



We target clinically underserved cancers

March 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; our existing collaboration with Novartis is, 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 including Notch and BCMA 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

Multiple potential value enhancing milestones

- Initial data from Phase 2/3 AL102 desmoid trial (2022)
- Additional Phase 2 AL101 R/M ACC data (2022)
- Phase 1 MM trial ongoing in partnership with Novartis

Strong corporate position to execute on strategy

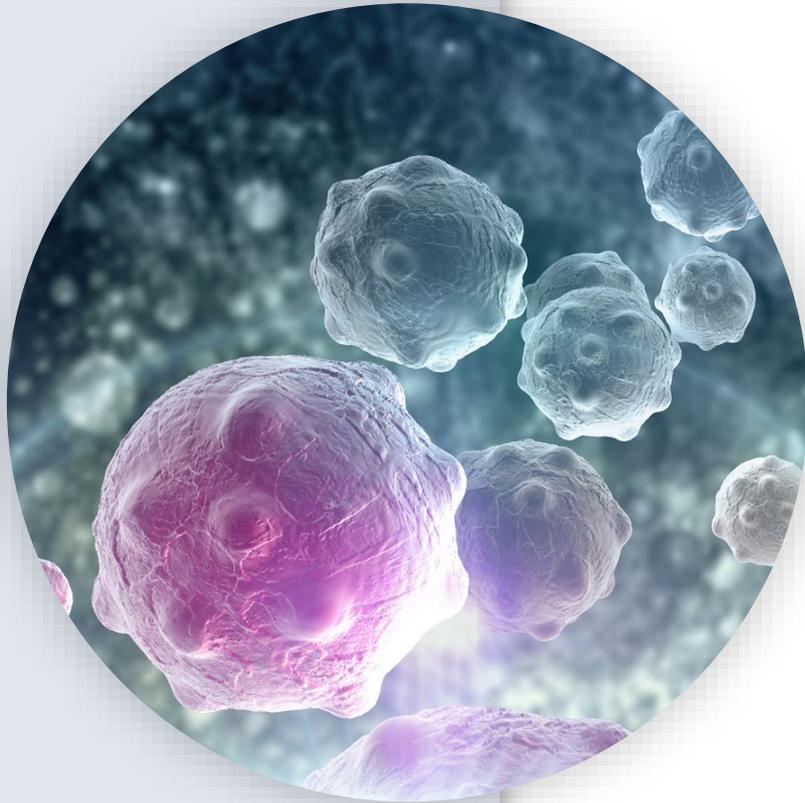
- Experienced management team in oncology and rare disease
- Validating partnership with  NOVARTIS

Late-Stage Pipeline Provides Multiple Opportunities for Value Creation

Indication	Product	Preclinical	Phase 1	Phase 2	Phase 3	Commercial Rights	Upcoming Milestones ¹
Desmoid	AL102						Initial data from Part A of Phase 2/3 trial mid-2022
R/M ACC	AL101						Additional data to be presented H2-2022
R/R MM	AL102 combo with Anti-BCMA					 ²	Initial clinical data (NVS to report)
R/R T-ALL	AL102						Initiate a Phase 2 trial H2-2022

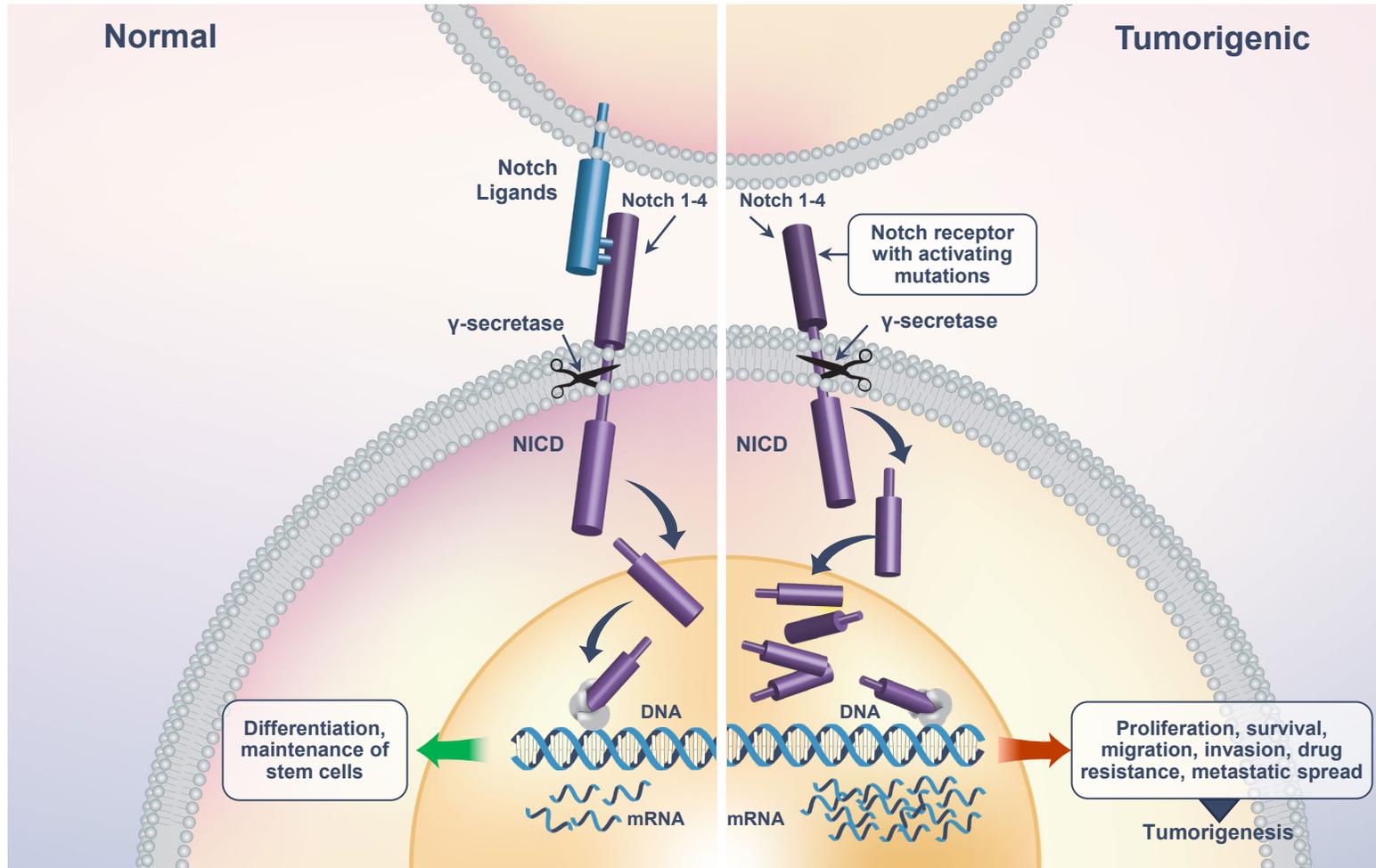
¹ Anticipated clinical milestones are subject to the impact of COVID-19 on our business

² If Novartis exercises its option to license AL102 for the treatment of MM we will be entitled to receive from Novartis an exercise fee and certain development, regulatory and commercial milestone payments as well as tiered royalties on net sales of licensed products



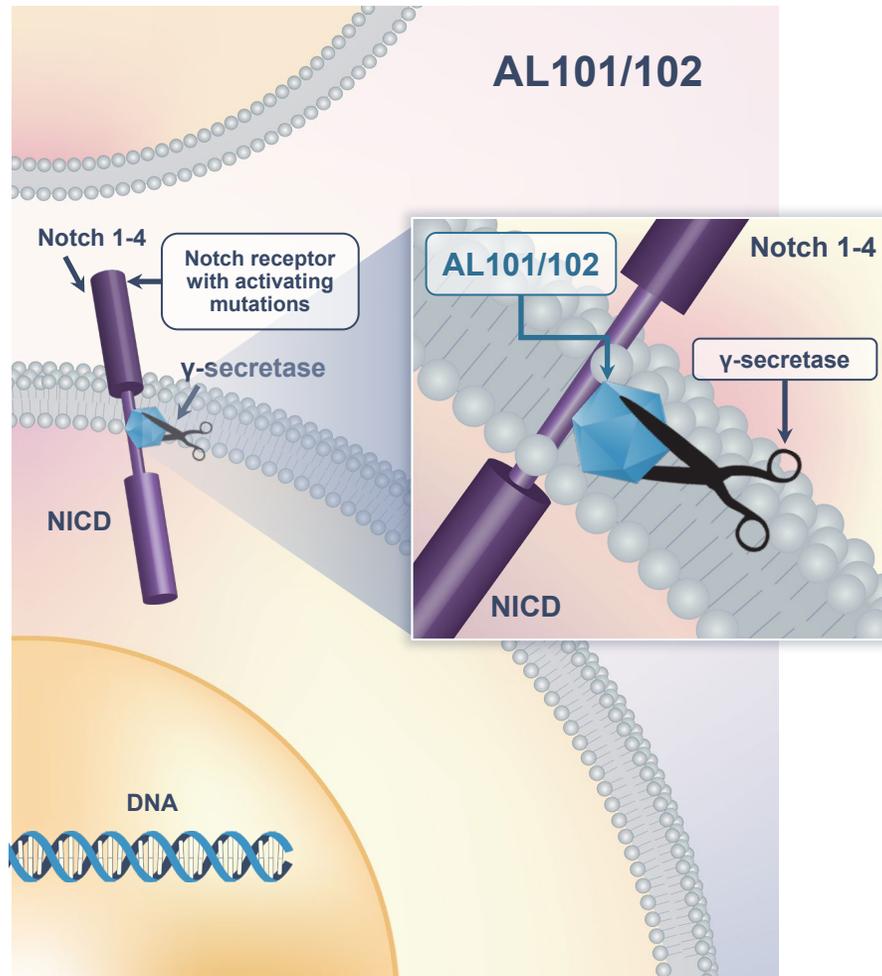
Targeting Notch Pathway Activation with Gamma Secretase Inhibitors

