## Evidence of Long-term Survival Benefit in ALS with **CNM-Au8 30 mg Treatment Across Three Study** Populations

**HEALEY ALS** Platform Trial **SCUE**ALS

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## **RESULTS:** Long-term follow-up from RESCUE-ALS and the HEALEY ALS Platform Trial provide evidence of improved survival with CNM-Au8 30mg, reinforced by real-world data from expanded access programs

CNM

Match

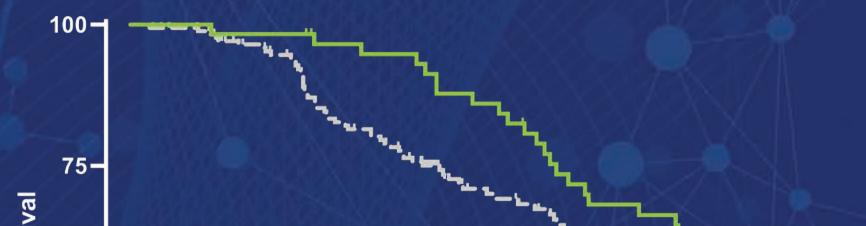
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HEALEY ALS **Platform Trial** 

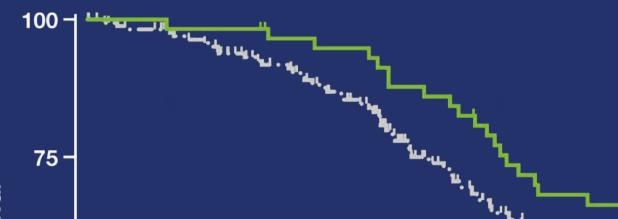
**Optimal Variable Ratio Matching** Prespecified Matching Methodology

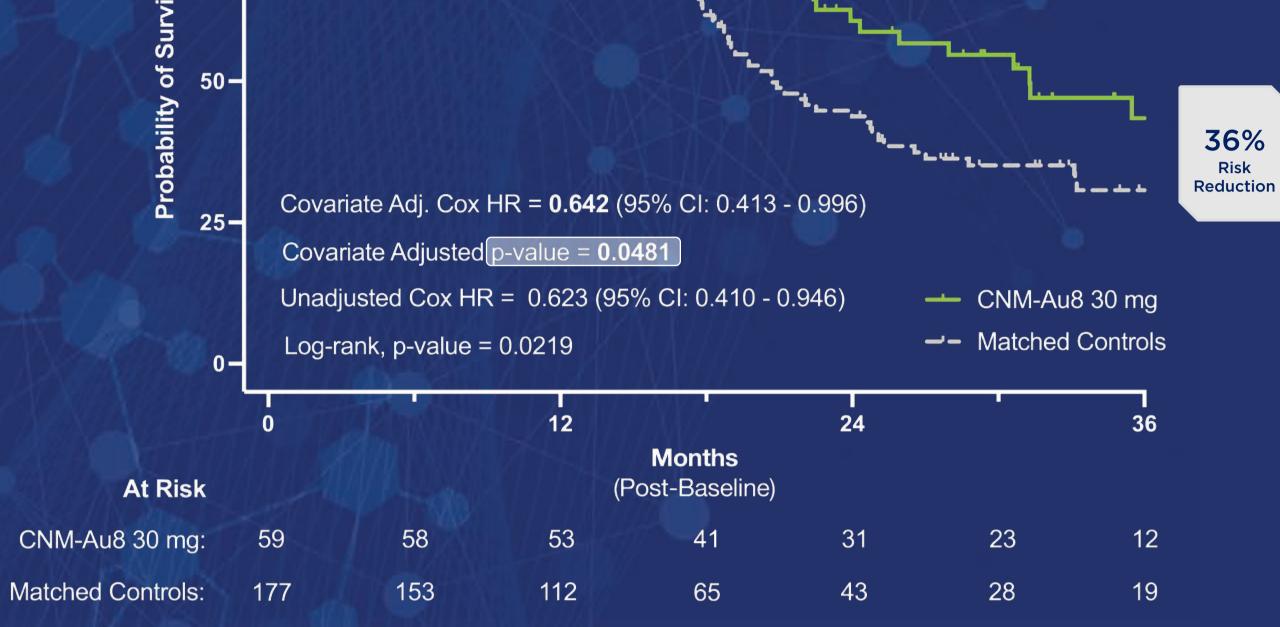
Original Randomized CNM-Au8 30 mg vs. Propensity Matched Controls HEALEY ALS Platform Trial | Optimal Variable Matching Pooled Matched Controls (PRO-ACT, ALS NHC, ANSWER-ALS)



