



## Clinical trial results:

**A Phase 3, Prospective, Randomized, Controlled, Open-Label, Multicenter, 2 Period Crossover Study With a Single Arm Continuation Evaluating the Safety and Efficacy of BAX 930 (rADAMTS13) in the Prophylactic and On-Demand Treatment of Subjects with Severe Congenital Thrombotic Thrombocytopenic Purpura (cTTP, Upshaw-Schulman Syndrome [USS], Hereditary Thrombotic Thrombocytopenic Purpura [hTTP])**

### Summary

|                          |                                     |
|--------------------------|-------------------------------------|
| EudraCT number           | 2017-000858-18                      |
| Trial protocol           | GB DE ES AT FR IT PL Outside EU/EEA |
| Global end of trial date | 30 May 2024                         |

### Results information

|                                |                                                     |
|--------------------------------|-----------------------------------------------------|
| Result version number          | v2                                                  |
| This version publication date  | 29 March 2025                                       |
| First version publication date | 13 December 2024                                    |
| Version creation reason        | • Correction of full data set<br>Updates to AE data |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 281102 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03393975 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |                                                                  |
|------------------------------|------------------------------------------------------------------|
| Sponsor organisation name    | Takeda Development Center Americas, Inc.                         |
| Sponsor organisation address | 95 Hayden Avenue, Lexington, Massachusetts, United States, 02421 |
| Public contact               | Study Director, Takeda, N/A N/A, TrialDisclosures@takeda.com     |
| Scientific contact           | Study Director, Takeda, N/A N/A, TrialDisclosures@takeda.com     |

Notes:

### Paediatric regulatory details

|                                                                      |                     |
|----------------------------------------------------------------------|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-001160-PIP01-11 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No                  |

|                                                                      |    |
|----------------------------------------------------------------------|----|
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
|----------------------------------------------------------------------|----|

Notes:

## Results analysis stage

|                                                      |             |
|------------------------------------------------------|-------------|
| Analysis stage                                       | Final       |
| Date of interim/final analysis                       | 30 May 2024 |
| Is this the analysis of the primary completion data? | No          |

|                                  |             |
|----------------------------------|-------------|
| Global end of trial reached?     | Yes         |
| Global end of trial date         | 30 May 2024 |
| Was the trial ended prematurely? | No          |

Notes:

## General information about the trial

Main objective of the trial:

To determine the incidence of acute TTP episodes in subjects with severe cTTP receiving either standard of care (SoC) or BAX 930 as a prophylactic treatment.

Protection of trial subjects:

Each participant or legally authorized representative signed an informed consent form (ICF) before participating in the study.

Background therapy:

N/A

Evidence for comparator:

N/A

|                                                           |                 |
|-----------------------------------------------------------|-----------------|
| Actual start date of recruitment                          | 13 October 2017 |
| Long term follow-up planned                               | No              |
| Independent data monitoring committee (IDMC) involvement? | Yes             |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Germany: 4         |
| Country: Number of subjects enrolled | France: 8          |
| Country: Number of subjects enrolled | Italy: 1           |
| Country: Number of subjects enrolled | Japan: 5           |
| Country: Number of subjects enrolled | Spain: 6           |
| Country: Number of subjects enrolled | Austria: 1         |
| Country: Number of subjects enrolled | Poland: 6          |
| Country: Number of subjects enrolled | United Kingdom: 12 |
| Country: Number of subjects enrolled | United States: 11  |
| Worldwide total number of subjects   | 54                 |
| EEA total number of subjects         | 26                 |

Notes:

| <b>Subjects enrolled per age group</b>    |    |
|-------------------------------------------|----|
| In utero                                  | 0  |
| Preterm newborn - gestational age < 37 wk | 0  |
| Newborns (0-27 days)                      | 0  |
| Infants and toddlers (28 days-23 months)  | 0  |
| Children (2-11 years)                     | 9  |
| Adolescents (12-17 years)                 | 4  |
| Adults (18-64 years)                      | 40 |
| From 65 to 84 years                       | 1  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Participants took part in the study at various investigative sites globally from 13 October 2017 to 30 May 2024.

### Pre-assignment

Screening details:

Participants with a diagnosis of cTTP were enrolled in either prophylaxis/on demand cohorts. All participants received intravenous infusion of TAK-755/standard treatment in Prophylaxis Periods 1&2,&TAK-755 in Prophylaxis Period 3(hereafter Prophylaxis Periods 1, 2,&3 are referred to simply as Periods 1, 2, and 3).