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

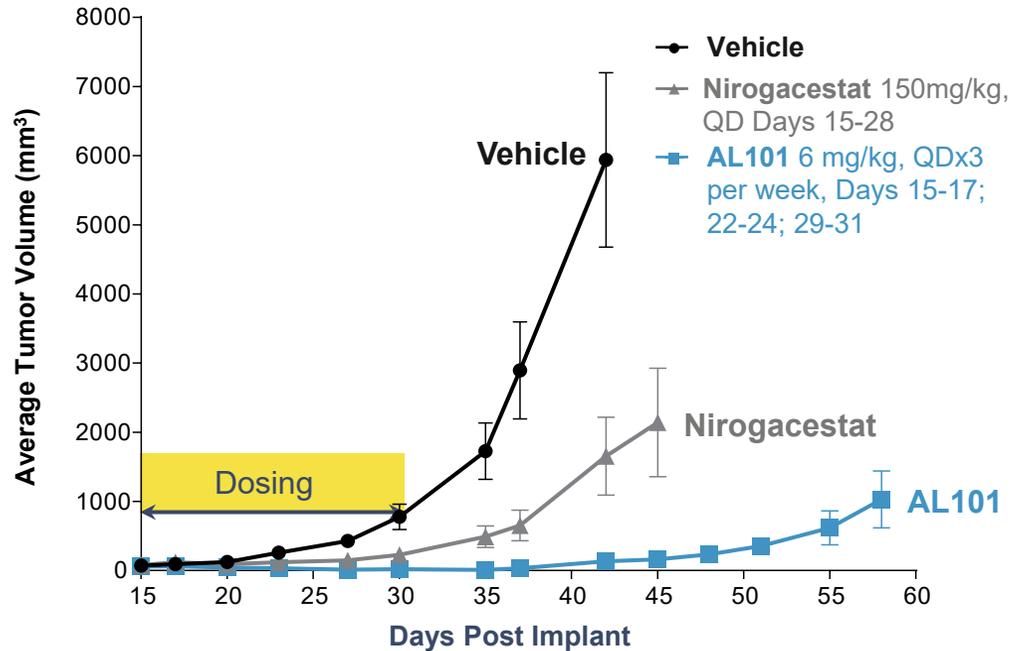
Lead Candidates AL101 and AL102 Inhibit the Notch Pathway



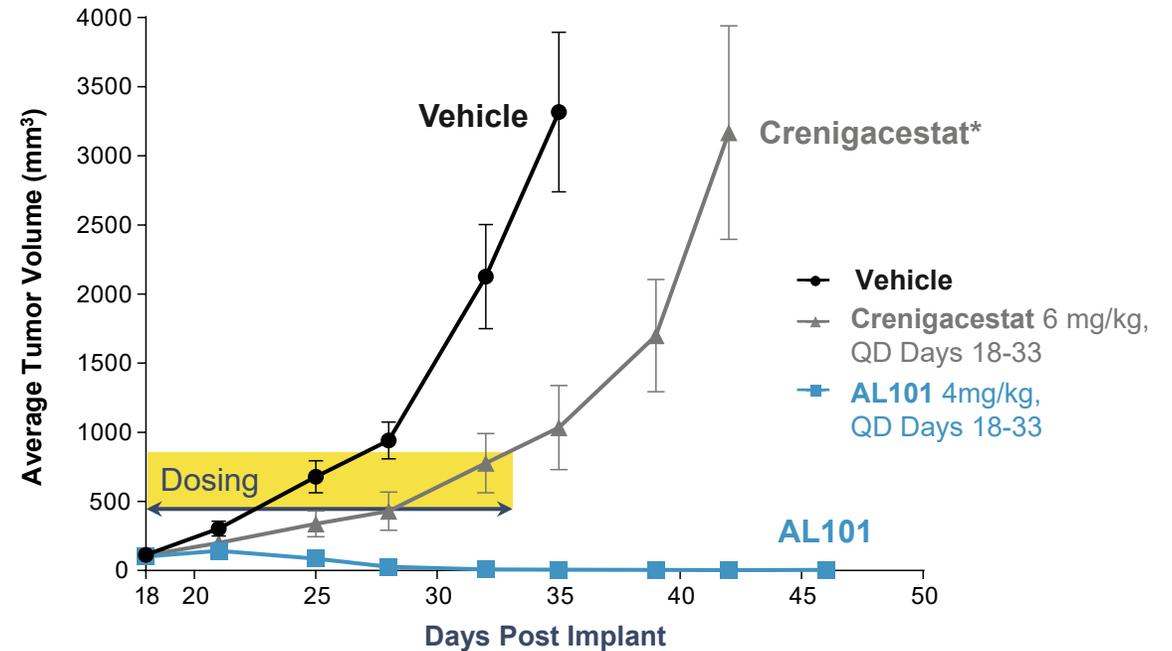
- AL101 and AL102 are potent small molecule gamma secretase inhibitors targeting the Notch pathway
- Gamma (γ) secretase enzyme is responsible for Notch activation

AL101 and AL102 Are Potent Notch Inhibitors

Effect on Tumor Growth in T-ALL Mouse Model



Tumor volume data are Mean ± 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

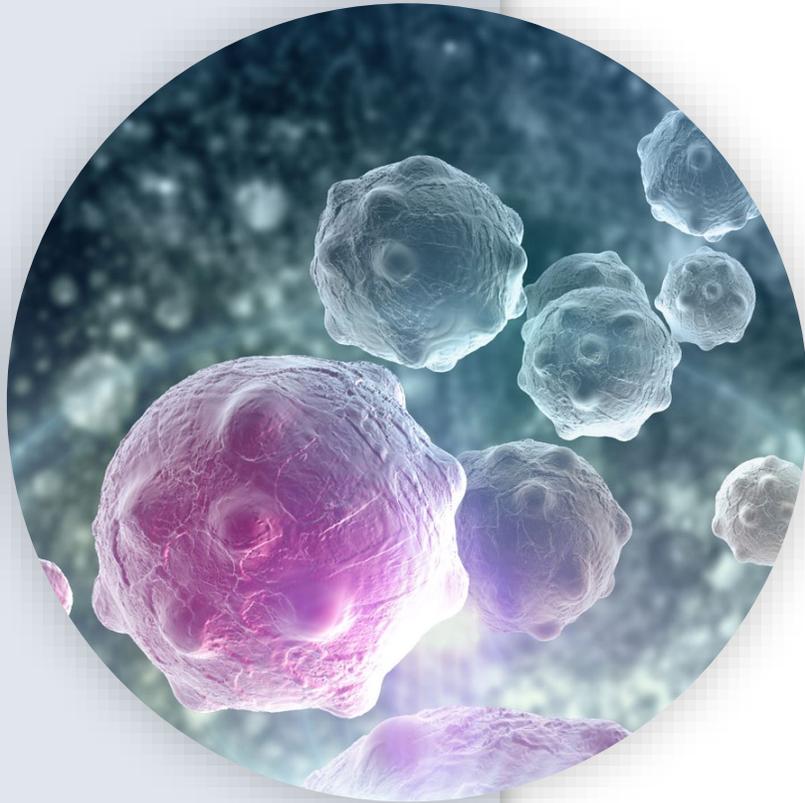
	AL101 (BMS-906024)	AL102 (BMS-986115)	Nirogacestat ² (PF-03084014)	RO-4929097 ³	MK-0752 ⁴
Notch1	1.6	6.1	13	3.8	354
Notch2	0.7	2.9	15	4.4	403
Notch3	3.4	8.1	17	22	955
Notch4	2.9	4.4	16	12	874

