To Whom It May Concern

Subject:	Request for Authorisation of Substantial Modification
Study title:	A Phase 2/3 Open-label Study Evaluating the Efficacy and Safety of Luveltamab Tazevibulin (STRO-002) versus Investigator's Choice (IC) Chemotherapy in Women with Relapsed Platinum-resistant Epithelial Ovarian Cancer (Including Fallopian Tube or Primary Peritoneal Cancers) Expressing Folate Receptor Alpha (FOLR1)
Protocol Number:	STRO-002-GM3
Protocol version and date	Protocol Version 3.0, Amend-1/EU-1.0, 05 Sep 2024
EU CT number:	2024-512477-27-00
Investigational Medicinal Product (IMP)	luveltamab tazevibulin (STRO-002)
Sponsor	Sutro Biopharma, Inc. 111 Oyster Point Boulevard South San Francisco CA 94080 United States
EU Legal Representative	Premier Research Group S.L.U

Dear Sir or Madam,

Premier Research, on behalf of the Sponsor Sutro Biopharma, Inc., would like to submit a substantial modification.

The Part I of the initial application received an approval with condition on 01 Jul 2024 therefore the trial applicable to the EU (phase 3-part 2) could not be initiated before submitting a substantial modification (SM) with the data of phase 2-part 1 of the trial, performed outside the EU and that supports the selected optimal dose.
Sponsor was also requested to update Part II documentation (Subject information and informed consent form as applicable) to align with the latest EU protocol.

Based on the above we hereby submit the protocol amendment Version 3.0, Amend-1/EU-1.0, 05 Sep 2024 that specifies the selected optimal dose regimen of luveltamab tazevibulin that will be used in Phase 3-Part 2 of the study.
The luveltamab tazevibulin dose regimen of 5.2 mg/kg q3w with prophylactic pegfilgrastim on Day 8 for 2 cycles followed by 4.3 mg/kg starting at Cycle 3 was selected for the Phase 3, Part 2 portion of Study REFRaME-O1. The selection of this dose was informed by the interim analysis of efficacy and safety in Part 1 of REFRaME-O1 which included at least 25 patients from both dose cohorts. Presentation of the data from the interim analysis, as well as a thorough analysis of the PK, safety and efficacy for the 4.3 and 5.2 mg/kg dosing regimens are presented in the response document included in the submission.

We also attach the updated country specific information sheets and consent forms specifying 5.2 mg/kg every 3 weeks (q3w) with prophylactic pegfilgrastim on Day 8 for 2 cycles followed by 4.3 mg/kg starting at Cycle 3 the optimized dose regimen for Part 2 of the study.

We also attach to the substantial modification the new version of the IMPD (v. 8.0) and Investigator's Brochure (Ed 10) to include update from frozen liquid formulation to lyophilized formulation and the associated changes.
The detailed list of changes in the IMPD are provided in the summary of changes.

We submit 5 additional sites for Germany and 6 sites for Italy, please see attached the site specific documentation attached to the application. Moreover, in Austria the PI has been changed at Medical University of Vienna therefore we attach the site specific documents from the new PI and also the updated insurance certificate.

List of Documents Attached

Part I:

No.	Document	Version No.	Date
B	**Cover letter**		
B1	Cover letter	N/A	30Sep24
B1	Cover letter for Hungary (bilingual)	N/A	30Sep24
B2	Proof of payment	N/A	As applicable for countries
D	**Protocol**		
D1	Protocol – *version for publication and version not for publication*	3.0 Amend-1/EU-1.0	05Sep24
D1	Protocol Synopsis English – *version for publication and version not for publication*	3.0 Amend-1/EU-1.0	05Sep24
D1	Protocol Synopsis – Spanish, Italian, Hungarian, German, French, Dutch, Czech– *version for publication and version not for publication*	3.0 Amend-1/EU-1.0	05Sep24
D1	Protocol_2024-512477-27-00 v3 0 Amend 1EU 1 0 dated 05 Sep 2024 rationale for optimal dose	N/A	N/A
D2	Compliance statement	N/A	05Sep24
D4	Study design	N/A	05Sep24