### Period 1

|                              |                         |
|------------------------------|-------------------------|
| Period 1 title               | Urgent Treatment Period |
| Is this the baseline period? | Yes                     |
| Allocation method            | Randomised - controlled |
| Blinding used                | Not blinded             |

### Arms

|                              |                             |
|------------------------------|-----------------------------|
| Are arms mutually exclusive? | No                          |
| <b>Arm title</b>             | On Demand Cohort I: TAK-755 |

Arm description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the TAK-755 cohort of the Urgent Treatment Period received initial dose of IV infusions 40 IU/kg [ $\pm$  4 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 1 followed by a subsequent dose IV infusion of 20 IU/kg [ $\pm$  2 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 2 and an additional daily dose IV infusions of 15 IU/kg [ $\pm$  1.5 IU/kg] TAK-755 on Day 3 until 2 days after the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.

|                                        |                 |
|----------------------------------------|-----------------|
| Arm type                               | Experimental    |
| Investigational medicinal product name | TAK-755         |
| Investigational medicinal product code |                 |
| Other name                             | BAK-930         |
| Pharmaceutical forms                   | Injection       |
| Routes of administration               | Intravenous use |

Dosage and administration details:

Daily

|                  |                          |
|------------------|--------------------------|
| <b>Arm title</b> | On Demand Cohort II: SoC |
|------------------|--------------------------|

Arm description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the SoC cohort of the Urgent Treatment Period received the investigator-recommended SoC and dosing regimen until the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.

|                                        |                  |
|----------------------------------------|------------------|
| Arm type                               | Experimental     |
| Investigational medicinal product name | Standard of care |
| Investigational medicinal product code |                  |
| Other name                             |                  |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Intravenous use  |

Dosage and administration details:

Daily

| <b>Number of subjects in period 1</b> | On Demand Cohort I: TAK-755 | On Demand Cohort II: SoC |
|---------------------------------------|-----------------------------|--------------------------|
| Started                               | 2                           | 4                        |
| Completed                             | 2                           | 3                        |
| Not completed                         | 0                           | 1                        |
| Physician decision                    | -                           | 1                        |

## Period 2

|                              |                         |
|------------------------------|-------------------------|
| Period 2 title               | Prophylaxis Period 1    |
| Is this the baseline period? | No                      |
| Allocation method            | Randomised - controlled |
| Blinding used                | Not blinded             |

## Arms

|                              |                                        |
|------------------------------|----------------------------------------|
| Are arms mutually exclusive? | Yes                                    |
| <b>Arm title</b>             | Prophylaxis Cohort I: TAK-755 Then SoC |

### Arm description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in Period 1 followed by SoC for 6 months in Period 2. Thereafter participants received TAK-755 SIN dose IV infusion of 40 IU/kg Q2W for 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

|                                        |                 |
|----------------------------------------|-----------------|
| Arm type                               | Experimental    |
| Investigational medicinal product name | TAK-755         |
| Investigational medicinal product code |                 |
| Other name                             | BAX-930         |
| Pharmaceutical forms                   | Injection       |
| Routes of administration               | Intravenous use |

### Dosage and administration details:

Daily

|                  |                                         |
|------------------|-----------------------------------------|
| <b>Arm title</b> | Prophylaxis Cohort II: SoC Then TAK-755 |
|------------------|-----------------------------------------|

### Arm description:

Participants received SoC for 6 months in Period 1 followed by IV infusions of 40 IU/kg dose of TAK-755 ORT Q2W in Period 2 for the next 6 months. Thereafter participants received TAK-755 SIN dose IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

|                                        |                  |
|----------------------------------------|------------------|
| Arm type                               | Experimental     |
| Investigational medicinal product name | Standard of care |
| Investigational medicinal product code |                  |
| Other name                             |                  |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Intravenous use  |

### Dosage and administration details:

Daily

| Number of subjects in period 2 | Prophylaxis Cohort I: TAK-755 Then SoC | Prophylaxis Cohort II: SoC Then TAK-755 |
|--------------------------------|----------------------------------------|-----------------------------------------|
| Started                        | 22                                     | 26                                      |
| Completed                      | 22                                     | 25                                      |
| Not completed                  | 0                                      | 1                                       |
| Reason not Specified           | -                                      | 1                                       |

### Period 3

|                              |                         |
|------------------------------|-------------------------|
| Period 3 title               | Prophylaxis Period 2    |
| Is this the baseline period? | No                      |
| Allocation method            | Randomised - controlled |
| Blinding used                | Not blinded             |

### Arms

|                              |                                        |
|------------------------------|----------------------------------------|
| Are arms mutually exclusive? | Yes                                    |
| <b>Arm title</b>             | Prophylaxis Cohort I: TAK-755 Then SoC |

#### Arm description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in Period 1 followed by SoC for 6 months in Period 2. Thereafter participants received TAK-755 SIN dose IV infusion of 40 IU/kg Q2W for 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

|                                        |                  |
|----------------------------------------|------------------|
| Arm type                               | Experimental     |
| Investigational medicinal product name | Standard of care |
| Investigational medicinal product code |                  |
| Other name                             |                  |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Intravenous use  |

#### Dosage and administration details:

Daily

|                  |                                         |
|------------------|-----------------------------------------|
| <b>Arm title</b> | Prophylaxis Cohort II: SoC Then TAK-755 |
|------------------|-----------------------------------------|

#### Arm description:

Participants received SoC for 6 months in Period 1 followed by IV infusions of 40 IU/kg dose of TAK-755 ORT Q2W in Period 2 for the next 6 months. Thereafter participants received TAK-755 SIN dose IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

|                                        |                 |
|----------------------------------------|-----------------|
| Arm type                               | Experimental    |
| Investigational medicinal product name | TAK-755         |
| Investigational medicinal product code |                 |
| Other name                             | BAX-930         |
| Pharmaceutical forms                   | Injection       |
| Routes of administration               | Intravenous use |