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

AL102 for the Potential Treatment of Desmoid Tumors

Desmoid are rare and aggressive connective tissue tumors



Desmoid Tumors

- Can aggressively infiltrate neurovascular structures and vital organs resulting in pain, loss of function and organ dysfunction with significant impact on quality of life
- Historically, surgery has been the initial intervention, followed-on by off label chemo and TKIs



Unmet Need

- Up to 72% of patients will relapse after surgical resection, with most often modest, not durable and poorly tolerated responses to follow-on treatment options
- No FDA-approved therapies for desmoid tumors
- Clear unmet need for more effective systemic therapies to treat recurrent/progressive tumors and prevent recurrence



Patient Population

- Annual incidence of ~1,700 in US with 5Y survival rates >95%
- 5,500-7,000 patients actively receiving treatment in the US in any given year

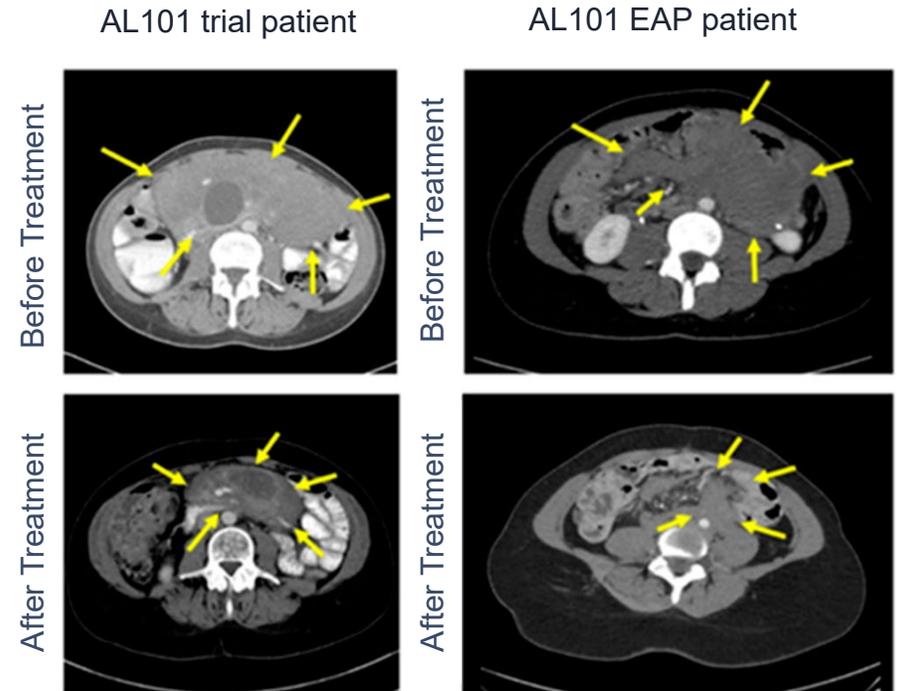


AL102 Opportunity

- AL102 is being developed as a potent, selective, oral GSI for the treatment of desmoid tumors
- Pivotal Phase 2/3 trial ongoing, initial data from Part A expected mid 2022

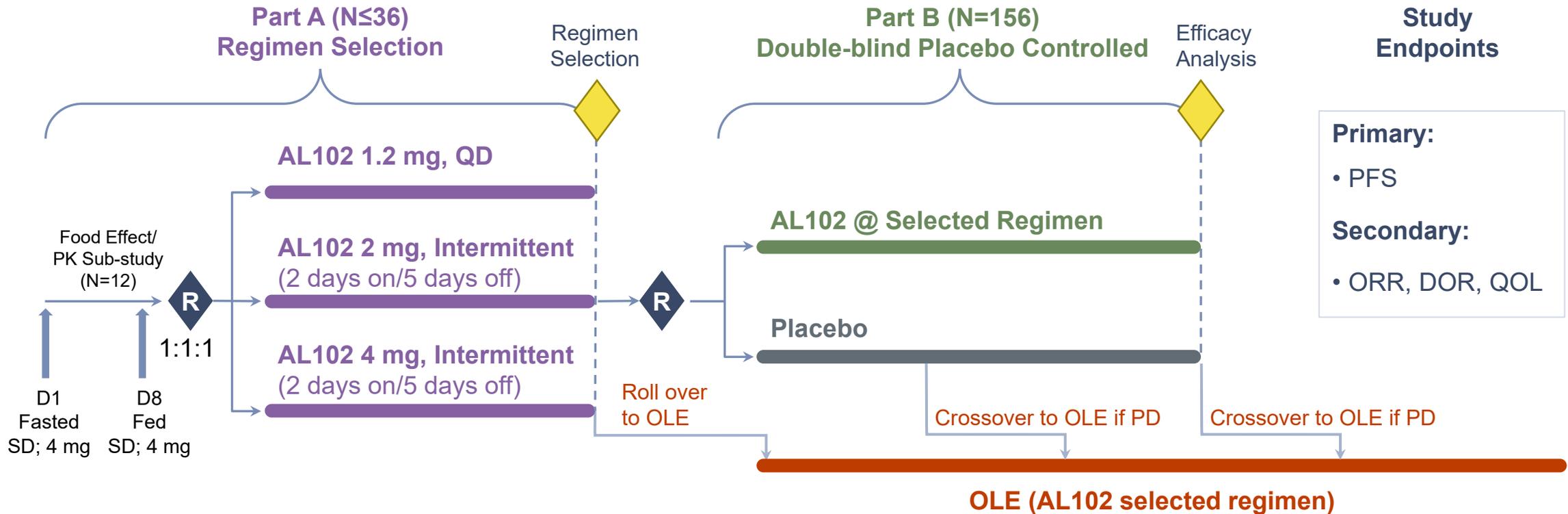
AL102 and AL101 Clinical Activity Demonstrated in Desmoid Tumors

- The one desmoid patient in the AL102 Phase 1 trial - achieved SD with 16.5% tumor shrinkage after 9 months of treatment
- In Phase 1 dose-escalation study of AL101 for patients with solid tumors, 3 patients had desmoid tumor
 - 2 had confirmed PR and 1 SD
 - The 2 PRs continued treatment in a post-trial EAP and had sustained responses
- One additional patient who received AL101 through EAP since 2017 had a sustained PR
- Most common toxicity was diarrhea (low grade)



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

Open label Part A enrollment completed; initial results expected mid-2022



Part A Key Inclusion Criteria

- R/R or TN DT with ≥10% unidimensional growth ≤18m or DT-related pain
- Age ≥18
- Measurable Lesion - MRI

Part B Key Inclusion Criteria

- R/R or TN DT with RECIST Progression ≤12m
- Age ≥12
- Measurable Lesion – MRI/CT



CT, computed tomography; DOR, duration of response; D, day; DT, desmoid tumor; MRI, magnetic resonance imaging; OLE, open-label extension; ORR, objective response rate; PFS, progression free survival; PK, pharmacokinetics; QD, once daily; QOL, quality of life; R, randomization, R/R, relapse/refractory; RECIST, Response Evaluation Criteria in Solid Tumors; TN, treatment-naive

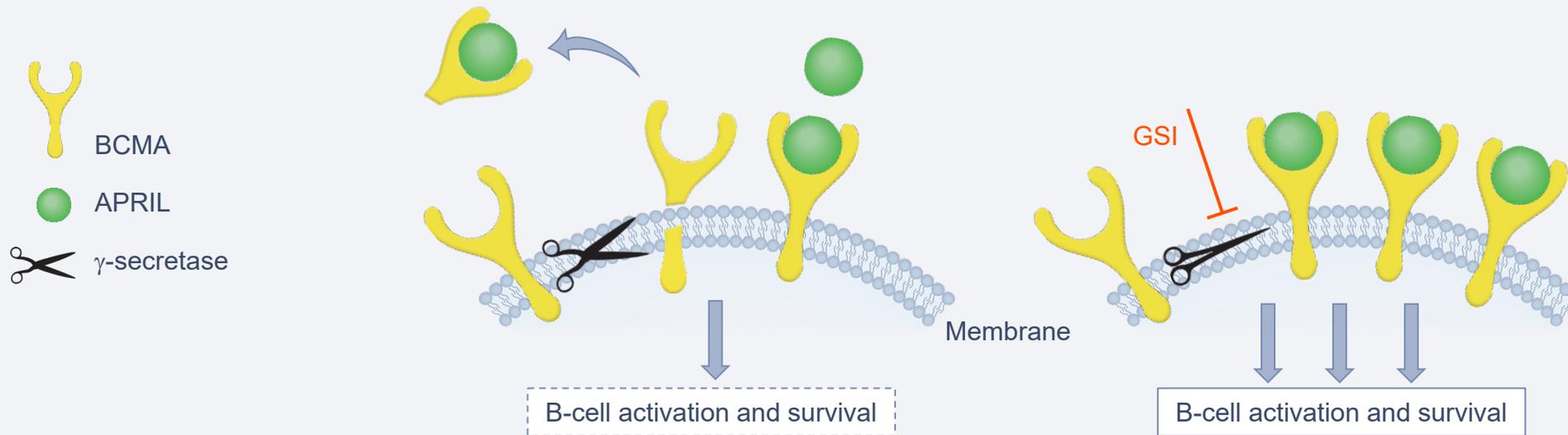
AL102 Has Potential to Enhance Anti-BCMA Efficacy in Multiple Myeloma

