4 SYNOPSIS

Name of Sponsor: invoX Pharma Limited

Name of Finished Product: FS118

Name of Active Ingredient: Immunoglobulin G1 bispecific human monoclonal antibody for lymphocyte-activation gene 3 (LAG-3) and programmed death-ligand 1 (PD-L1)

Title of Study: A Phase 2 Open-Label Basket Study of FS118, a LAG-3/PD-L1 Bispecific Antibody, in Subjects with Advanced and Early-Stage Malignancies

Investigators: Donchev, Martin; Gastinne, Thomas; Giorgadze, Davit; Maglakelidze, Marina; Makharadze,Tamta; Michot, Jeran-Marie; Vinogradov, Igori.

Study Sites: Bulgaria (1), France (2), Georgia (3), Republic of Moldova (4).

Publications (references): (1) Jean-Marie Michot, Abhay Patki, Marina Maglakelidze, Regis Costello, Martin Donchev, Vincent Ribrag, Igori Vinogradov. Open-Label Phase 2 Study Results of FS118, a LAG-3/PD-L1 Bispecific Antibody, in Patients with Relapsed/Refractory Diffuse Large B-cell Lymphoma. Accepted for Presentation at 66th American Society of Hematology (ASH) Annual Meeting and Exposition, December 7–10, 2024, San Diego, CA, USA

Study Period: Approximately 34 months (First Patient First Visit: 26 January 2022; Last Patient Last Treatment: 15 August 2024; Last Patient Last Visit: 07 November 2024)

Phase of Development: Phase 2

Study Objectives and Endpoints:

The primary and secondary study objectives and endpoints are presented in Table 1. Due to early study termination, exploratory endpoints were not analyzed.

In addition, Cohort B was never initiated due to early study termination; therefore, for the purpose of this report, although Cohort B is presented per the Clinical Study Protocol (CSP), Cohort B will not be presented hereinafter within the results of this study report. For the complete list of exploratory objectives and endpoints, see the CSP (Appendix 16.1.1).

Table 1 Primary and Secondary Objectives and Endpoints

	Objectives	Endpoints
PRIMARY		
Cohort A: NSCLC		
Efficacy	• To assess the efficacy of FS118 in terms of radiological response in all subjects	• ORR as per RECIST v1.1
Cohort B: NSCLC WOO		
Biomarker/ Pharmacodynamic Markers	• To evaluate changes in specific T cell (e.g., CD8 T cells and Tregs) density (cells/mm^2) in tumor samples collected pre- and post-treatment with FS118. • To assess the ratio of CD8/Tregs in tumor samples collected pre-	• Change in tumor infiltrating T cells subtypes in response to FS118

	Objectives	Endpoints
	and post-treatment with FS118	
Cohort C: DLBCL		
Efficacy	• To assess the efficacy of FS118 in terms of radiological response	• ORR as per the Lugano Classification
SECONDARY		
Cohort A: NSCLC		
Efficacy	• To assess the efficacy of FS118 in all subjects by alternative endpoints	• Assessment of antitumor activity include DCR, DoR, DoC, and PFS/iPFS as assessed by RECIST v1.1 and iRECIST. • OS
PK	• To assess PK parameters for FS118	• PK endpoints include, but are not limited to the following parameters: Cycle 1: C_{max}, T_{max}, C_{trough}, AUC, $T_{1/2}$, $AUC_{0-\tau}$, C_{avg} (= $AUC_{0-\tau/\tau}$), CL, V_d, and R_{ac} for $AUC_{0-\tau}$ • Cycle 2 onwards: C_{max}, T_{max}, C_{trough}
Safety	• Assessment of the safety and tolerability of FS118	• Incidence, severity, and duration of AEs as defined by CTCAE v5.0
Cohort B: NSCLC WOO		
Efficacy	• Assessment of major pathological response (MPR) to pre-operative FS118 therapy in resected tumor and lymph nodes	• MPR defined as <10% residual viable tumor cells in the resection specimen
Efficacy	• Assessment of radiographic response to pre-operative FS118 therapy	• ORR assessed as per RECIST v1.1
Safety	• To assess the safety and tolerability of FS118 given in a pre-operative setting	• The number of subjects with Grade 2, 3 and 4 laboratory abnormalities, as defined by CTCAE v5.0 • The number of Grade 2, 3 and 4 AEs that occur while a subject is participating in the study, as defined by CTCAE v5.0
PK	• To assess PK parameters for FS118	• PK endpoints include, but are not limited to the following parameters: • Cycle 1: C_{max}, T_{max}, C_{trough}, AUC, $T_{1/2}$, $AUC_{0-\tau}$, C_{avg} (= $AUC_{0-\tau/\tau}$), CL, V_d, and R_{ac} for $AUC_{0-\tau}$
Biomarker/ Pharmacology/ Pharmacodynamic	• To evaluate soluble receptors (LAG-3 and PD-L1) following	• Fold induction of sLAG-3 and sPD-L1

	Objectives	Endpoints
	pre-operative FS118 therapy	
Cohort C: DLBCL		
Efficacy	• To assess the efficacy of FS118 in all subjects by alternative endpoints	• Assessments of antitumor activity include DCR, DoR, duration of disease control (DoC), and PFS as assessed by the Lugano Classification • OS
PK	• To assess PK parameters for FS118	• PK endpoints include, but are not limited to the following parameters: Cycle 1: C_{max}, T_{max}, C_{trough}, AUC, $T_{1/2}$, $AUC_{0-\tau}$, C_{avg} (= $AUC_{0-\tau/\tau}$), CL, V_d, and R_{ac} for $AUC_{0-\tau}$ • Cycle 2 onwards: C_{max}, T_{max}, C_{trough}
Safety	• Assessment of the safety and tolerability of FS118	• Incidence, severity, and duration of AEs as defined by CTCAE v5.0

Methodology:

This was a Phase 2 open-label basket study of FS118 in checkpoint inhibitor (CPI) naïve adult subjects with advanced and early-stage cancers. It consisted of multiple single-arm tumor-specific expansion cohorts and was primarily designed to assess efficacy in advanced cancers, initially CPI naïve NSCLC (Cohort A), DLBCL (Cohort C) and in pre-operative early-stage NSCLC (Cohorts B1 and B2). Cohort B (B1 and B2) and Cohort D was never initiated. Additionally, FS118 PK/PD data combined with other exploratory readouts were not investigated.

A schematic of the study design is presented in

Figure 1.