E	**Investigator's Brochure**		
E1	Investigator's Brochure clean and tracked changes	Ed 10	20Aug2024
G	**Investigational Medicinal Product Dossier (IMPD)**		
G1	Investigational Medicinal Product Dossier (IMPD) – Quality for Active Substance	8.0	Sept24
G1	IMPD Summary of Changes	N/A	Sep2024
I	**Labelling**		
I1	Vial booklet label	N/A	13Sep24
I1	Carton booklet label	N/A	13Sep24

Part II: AUSTRIA

Recruitment Arrangements			
Subject Information Sheet and Informed Consent Form			
L1	Main ICF (German) *version for publication and version not for publication*	3.0	16Sep2024
L1	Site contact details for ICF *version for publication and version not for publication*	3.0	19Sep2024
Suitability of the Investigators			
M1	CV Investigator PI Concin MU Wien	N/A	12Aug2024
M2	DoI Investigator PI Concin MU Wien	N/A	26Aug2024
M3	GCP Investigator PI Concin MU Wien	N/A	10Sep2024
Suitability of the facilities			
N1	Site suitability form MU Wien	N/A	26Aug2024
Proof of insurance cover			
O1	Trial participant insurance certificate	N/A	23Sep2024

Part II: BELGIUM

Subject Information Sheet and Informed Consent Form			
L1	Main ICF (French; Dutch; German) *version for publication and version not for publication*	4.0	10Sep2024

Part II: CZECH REPUBLIC

No. / *Č.*	**Document / *Dokument***	**Version No. / *Verze č.***	**Date / *Datum***
L. Subject Information, Informed Consent Form, other subject information material / *Informace pro subjekty a formulář informovaného souhlasu, další informační materiály pro subjekty*			
L1	Main ICF -Participant Information Sheet and Informed Consent Form / *Informace pro účastníka a formulář informovaného souhlasu*	2.0	10Sep24

	Language / *jazyk*: Czech / *čeština* *version for publication and version not for publication / verze ke zveřejnění a verze k nezveřejnění*		
The following document was uploaded in response to the country decision with condition:			
N4	Clinical performance study approval_CZE Language: Czech	N/A	22-Jul-2024

Part II: GERMANY

Subject Information Sheet and Informed Consent Form			
L1	Main ICF (German) *version for publication and version not for publication*	v3.0	16Sep2024
Suitability of the Investigators			
Site 1701 PI Pietzner, Charité			
M1	CV PI Pietzner, Charité	NA	11Mar2024
M1	CV Braicu, Charité	NA	01Mar2024
M1	GCP PI Pietzner, Charité	NA	01Dec2022
M1	GCP Braicu, Charité	NA	01Dec2022
M2	Declaration of Interest PI Pietzner, Charité	NA	26Feb2024
M2	Declaration of Interest Braicu, Charité	NA	26Feb2024
Site 1706 PI Ignatov, Uni Magdeburg			
M1	CV PI Ignatov, UniMagdeb	NA	05Mar2024
M1	CV Meszaros, UniMagdeb	NA	08Mar2024
M1	GCP PI Ignatov, UniMagdeb	NA	31Mar2022
M1	GCP Meszaros, Uni Magdeb	NA	10Oct2023
M2	Declaration of Interest PI Ignatov, UniMagdeb	NA	08Mar2024
M2	Declaration of Interest Meszaros, UniMagdeb	NA	08Mar2024
Site 1707 PI Marmé, UMM			
M1	CV PI Marmé, UMM	NA	12Mar2024
M1	CV Mavratzas, UMM	NA	12Mar2024
M1	GCP PI Marmé, UMM	NA	29Jun2022
M1	GCP Mavratzas, UMM	NA	05Jul2021
M2	Declaration of Interest PI Marmé, UMM	NA	12Mar2024
M2	Declaration of Interest Mavratzas, UMM	NA	19Aug2024
Site 1710 PI Mustea, UKBonn			
M1	CV PI Mustea, UKBonn	NA	27Feb2024
M1	CV Otten, UKBonn	NA	22Feb2024
M1	GCP PI Mustea, UKBonn	NA	16Mar2022
M1	GCP Otten, UKBonn	NA	16Mar2022
M2	Declaration of Interest PI Mustea, UKBonn	NA	05Mar2024
M2	Declaration of Interest Otten, UKBonn	NA	05Mar2024
Site 1711 PI Heitz, KEM			
M1	CV PI Heitz, KEM	NA	14Feb2024
M1	CV Kaiser, KEM	NA	16Feb2024
M1	GCP PI Heitz, KEM	NA	15Feb2022
M1	GCP Kaiser, KEM	NA	18Aug2024