Multiple Myeloma:

- MM is the second most common blood cancer in the US
- MM is still considered incurable, and relapse remains nearly inevitable
- US incidence of ~27,000 new patients in the relapsed/refractory setting
- Anti-BCMA class emerging as promising therapeutic option for R/R MM, estimated sales of >\$6 billion by 2027

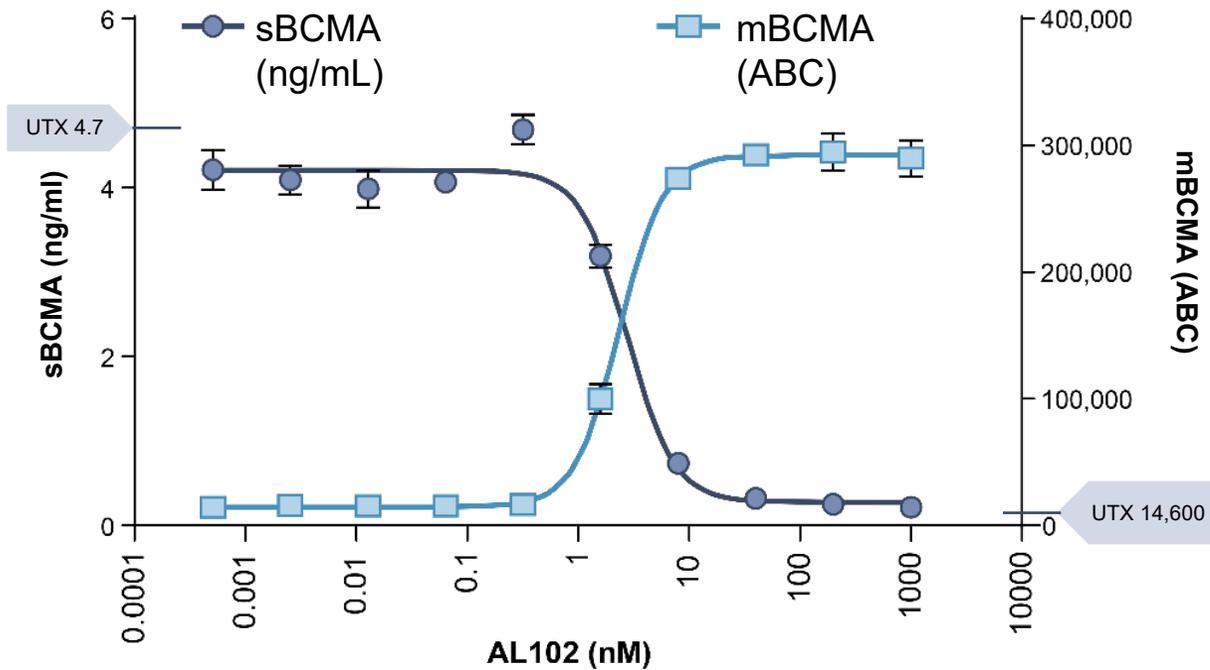
AL102 has the potential to enhance anti-BCMA therapies by:

- 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

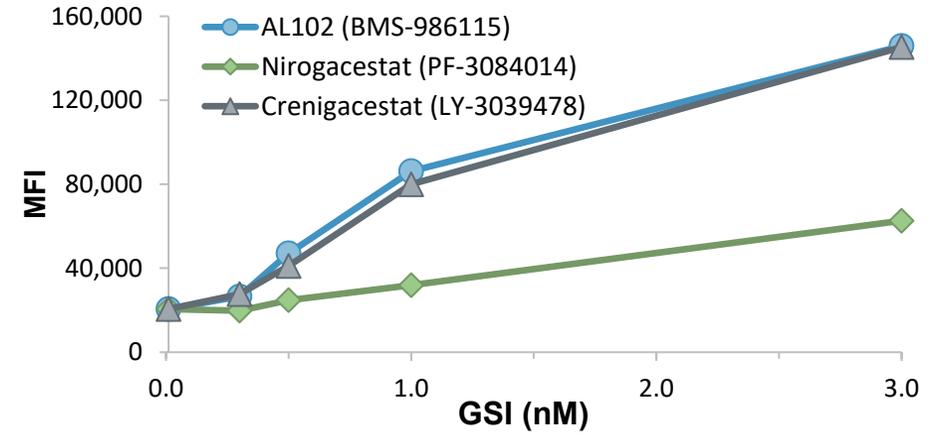
Shed & Membrane BCMA¹



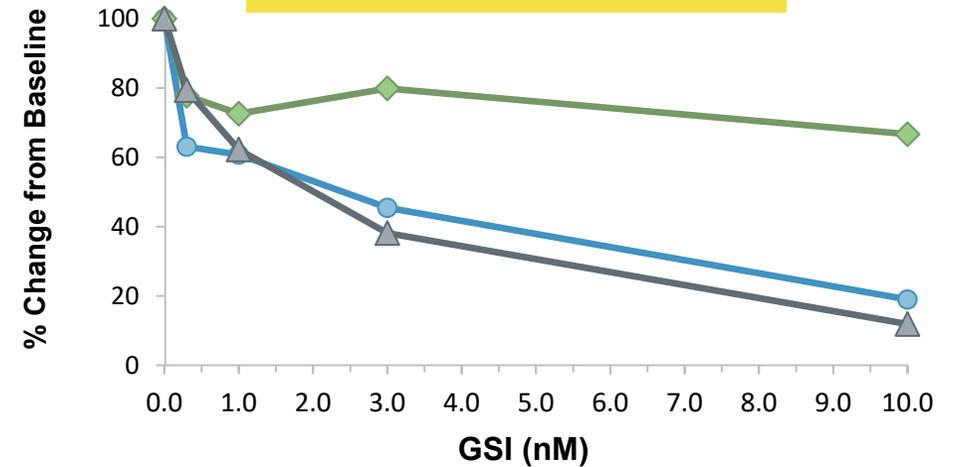
sBCMA drops below LLoQ and mBCMA increases ~20 fold¹

