Phase 1 Clinical Data for Single-Dose Subcutaneous Injection of RLYB116, a C5 Blocking Affibody® Molecule Linked to an Albumod® Albumin Binding Domain

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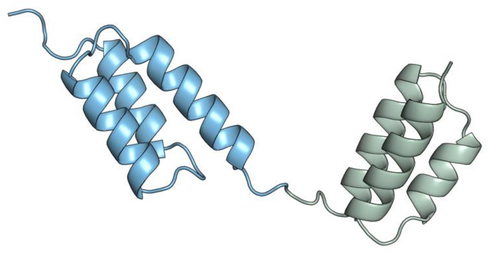
Introduction

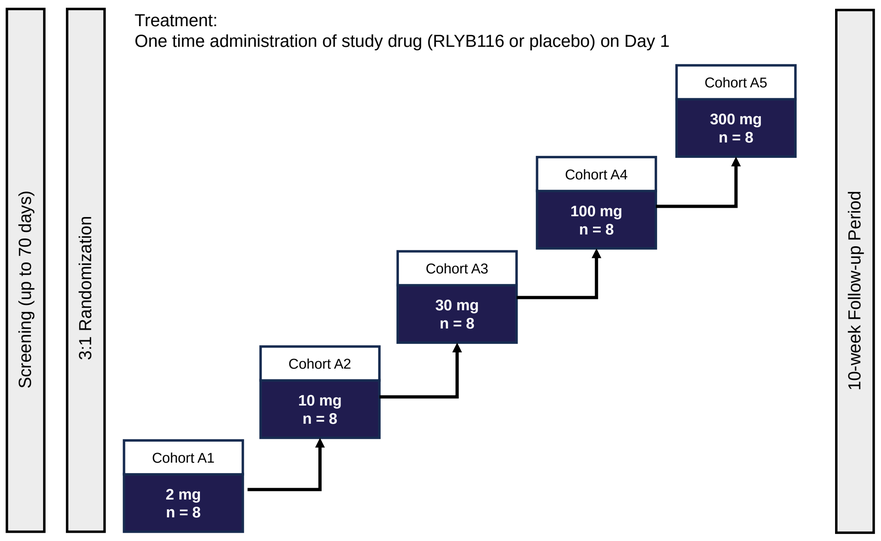
RLYB116 is an Affibody molecule with high affinity for blocking C5 linked to an albumin binding domain for half-life extension. It is in Phase 1 clinical development. The Affibody platform presents an opportunity for a small molecular sized protein with high specificity for target to be administered infrequently with low volume subcutaneous injection that may be suitable for autoinjector use.

The RLYB116 molecule contains 108 amino acids and has a molecular weight of ~11.9kDa. The Affibody component of the molecule is connected to an albumin binding domain with a short linker sequence.



Study Design and Study Population

The study has a randomized, parallel group, single-blind, placebo-controlled, ascending dose design. The single-ascending dose (SAD) phase includes a 10-week follow up period after dosing.



A Phase 1 single-blind, placebo-controlled single and multiple ascending dose study was initiated with objectives including evaluation of the safety and tolerability as well as pharmacokinetic and pharmacodynamic properties of RLYB116 in healthy participants. The single dose phase of the study included doses of 2, 10, 30, 100, and 300 mg administered by subcutaneous injection in sequential cohorts of 8 participants each. Each cohort included 6 assigned to RLYB116 and 2 to placebo.

The study population included healthy participants aged 18 to 55 with a BMI of 18.0 to 32.0 kg/m^2. Participants were excluded with a clinically significant medical history, current medical, psychiatric, or any other condition that, in the opinion of the investigator, would interfere with the participant's ability to participate in the study or increase the risk of participation for that participant.

Methods

Serum concentrations of RLYB116 were measured utilizing LC-MS/MS and the pharmacodynamic measure of free C5 serum concentration was assessed utilizing a Gyrolab® immunoassay.

Serum concentrations of RLYB116 (PK) and free C5 (PD) with nominal times were evaluated using Phoenix WinNonlin® software, version 8.3 (Pharsight Corporation, USA). Noncompartmental analysis was performed (Model type: Plasma 200-202) using extravascular dosing option. All AUC determinations were determined using the 'linear up-log down trapezoidal' method.

The pharmacokinetic assay for RLYB116 has a lower limit of quantification (LLOQ) of 0.02 µM and an upper limit of quantification (ULOQ) of 20 µM.

