Visit 1: Screening / Pre-Treatment

Date of Visit: _____/_____/_____

INFORMED CONSENT:

Date Informed Consent signed: _____/_____/_____ Time signed: _____am / pm

Signed by: ☐ Patient ☐ Other: describe relationship: _____

Date Local required documents signed (if applicable): _____/_____/_____

Comments: _____

Narrative description of process (should include at least the following):

Patient or Legally Authorized Representative (LAR) was given sufficient time to read and evaluate ICF	☐
Patient / LAR expressed understanding of the following study details:	
Medication and condition under investigation, purpose of the study, and the approximate number of patients involved in the study	☐
Voluntary nature of participation, including the right to withdraw at any time for any reason without penalty or loss of benefits to which patient is otherwise entitled, and procedures for such withdrawal	☐
Possible risks and benefits; significant new developments during the course of the research which may affect the patient's willingness to continue participation will be provided to the patient	☐
Patient compensation for time and travel **OR** Patient informed that they will be not be compensated for time or travel *(dependent upon site-specific ICF)*	☐
Patient's rights and responsibilities	☐
Study visit schedule, including necessary tests and procedures	☐
Alternative treatments	☐
Confidentiality of study information, and who will have access to records	☐
Compensation and available medical treatments if injury occurs	☐
Anticipated circumstances under which the patient's participation may be terminated by the investigator without regard to the patient's consent	☐
Contact information in case of emergency (principal investigator), study-related questions (coordinator or investigator), and questions relating to patient rights (IRB)	☐
All questions were answered to the patient's / LAR's satisfaction and patient was informed of availability of principal investigator for further questions	☐
Patient / LAR expressed willingness to participate in research study	☐
A signed copy of the consent form was provided to the patient / LAR	☐
The original signed consent was filed in the patient's medical or research record	☐

CONSENT OBTAINED BY: _____ _____ ____/____/____
Printed Name and Qualification(s) ***Signature*** ***Date***

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*Patients will be eligible for inclusion into the study if they meet **all** of the following criteria:*

INCLUSION CRITERIA - ***If any answers are NO, the subject is <u>not eligible</u>***			
1	Male or female > 18 years of age with documented or verbal informed consent form	Yes ☐	No ☐
2	History or documentation of ticagrelor intake within the prior 3 days	Yes ☐	No ☐
3	Patients described below who require urgent reversal of the antiplatelet effects of ticagrelor: <u>Patients with uncontrolled major or life-threatening bleeding</u>, requiring urgent reversal of the antiplatelet effects of ticagrelor. It is expected that enrolled patients would have characteristics similar to those described below: • Potentially life-threatening bleeding with signs or symptoms of hemodynamic compromise, e.g., systolic blood pressure < 90 mm Hg and signs or symptoms of low cardiac output not otherwise explained • Bleeding in a critical organ or closed space, such as intracranial, intraspinal, intraocular, retroperitoneal, intra-articular, pericardial, or intramuscular bleed with compartment syndrome • Visible, uncontrolled bleeding associated with a corrected hemoglobin level < 8.0 g/dL, a fall in hemoglobin level of ≥ 2.0 g/dL (1.24 mmol/L) from a known baseline, or requirement for transfusion of 2 or more units of packed red blood cells (PRBC) **Other Reason:**	Yes ☐ Check all that apply ☐ ☐ ☐ ☐	No ☐
	OR		
	<u>Patients requiring urgent surgery or invasive procedure</u> when it is not medically advisable either to proceed urgently with impaired hemostasis or to delay the urgent procedure for 3 or more days due to the high risk of bleeding. These patients may typically be in any of the following clinical situations: • Requires urgent surgery or invasive procedure known to be associated with a risk of significant bleeding (such as cardiac surgery, neurosurgery, or major orthopedic surgery) • Requires urgent surgery or invasive procedure that may have an adverse procedural outcome if hemostasis is impaired (such as neurological, spinal, ophthalmological, urological, or orthopedic surgery) • At risk of experiencing life-threatening events, such as, shock, myocardial infarction, or stroke, if significant intraoperative or postoperative bleeding occurs (such as in elderly patients or patients with underlying cardiac or pulmonary disease who have limited cardiopulmonary reserve)	Yes ☐ Check all that apply ☐ ☐ ☐	No ☐