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

Membrane BCMA



Shed BCMA

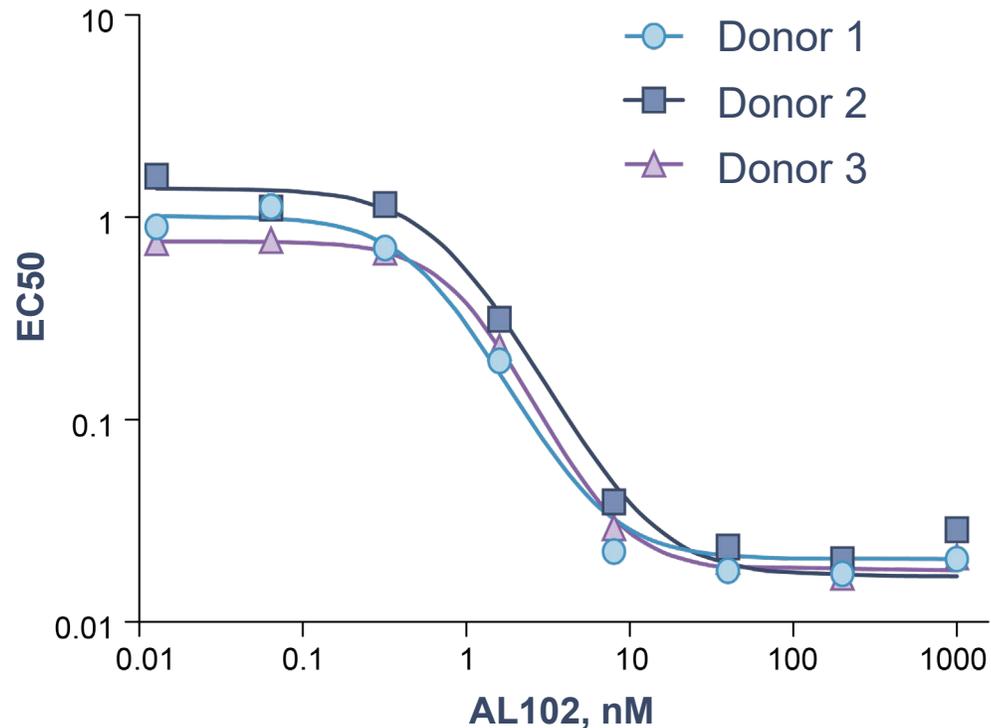


20-fold increase in the levels of cell surface BCMA

AL102 Enhanced Novartis' Anti-BCMA (BisAb) Candidate in an Ex-Vivo Assay



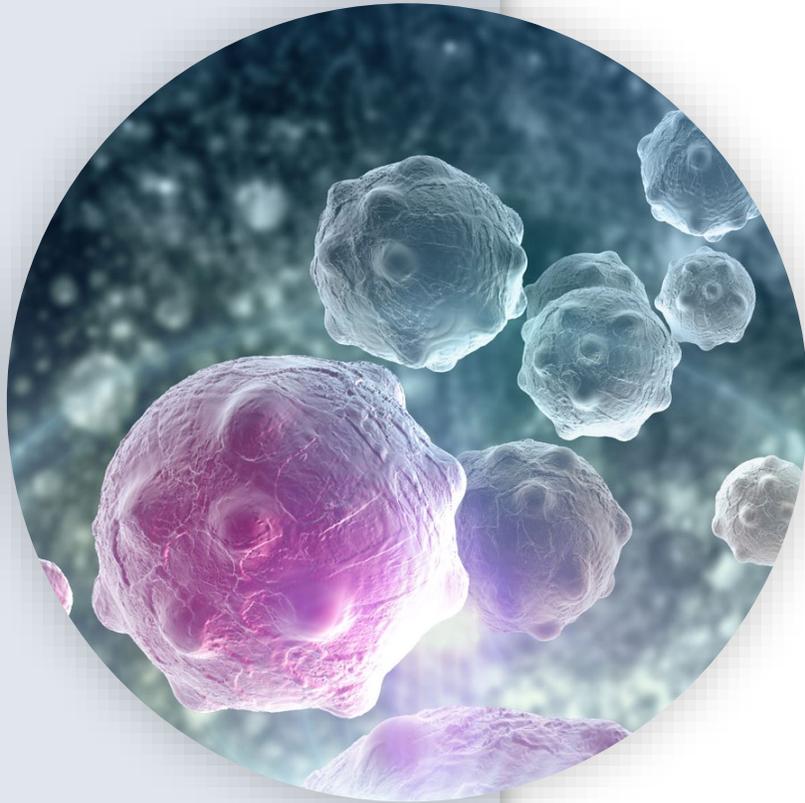
AL102 enhanced NVS BisAb redirected T-cell Cytotoxicity on MM cell line¹



Ongoing Phase 1 Trial is evaluating safety and efficacy of the combination

- WVT078 is a BCMA/CD3 bispecific mAb
- The trial is designed to assess the safety, tolerability and recommended dose regimen(s) of WVT078 alone and in combination with AL102
- Trial will also assess preliminary anti-MM response and characterize the PK and immunogenicity of WVT078 alone and in combination with AL102

AL102 makes the bispecific about 100-fold more potent, to improve efficacy



AL101 – Investigational Targeted
Therapy for Notch Activation

AL101 for Potential Treatment of the 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 more quickly and are tougher to remove surgically



Patient Population

- Annual US incidence ~3,400
- R/M ACC ~1,700
- Notch-activating mutations 20%



Unmet Need

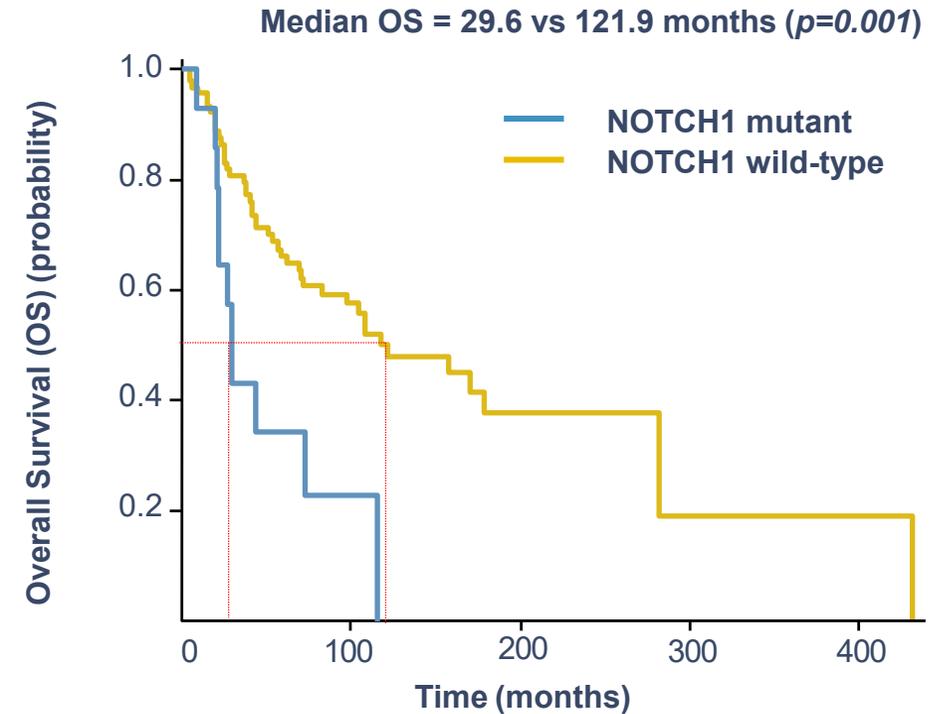
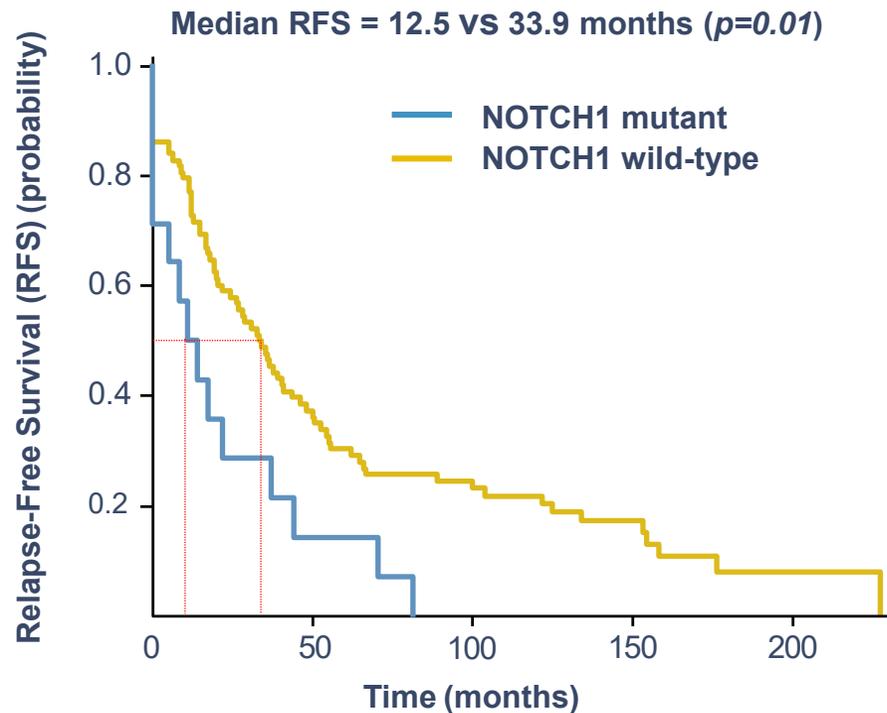
- No FDA approved therapy, limited treatment options
- SOC surgery and radiation in early disease and chemo or lenvatinib for advanced disease



AL101 Opportunity

- More than 37 Phase 2 clinical trials: No treatments advanced into registration trials or approval in ACC
- In 18 of the 37 trials, a 0% ORR was observed, ORR average across all trials ~5%
- 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) and similar results were observed in 84 ACC subjects (MSKCC)