#### Dosage and administration details:

Daily

| <b>Number of subjects in period 3</b> | Prophylaxis Cohort I: TAK-755 Then SoC | Prophylaxis Cohort II: SoC Then TAK-755 |
|---------------------------------------|----------------------------------------|-----------------------------------------|
| Started                               | 22                                     | 25                                      |
| Completed                             | 22                                     | 24                                      |
| Not completed                         | 0                                      | 1                                       |
| Reason not Specified                  | -                                      | 1                                       |

#### Period 4

|                              |                         |
|------------------------------|-------------------------|
| Period 4 title               | Prophylaxis Period 3    |
| Is this the baseline period? | No                      |
| Allocation method            | Randomised - controlled |
| Blinding used                | Not blinded             |

#### Arms

|                              |                                        |
|------------------------------|----------------------------------------|
| Are arms mutually exclusive? | Yes                                    |
| <b>Arm title</b>             | Prophylaxis Cohort I: TAK-755 Then SoC |

##### Arm description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in Period 1 followed by SoC for 6 months in Period 2. Thereafter participants received TAK-755 SIN dose IV infusion of 40 IU/kg Q2W for 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

|                                        |                 |
|----------------------------------------|-----------------|
| Arm type                               | Experimental    |
| Investigational medicinal product name | Tak-755         |
| Investigational medicinal product code |                 |
| Other name                             | Bax-930         |
| Pharmaceutical forms                   | Injection       |
| Routes of administration               | Intravenous use |

##### Dosage and administration details:

Daily

|                  |                                         |
|------------------|-----------------------------------------|
| <b>Arm title</b> | Prophylaxis Cohort II: SoC Then TAK-755 |
|------------------|-----------------------------------------|

##### Arm description:

Participants received SoC for 6 months in Period 1 followed by IV infusions of 40 IU/kg dose of TAK-755 ORT Q2W in Period 2 for the next 6 months. Thereafter participants received TAK-755 SIN dose IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

|                                        |                 |
|----------------------------------------|-----------------|
| Arm type                               | Experimental    |
| Investigational medicinal product name | TAK-755         |
| Investigational medicinal product code |                 |
| Other name                             | BAX-930         |
| Pharmaceutical forms                   | Injection       |
| Routes of administration               | Intravenous use |

##### Dosage and administration details:

Daily

| <b>Number of subjects in period 4</b> | Prophylaxis Cohort<br>I: TAK-755 Then<br>SoC | Prophylaxis Cohort<br>II: SoC Then TAK-<br>755 |
|---------------------------------------|----------------------------------------------|------------------------------------------------|
| Started                               | 22                                           | 24                                             |
| Completed                             | 22                                           | 24                                             |



## Baseline characteristics

### Reporting groups<sup>[1]</sup>

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | On Demand Cohort I: TAK-755 |
|-----------------------|-----------------------------|

#### Reporting group description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the TAK-755 cohort of the Urgent Treatment Period received initial dose of IV infusions 40 IU/kg [ $\pm$  4 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 1 followed by a subsequent dose IV infusion of 20 IU/kg [ $\pm$  2 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 2 and an additional daily dose IV infusions of 15 IU/kg [ $\pm$  1.5 IU/kg] TAK-755 on Day 3 until 2 days after the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.

|                       |                          |
|-----------------------|--------------------------|
| Reporting group title | On Demand Cohort II: SoC |
|-----------------------|--------------------------|

#### Reporting group description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the SoC cohort of the Urgent Treatment Period received the investigator-recommended SoC and dosing regimen until the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.

#### Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.

Justification: The arms reported in the baseline period represent only the On Demand cohorts of this study.

