44 Phase 2 clinical trials: No treatments advanced into registration trials or approval in ACC
- In 21 of the 44 trials, a 0% ORR was observed, ORR average across all trials ~6%³
- AL101 is the only candidate targeting Notch activated mutations being developed as monotherapy

Notch is a Tumorigenic Driver in ACC and Correlates with Poorer Prognosis



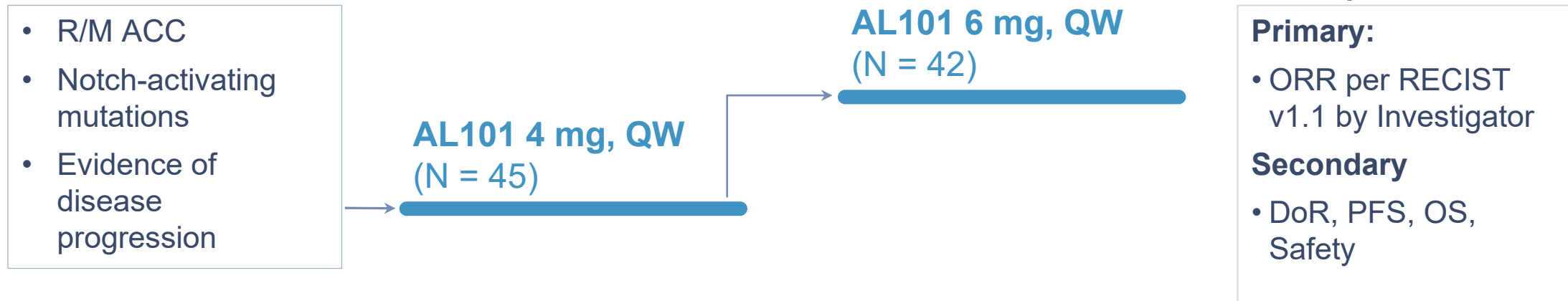
Results from 102 subjects (MD Anderson)¹ and similar results were observed in 84 ACC subjects (MSKCC)²

ACC Patients with Notch1 mutations expected to have shorter relapse-free survival and overall survival

Ongoing Phase 2 ACCURACY Trial in R/M Adenoid Cystic Carcinoma with Notch-Activating Mutations Trial Design

Trial Overview/Summary

Majority of patients heavily pre-treated before entering the study including surgery, radiation and systemic therapies

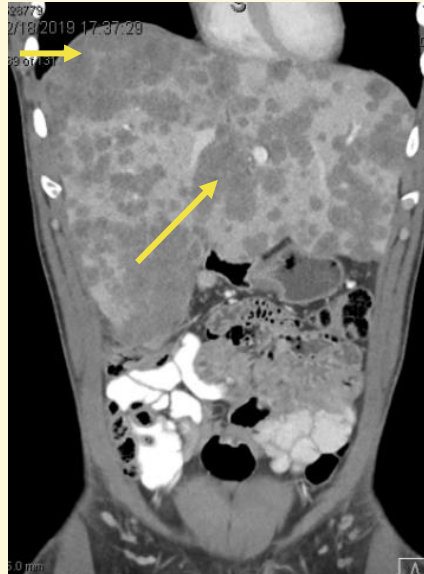


AL101 has received Orphan Drug Designation and Fast Track from the FDA

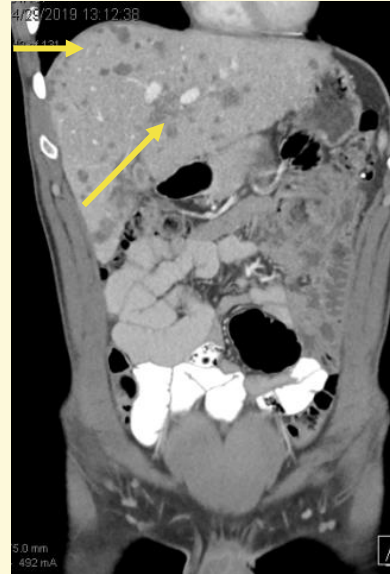
Clinical Activity Demonstrated in Phase 2 ACCURACY

