



**RINGSIDE Phase 2/3 Trial of AL102 for Treatment of
Desmoid Tumors (DT)**

Updated Phase 2 Results Presented at ASCO 2023

Investor Call June 7, 2023

Forward Looking Statement

This presentation contains forward-looking statements that involve a number of risks and uncertainties. Forward-looking statements generally include statements that are predictive in nature and depend upon or refer to future events or conditions, and include words such as “may,” “will,” “should,” “would,” “expect,” “anticipate,” “plan,” “likely,” “believe,” “estimate,” “project,” “intend,” and other similar expressions among others. Statements that are not historical facts are forward-looking statements. Forward-looking statements are based on current beliefs and assumptions that are subject to risks and uncertainties and are not guarantees of future performance. The factors that could cause our actual results to differ materially include, without limitation: the success and timing of our clinical trials, including subject accrual; our ability to avoid and quickly resolve any clinical holds; our ability to obtain and maintain regulatory approval and/or reimbursement of our product candidates for marketing; our ability to obtain the appropriate labeling of our products under any regulatory approval; our plans to develop and commercialize our products; our ability to operate as a going concern, our levels of available cash and our need to raise additional capital, including to support current and planned clinical activities; the successful development and implementation of our sales and marketing campaigns; the size and growth of the potential markets for our product candidates and our ability to serve those markets; our ability to successfully compete in the potential markets for our product candidates, if commercialized; regulatory developments in the United States and other countries; the rate and degree of market acceptance of any of our product candidates; new products, product candidates or new uses for existing products or technologies introduced or announced by our competitors and the timing of these introductions or announcements; market conditions in the pharmaceutical and biotechnology sectors; uncertainties as to our ability to obtain a listing of our common stock on Nasdaq; our ability to integrate our various business areas successfully and to achieve anticipated synergies following our recent merger and the possibility that other anticipated benefits of the transaction will not be realized; potential litigation relating to the transaction; our ability to obtain and maintain intellectual property protection for our product candidates; the success and timing of our preclinical studies including IND-enabling studies; the timing of our IND submissions; our ability to get FDA approval for study amendments; the timing of data read-outs; the ability of our product candidates to successfully perform in clinical trials; our ability to initiate, enroll, and execute pilots and clinical trials; our ability to maintain our existing collaborations; our ability to manufacture and the performance of third-party manufacturers; the performance of our clinical research organizations, clinical trial sponsors and clinical trial investigators; our ability to successfully implement our strategy; and other risk factors identified from time to time in our reports filed with the SEC. Any forward-looking statements set forth in this presentation speak only as of the date of this presentation. We do not intend to update any of these forward-looking statements to reflect events or circumstances that occur after the date hereof.

RINGSIDE Phase 2/3 Trial of AL102 for Treatment of Desmoid Tumors (DT): Updated Phase 2 Results

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Desmoid Tumors Are Rare, Highly Debilitating Soft Tissue Tumors with No Approved Therapies

Desmoid tumors (DT) are locally aggressive, invasive connective tissue tumor associated with a high recurrence rate but with no metastatic potential

- Infiltrate surrounding tissues and affect organs and nerves¹
- Associated with significant morbidity, with symptoms including lesion ulceration, organ dysfunction, amputation, long-lasting pain due to nerve compression or tumor pressure, disfigurement and restricted range-of-motion¹

Incidence of about 1,700 annually in US²

- Given high rate of recurrence between 6,600 – 8,000 persons receive treatment for DT annually,³ representing ~20 – 25% of prevalent patient population^{4,5}

Substantial burden of illness due to chronic symptoms, decreased QOL, and increased financial burden²

- No approved therapies
- SOC includes off label chemo, radiation and TKIs, which are often poorly tolerated with inconsistent efficacy
- Move away from surgery leaves a treatment gap/opportunity