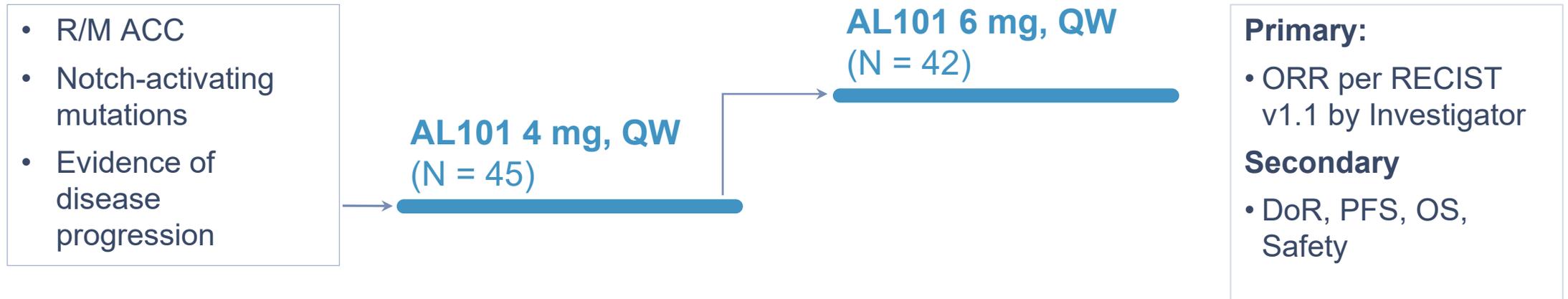
ACC Patients with Notch1 mutations expected to have shorter relapse-free survival and overall survival

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

Study is fully enrolled: Additional results expected 2H 2022

Trial Overview/Summary

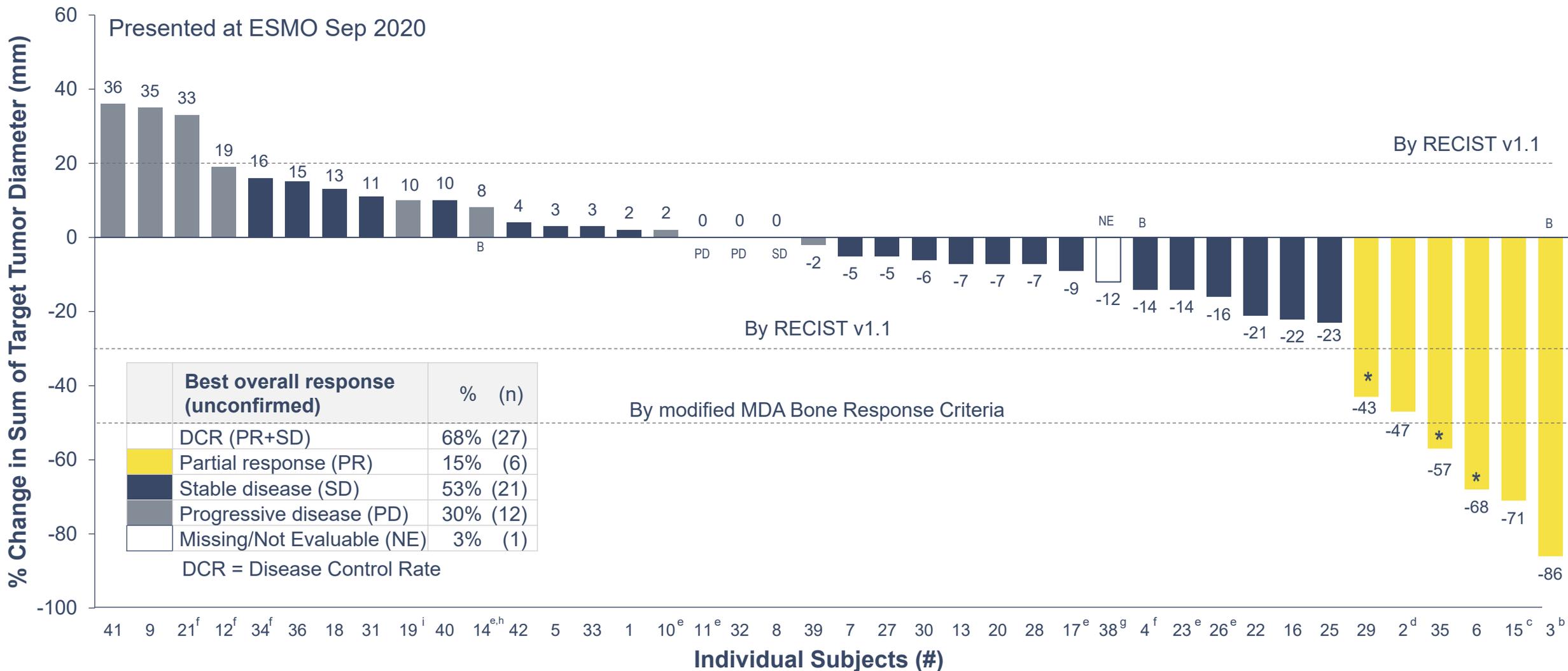
Majority of patients heavily pre-treated before entering the study including surgery, radiation and systemic therapies



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

Clinical Activity Demonstrated in Phase 2 ACCURACY Initial Results

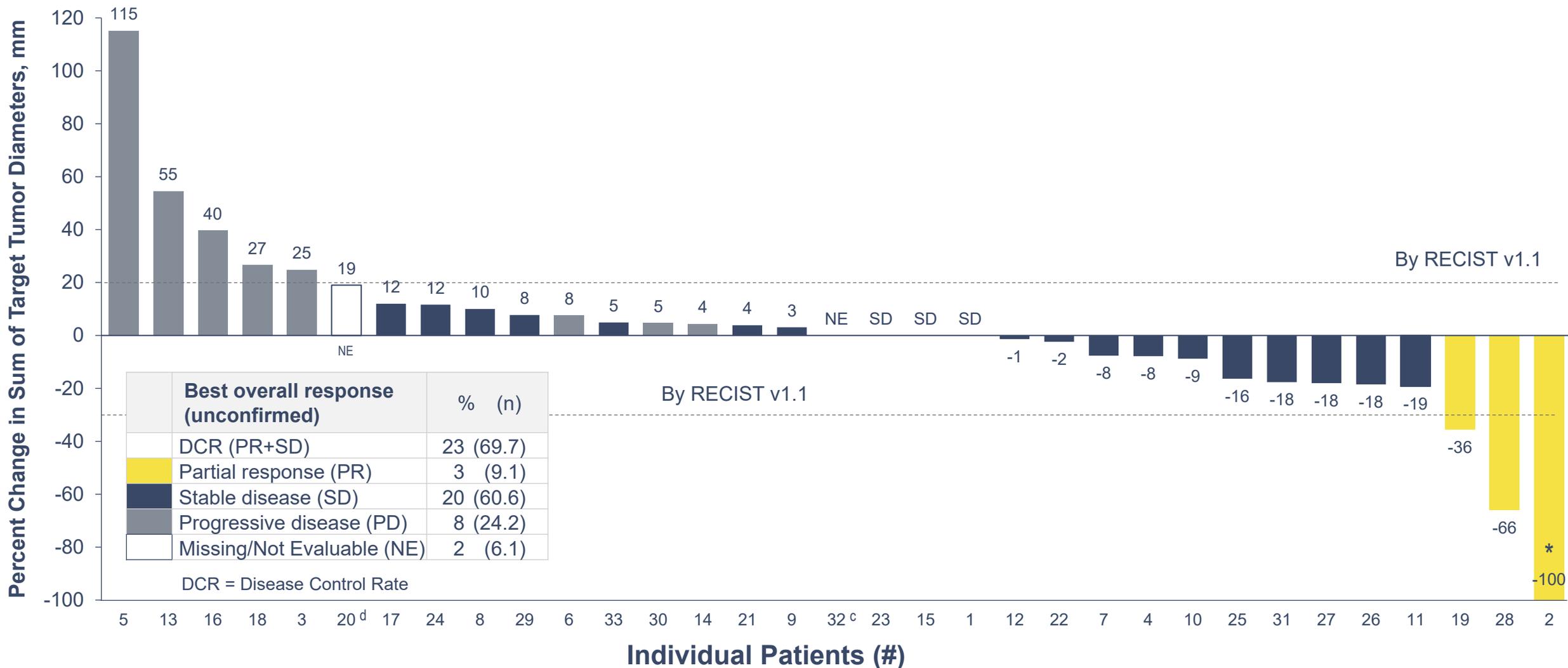
Best Overall Responses by Investigator Review 4mg (n=40)^a



^aconfirmed responses. B, bone-only disease. ^gIncludes efficacy-evaluable subjects only (data cutoff: July 30, 2020); #24 not included because the patient withdrew consent; #37 not included because died before disease assessment. ^bSubject #3, with bone-only disease, had an unconfirmed PR at week 32 by the investigator per modified MDA Bone Response Criteria. ^cSubject #15 had an unconfirmed PR at week 8. ^dSubject #2 had an unconfirmed PR at week 16. ^eThese subjects had clinical PD. ^fSubject #4, with bone-only disease, had SD at week 16 by the investigator per modified MDA Bone Response Criteria. ^gSubject #38 was NE because only one scan demonstrating SD was performed at week 7. ^hSubject #14, with bone-only disease, had PD at week 8 by the investigator per modified MDA Bone Response Criteria. ⁱSubject #19 had radiographic PD.