**Nearest Neighbor (Greedy) Matching** Sensitivity Matching Methodology

Original Randomized CNM-Au8 30 mg vs. Propensity Matched Controls HEALEY ALS Platform Trial | Greedy Nearest Neighbor Match Pooled Matched Controls (PRO-ACT, ALS NHC, ANSWER-ALS)



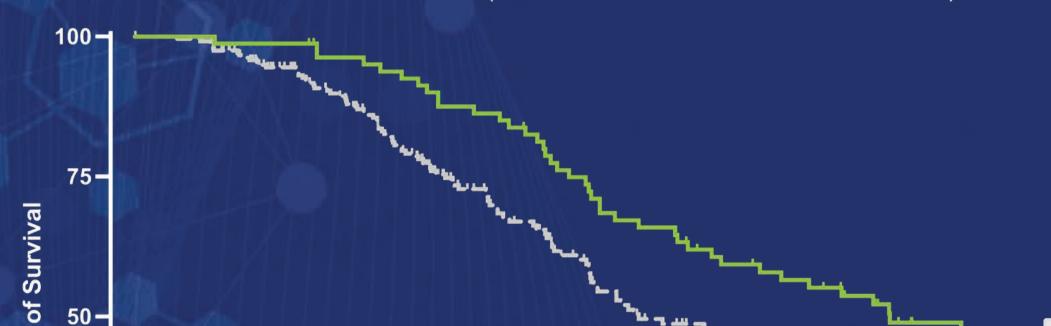




**ESCUE**ALS

**Optimal Variable Ratio Matching** Prespecified Matching Methodology

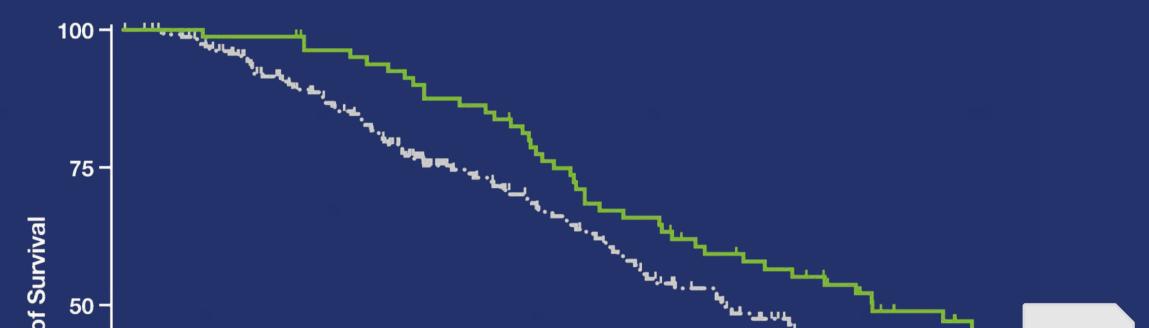
Original Randomized CNM-Au8 30 mg vs. Propensity Matched Controls Pooled HEALEY ALS Platform Trial & RESCUE-ALS | Optimal Variable Matching Pooled Matched Controls (PRO-ACT, ALS NHC, ANSWER-ALS)



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Probability of Su	)-				- حد ا حله ، <sup>ار الله</sup>	حما من <sup>عد م</sup> ن <sup>عر م</sup> ن <sup>عر م</sup> ن		<b>44%</b> Risk Reductior	
<u>م</u> 25	;-	Covariate Adjusted	Cox HR = 0.5	5 <b>62</b> (95% CI: 0	0.357 - 0.887)		<b>L</b>		
		Covariate Adjusted	p-value = 0.0	0132					
		Unadjusted Cox HF	R = 0.644 (95°	% CI: 0.416 - (	0.995) —	CNM-Au8 30	mg		
0-		Log-rank, p-value =			ntrols				
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	0		12		24		36		
At Risk			(F	<b>Months</b> Post-Baseline)	)				
I-Au8 30 mg:	59	58	53	41	31	23	12		
ned Controls:	172	144	110	52	31	21	10		