Receive treatment annually³



Prevalence of chronic pain as leading cause of disability²



Adults with sleep disturbance due to chronic pain²



Recurrence rate after surgery²



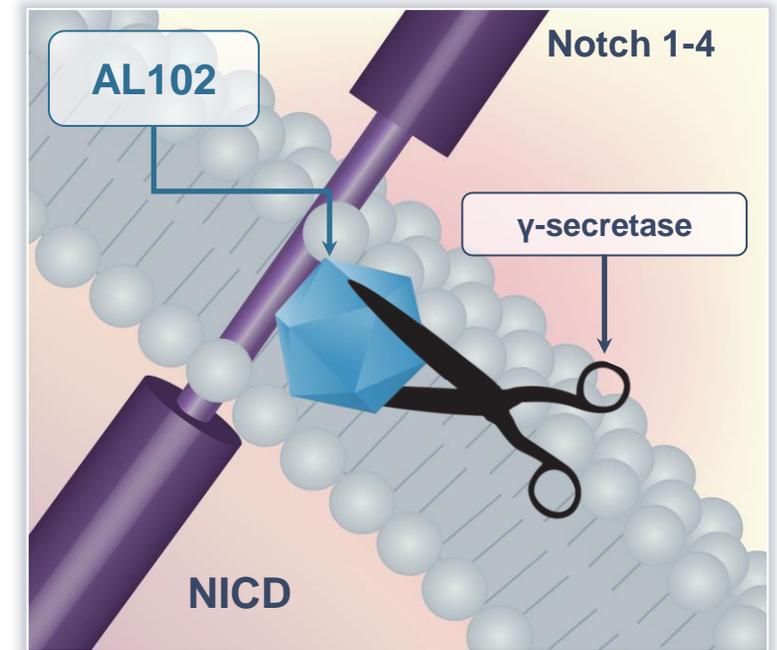
Persons with inability to hold full-time job or definitive work stoppage due to chronic pain⁶

QOL, Quality of Life; SOC, Standard of Care; TKI, Tyrosine kinase inhibitors

1 Gounder, MM., et al., Locally aggressive connective tissue tumors, J Clin Oncol, 2018, 36(2):202-209; 2 Fernandez, M., et al., Burden of illness of desmoid tumors. Poster presented at the 2022 CTOS Annual Meeting, November 16, 2022, Vancouver, Canada. Previously presented at the 2022 Desmoid Tumor Research Foundation (DTRF) Annual Meeting. 3 The Nemetz Group LLC analysis, 2022; 4 Anneberg, M., et al., Cancer Epidemiology, 2022; 5 SpringWorks analysis of EMR data and KOL Qualitative Interviews In SpringWorks JP Morgan Presentation, January 9, 2023; 6 Rigaux, P., et al., Pain burden in desmoid tumor patients: a survey of the French Advocacy Group SOS Desmoid. Bull Cancer 2015;102:213-216.