This study is registered in the Australia New Zealand Clinical Trials Registry (ANZCTR): ACTRN12621001571864.

Safety

The most commonly reported treatment emergent adverse events were headache (22.5%), diarrhea (15%), and abdominal pain (10%). There was 1 case of mild injection site erythema. Most adverse events were mild in severity. There were no severe or serious adverse events reported and no study discontinuations due to an adverse event.

Disclaimer

Any information and recommendations provided by Rallybio during this presentation are proprietary to Rallybio. The data presented in this poster is preliminary and subject to change with finalization of the clinical study report.

Note: RLYB116 has not been approved by the U.S. Food and Drug Administration (FDA), the European Commission, or any other health authority for any indication, and the safety and effectiveness of this molecule have not been established.

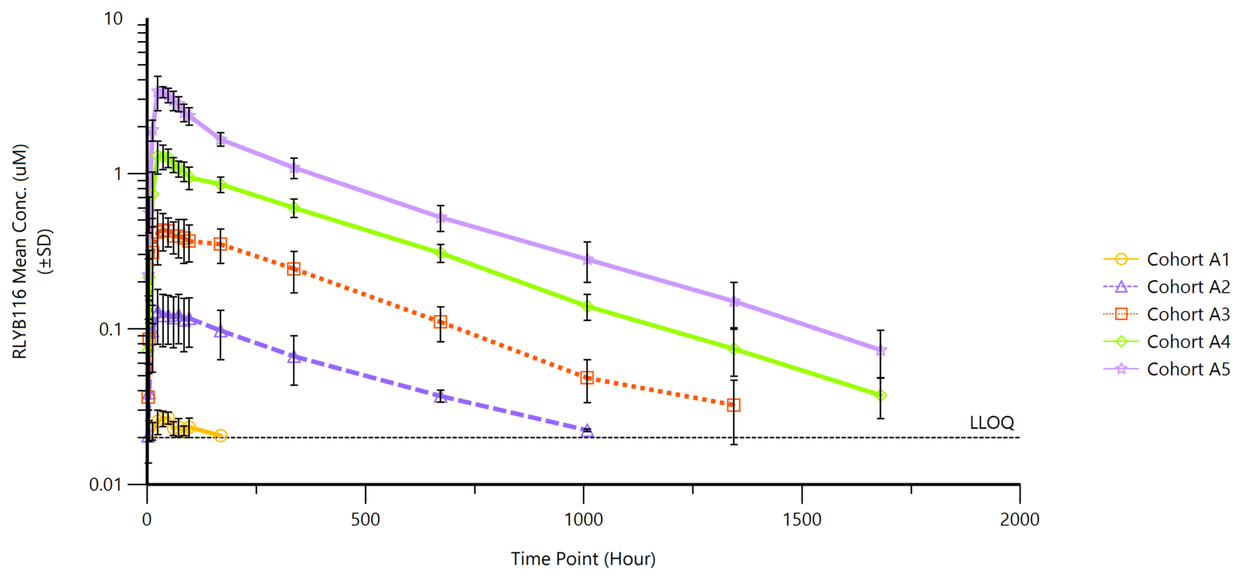
Results

RLYB116 exhibited a characteristic absorption pattern when administered subcutaneously. Non-compartmental analysis (NCA) yielded the PK parameters outlined in the table below. The PK profiles demonstrated consistent increases in exposure with increasing dose levels, ranging from 2 mg to 300 mg, with an observed increase in proportionality. Furthermore, the 100 mg and 300 mg dose cohorts demonstrated low inter-subject variation (%CV), which remained below 20%, for PK parameters that included C_{max}, AUC_{0-t}, AUC_{0-inf}, $t_{1/2}$, V_d, and CL. The elimination half-life of RLYB116 is greater than 300 hours.
The minimum concentrations (Cmin) of free C5 demonstrated a direct relationship with the escalating dose of RLYB116. Free C5 concentrations measured for each participant were reduced by greater than 99% at 24 hours after the 100 mg dose and at 12, 24, and 72 hours after the 300 mg dose of RLYB116.