**Nearest Neighbor (Greedy) Matching** Sensitivity Matching Methodology

Original Randomized CNM-Au8 30 mg vs. Propensity Matched Controls HEALEY ALS Platform Trial & RESCUE-ALS | Greedy Nearest Neighbor Match Pooled Matched Controls (PRO-ACT, ALS NHC, ANSWER-ALS)

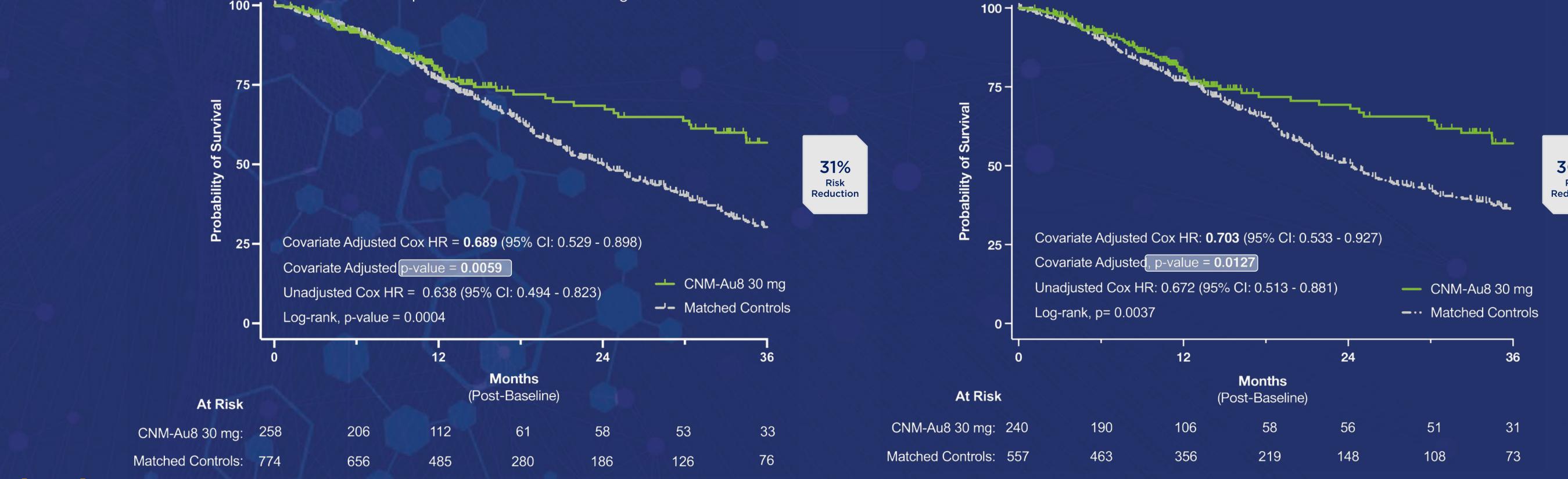




**Optimal Variable Ratio Matching** Prespecified Matching Methodology



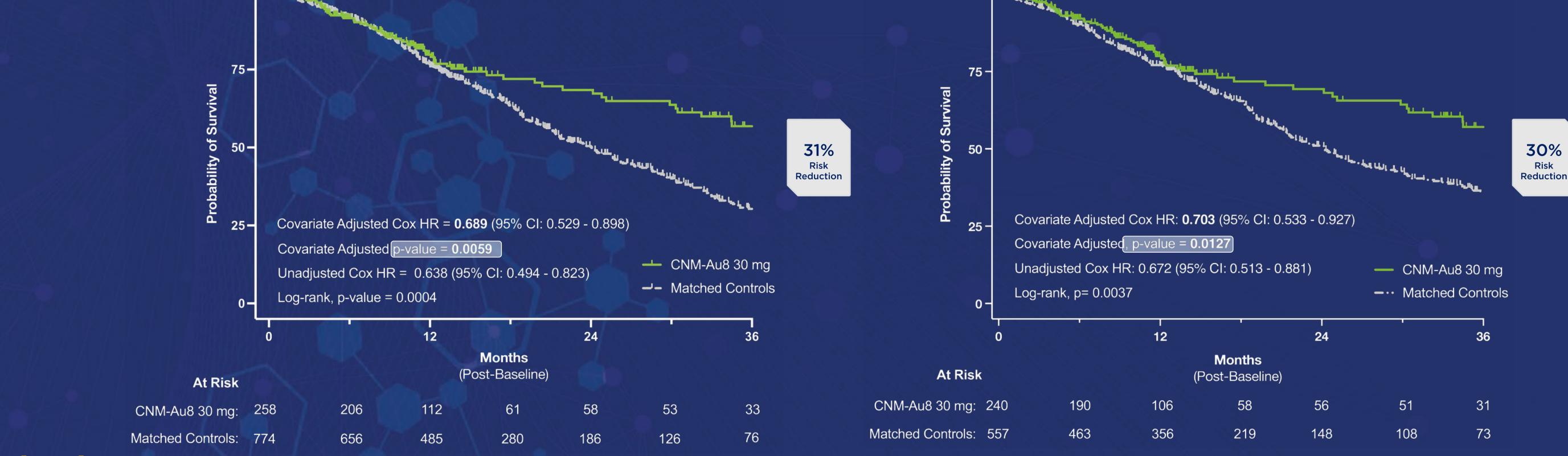
CNM-Au8 30 mg EAP Participants vs. Propensity Matched Controls CNM-Au8 30 mg (EAP01 & EAP02) All Evaluable with Baseline Covariates vs. Pooled Matched Controls (PRO-ACT, ALS NHC, ANSWER-ALS) **Optimal Variable Ratio Matching** 



Probability o 52 1						<sup>7</sup> 4. —, L	·	<b>31%</b> Risk Reduction				
<u>ک</u> 25 –		Covaraite Adjusted Cox HR = <b>0.694</b> (95% CI: 0.482 - 0.998)										
		Covariate Adjusted, p-value = 0.049										
		Unadjusted Cox H	IR = 0.667 (95	5% CI: 0.469	- 0.949)	0.949) — CNM-Au8 30 mg —— Matched Controls						
0 -		Log-rank, p-value	Matched Controls									
·	۲ 0		12		24		 36					
At Risk	U			<b>Months</b> Post-Baseline								
M-Au8 30 mg: 8	82	81	73	59	45	35	23					
ched Controls: 2	.41	197	144	83	59	36	21					

## **Nearest Neighbor (Greedy) Matching** Sensitivity Matching Methodology

CNM-Au8 30 mg EAP Participants vs. Propensity Matched Controls CNM-Au8 30 mg (EAP01 & EAP02) All Evaluable with Baseline Covariates vs. Pooled Matched Controls (PRO-ACT, ALS NHC, ANSWER-ALS) Nearest Neighbor Matching | Matched Population Only