New Investigational Drug AL102: Potential Treatment for DT

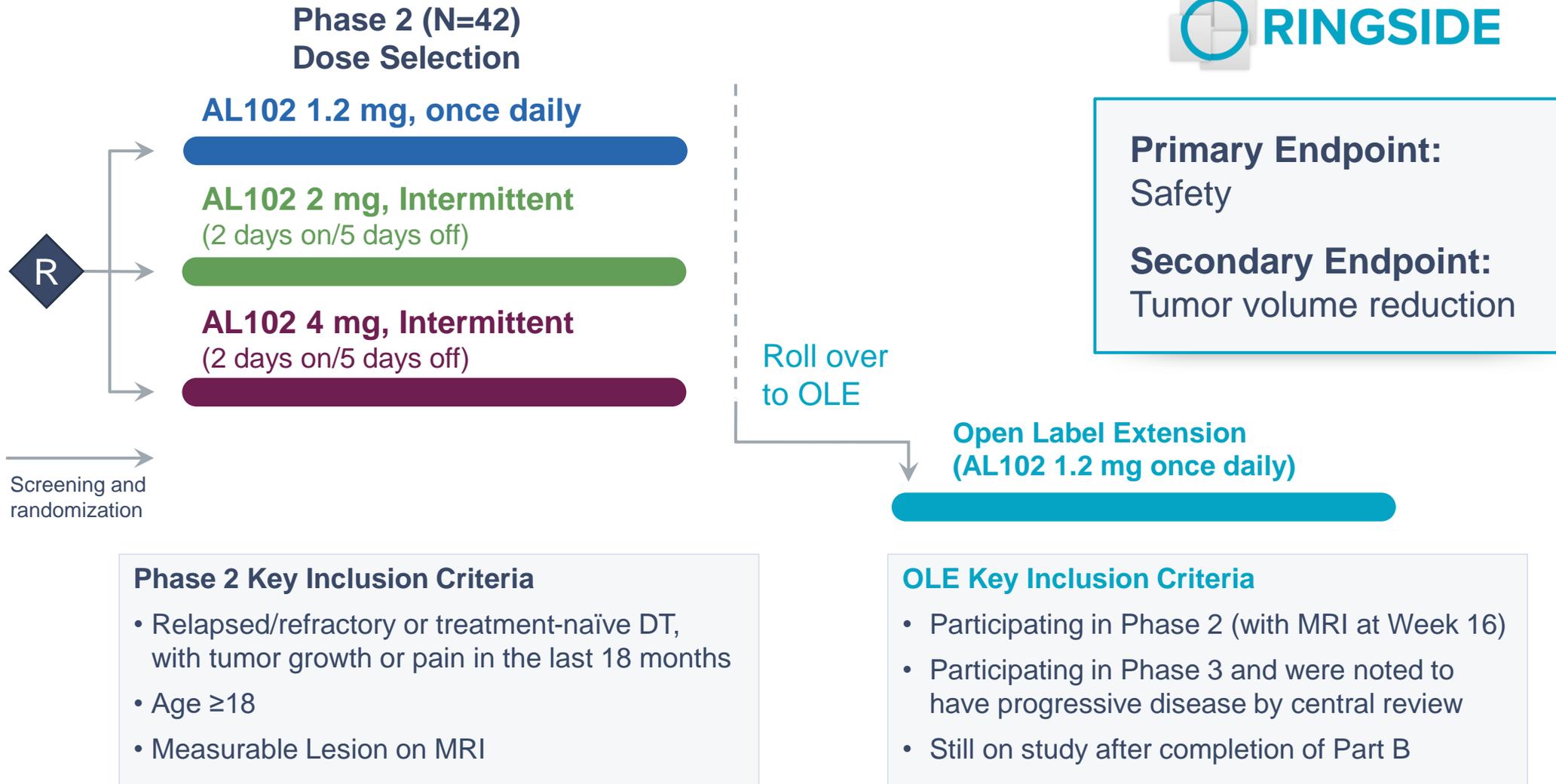
- Desmoid tumors (DT) are characterized by CTNNB1 (somatic) mutations (~85%) or APC (germline) mutations (10-15%), both result in activation of the Wnt Pathway¹
- There is overlap as well as direct cross talk between Notch target gene activation and Wnt Pathway, providing additional therapeutic targets in DTs ²
- GSIs are potent modulators of Notch, providing a mechanistic rationale for GSI therapy in DT²
- Strong clinical evidence supports the role of GSI class in DT
 - Tumor shrinkage (per RECIST criteria) and volume reduction (in MRI) have been documented with Ayala's GSIs AL101 and AL102³⁻⁵ in clinical studies, as well as with nirogacestat in late-stage clinical studies^{6,7}