Scans of subjects with partial response per RECISTv1.1

Subject #6 (4mg)

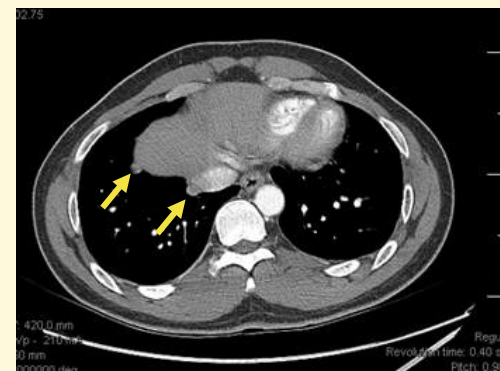


Baseline Scan

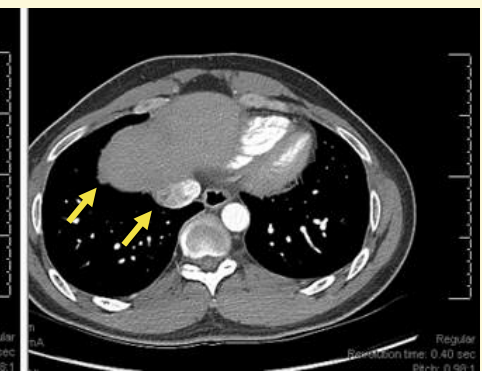


Post-treatment Scan (C3/D1): PR

Subject #29 (4mg)

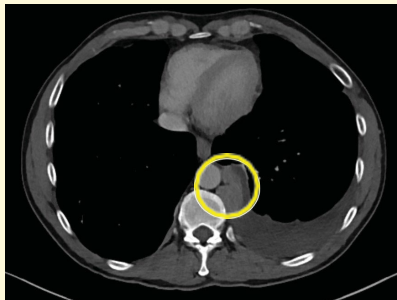


Baseline Scan

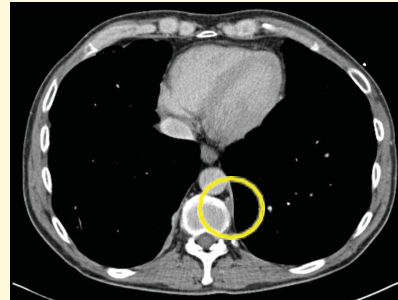


Post-treatment Scan (C3/D8): PR

Subject #2 (6mg)

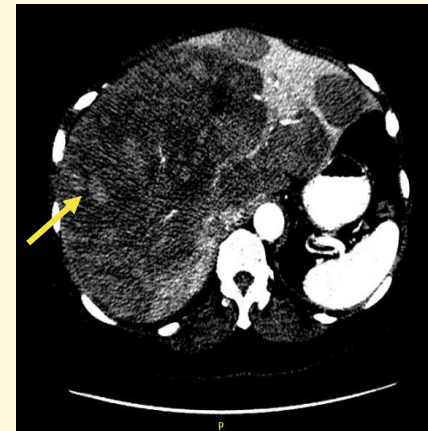


Baseline Scan

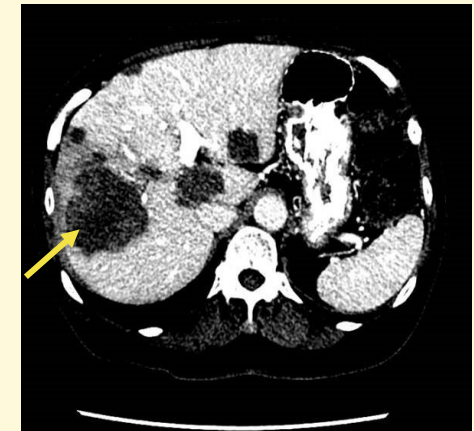


Post-treatment Scan (3 months): PR

Subject #35 (4mg)



