Inclusion criteria

1) Subjects were ≥18 years of age and ≤65 years of age, with no gender requirement.
2) Pre-screening clinical diagnosis of chronic immune thrombocytopenia (cITP). Platelet count of < 30 × 10^9/L at the time of both screening and pre-administration visit (D0).
3) ITP diagnosed by bone marrow examination carried out within the screening period, excluding myelodysplastic syndrome (MDS), immune diseases such as systemic lupus erythematosus (SLE), early aplastic anemia (AA), atypical aplastic anemia, thrombocytopenic purpura (TTP), pseudo thrombocytopenia, and secondary thrombocytopenia (STP) caused by other reasons.
4) The patient has poor response to at least one ITP therapy or relapses after treatment. Past treatments for chronic ITP include, but are not limited to, corticosteroids, immunomodulators (intravenous gamma globulin or anti-D immunoglobulin), azathioprine, danazol, cyclophosphamide and immunomodulators, and splenectomy.
5) Past rescue treatments for ITP (include but not limited to corticosteroids, immunoglobulins, immunomodulators, and cyclophosphamide) must be completed at least 2 weeks pre-administration (refer to item 4 in inclusion criteria).
6) Patients receiving immunosuppressants (including but not limited to corticosteroids, azathioprine, danazol, cyclosporin A, mycophenolate mofetil) for maintenance treatment must have a stable dose at least 4 weeks before the study.
7) Prothrombin time (PT) does not exceed the normal value range by ± 3 s; activated partial thromboplastin time (APTT) does not exceed the normal value range by ± 10 s; there was no history of other coagulopathy except ITP.
8) The whole blood cell count was within the reference value range (those with a whole blood cell count exceeding the reference value range can be enrolled if they are judged as “abnormal but not clinically significant” by the Investigator. e.g., abnormalities caused by corticosteroids), but the following conditions should be treated specially:
   • Platelet count of <30 × 10^9/L meets the inclusion criteria.
   • Hemoglobin: female and male with ≥10 g/dL meet the inclusion criteria.
   • Those with an absolute neutrophil count (ANC) of ≥1,500/µL (1.5 × 10^9/L) can be enrolled.
9) Patients with potential fertility (i.e., except for females undergoing hysterectomy, bilateral salpingectomy, bilateral tubal ligation or more than 1 year after menopause; males undergoing bilateral vasectomy) must take effective contraceptive measures in at least two weeks before the first administration of the investigational drug, during the entire study period, and within 28 days after the end of the study (or early study termination).
10) Women with potential fertility must be negative for a pregnancy test during the screening period and on D0 of the study.
11) Understand the study procedures and voluntarily agree to sign the informed consent form in writing.

Exclusion criteria (those who meet any of the followings are ineligible)

1) The patient has experienced any arterial or venous thrombosis (stroke, transient ischemic attack, myocardial infarction, deep vein thrombosis or pulmonary embolism) or has clinical symptoms and medical history suggesting thromboembolic disorders.
2) History of malignant tumors.
3) Heart disease within the past 3 months, including NHYA grade III/IV congestive heart failure and arrhythmias requiring medical treatment. Or any of the following: arrhythmias (such as atrial fibrillation) known to increase the risk of a thrombotic event, or patients with a corrected QT interval (QTc) of >450 msec (QTc of >480 msec for patients with bundle branch block).
4) Pregnant or lactating women.
5) Participated in the treatment of other investigational drugs within 30 days or 5 half-lives (whichever is longer) before the first administration of the investigational drug.
6) Have received within 30 days or 5 half-lives (whichever is longer) before the first administration of the investigational drug or are currently receiving treatment with eltrombopag or any other thrombopoietin receptor agonist.
7) Patients who had received rituximab and splenectomy within 6 months before the first administration of the
investigational drug.

8) Within 2 weeks before the start of the study, subjects have continuously used medications affecting platelet functions (including but not limited to aspirin, aspirin-containing complexes, clopidogrel, salicylate, and/or non-steroidal anti-inflammatory drugs (NSAIDs) or anticoagulants for more than 3 days.

9) Clinical history of all laboratory or clinical HIV infections and past hepatitis C infections, chronic hepatitis B infections, or evidence of active hepatitis found during screening. Laboratory tests carried out during the screening period suggest hepatitis C or hepatitis B infection.