| Reporting group values                    | On Demand Cohort I: TAK-755 | On Demand Cohort II: SoC | Total |
|-------------------------------------------|-----------------------------|--------------------------|-------|
| Number of subjects                        | 2                           | 4                        | 6     |
| Age categorical                           |                             |                          |       |
| Units: Subjects                           |                             |                          |       |
| ≥18 years                                 | 2                           | 3                        | 5     |
| 12 to <18 years                           | 0                           | 0                        | 0     |
| 6 to <12 years                            | 0                           | 0                        | 0     |
| <6 years                                  | 0                           | 1                        | 1     |
| Gender categorical                        |                             |                          |       |
| Units: Subjects                           |                             |                          |       |
| Female                                    | 1                           | 1                        | 2     |
| Male                                      | 1                           | 3                        | 4     |
| Race (NIH/OMB)                            |                             |                          |       |
| Units: Subjects                           |                             |                          |       |
| American Indian or Alaska Native          | 0                           | 0                        | 0     |
| Asian                                     | 1                           | 0                        | 1     |
| Native Hawaiian or Other Pacific Islander | 0                           | 0                        | 0     |
| Black or African American                 | 0                           | 1                        | 1     |
| White                                     | 1                           | 2                        | 3     |
| More than one race                        | 0                           | 1                        | 1     |
| Unknown or Not Reported                   | 0                           | 0                        | 0     |
| Ethnicity (NIH/OMB)                       |                             |                          |       |
| Units: Subjects                           |                             |                          |       |
| Hispanic or Latino                        | 0                           | 0                        | 0     |
| Not Hispanic or Latino                    | 2                           | 4                        | 6     |
| Unknown or Not Reported                   | 0                           | 0                        | 0     |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                         |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | On Demand Cohort I: TAK-755             |
| Reporting group description:<br>Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the TAK-755 cohort of the Urgent Treatment Period received initial dose of IV infusions 40 IU/kg [ $\pm$ 4 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 1 followed by a subsequent dose IV infusion of 20 IU/kg [ $\pm$ 2 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 2 and an additional daily dose IV infusions of 15 IU/kg [ $\pm$ 1.5 IU/kg] TAK-755 on Day 3 until 2 days after the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely. |                                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | On Demand Cohort II: SoC                |
| Reporting group description:<br>Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the SoC cohort of the Urgent Treatment Period received the investigator-recommended SoC and dosing regimen until the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.                                                                                                                                                                                                                                                              |                                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Prophylaxis Cohort I: TAK-755 Then SoC  |
| Reporting group description:<br>Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in Period 1 followed by SoC for 6 months in Period 2. Thereafter participants received TAK-755 SIN dose IV infusion of 40 IU/kg Q2W for 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.                                                                                                                                                                                                                                                                                                                  |                                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Prophylaxis Cohort II: SoC Then TAK-755 |
| Reporting group description:<br>Participants received SoC for 6 months in Period 1 followed by IV infusions of 40 IU/kg dose of TAK-755 ORT Q2W in Period 2 for the next 6 months. Thereafter participants received TAK-755 SIN dose IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.                                                                                                                                                                                                                                                                                                |                                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Prophylaxis Cohort I: TAK-755 Then SoC  |
| Reporting group description:<br>Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in Period 1 followed by SoC for 6 months in Period 2. Thereafter participants received TAK-755 SIN dose IV infusion of 40 IU/kg Q2W for 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.                                                                                                                                                                                                                                                                                                                  |                                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Prophylaxis Cohort II: SoC Then TAK-755 |
| Reporting group description:<br>Participants received SoC for 6 months in Period 1 followed by IV infusions of 40 IU/kg dose of TAK-755 ORT Q2W in Period 2 for the next 6 months. Thereafter participants received TAK-755 SIN dose IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.                                                                                                                                                                                                                                                                                                |                                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Prophylaxis Cohort I: TAK-755 Then SoC  |
| Reporting group description:<br>Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in Period 1 followed by SoC for 6 months in Period 2. Thereafter participants received TAK-755 SIN dose IV infusion of 40 IU/kg Q2W for 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.                                                                                                                                                                                                                                                                                                                  |                                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Prophylaxis Cohort II: SoC Then TAK-755 |
| Reporting group description:<br>Participants received SoC for 6 months in Period 1 followed by IV infusions of 40 IU/kg dose of TAK-755 ORT Q2W in Period 2 for the next 6 months. Thereafter participants received TAK-755 SIN dose IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.                                                                                                                                                                                                                                                                                                |                                         |
| Subject analysis set title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Prophylaxis Cohort: TAK-755             |
| Subject analysis set type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Sub-group analysis                      |
| Subject analysis set description:<br>Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                         |

or Period 2. Thereafter participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

|                            |                             |
|----------------------------|-----------------------------|
| Subject analysis set title | On Demand Cohort I: TAK-755 |
| Subject analysis set type  | Sub-group analysis          |

Subject analysis set description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the TAK-755 cohort of the Urgent Treatment Period received initial dose of IV infusions 40 IU/kg [ $\pm$  4 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 1 followed by a subsequent dose IV infusions of 20 IU/kg [ $\pm$  2 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 2 and an additional daily dose IV infusions of 15 IU/kg [ $\pm$  1.5 IU/kg] TAK-755 on Day 3 until 2 days after the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.

|                            |                             |
|----------------------------|-----------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 |
| Subject analysis set type  | Sub-group analysis          |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. Thereafter participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

|                            |                         |
|----------------------------|-------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC |
| Subject analysis set type  | Sub-group analysis      |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

|                            |                             |
|----------------------------|-----------------------------|
| Subject analysis set title | On Demand Cohort I: TAK-755 |
| Subject analysis set type  | Sub-group analysis          |

Subject analysis set description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the TAK-755 cohort of the Urgent Treatment Period received initial dose of IV infusions 40 IU/kg [ $\pm$  4 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 1 followed by a subsequent dose IV infusion of 20 IU/kg [ $\pm$  2 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 2 and an additional daily dose IV infusions of 15 IU/kg [ $\pm$  1.5 IU/kg] TAK-755 on Day 3 until 2 days after the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.

|                            |                          |
|----------------------------|--------------------------|
| Subject analysis set title | On Demand Cohort II: SoC |
| Subject analysis set type  | Sub-group analysis       |

Subject analysis set description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the SoC cohort of the Urgent Treatment Period received the investigator-recommended SoC and dosing regimen until the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.

|                            |                                 |
|----------------------------|---------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 SIN |
| Subject analysis set type  | Sub-group analysis              |

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.

|                            |                                 |
|----------------------------|---------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 SIN |
| Subject analysis set type  | Sub-group analysis              |

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.