Baseline Scan



Post-treatment Scan (C3/D1): PR

Clinical Activity Demonstrated in Phase 2 ACCURACY

Best Overall Responses by Investigator Review

Disease control (PR+SD) rate across both dose cohorts 69% (53/77)

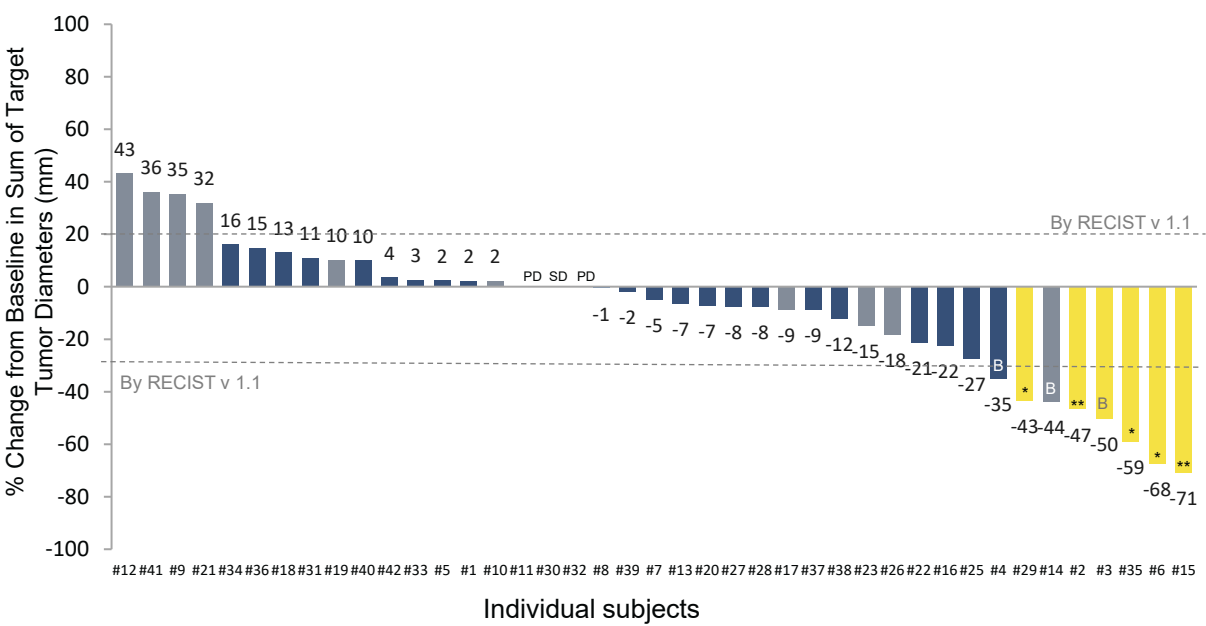
Best Tumor Response	AL101 4 mg (N=41) n (%)	AL101 6 mg (N=36) n (%)
Partial Response (PR)	6 (14.6%)	3 (8.3%)
Stable Disease (SD)	23 (56.1%)	21 (58.3%)
Progressive Disease (PD)	12 (29.3%)	10 (27.8%)
Missing or Not Evaluable (NE)	0 (0.0%)	2 (5.6%)
Objective Response Rate (CR or PR)	6 (14.6%)	3 (8.3%)
Disease control (PR+SD) rate	29 (70.7%)	24 (66.7%)

*Confirmed and unconfirmed responses. Central Review is ongoing and shows results consistent with the investigator's evaluations.