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EXCLUSION CRITERIA - ***If any answers are YES, the patient is <u>not eligible</u>***			
1	Known sensitivity or contraindication to PB2452 or any of its excipients	Yes ☐	No ☐
2	Patients in whom ticagrelor reversal is not considered urgent, e.g., patients with stable or non-acute conditions who have low hemoglobin due to chronic, low-grade gastrointestinal bleeding or who have stable, remote, or asymptomatic intracranial hemorrhage	Yes ☐	No ☐
3	Patients expected to be clinically unsalvageable, such as, patients with intracranial hemorrhage with Glasgow Coma Scale ≤ 8, or an intracerebral hematoma volume > 60 cc or patients with overwhelming sepsis	Yes ☐	No ☐
4	Any condition which, in the opinion of the investigator, would make it unsafe or unsuitable for the patients to participate in this study. This includes assessment of likelihood to cooperate with study follow-up visits and procedures • Known pregnancy may be exclusionary in some regions or countries as directed by national health authorities and/or local IRBs/Ethics Committees	Yes ☐	No ☐
5	Known use of clopidogrel, prasugrel, or ticlopidine within 5 days of study drug administration; known use of antiplatelet GPIIb/IIIa inhibitors, or cangrelor within 5 half lives of expected study drug administration; or known use of warfarin, dabigatran, rivaroxaban, apixaban, or edoxaban within 5 half-lives of expected study drug administration.	Yes ☐	No ☐
6	Known recent use (< 5 day) of vitamin K, prothrombin complex concentrate, recombinant factor VIIa, whole blood or plasma transfusions, idarucizumab, or andexanet-alfa (coagulation factor Xa (recombinant), inactivated-zhzo)	Yes ☐	No ☐

<u>PATIENT ELIGIBILITY CONFIRMATION</u>

By signing below, I confirm I have reviewed all available patient information.
This patient meets <u>ALL</u> Inclusion Criteria, <u>NO</u> Exclusion Criteria and <u>IS</u> eligible to enter the study:
☐ **Yes** ☐ **No*** ***If NO, the patient is a SCREEN FAILURE**

_____ _____ _____ /_____ /____
Investigator Name ***Investigator Signature*** ***Date***

I am signing as (check one):
Principal Investigator (PI) ☐ ***OR*** Sub-Investigator ☐

<u>Principal Investigator (PI) Confirmation</u>

If signature above is a Sub-Investigator, PI signature is required to signify review ☐ N/A

_____ _____ _____ /_____ /____
PI Printed Name ***PI Signature*** ***Date***

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DEMOGRAPHICS

Sex at birth:

☐ Male ☐ Female Date of Birth: _____/_____/_____

What ethnicity does patient identify as?

☐ Hispanic/Latino

☐ Not Hispanic/Latino

What race does the patient identify as?

☐ American Indian or Alaska Native

☐ Asian: if Asian:

☐ South Asian:

☐ Indian ☐ Pakistani ☐ Afghan

☐ East Asian

☐ Chinese ☐ Japanese ☐ Korean

☐ Other Asian: _____

☐ Black or African American

☐ Native Hawaiian or Other Pacific Islander

☐ White

☐ Other: _____

Has the patient previously been treated with PB2452: ☐ No ☐ Yes, if yes details:

_____

_____

_____

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MEDICAL HISTORY (Confirmed by Medical Records):

Please record all medical or surgical conditions within the last 3 years. Also include all other relevant past medical history including intracranial hemorrhages, cardiac conditions, thrombosis, bleeding events etc.

Condition / Diagnosis with additional information (if any)	Start Date	Stop Date or ongoing	Therapy* (Y/N)

** If condition is currently under therapy, please record details on Concomitant Therapy Page*

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TICAGRELOR HISTORY

How was Ticagrelor usage confirmed prior to administration of PB2452 (study medication):

☐ Patient ☐ Relative ☐ Medical Records ☐ Other

Please describe process for confirming ticagrelor use: _____

_____

Start date of ticagrelor: _____/_____/_____ Start time: _____am / pm ☐ Unknown

Date of last ticagrelor dose: _____/_____/_____ Time of last ticagrelor dose: _____am / pm

Dose of ticagrelor: _____mg Frequency: _____

Indication for ticagrelor:

☐ MI ☐ Percutaneous coronary interventions (PCI)

☐ Stroke ☐ Coronary artery bypass graft (CABG)

☐ Other: Specify: _____

ASPIRIN HISTORY ☐ NA

Start date of aspirin: _____/_____/_____ Start time: _____am / pm ☐ Unknown

Date of last aspirin dose: _____/_____/_____ Time of last aspirin dose: _____am / pm