## Methods

Propensity Matching: Optimal Variable Ratio (Prespecified) and Nearest Neighbor (Sensitivity); Pooled Control Set: PRO-ACT, ALS Natural History Consortium (ALS NHC), ANSWER-ALS (i.e., widest possible pool for matching); Matching Allocation: 1:3 (active:control) match; Logit Caliper Width: 0.2; Matching Covariates: (i) BMI, (ii) Sex, (iii) Bulbar Onset, (v) Onset Age, (vi) Diagnostic Delay (Months), (vii) ALSFRS-R Pre-Treatment Slope, (viii) ALSFRS-R Total Score, (ix) Vital Capacity (% predicted), (x) VC Onset, (ii) Onset Age, (iii) Sex, (iv) BMI, (v) Pre-treatment ALSFRS-R slope, (vi) ALSFRS-R Total Score, (vii) Diagnostic Delay (in months), (viii) Vital Capacity (% predicted), (ix) Pre-Treatment Vital Capacity Slope, and (x) TRICALS Risk Score. Notes: Includes all evaluable participants with complete baseline covariates for matching. Participants are right censored at last observation (death or any reported clinical or laboratory value). When less than ~10% follow-up information is available in both groups (active and matched controls), Kaplan-Meier figures are truncated thereafter (Hazard Ratios include all follow-up data in all participants). Survival (time to all-cause mortality) does not include permanent assisted ventilation, which was not tracked consistently in the control datasets. Acknowledgements: We are indebted to the participants and investigators of the HEALEY ALS Platform Trial, the RESCUE-ALS trial, and the U.S. Expanded Access Protocols (EAPs).