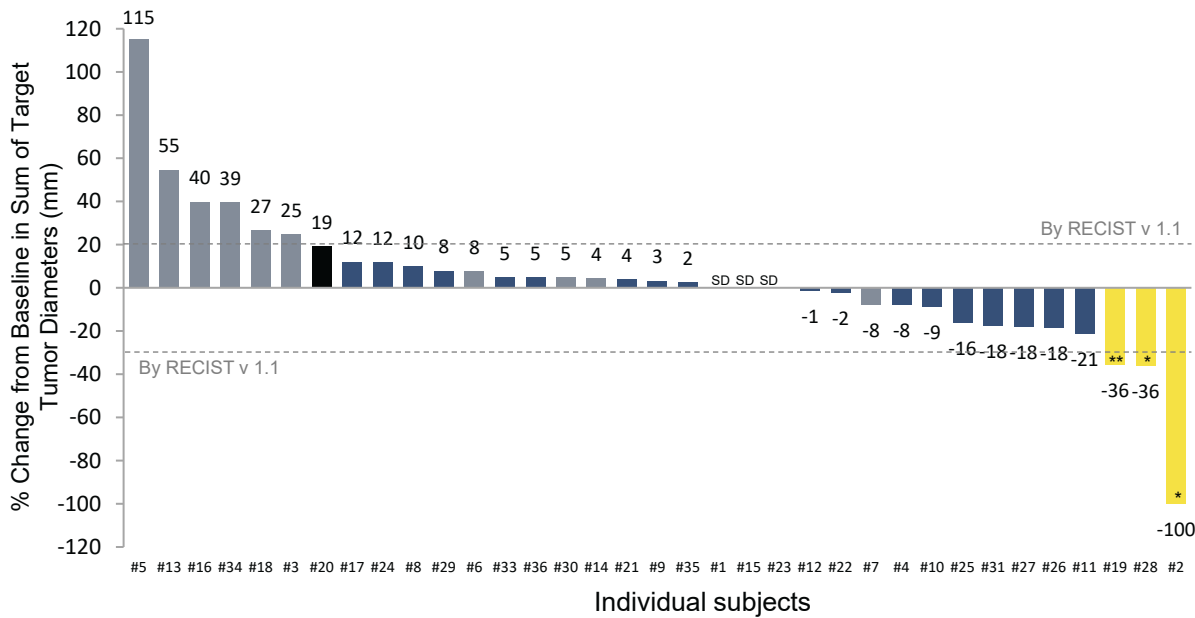
Clinical Activity Demonstrated in Phase 2 ACCURACY

Best Overall Responses by Investigator Review

AL101 4 mg



AL101 6 mg



Best overall response

PR SD PD

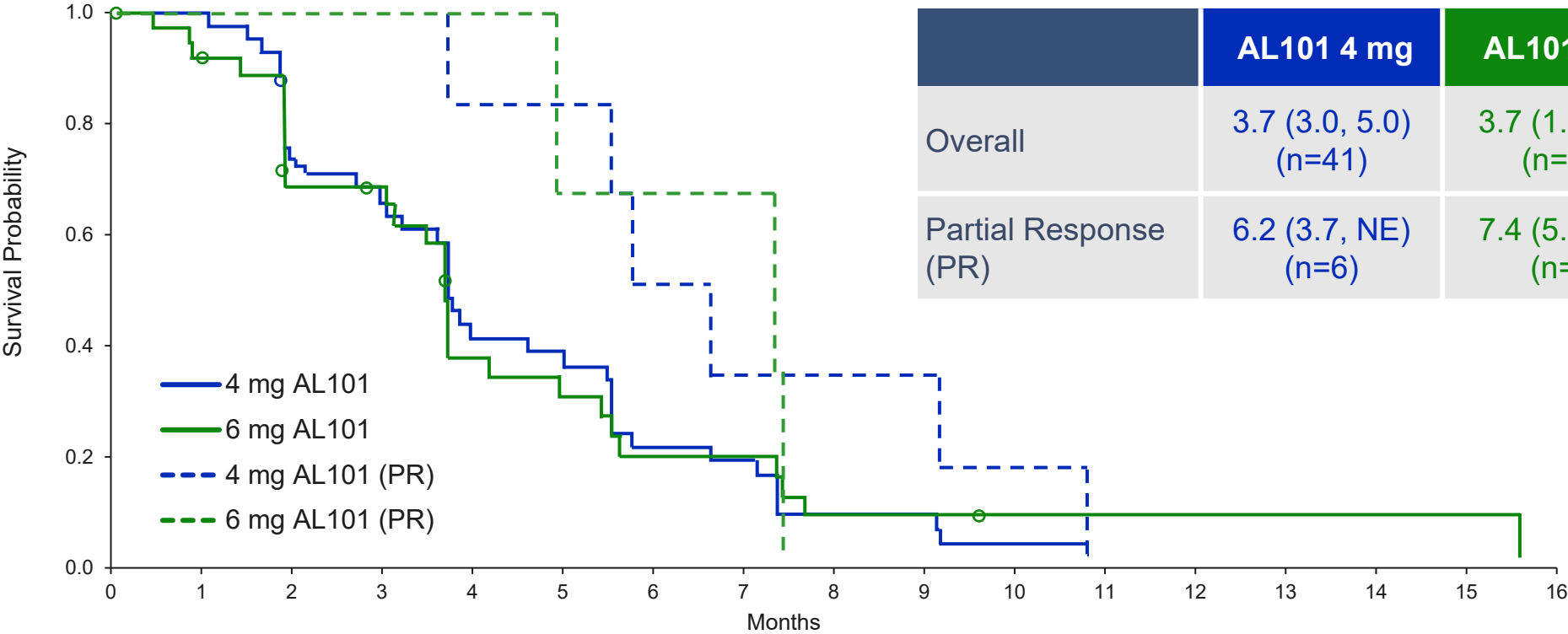
*Confirmed response; **Unconfirmed response; B: indicates bone-only subjects. Central Review is ongoing and shows results consistent with the investigator's evaluations.