M2	Declaration of Interest PI Heitz, KEM	NA	14Feb2024
M2	Declaration of Interest Kaiser, KEM	NA	16Feb2024
Suitability of the facilities			
N1	Site suitability form, 1701, Charité	NA	13Mar2024
N1	Site suitability form, 1706, UniMagdeb	NA	16Sep2024
N1	Site suitability form, 1707 UMM	NA	12Mar2024
N1	Site suitability form, 1710 UKBonn	NA	14Mar2024
N1	Site suitability form, 1711 KEM	NA	14Mar2024

Part II: HUNGARY

L. Subject Information Sheet and Informed Consent Form / Tájékoztatáson alapuló beleegyező nyilatkozat			
L1	Main ICF – redacted version for publication and clean version not for publication, Language: Hungarian / *Fő tájékoztatáson alapuló beleegyező nyilatkozat – kitakart, közzétételre szánt verzió és tisztázott, nem közzétételre szánt verzió* *Nyelv: magyar*	v3.0	13Sep2024

Part II: IRELAND

Subject Information Sheet and Informed Consent Form			
L1	Main ICF (English)	2.0	17Sep2024

Part II: ITALY

The referent Italian Ethic Committee is: "Comitato Etico Territoriale Lombardia 1".
We would like to confirm that the Patient's information sheets and Informed consent forms for Italy have been prepared following the Guidelines of National coordination centre (CCN) of ethics committees for clinical trials.

We declare that the Stamp Duty related to this application has been paid through F23 dated 10 September 2024.

Subject Information Sheet and Informed Consent Form			
L1	Main ICF Italian version for publication and version not for publication	3.0	10Sep2024
Suitability of the Investigators			
Site 0605 PI Raspagliesi, Istituto Nazionale Tumori			
M1	CV PI	NA	30Apr2024
M2	Declaration of Interest PI	NA	26Sep2024
Site 0607 PI Tasca, Istituto Oncologico Veneto - IRCSS			
M1	CV PI	NA	19Feb2024

M2	Declaration of Interest PI	NA	24Jan2024
Site 0608 PI Sikokis, Azienda Ospedale Universita Parma			
M1	CV PI	NA	14May2024
M2	Declaration of Interest PI	NA	14May2024
Site 0610 PI Piovano, A.O.U. Citta della Salute e della Scienza di Torino			
M1	CV PI	NA	23Apr2024
M2	Declaration of Interest PI	NA	28May2024
Site 0612 PI Cecere, Istituto Nazionale Tumori IRCCS Fondazione G. Pascale			
M1	CV PI	NA	12Feb2024
M2	Declaration of Interest PI	NA	19Mar2024
Site 0616 PI Scandurra, Ospedale Cannizzaro			
M1	CV PI	NA	12Mar2024
M2	Declaration of Interest PI	NA	12Mar2024
Suitability of the facilities			
N1	Site suitability form, Site 0607	NA	28May2024
N1	Site suitability form Signature Delegation, Site 0607	NA	08Mar2024
N1	Site suitability form, Site 0608	NA	22Apr2024
N1	Site suitability form, Site 0610	NA	14Jun2024
N1	Site suitability form, Site 0612	NA	19Mar2024
N1	Site suitability form, Site 0616	NA	18Mar2024
N1	Site suitability form, Site 0605	NA	27Sep2024
N1	PI suitability Italy	NA	24Sep2024

Part II: SPAIN

Recruitment Arrangements			
K2	Recruitment Material: STR-002-GM3_REFRaME-O1 Patient Leave Behind (Spanish)	2.0	26Oct2023
Subject Information Sheet and Informed Consent Form			
L1	Main ICF (Spanish) *version for publication and version not for publication*	3.0	10Sep2024

I trust the information provided is adequate and complete, but should you have any queries about the submission content, please do not hesitate to contact me.

I look forward to receiving your response to this application.

Yours sincerely,

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