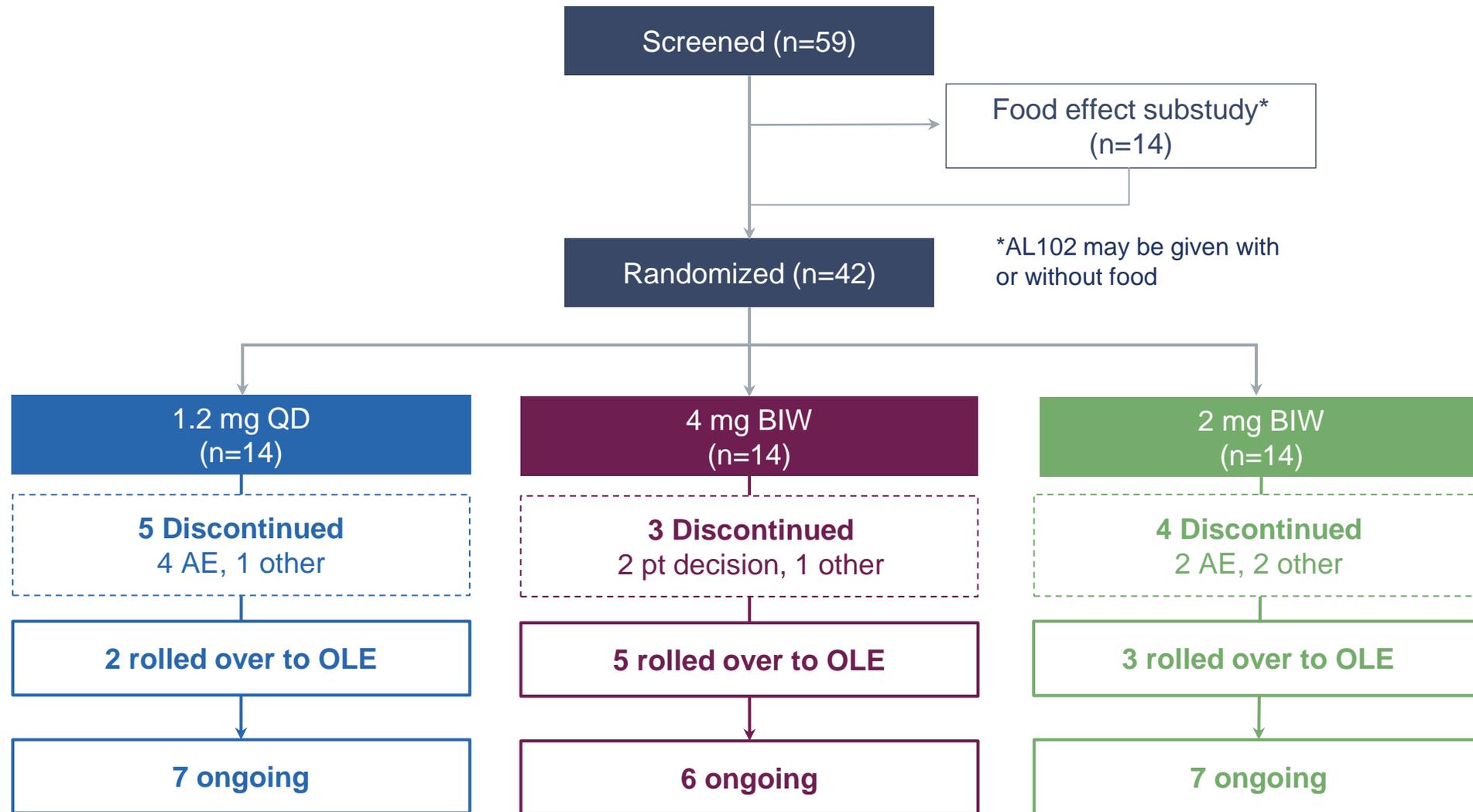
1 Lazar, AJ., et al., Specific mutations in the beta-catenin gene (CTNNB1) correlate with local recurrence in sporadic desmoid tumors, Am J Pathol. 2008; 2 Ungerback, J., et al., The Notch-2 gene is regulated by Wnt signaling in cultured colorectal cancer cells, PLoS One. 2011; 3 Chan, et al., Activity of the Gamma Secretase Inhibitor AL101 in Desmoid Tumors: A Case Report of 2 Adult Cases, Curr Oncol. 2021, 28, 3659–3667; 4 Kasper, B., et al., ESMO Congress 2022, presentation #1488MO; Data cut Jul 14, 2022; 5 Aung, KL., et al., Invest New Drugs 2018, 36:1026; 6 Kummar, S. et al., JCO 2017; 7 Kasper, B., et al., ESMO Congress 2022. #LBA2.