|                            |                                           |
|----------------------------|-------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                        |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

|                            |                                           |
|----------------------------|-------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                        |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

|                            |                                           |
|----------------------------|-------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                        |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

|                            |                                           |
|----------------------------|-------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                        |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

|                            |                                           |
|----------------------------|-------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                        |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

|                            |                                           |
|----------------------------|-------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                        |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

|                            |                                           |
|----------------------------|-------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                        |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

|                            |                                           |
|----------------------------|-------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                        |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

|                            |                                           |
|----------------------------|-------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                        |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

|                            |                                   |
|----------------------------|-----------------------------------|
| Subject analysis set title | Prophylaxis Cohort I: TAK-755 SIN |
| Subject analysis set type  | Sub-group analysis                |

Subject analysis set description:

Participants received TAK-755 SIN prophylactic dose of IV infusions of 40 IU/kg for another 6 months in Period 3.

|                            |                                   |
|----------------------------|-----------------------------------|
| Subject analysis set title | Prophylaxis Cohort I: TAK-755 SIN |
| Subject analysis set type  | Sub-group analysis                |

Subject analysis set description:

Participants received TAK-755 SIN prophylactic dose of IV infusions of 40 IU/kg for another 6 months in Period 3.

|                            |                                   |
|----------------------------|-----------------------------------|
| Subject analysis set title | Prophylaxis Cohort I: TAK-755 SIN |
| Subject analysis set type  | Sub-group analysis                |

Subject analysis set description:

Participants received TAK-755 SIN prophylactic dose of IV infusions of 40 IU/kg for another 6 months in Period 3.

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|----------------------------|-----------------------------------|
| Subject analysis set title | Prophylaxis Cohort I: TAK-755 ORT |
| Subject analysis set type  | Sub-group analysis                |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT once Q2W for 6 months in either Period 1 or Period 2.

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|----------------------------|-----------------------------------|
| Subject analysis set title | Prophylaxis Cohort I: TAK-755 SIN |
| Subject analysis set type  | Sub-group analysis                |

Subject analysis set description:

Participants received TAK-755 SIN prophylactic dose of IV infusions of 40 IU/kg for another 6 months in Period 3.

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|----------------------------|---------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755-ORT |
| Subject analysis set type  | Sub-group analysis              |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria.

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|----------------------------|---------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755-SIN |
| Subject analysis set type  | Sub-group analysis              |

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.

|                            |                         |
|----------------------------|-------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC |
| Subject analysis set type  | Sub-group analysis      |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

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|----------------------------|---------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755-ORT |
| Subject analysis set type  | Sub-group analysis              |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria.

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|----------------------------|---------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755-SIN |
| Subject analysis set type  | Sub-group analysis              |

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.

|                            |                         |
|----------------------------|-------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC |
| Subject analysis set type  | Sub-group analysis      |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

|                            |                             |
|----------------------------|-----------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 |
| Subject analysis set type  | Sub-group analysis          |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. Thereafter participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

|                            |                         |
|----------------------------|-------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC |
| Subject analysis set type  | Sub-group analysis      |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

|                            |                             |
|----------------------------|-----------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 |
| Subject analysis set type  | Sub-group analysis          |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. Thereafter participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

|                            |                         |
|----------------------------|-------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC |
| Subject analysis set type  | Sub-group analysis      |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

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|----------------------------|---------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 ORT |
| Subject analysis set type  | Sub-group analysis              |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria.

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|----------------------------|-------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC |
| Subject analysis set type  | Sub-group analysis      |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2. (except for PK-II where they did not receive SoC).

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|----------------------------|---------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 ORT |
| Subject analysis set type  | Sub-group analysis              |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria.

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|----------------------------|-------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC |
| Subject analysis set type  | Sub-group analysis      |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

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|----------------------------|---------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 ORT |
| Subject analysis set type  | Sub-group analysis              |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria.

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|----------------------------|---------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 SIN |
| Subject analysis set type  | Sub-group analysis              |

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.

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|----------------------------|-------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC |
| Subject analysis set type  | Sub-group analysis      |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

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|----------------------------|---------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755-ORT |
| Subject analysis set type  | Sub-group analysis              |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria.

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|----------------------------|---------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 SIN |
| Subject analysis set type  | Sub-group analysis              |

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.

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|----------------------------|-------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC |
| Subject analysis set type  | Sub-group analysis      |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

|                            |                                 |
|----------------------------|---------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755-ORT |
|----------------------------|---------------------------------|