Progression-free Survival by Investigator Review

- Subjects achieving a PR had a median PFS approximately double that of the group as a whole

Progression-free Survival (Months) – Median (95% CI)

	AL101 4 mg	AL101 6 mg	Total
Overall	3.7 (3.0, 5.0) (n=41)	3.7 (1.9, 4.2) (n=36)	3.7 (3.2, 4.0) (n=77)
Partial Response (PR)	6.2 (3.7, NE) (n=6)	7.4 (5.0, NE) (n=3)	6.7 (3.7, 9.2) (n=9)



4 mg AL101	41	41	29	26	16	15	8	7	3	3	1	0	0	0	0	0
6 mg AL101	36	31	21	20	10	8	5	5	2	2	1	1	1	1	1	0
4 mg AL101 (PR)	6	6	6	6	5	5	3	2	2	2	1	0	0	0	0	0
6 mg AL101 (PR)	3	1	3	3	3	2	2	2	0	0	0	0	0	0	0	0

Treatment-Related AEs Reported in ≥20% of Subjects in Either Cohort

	AL101 4 mg (N=45) n (%)	AL101 6 mg (N=42) n (%)	Total (M=87) n (%)
Diarrhoea	28 (62.2%)	33 (78.6%)	61 (70.1%)
Fatigue	23 (51.1%)	21 (50.0%)	44 (50.6%)
Nausea	24 (53.3%)	17 (40.5%)	41 (47.1%)
Hypophosphataemia	20 (44.4%)	13 (31.0%)	33 (37.9%)
Vomiting	13 (28.9%)	11 (26.2%)	24 (27.6%)
Cough	12 (26.7%)	10 (23.8%)	22 (25.3%)
Epistaxis	10 (22.2%)	7 (16.7%)	17 (19.5%)
Decreased appetite	5 (11.1%)	10 (23.8%)	15 (17.2%)
Dry mouth	4 (8.9%)	9 (21.4%)	13 (14.9%)