RINGSIDE: Pivotal Phase 2/3 Trial Evaluating AL102 in DT

Phase 2 fully enrolled (March 2022), data cut 3 Jan 2023, treatment ongoing



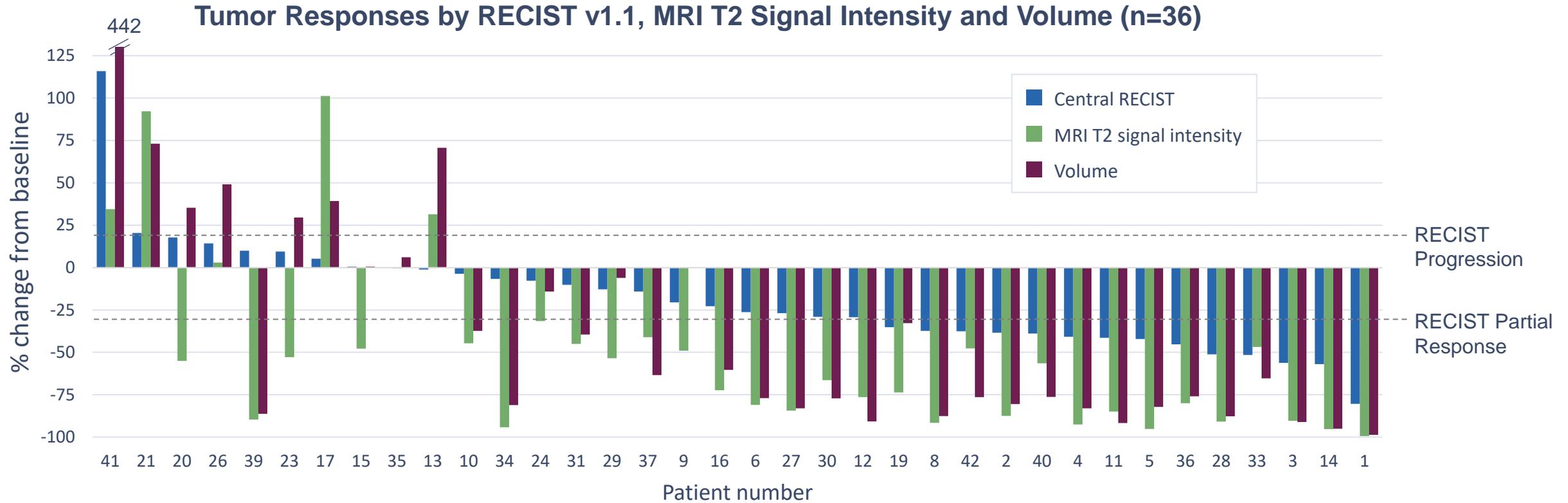
Patient Disposition from RINGSIDE Part A



Baseline Characteristics Were Generally Balanced Across Treatment Groups

Baseline Patient and Disease Characteristics	1.2 mg QD (N=14) n (%)	4 mg BIW (N=14) n (%)	2 mg BIW (N=14) n (%)	Total (N=42) n (%)
Age (years), Median (range)	44 (24-61)	36 (24-69)	32.5 (19-72)	38.5 (19-72)
Gender				
Female	11 (78.6)	11 (78.6)	9 (64.3)	31 (73.8)
Male	3 (21.4)	3 (21.4)	5 (35.7)	11 (26.2)
Location of Tumor at Initial Diagnosis				
Intra Abdominal	4 (28.6)	3 (21.4)	4 (28.6)	11 (26.2)
Extra Abdominal	10 (71.4)	11 (78.6)	10 (71.4)	31 (73.8)
Size of Tumor, Measured (n)	14	13	12	39
Median in mm (min, max)	62.0 (35, 169)	65 (11, 110)	55.5 (0, 120)	61.0 (0, 169)
Prior Desmoid Cancer Therapies	9 (64.3)	7 (50.0)	13 (92.9)	29 (69.0)
Chemotherapy	7 (50)	4 (28.6)	9 (64.3)	20 (47.6)
Targeted Small Molecule	2 (14.3)	4 (28.6)	6 (42.9)	12 (28.6)
Hormonal Therapy	3 (21.4)	2 (14.3)	4 (28.6)	9 (21.4)
Prior Desmoid Cancer Surgeries	7 (50.0)	5 (35.7)	8 (57.1)	20 (47.6)
Prior Desmoid Radiation Therapies	1 (7.1)	1 (7.1)	2 (14.3)	4 (9.5)