|                                                                                                                                                                                                                                                                       |                                 |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|
| Subject analysis set type                                                                                                                                                                                                                                             | Sub-group analysis              |
| Subject analysis set description:<br>Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria. |                                 |
| Subject analysis set title                                                                                                                                                                                                                                            | Prophylaxis Cohort: TAK-755 SIN |
| Subject analysis set type                                                                                                                                                                                                                                             | Sub-group analysis              |
| Subject analysis set description:<br>Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.         |                                 |
| Subject analysis set title                                                                                                                                                                                                                                            | Prophylaxis Cohort: SoC         |
| Subject analysis set type                                                                                                                                                                                                                                             | Sub-group analysis              |
| Subject analysis set description:<br>Participants received SoC for 6 months in either Period 1 or Period 2.                                                                                                                                                           |                                 |
| Subject analysis set title                                                                                                                                                                                                                                            | Prophylaxis Cohort: TAK-755-ORT |
| Subject analysis set type                                                                                                                                                                                                                                             | Sub-group analysis              |
| Subject analysis set description:<br>Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2..TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria. |                                 |
| Subject analysis set title                                                                                                                                                                                                                                            | Prophylaxis Cohort: TAK-755 SIN |
| Subject analysis set type                                                                                                                                                                                                                                             | Sub-group analysis              |
| Subject analysis set description:<br>Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.         |                                 |
| Subject analysis set title                                                                                                                                                                                                                                            | Prophylaxis Cohort: SoC         |
| Subject analysis set type                                                                                                                                                                                                                                             | Sub-group analysis              |
| Subject analysis set description:<br>Participants received SoC for 6 months in either Period 1 or Period 2.                                                                                                                                                           |                                 |
| Subject analysis set title                                                                                                                                                                                                                                            | Prophylaxis Cohort: TAK-755-ORT |
| Subject analysis set type                                                                                                                                                                                                                                             | Sub-group analysis              |
| Subject analysis set description:<br>Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria. |                                 |
| Subject analysis set title                                                                                                                                                                                                                                            | Prophylaxis Cohort: TAK-755 SIN |
| Subject analysis set type                                                                                                                                                                                                                                             | Sub-group analysis              |
| Subject analysis set description:<br>Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.         |                                 |
| Subject analysis set title                                                                                                                                                                                                                                            | Prophylaxis Cohort: SoC         |
| Subject analysis set type                                                                                                                                                                                                                                             | Sub-group analysis              |
| Subject analysis set description:<br>Participants received SoC for 6 months in either Period 1 or Period 2.                                                                                                                                                           |                                 |
| Subject analysis set title                                                                                                                                                                                                                                            | Prophylaxis Cohort: TAK-755-ORT |
| Subject analysis set type                                                                                                                                                                                                                                             | Sub-group analysis              |
| Subject analysis set description:<br>Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria. |                                 |
| Subject analysis set title                                                                                                                                                                                                                                            | Prophylaxis Cohort: TAK-755 SIN |
| Subject analysis set type                                                                                                                                                                                                                                             | Sub-group analysis              |

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.

|                            |                         |
|----------------------------|-------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC |
| Subject analysis set type  | Sub-group analysis      |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

|                            |                                 |
|----------------------------|---------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755-ORT |
| Subject analysis set type  | Sub-group analysis              |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria.

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|----------------------------|---------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 SIN |
| Subject analysis set type  | Sub-group analysis              |

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.

|                            |                         |
|----------------------------|-------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC |
| Subject analysis set type  | Sub-group analysis      |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

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|----------------------------|-----------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                            |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

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|----------------------------|----------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 (Period 3) |
| Subject analysis set type  | Sub-group analysis                     |

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

|                            |                                           |
|----------------------------|-------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                        |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

|                            |                                               |
|----------------------------|-----------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                            |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

|                            |                                        |
|----------------------------|----------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 (Period 3) |
| Subject analysis set type  | Sub-group analysis                     |

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

|                            |                                           |
|----------------------------|-------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                        |



Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

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|----------------------------|-----------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                            |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

|                            |                                        |
|----------------------------|----------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 (Period 3) |
| Subject analysis set type  | Sub-group analysis                     |

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

|                            |                                           |
|----------------------------|-------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                        |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

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|----------------------------|-----------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                            |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

|                            |                                        |
|----------------------------|----------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 (Period 3) |
| Subject analysis set type  | Sub-group analysis                     |

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

|                            |                                           |
|----------------------------|-------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                        |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

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|----------------------------|-----------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                            |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

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|----------------------------|----------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 (Period 3) |
| Subject analysis set type  | Sub-group analysis                     |

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

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|----------------------------|-------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                        |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

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|----------------------------|-----------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                            |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

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|----------------------------|----------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 (Period 3) |
| Subject analysis set type  | Sub-group analysis                     |

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

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|----------------------------|-------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                        |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

|                            |                                               |
|----------------------------|-----------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                            |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

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|----------------------------|----------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 (Period 3) |
| Subject analysis set type  | Sub-group analysis                     |

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

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|----------------------------|-------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                        |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

|                            |                                               |
|----------------------------|-----------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                            |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

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|----------------------------|----------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 (Period 3) |
| Subject analysis set type  | Sub-group analysis                     |

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

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|----------------------------|-------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                        |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

|                            |                                               |
|----------------------------|-----------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                            |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

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|----------------------------|----------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 (Period 3) |
| Subject analysis set type  | Sub-group analysis                     |

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

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|----------------------------|-------------------------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC (Periods 1 and 2) |
| Subject analysis set type  | Sub-group analysis                        |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

|                            |                                        |
|----------------------------|----------------------------------------|
| Subject analysis set title | Prophylaxis Cohort I: TAK-755 Then SoC |
| Subject analysis set type  | Sub-group analysis                     |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in Period 1 followed by SoC for 6 months in Period 2. Thereafter participants received TAK-755 SIN dose IV infusion of 40 IU/kg Q2W for 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

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|----------------------------|-----------------------------------------|
| Subject analysis set title | Prophylaxis Cohort II: SoC Then TAK-755 |
| Subject analysis set type  | Sub-group analysis                      |

Subject analysis set description:

Participants received SoC for 6 months in Period 1 followed by IV infusions of 40 IU/kg dose of TAK-755 ORT Q2W in Period 2 for the next 6 months. Thereafter participants received TAK-755 SIN dose IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

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|----------------------------|----------------------------------------|
| Subject analysis set title | Prophylaxis Cohort I: TAK-755 Then SoC |
| Subject analysis set type  | Sub-group analysis                     |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in Period 1 followed by SoC for 6 months in Period 2. Thereafter participants received TAK-755 SIN dose IV infusion of 40 IU/kg Q2W for 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

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|----------------------------|-----------------------------------------|
| Subject analysis set title | Prophylaxis Cohort II: SoC Then TAK-755 |
| Subject analysis set type  | Sub-group analysis                      |

Subject analysis set description:

Participants received SoC for 6 months in Period 1 followed by IV infusions of 40 IU/kg dose of TAK-755 ORT Q2W in Period 2 for the next 6 months. Thereafter participants received TAK-755 SIN dose IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

|                            |                                        |
|----------------------------|----------------------------------------|
| Subject analysis set title | Prophylaxis Cohort I: TAK-755 Then SoC |
| Subject analysis set type  | Sub-group analysis                     |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in Period 1 followed by SoC for 6 months in Period 2. Thereafter participants received TAK-755 SIN dose IV infusion of 40 IU/kg Q2W for 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

|                            |                                         |
|----------------------------|-----------------------------------------|
| Subject analysis set title | Prophylaxis Cohort II: SoC Then TAK-755 |
| Subject analysis set type  | Sub-group analysis                      |

Subject analysis set description:

Participants received SoC for 6 months in Period 1 followed by IV infusions of 40 IU/kg dose of TAK-755 ORT Q2W in Period 2 for the next 6 months. Thereafter participants received TAK-755 SIN dose IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

|                            |                                 |
|----------------------------|---------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 ORT |
| Subject analysis set type  | Sub-group analysis              |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria.

|                            |                                 |
|----------------------------|---------------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 SIN |
| Subject analysis set type  | Sub-group analysis              |

Subject analysis set description:

Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.

|                            |                         |
|----------------------------|-------------------------|
| Subject analysis set title | Prophylaxis Cohort: SoC |
| Subject analysis set type  | Sub-group analysis      |

Subject analysis set description:

Participants received SoC for 6 months in either Period 1 or Period 2.

|                            |                             |
|----------------------------|-----------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 |
| Subject analysis set type  | Sub-group analysis          |

Subject analysis set description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. Thereafter participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

|                            |                             |
|----------------------------|-----------------------------|
| Subject analysis set title | On Demand Cohort I: TAK-755 |
| Subject analysis set type  | Sub-group analysis          |

Subject analysis set description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the TAK-755 cohort of the Urgent Treatment Period received initial dose of IV infusions 40 IU/kg [ $\pm$  4 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 1 followed by a subsequent dose IV infusions of 20 IU/kg [ $\pm$  2 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 2 and an additional daily dose IV infusions of 15 IU/kg [ $\pm$  1.5 IU/kg] TAK-755 on Day 3 until 2 days after the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.

|                            |                          |
|----------------------------|--------------------------|
| Subject analysis set title | On Demand Cohort II: SoC |
| Subject analysis set type  | Sub-group analysis       |

Subject analysis set description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the SoC cohort of the Urgent Treatment Period received the investigator-recommended SoC and dosing regimen until the acute event was resolved.

|                            |                             |
|----------------------------|-----------------------------|
| Subject analysis set title | On Demand Cohort I: TAK-755 |
| Subject analysis set type  | Sub-group analysis          |

Subject analysis set description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the TAK-755 cohort of the Urgent Treatment Period received initial dose of IV infusions 40 IU/kg [ $\pm$  4 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 1 followed by a subsequent dose IV infusions of 20 IU/kg [ $\pm$  2 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 2 and an additional daily dose IV infusions of 15 IU/kg [ $\pm$  1.5 IU/kg] TAK-755 on Day 3 until 2 days after the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.

|                            |                          |
|----------------------------|--------------------------|
| Subject analysis set title | On Demand Cohort II: SoC |
| Subject analysis set type  | Sub-group analysis       |

Subject analysis set description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the SoC cohort of the Urgent Treatment Period received the investigator-recommended SoC and dosing regimen until the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.

|                            |                             |
|----------------------------|-----------------------------|
| Subject analysis set title | Prophylaxis Cohort: TAK-755 |
|----------------------------|-----------------------------|