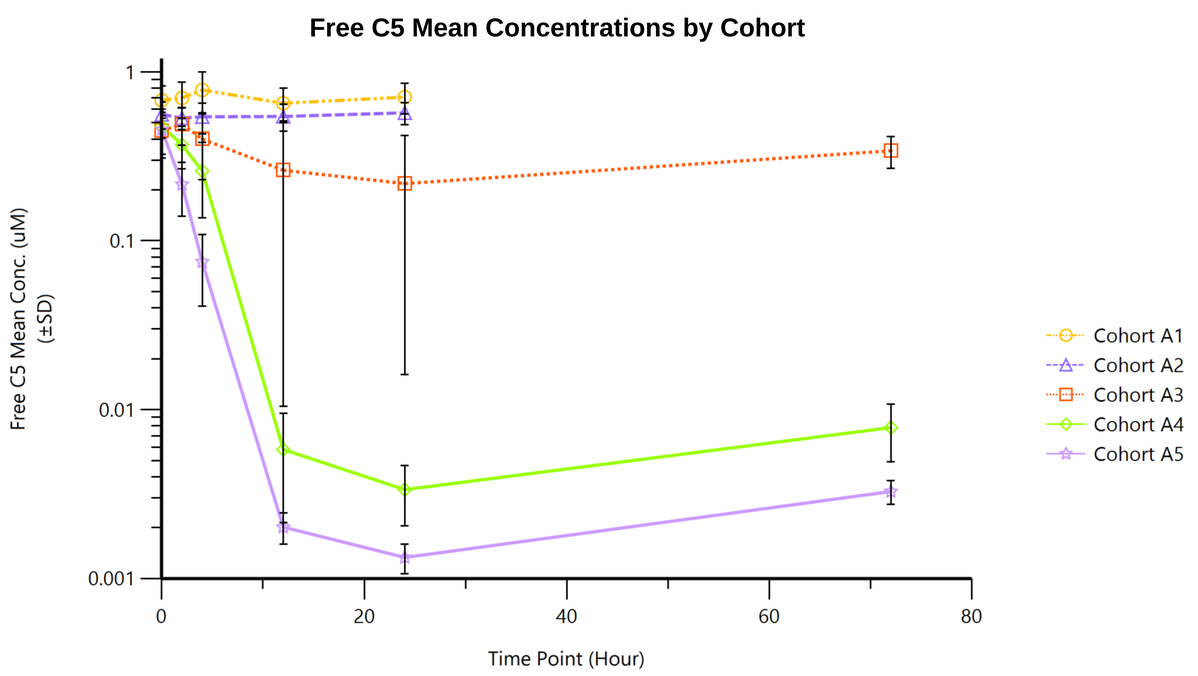
Cohorts	Treatment	Dose (µmol)	Stat	T_{max} (hr)	C_{max} (µM)	AUC_{0-t} (hr*µM)	AUC_{0-inf} (hr*µM)	$t_{1/2}$ (hr)	V_d (L)	CL (L/h)
A1	2 mg RLYB116	0.17	Mean	31.2	0.03	19.6	NC	NC	NC	NC
			CV%	43.9	22.10	15.0	NC	NC	NC	NC
A2	10 mg RLYB116	0.84	Mean	40.0	0.15	68.8	74.3	379.2	6.3	0.01
			CV%	49.0	20.00	13.8	12.4	7.6	19.7	12.80
A3	30 mg RLYB116	2.52	Mean	52.0	0.50	206.4	210.6	289.9	5.3	0.01
			CV%	51.9	30.70	25.1	24.5	6.7	28.5	24.90
A4	100 mg RLYB116	8.4	Mean	30.0	1.40	504.9	552.7	314.5	6.8	0.02
			CV%	33.5	18.70	17.6	9.3	19.1	19.6	9.50
A5	300 mg RLYB116	25.21	Mean	34.0	3.70	1118.7	1155.4	338.5	10.8	0.02
			CV%	26.6	16.40	14.0	14.6	10.7	12.5	17.70

NC = not calculated

RLYB116 Mean Concentrations by Cohort



Free C5 Mean Concentrations by Cohort



Conclusion

- RLYB116 is a low molecular weight protein containing an Affibody molecule with C5 binding specificity linked to an albumin binding domain for half-life extension.
- Phase 1 data has demonstrated that single-dose administration of 100 and 300 mg resulted in maximum exposures greater than 1 µM and 3 µM, respectively, and greater than 99% reduction in free C5 concentrations.
- Single-dose administration of RLYB116 was characterized by no severe or serious adverse events.
- Further investigation of RLYB116 with multiple-dose administration in healthy participants is ongoing.

References

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Acknowledgments

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