Clinical Activity Demonstrated in Phase 2 ACCURACY Initial Results

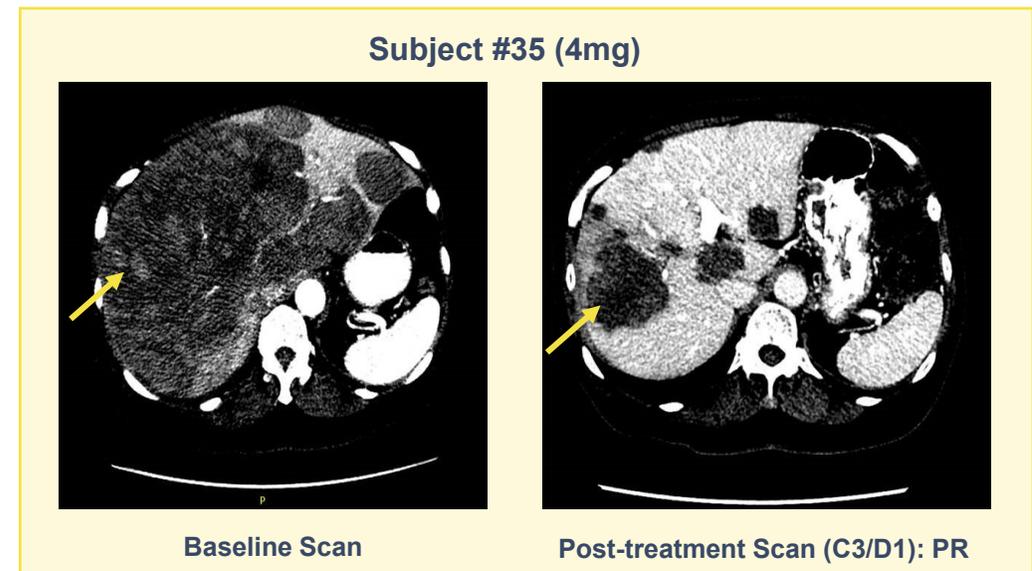
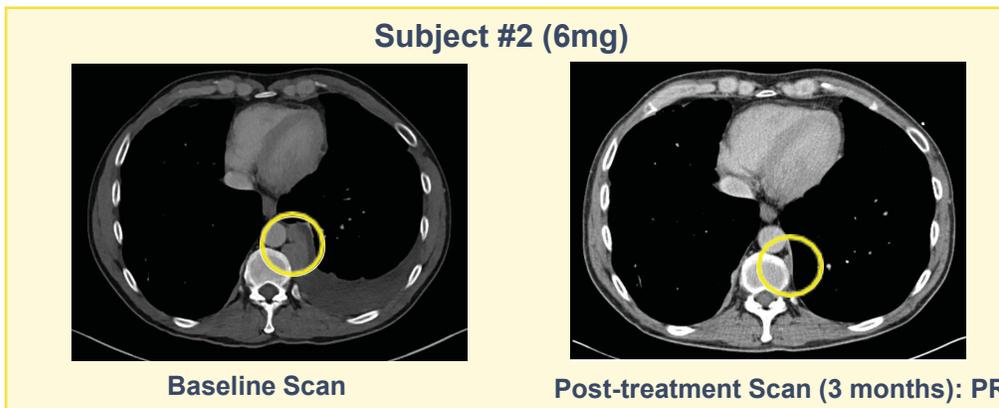
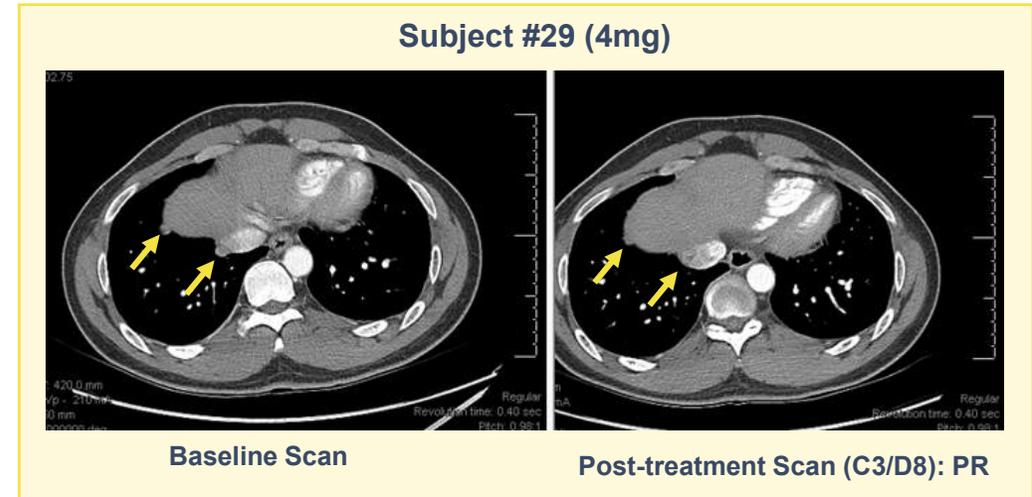
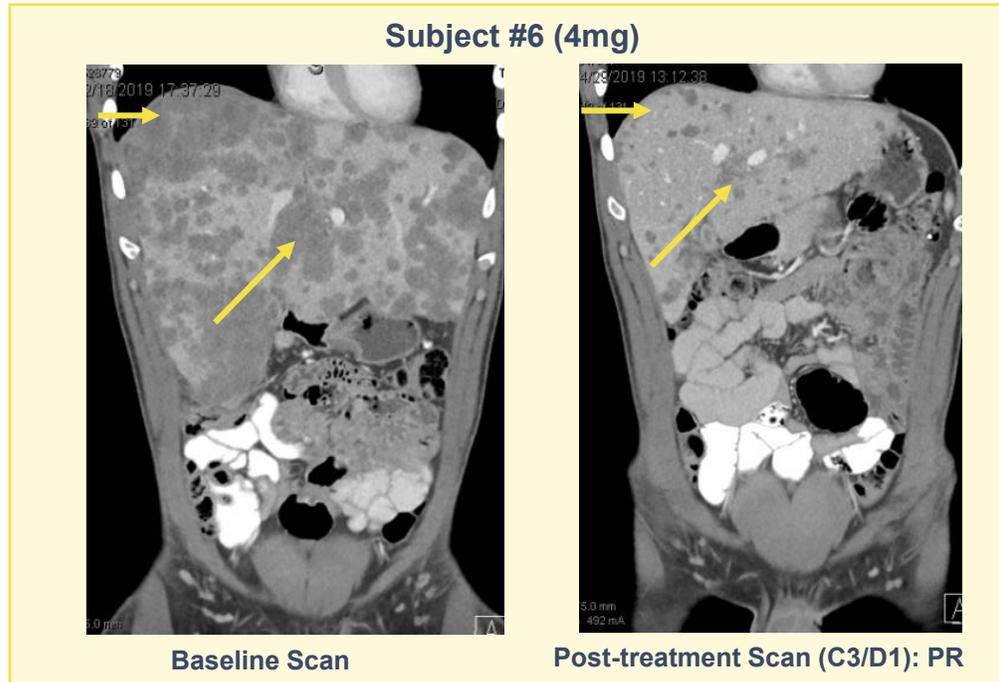
Presented at ESMO Sep 2021 6mg (n=33)^a



Data cutoff as of July 9, 2021. ^aResponse as assessed by investigator per RECIST version 1.1. ^bIncludes all efficacy-evaluable patients. ^cPatient #32 has a best overall response of NE because no post baseline measurements were recorded but is included here as zero for completeness. ^dPatient #20 has a best overall response of NE; the percent change calculation excludes tumors that are measured at screening only (T5). *Confirmed responses. **Unconfirmed response. DCR, disease control rate; NE, not evaluable; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