10) The following blood biochemistry indicators: ALT and AST are more than 1.5 times the upper limit of normal; total bilirubin, blood creatinine and alkaline phosphatase are more than 1.2 times the upper limit of normal; serum albumin lower than 10% the lower limit of normal;

11) Clinical findings of abnormalities other than ITP or any medical history or condition in the screening stage deemed by the Investigator as unsuitable for participation in this study.
**Table S1** Participating sites

| Principal investigator | Institution                                                                 | Number of patients | Ethics committee approval number/ID |
|------------------------|-----------------------------------------------------------------------------|--------------------|-------------------------------------|
| Xiequn Chen            | The First Affiliated Hospital of Air Force Medical University, Xi'an, China  | 14                 | YS20160713-1                       |
| Yu Hu/ Heng Mei        | Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China | 11                 | 2015-110-2                         |
| Jianfeng Zhou          | Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China | 5                  | 2015-110-3                         |
| Jianmin Luo            | The Second Hospital of Hebei Medical University, Shijiazhuang, China          | 3                  | 2015EC10-03-XZ-3                   |
| Qingzhi Shi            | The Second Affiliated Hospital of Nanchang University, Nanchang, China        | 1                  | None                               |
| Hua Lu                 | The First Affiliated Hospital of Nanjing Medical University, Jiangsu Province Hospital, Nanjing, China | 1                  | 2015-MD-158.A2                     |
| Jing Liu               | The Third Xiangya Hospital of Central South University, Changsha, China       | 1                  | 16029                              |
| Depei Wu               | The First Affiliated Hospital of Soochow University, Suzhou, China            | 1                  | 2015-068-2                         |

**Table S2** Dose modification scheme of hetrombopag

| Weeks     | Current dose | Platelet counts | Dose should be interrupted until platelet counts reach ≤150×10^9/L, and then mg was given |
|-----------|--------------|-----------------|-----------------------------------------------------------------------------------------|
| Week 0-2  | 5 mg         | 5 mg            | 3.75 mg reduce to 3.75 mg                                                                 |
|           |              | ≥50×10^9/L       |                                                                                         |
|           |              | 100×10^9/L       |                                                                                         |
| Week 3-6  | 2.5 mg       | increase to 3.75 mg | 2.5 mg reduce to 2.5 mg                                                                  |
|           |              | ≥200×10^9/L      |                                                                                         |
| 3.75 mg   | increase to 5 mg | 3.75 mg reduce to 2.5 mg |                                                                                         |
| 5 mg      | increase to 7.5 mg | 5 mg reduce to 3.75 mg |                                                                                         |
| 7.5 mg    | 7.5 mg       | 7.5 mg reduce to 5 mg |                                                                                         |

All doses were give once daily.
### Table S3: Treatment interruption and dose modification per protocol

| Patients (n=37) |
|----------------|
| Treatment interruption | 4 (10.8%) |
| Duration of treatment interruption, days |
| Median (IQR) | 10.0 (8.0–11.0) |
| Mean±SD | 9.5±1.9 |
| Final dose |
| 2.5 mg once every other day | 1 (2.7%) |
| 2.5 mg once daily | 4 (10.8%) |
| 3.75 mg once daily | 4 (10.8%) |
| 5 mg once daily | 9 (24.3%) |
| 7.5 mg once daily | 19 (51.4%) |
| Dose, mg/d |
| Median (IQR) | 5.9 (4.2–6.7) |
| Mean±SD | 5.5±1.3 |
| Dose adjustment times |
| 0 | 2 (5.4%) |
| 1 | 22 (59.5%) |
| 2 | 7 (18.9%) |
| 3 | 2 (5.4%) |
| 4 | 2 (5.4%) |
| 6 | 2 (5.4%) |

Data are presented as n (%), unless otherwise specified.
Table S4  Treatment-related adverse events

|                                | Patients (n=37) |
|--------------------------------|-----------------|
|                                | Any grade       | Grade 3-4      |
| Any                            | 13 (35.1%)      | 2 (5.4%)       |
| Blood lactate dehydrogenase increased | 5 (13.5%)    | 0              |
| Alanine aminotransferase increased | 4 (10.8%)      | 1 (2.7%)       |
| Aspartate aminotransferase increased | 2 (5.4%)       | 0              |
| Blood uric acid increased      | 2 (5.4%)        | 0              |
| Alpha hydroxybutyrate dehydrogenase increased | 1 (2.7%)     | 0              |
| Gamma-glutamyltransferase increased | 1 (2.7%)      | 0              |
| Bilirubin conjugated increased | 1 (2.7%)        | 0              |
| Blood bilirubin increased      | 1 (2.7%)        | 0              |
| Blood pressure increased       | 1 (2.7%)        | 0              |
| Hyperuricemia                  | 1 (2.7%)        | 1 (2.7%)       |
| Decreased appetite             | 1 (2.7%)        | 0              |
| Somnolence                     | 1 (2.7%)        | 0              |
| Headache                       | 1 (2.7%)        | 0              |
| Face edema                     | 1 (2.7%)        | 0              |
| Fatigue                        | 1 (2.7%)        | 0              |
| Edema peripheral               | 1 (2.7%)        | 0              |
| Nausea                         | 1 (2.7%)        | 0              |
| Abdominal distension           | 1 (2.7%)        | 0              |
| Back pain                      | 1 (2.7%)        | 0              |
| Optic atrophy                  | 1 (2.7%)        | 0              |

Data are presented as n (%). The treatment-related adverse events refers to the correlation of the adverse events with study treatment was “definitely related”, “possibly related”, or “unassessable”, as judged by investigators.