Listed in order of descending frequency in the total study population

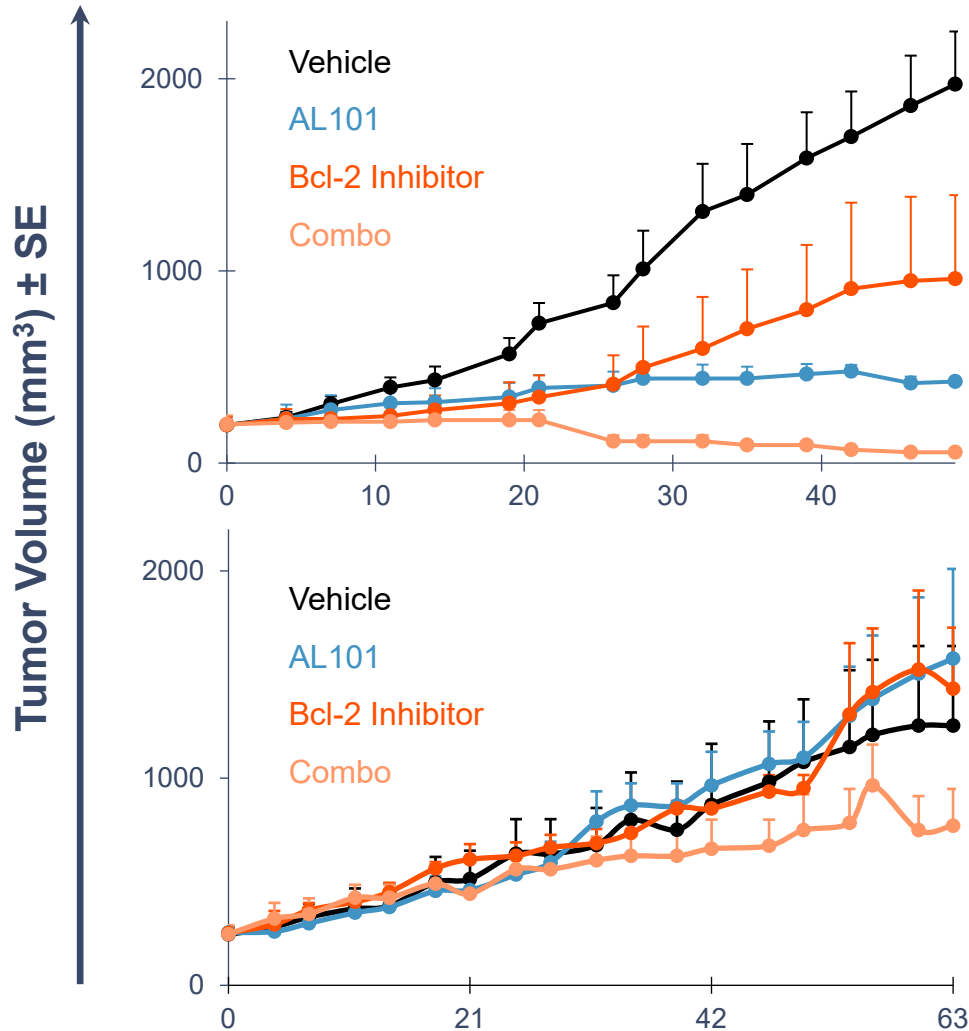
Registrational Path for AL101 as Monotherapy in Advanced ACC

- ACCURACY is the only prospective study conducted to date in ACC patients carrying Notch activating mutations
- Benchmark is missing on this patient population because no therapies have been approved and no studies conducted
- Therefore, to put the efficacy and safety results of ACCURACY in perspective of this specific patient population, a Systemic Literature Review (SLR) meta-analysis study is being conducted
- We plan to utilize the SLR results to establish a threshold for AL101 clinical benefit in the ACC Notch positive population to facilitate discussions with FDA and expect to obtain clarity on a registrational path in early 2023