Substantial Reductions in Tumor Size – Consistent Across All Measures



Changes in tumor volume and T2 signal intensity typically preceded RECIST responses and were deeper than those in the RECIST evaluation

A decrease in T2 signal intensity, as measured by MRI, reflects a decrease in tumor cellularity and in DT is considered a strong indicator of anti-tumor activity

Tumor volume shrinkage consistently deepens over time and some patients continue to PRs by RECIST with longer follow-up

Interim Phase 2 – Substantial Reductions in Tumor Size – Best Overall Response¹

Median time on treatment 10.3 months (study ongoing)

Evaluable² population

Evaluable population	1.2 mg OD (n= 12)	4 mg BIW (n=13)	2 mg BIW (n=11)
Objective Response rate (CR + PR), n (%)	6 (50)	3 (23.1)	5 (45.5)
Best Overall Response			
Complete Response (CR)	0	0	0
Partial Response (PR)	6 (50)	3 (23.1)	5 (45.5)
Stable Disease (SD)	6 (50)	10 (76.9)	4 (36.4)
Progressive Disease (PD)	0	0	2 (18.1)
Disease Control Rate (DCR)	100%	100%	81.9%
Non Evaluable	2	1	3
Time to objective response, median (range), months	6.7 (3.8-9.4)	9.8 (9.0-12.3)	9.2 (6.4-9.2)

ITT population

Intention-To-Treat (ITT) population	1.2 mg OD (n= 14)	4 mg BIW (n=14)	2 mg BIW (n=14)
Objective Response rate (CR + PR), n (%)	6 (42.9)	3 (21.4)	5 (35.7)
Best Overall Response			
Complete Response (CR)	0	0	0
Partial Response (PR)	6 (42.9)	3 (21.4)	5 (35.7)
Stable Disease (SD)	6 (42.9)	10 (71.4)	4 (28.6)
Progressive Disease (PD)	0	0	2 (14.3)
Disease Control Rate (DCR)	85.8%	92.8%	64.3%

Gounder M., et al., ASCO Annual Meeting 2023, Abstr #11515 | AL102 Data Cut Date: 03 Jan 2023