Dose of aspirin: _____mg Frequency: _____

CYP3A INHIBITOR HISTORY ☐ NA

Is there recent history of concomitantly taking a **moderate** or **strong** CYP3A inhibitor? *(See protocol Appendix 4)*

CYP3A Name: _____

Start date of CYP3A: _____/_____/_____ Start time: _____am / pm ☐ Unknown

Date of last CYP3A dose: _____/_____/_____ ___Time of last CYP3A dose: _____am / pm

Is this a strong or moderate CYP3A inhibitor ☐ strong ☐ moderate

Indication for CYP3A: _____

PHYSICAL EXAMINATION:

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Height: _____cm/ in Weight: _____kg

Body System	Overall interpretation, findings, abnormalities etc.	*Clinically Significant?
Skin		
Lungs		
Cardiovascular		
Abdomen		
Upper Extremities		
Lower Extremities		
Other:		
Other:		
Other:		

*If any abnormal findings are clinically significant, record in medical history / baseline conditions:

<u>SIGNATURE SECTION</u> – Physical Examination Completed by:

_____ _____ ____/____/___

Printed name and qualification(s) Signature Date

Additional information: _____

_____

_____

_____

VITAL SIGNS

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Date vital signs completed: _____/_____/_____ Time completed: ____________am / pm

Blood pressure: ________ / _________mmHg Location: ☐ Arm ☐ Leg ☐ Right ☐ Left

Heart rate: _______________bpm Respiratory rate: __________breaths / min

Temperature: ______ ☐ °F or ☐ °C

Temperature Method: ☐ Oral ☐ Rectal ☐ Axillary ☐ Tympanic (Ear) ☐ Cutaneous Infrared ☐ Other: _______________________________

ECG

Was the ECG taken? ☐ Yes ☐ No: Specify reason: ___________________________________

Time of screening ECG: __________________

Subject Position:

☐ Supine ☐ Semi-Recumbent

☐ Sitting ☐ Other: ____

Tracing to be reviewed/assessed as clinically significant or non-clinically significant and initialized and dated by investigator; file original and record any findings judged clinically relevant in Medical History / Baseline Conditions.
Transcribe all findings from the ECG in EDC. QTcF and QTcB will be auto calculated in EDC

INTRACRANIAL HEMORRHAGE (ICH) PATIENTS ONLY ☐ NA

Standard of Care imaging: ☐ Yes ☐ No* Time completed: ____________am / pm

(Must be within 2 hours of study drug administration – the diagnostic scan may be repeated to meet this requirement)

**If* No*, reason:* ____

Diagnostic Scan Type: ☐ CT ☐ MRI

Scan with contrast: ☐ Yes ☐ No

Reminder: *1 (one) follow-up CT/MRI scan of the head is required between 12 and 24 hours after completion of the PB2452 infusion. The standard of care diagnostic CT/MRI scans taken at any other timepoint throughout the study will be collected as part of the eCRF.*

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PREGNANCY TEST – Taken Locally

Pregnancy test for women < 55 years old only or as clinically indicated. Day 1 (Visit 1) can be either a serum and/or a urine pregnancy test. ** If positive follow protocol guidance*

Pregnancy test performed ☐ N/A ☐ Yes ☐ No - comment: _____

Urine ☐ Serum ☐ *(if local requirement)*

Brand name of urine test: _____

Expiration date: _____

Result: ☐ Negative ☐ Positive* **Completed by (initials):_____**

END OF SCREENING REMINDERS!

Please complete the following additional source documents

- Central Laboratory Samples (see Laboratory Draw Worksheet) ☐ No ☐ Yes
- Bleeding Location and Hemostasis Assessment ☐ No ☐ Yes
- Surgery/Invasive Procedure Assessment ☐ No ☐ Yes
- Adverse Events ☐ No ☐ Yes
- Concomitant Therapies ☐ No ☐ Yes
- Blood Products and / or additional supportive treatments ☐ No ☐ Yes

Do not transcribe data points already captured in patient's medical records. Line through and initial duplicate sections above and indicate where source is located.

Additional Information: _____

_____

_____

_____

<u>SIGNATURE SECTION</u> – Visit 1 source documents completed by:

_____ _____ ____/____/____

Printed Name and qualification(s) Signature Date

<u>PI SIGNATURE SECTION</u> – Principal Investigator signature is required below to signify review:

_____ _____ ____/____/____

Printed Name Signature Date