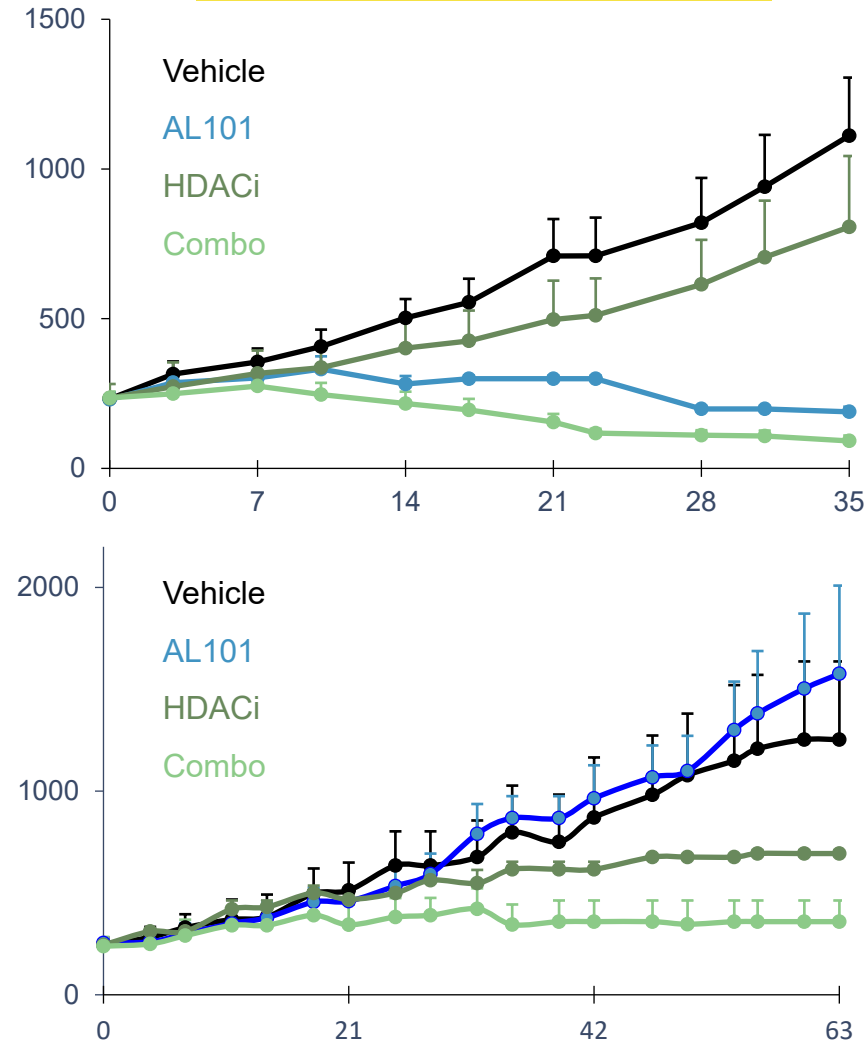
Enhancing the Efficacy of AL101 by Employing Combination Therapy

Preclinical PDX Models

AL101+ Bcl2 inhibitor



AL101+ HDAC inhibitor



Notch Activated
(ACCx11)

Notch Wild Type
(ACCx5M1)

Ayala Achieved and Upcoming Potential Milestones



Received Orphan Drug and Fast Track Designations for AL101



Reported Positive Interim data from Phase 2 ACCURACY trial in ACC



Fully enrolled Part A of AL102 desmoid tumor Pivotal Phase 2/3 trial



Reported interim data from Part A of Pivotal Phase 2/3 RINGSIDE trial in desmoid tumors



2H-2022 – Enroll 1st Patient in Part B of the RINGSIDE trial



Mid 2023 – Present long-term data from the selected dose from the RINGSIDE study with AL102



Early 2023 – Gain clarity on registration in R/M ACC



H2-2022 – Initiate Phase 2 clinical trial in R/R T-ALL

Pioneers in Targeting Novel Cancer Drivers



Ayala is targeting key biological pathways implicated in rare and aggressive cancers through the inhibition of gamma secretase



Broad portfolio of innovative clinical-stage programs



Clinical proof-of-concept demonstrated for lead candidates AL101 and AL102



Multiple potential value-enhancing milestones over the next 12 months



Experienced management team with track record in oncology and rare disease

Thank you.