Initial Results Support Continuing Development of AL101 in ACC

Scans of subjects with partial response per RECISTv1.1

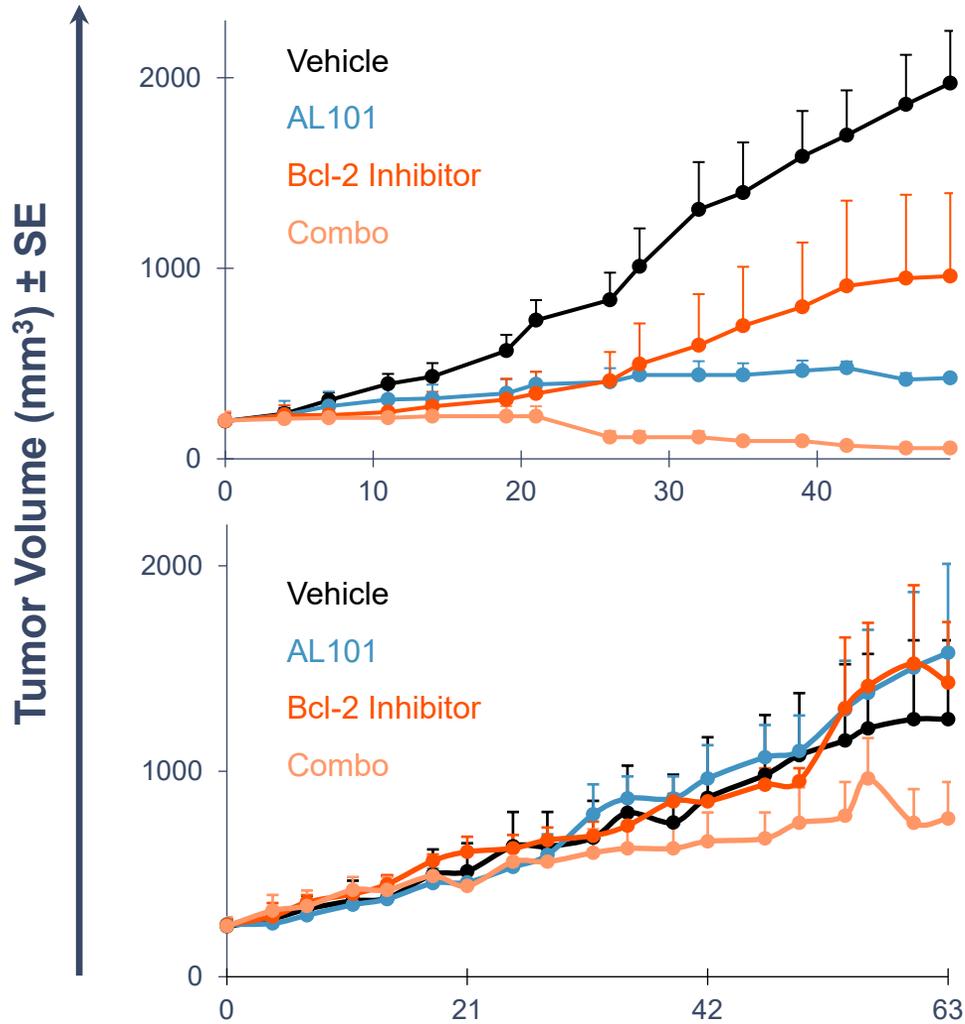


Treatment-Related AEs (TRAEs) Reported in ≥15% of Subjects*

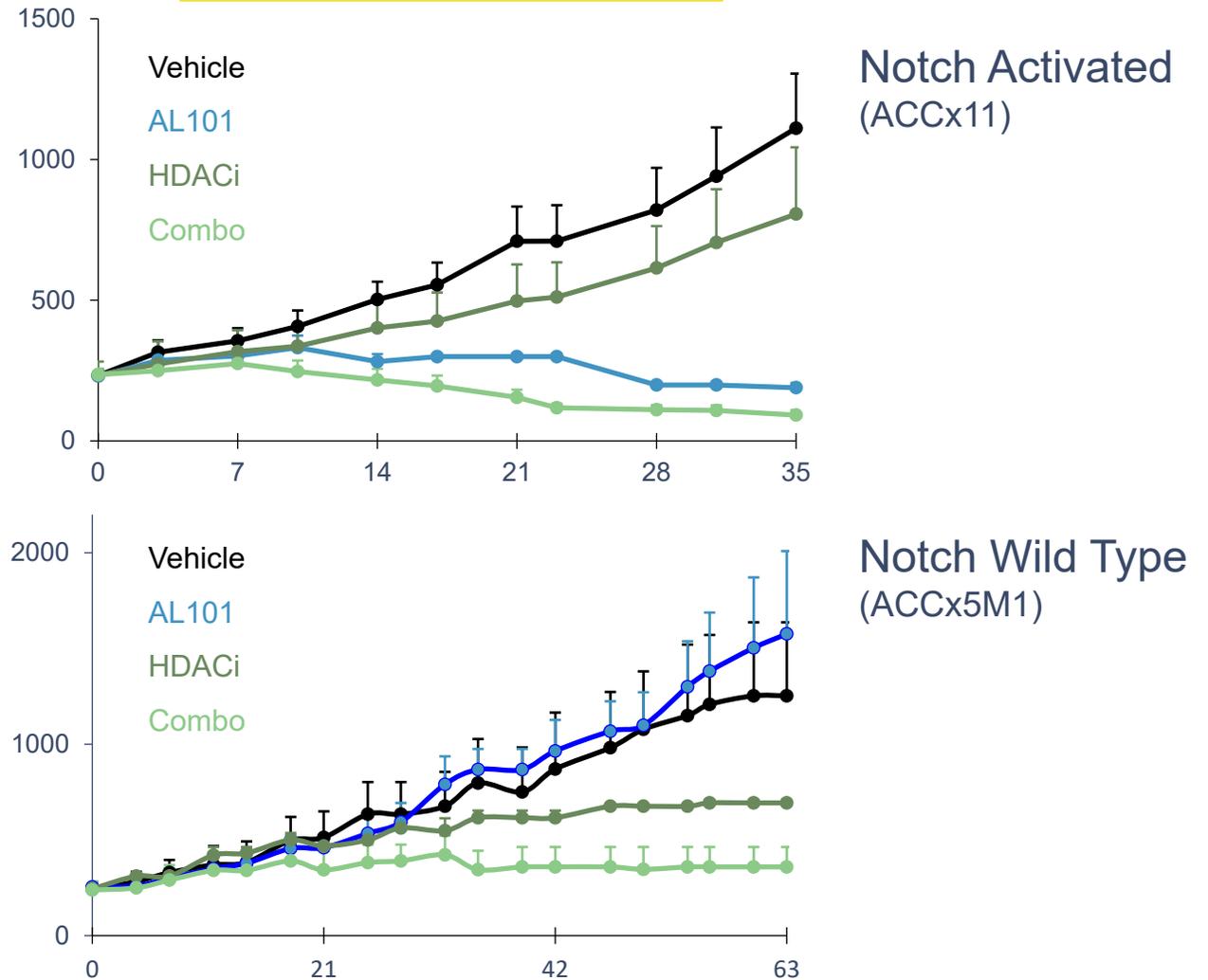
	Safety Population (N=45) 4 mg IV QW		Safety Population (N=42) 6 mg IV QW	
	Any Grade, n (%)	Grade 3/4, n (%)	Any Grade, n (%)	Grade 3/4, n (%)
Any TRAE	45 (100)	9 (20)	41 (98)	27 (64)
Diarrhea	27 (60)	2 (4)	32 (76)	6 (14)
Fatigue	23 (51)	2 (4)	20 (48)	2 (5)
Nausea	22 (49)	1 (2)	17 (41)	2 (5)
Hypophosphatemia	19 (42)	2 (4)	12 (29)	1 (2)
Cough	12 (27)	0	8 (19)	0
Vomiting	12 (27)	0	11 (26)	2 (5)
Epistaxis	9 (20)	0	7 (17)	0
Rash maculo-papular	8 (18)	0	9 (21)	0
Decreased appetite	7 (16)	1 (2)	11 (26)	1 (2)
Dysgeusia	7 (16)	0	6 (14)	0
Dry mouth	4 (9)	0	9 (21)	0
Dermatitis acneiform	4 (9)	0	7 (17)	0

Potential of AL101 Combinations to Further Improve Efficacy as Demonstrated in ACC Preclinical PDX Models

AL101+ Bcl2 inhibitor



AL101+ HDAC inhibitor



Novartis Collaboration for AL102 in Combination with BCMA-Targeting Agents

- ✓ Established license agreement with Novartis in 2018 for the development and commercialization of AL102 in combination with BCMA-targeting agents for the treatment of multiple myeloma
- ✓ Ayala to retain full rights to AL102 for all other indications
- ✓ Ayala is eligible to receive clinical, regulatory and commercial milestones of up to \$245M and tiered royalties
- ✓ Novartis led Series B round with \$10M investment in Ayala



In Licensing from BMS – Main Terms

- ✓ Upfront payment of \$6M
- ✓ Grant of 8% equity in Ayala
- ✓ Regulatory and commercial milestones totaling ~\$145M
- ✓ High single digit to low double-digit royalties (with a carve out for certain revenues earned from the NVS collaboration)



Ayala Achieved and Upcoming Potential Milestones¹



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



Dosed first patient in Phase 1 combo trial of AL102 and Novartis' anti-BCMA therapy in MM



Mid-'22 – Report initial data from Part A of Pivotal Phase 2/3 RINGSIDE trial in desmoid tumors



H2-2022 – Report additional data from Phase 2 ACCURACY trial 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 including Notch and BCMA 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 in 2022



Validating partnership with Novartis



Experienced management team with track record in oncology and rare disease

Thank you.

ayaia
pharmaceuticals

