**Annex No. 6**
*to Methodological Norms*

**RO-Form describing the facilities of the investigational site for participation in the study _ V1_May 2022**

- **Protocol Title**: An Open-label Extension Study Evaluating the Long-term Safety and Efficacy of Seralutinib Orally Inhaled for the Treatment of Pulmonary Arterial Hypertension (PAH)
- **Protocol code**: GB002-3102
- **EU trial number**: 2023-506334-75-00
- **Name of site:** Institutul Inimii De Urgenta Pentru Boli Cardiovasculare "Niculae Stancioiu" Cluj-Napoca, Cardiologie 1
- **Adress**: Calea Motilor 19-21, 400001, Cluj-Napoca, România
- **Principal Investigator:** Raluca-Alina Rancea

| *Part I* |
|---|
| a) Please provide a comprehensive written statement regarding the suitability of the investigational site as to the nature and use of the investigational drug.<br><br>The Cardiology 1 department at "Niculae Stancioiu" Emergency Heart Institute for Cardiovascular Diseases Cluj-Napoca has enough staff availability with experience in management and treatment of Pulmonary Arterial Hypertension. The site has applicable equipment and qualified staff to conduct the study according to the applicable regulations and requirements.<br><br>IP management processes are in accordance with protocol/ICH-GCP/regulatory requirements. Delegated site personnel will receive the IP, they have secure storage (with restricted access to the dedicated clinical studies room), separate preparation/dispensation room, accountability is performed regularly after each administration or new IP shipment. The IP will be stored at controlled room temperature between 20°C and 25°C. There is a power generator in case of power outages at site. |
| *- provide the reasoning for choosing the healthcare unit/medical department depending on the specifics of the study, including the certifications of the healthcare unit*<br>**ASF (Autorizatie sanitara de functionare [Healthcare Operating Permit]): 284/19.06.2023.**<br><br>**Phase I authorization/bioequivalence:** *-Not Applicable*<br>**Quality assurance at the investigational site:**<br>The Principal Investigator has experience in coordinating clinical trials, informing and recruiting patients, source documentation and IP management.<br><br>For the conduct of the clinical trial, there will be dedicated staff available for the collection, processing and shipping of the samples to the central lab, for the 6-minute walk tests, ECG and all study assessments and procedures.<br><br>All the staff will be properly trained. |
| b) Please describe in detail the facilities in order to determine suitability |
| The place of investigation has:<br>- Facilities for admitting patients Yes |

- Specialized outpatient clinic Yes
- Immediate access to ICU Yes
- Immediate access to an emergency medical service Yes
- Its own medical laboratory Yes

- Suitable pharmacy/facilities for managing study medication Yes
- Is it clearly established who is responsible for study medication and accounting for medication ? Yes
-Is it clearly established who is responsible for processing biological samples for laboratory tests? Yes
-Are the source documents kept in a secure place and does the investigator have access to the source documents at all times? Yes
Source documents:
The site has the facilities to conduct the study according to Protocol and local regulation: location where subjects will be seen, special equipment location, monitoring room. Three treatment rooms and one emergency room are available at site. The access in these rooms is limited to site personnel (door access code).

It is clearly established who is responsible for study medication, medication counting and processing biological samples for laboratory analysis.

The source documents will be maintained in paper records. No records are being kept electronically. Site staff will keep source data in compliance with ALCOA/CCEA principles and ICH/GCP requirements.

c) Please describe accurately the suitability of the medical equipment

Site equipment and systems that will be used during the study are adequate according to study requirements and local regulations.

Equipment available at site: -20°C freezer, ECG machine, Min/max thermometers (for freezer and IP), echocardiography facility, weight device, height machine, fully automated sphygmomanometer, emergency equipment at site, emergency medications, automatic external defibrillator, cardio-pulmonary resuscitation staff, hallway (20 m) for 6MWT test.

The site has capacity to use a back-up during power outages.

Telephone/fax/copier/scanner/high-speed internet access is available.

d) Please provide a detailed description of all study procedures that will be performed at the investigational site.

Participants will sign the informed consent document(s), prior to completion of any procedures.

List of procedures to be done locally:

- Informed consent collection
- Eligibility criteria review
- Demography data collection
- Medical history review/collection
- PAH diagnosis and background PAH disease specific medication(s)
- Prior/concom. medications review
- Vital signs, body weight, height, and BMI
- Physical examination
- 12-lead electrocardiogram
- WHO FC assessment
- Six-minute walk test with Dyspnea Scale

- PFTs and DLCO
- Echocardiogram
- Head CT scan
- Assessment of Risk Score
- Assessment of Clinical Worsening
- EQ-5D-5L survey
- PAH-SYMPAC assessment
- Haematology, Clinical Chemistries, and Coagulation tests
- Serology and urine drug screen test
- NT-proBNP test
- Urinalysis
- Testosterone, LH, FSH, estradiol, and inhibin B tests
- LH, FSH, and estradiol tests
- Pregnancy test (WOCBP)
- Serum digoxin concentration test
- Biomarkers samples collection
- Seralutinib pharmacokinetic (PK) samples collection
- Background PAH disease specific medication PK samples collection
- Randomization
- IP dispensation
- Inhalation and DPI device training/re-training
- Dose Escalation

- Administer oral and/or inhaled background PAH disease-specific medication(s) in the clinic after 6MWT.
  - Collect used/unused IP and conduct accountability.
  - Adverse events collection
  - Study specific User Survey

- Physical evaluation: height, weight, vital signs, BMI, physical examination

- Lab samples collection (Hematology, Clinical Chemistries, and Coagulation;,; NT-proBNP; Urinalysis; Testosterone, LH, FSH, estradiol, and inhibin B; LH, FSH, and estradiol, Pregnancy test, Serum digoxin concentration, biomarkers, PK,)

- 12-lead electrocardiogram Pulmonary function tests and diffusion capacity of lungs for carbon monoxide

- 6-minute walk tests

Assessments: WHO FC assessment, Assessment of Risk Score, Assessment of Clinical Worsening, PAH-SYMPACT™ assessment.

e) information regarding Human Resources and expertise at the investigational site

Site has the adequate staff with time and availability to conduct the study as per the requirements.

**Principal Investigator:** Dr. Raluca-Alina Rancea, Senior Specialist in Cardiology

**Sub-Investigators :-**Dr. Mihai Cocoi, Sr. Specialist in Cardiology

- Dr. Sabina Istratoaie, Resident in Cardiology

***Part II***

By authorizing this document, I confirm that the necessary facilities and equipment [are] available at the investigational site and the investigational team is competent in terms of structure and training to carry out the clinical study, in accordance with EU Regulation 536/2014. I confirm that all identified conditions that could affect the impartiality of any investigators have been addressed

Principal Investigator: Raluca-Alina Rancea

Date: 13.03.2024

Signature: _____

Head *of department/clinic/ward* :

Date: 14.03.2024

Signature: _____

*Manager/General Manager/General Director* :

MANAGER
Jr. Florin Crișan

Date: 18.03.2024

Signature: _____