RECIST, Response Evaluation Criteria in Solid Tumors

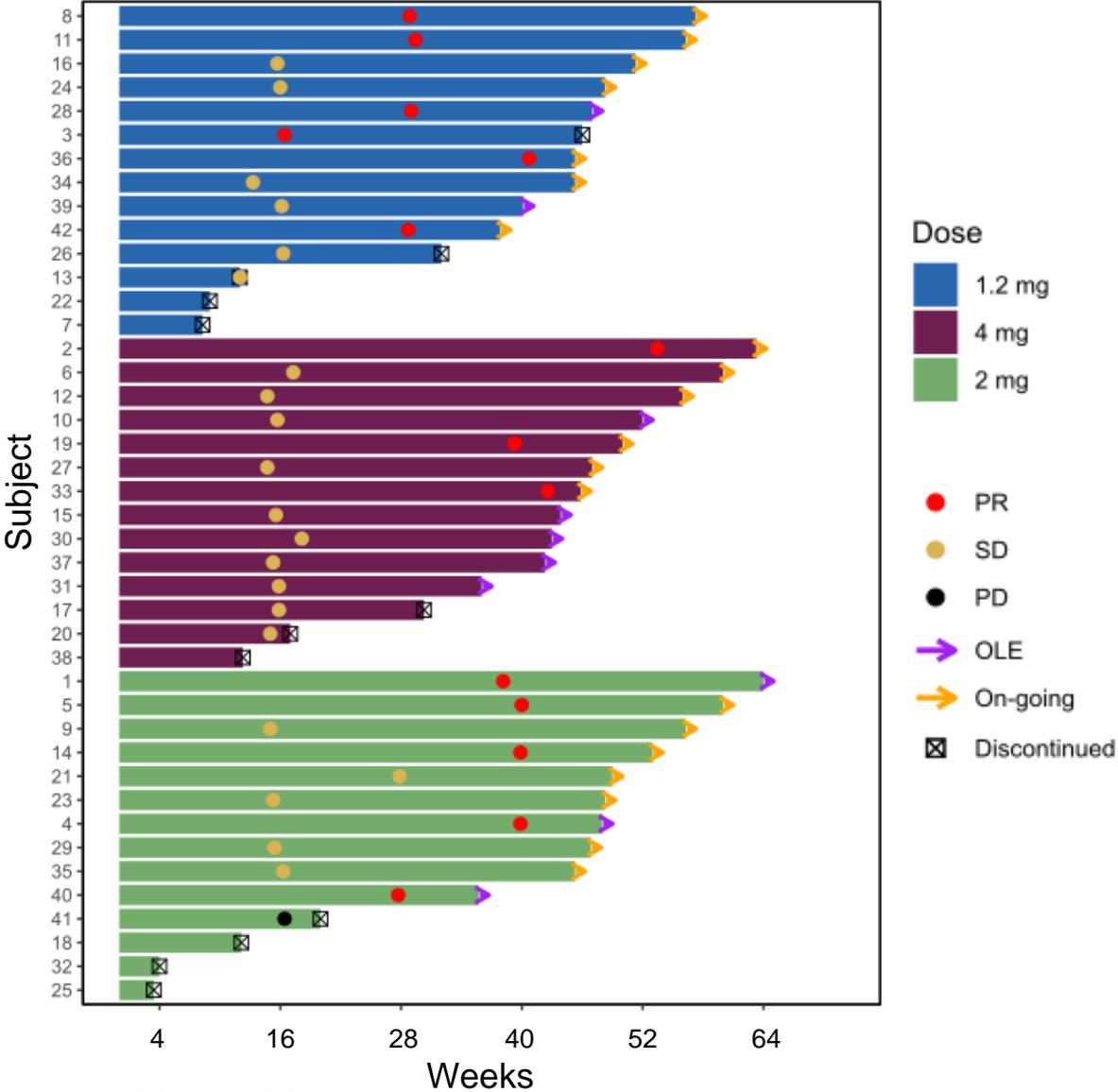
¹ Change from baseline in tumor shrinkage as measured on MRI by Blinded independent Central Review (BICR)

² Evaluable population includes patients with baseline and at least one follow-up MRI scans

Consistent Pattern of Deeper, More Rapid and Persistent Tumor Responses for 1.2 mg Once Daily

Study Visit	Median % Change from Baseline		
	1.2 mg QD (n= 12)	4 mg BIW (n=13)	2 mg BIW (n=11)
Tumor Volume			
Week 16	-51.9	-9.5	-15.2
Week 28	-76.4	-35.5	-51.2
Week 40	-75.9	-63.4	-61.2
T2W Signal Intensity (cellularity)			
Week 16	-58.4	-37.9	-28.2
Week 28	-77.8	-42.1	-50.2
Week 40	-85.2	-56.6	-54.9
RECIST (sum of diameters)			
Week 16	-13.3	1.7	-7.2
Week 28	-29.4	-9.6	-7.0
Week 40	-22.8	-16.7	-22.0

Most PRs in 1.2 mg Arm Achieved at 16 to 28 Weeks



Safety Outcomes

● **AL102 was generally well tolerated with a manageable safety profile across all dose arms**

- Regardless of dose regimen, adverse events (AEs) were predominantly Grade 1 (~71%) or Grade 2 (~25%) | Most common were diarrhea, nausea, fatigue, alopecia, and dry skin
- There were no Grade 4-5 related AEs
- Serious AEs were reported in 6/42 patients (14%) and assessed as unrelated to AL102 by investigators

● **Discontinuation due to AEs occurred in 6/42 of patients (14%)**

- These were Grade 2 rash, keratitis, stomatitis, diarrhea, ALT elevation
- All occurred within 3 months of treatment initiation

● **Ovarian dysfunction was reported in 10/23 (43%) women of childbearing potential across all dose arms, but only in 3/9 (33%) with 1.2 mg once daily***

*Ovarian dysfunction defined as premature menopause, menopause, ovarian failure, amenorrhea, and irregular menstruation

Adverse Events Reported in ≥20% of Patients

Preferred Term	1.2 mg QD (N=14) n (%)				4 mg BIW (N=14) n (%)				2 mg BIW (N=14) n (%)			
	Grade 1	Grade 2	Grade 3	Total	Grade 1	Grade 2	Grade 3	Total	Grade 1	Grade 2	Grade 3	Total
Diarrhea	8 (57.1)	3 (21.4)	2 (14.3)	13 (92.9)	6 (42.9)	3 (21.4)	1 (7.1)	10 (71.4)	5 (35.7)	1 (7.1)	1 (7.1)	7 (50)
Nausea	5 (35.7)	3 (21.4)	—	8 (57.1)	6 (42.9)	3 (21.4)	—	9 (64.3)	4 (28.6)	—	—	4 (28.6)
Fatigue	7 (50)	—	—	7 (50)	4 (28.6)	2 (14.3)	—	6 (42.9)	3 (21.4)	2 (14.3)	—	5 (35.7)
Alopecia	7 (50)	—	—	7 (50)	4 (28.6)	—	—	4 (28.6)	2 (14.3)	—	—	2 (14.3)
Dry skin	7 (50)	—	—	7 (50)	4 (28.6)	—	—	4 (28.6)	1 (7.1)	—	—	1 (7.1)
Hypophosphataemia	3 (21.4)	2 (14.3)	—	5 (35.7)	2 (14.3)	—	—	2 (14.3)	1 (7.1)	3 (21.4)	—	4 (28.6)
Hot flush	3 (21.4)	—	—	3 (21.4)	4 (28.6)	—	—	4 (28.6)	4 (28.6)	—	—	4 (28.6)
Dry mouth	5 (35.7)	1 (7.1)	—	6 (42.9)	2 (14.3)	3 (21.4)	—	5 (35.7)	—	—	—	—
Stomatitis	3 (21.4)	3 (21.4)	1 (7.1)	7 (50)	—	2 (14.3)	—	2 (14.3)	1 (7.1)	1 (7.1)	—	2 (14.3)
Headache	1 (7.1)	—	—	1 (7.1)	3 (21.4)	2 (14.3)	—	5 (35.7)	4 (28.6)	1 (7.1)	—	5 (35.7)
Cough	3 (21.4)	—	—	3 (21.4)	4 (28.6)	—	—	4 (28.6)	3 (21.4)	—	—	3 (21.4)
Vomiting	2 (14.3)	1 (7.1)	—	3 (21.4)	1 (7.1)	1 (7.1)	1 (7.1)	3 (21.4)	4 (28.6)	—	—	4 (28.6)
Aspartate aminotransferase increased	4 (28.6)	—	—	4 (28.6)	2 (14.3)	1 (7.1)	—	3 (21.4)	2 (14.3)	—	—	2 (14.3)
Alanine aminotransferase increased	3 (21.4)	—	—	3 (21.4)	2 (14.3)	—	—	2 (14.3)	2 (14.3)	1 (7.1)	1 (7.1)	4 (28.6)

— Not reported by patients taking this dose

RINGSIDE Phase 3 Enrolling Globally



Study running in:

- USA
- Australia
- Israel
- Spain
- Poland
- Netherlands
- South Korea
- UK
- Germany

Planned:

- Belgium
- France
- Italy
- India

Summary

- **Phase 2 of RINGSIDE demonstrated anti-tumor activity for AL102 across all dose arms**
- **Manageable safety profile consistent with the GSI drug class**
- **AL102 has best in class potential**
 - Sizable reductions in tumor volume, cellularity and size in a Phase 2 study
 - Potential for fewer AEs such as ovarian dysfunction
- **Patients strongly prefer AL102 once-daily dosing versus BID dosing**
 - Patient acceptability and potential adherence advantage
- **Further update from Phase 2 of RINGSIDE expected in 2H 2023**
- **Enrollment is well underway in Phase 3 and Open-Label Extension**



Questions?

Answers.

Thank you.

aya**a**
pharmaceuticals