|                                                                                                                                                                                                                                                                                                                                                     |                                 |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|
| Subject analysis set type                                                                                                                                                                                                                                                                                                                           | Sub-group analysis              |
| Subject analysis set description:                                                                                                                                                                                                                                                                                                                   |                                 |
| Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. Thereafter participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria. |                                 |
| Subject analysis set title                                                                                                                                                                                                                                                                                                                          | Prophylaxis Cohort: SoC         |
| Subject analysis set type                                                                                                                                                                                                                                                                                                                           | Sub-group analysis              |
| Subject analysis set description:                                                                                                                                                                                                                                                                                                                   |                                 |
| Participants received SoC for 6 months in either Period 1 or Period 2.                                                                                                                                                                                                                                                                              |                                 |
| Subject analysis set title                                                                                                                                                                                                                                                                                                                          | Prophylaxis Cohort: TAK-755-ORT |
| Subject analysis set type                                                                                                                                                                                                                                                                                                                           | Sub-group analysis              |
| Subject analysis set description:                                                                                                                                                                                                                                                                                                                   |                                 |
| Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria.                                                                                                                    |                                 |
| Subject analysis set title                                                                                                                                                                                                                                                                                                                          | Prophylaxis Cohort: TAK-755-SIN |
| Subject analysis set type                                                                                                                                                                                                                                                                                                                           | Sub-group analysis              |
| Subject analysis set description:                                                                                                                                                                                                                                                                                                                   |                                 |
| Participants received TAK-755 SIN prophylactic dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.                                                                                                               |                                 |
| Subject analysis set title                                                                                                                                                                                                                                                                                                                          | Prophylaxis Cohort: SoC         |
| Subject analysis set type                                                                                                                                                                                                                                                                                                                           | Sub-group analysis              |
| Subject analysis set description:                                                                                                                                                                                                                                                                                                                   |                                 |
| Participants received SoC for 6 months in either Period 1 or Period 2.                                                                                                                                                                                                                                                                              |                                 |
| Subject analysis set title                                                                                                                                                                                                                                                                                                                          | Prophylaxis Cohort: TAK-755-ORT |
| Subject analysis set type                                                                                                                                                                                                                                                                                                                           | Sub-group analysis              |
| Subject analysis set description:                                                                                                                                                                                                                                                                                                                   |                                 |
| Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. TAK-755 ORT could also be continued in Period 3 depending on availability of TAK-755 SIN and other criteria.                                                                                                                    |                                 |
| Subject analysis set title                                                                                                                                                                                                                                                                                                                          | Prophylaxis Cohort: TAK-755-SIN |
| Subject analysis set type                                                                                                                                                                                                                                                                                                                           | Sub-group analysis              |
| Subject analysis set description:                                                                                                                                                                                                                                                                                                                   |                                 |
| Participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 SIN could also be given in Periods 1 and 2 depending on availability of TAK-755 ORT and other criteria.                                                                                                                            |                                 |
| Subject analysis set title                                                                                                                                                                                                                                                                                                                          | Prophylaxis Cohort: SoC         |
| Subject analysis set type                                                                                                                                                                                                                                                                                                                           | Sub-group analysis              |
| Subject analysis set description:                                                                                                                                                                                                                                                                                                                   |                                 |
| Participants received SoC for 6 months in either Period 1 or Period 2.                                                                                                                                                                                                                                                                              |                                 |

### **Primary: Number of Participants With Acute Thrombotic Thrombocytopenic Purpura (TTP) Events During Prophylactic Treatment**

|                                                                                                                                                                                                                                                                                                  |                                                                                                                                 |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                  | Number of Participants With Acute Thrombotic Thrombocytopenic Purpura (TTP) Events During Prophylactic Treatment <sup>[1]</sup> |
| End point description:                                                                                                                                                                                                                                                                           |                                                                                                                                 |
| As per planned analysis, data for this outcome measure were collected and reported only for the prophylaxis cohorts, in a combined manner for Periods 1 and 2 for TAK-755 and SoC treatments respectively, and separately for Period 3 in which all participants received TAK-755. Modified FAS. |                                                                                                                                 |
| End point type                                                                                                                                                                                                                                                                                   | Primary                                                                                                                         |

End point timeframe:

Up to 74.5 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only one event was observed under SOC. Due to the sparseness of data, only summary analysis was provided.

| End point values            | Prophylaxis Cohort: TAK-755 (Periods 1 and 2) | Prophylaxis Cohort: TAK-755 (Period 3) | Prophylaxis Cohort: SoC (Periods 1 and 2) |  |
|-----------------------------|-----------------------------------------------|----------------------------------------|-------------------------------------------|--|
| Subject group type          | Subject analysis set                          | Subject analysis set                   | Subject analysis set                      |  |
| Number of subjects analysed | 45                                            | 45                                     | 46                                        |  |
| Units: participants         | 0                                             | 0                                      | 1                                         |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Acute Thrombotic Thrombocytopenic Purpura (TTP) Events Responding to TAK-755

|                 |                                                                                            |
|-----------------|--------------------------------------------------------------------------------------------|
| End point title | Percentage of Acute Thrombotic Thrombocytopenic Purpura (TTP) Events Responding to TAK-755 |
|-----------------|--------------------------------------------------------------------------------------------|

End point description:

Percentage of acute TTP events responding to TAK-755, was defined as not requiring the use of another human disintegrin and metalloprotease with a thrombospondin type 1 motif, member 13 (ADAMTS13)-containing agent. As per planned analysis, data for this outcome measure were collected and reported only for the TAK-755 treatment arm of both the prophylaxis (irrespective of the prophylaxis periods) and on demand cohorts. Modified Full Analysis Set (MFAS)

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 79.6 months

| End point values            | Prophylaxis Cohort: TAK-755 | On Demand Cohort I: TAK-755 |  |  |
|-----------------------------|-----------------------------|-----------------------------|--|--|
| Subject group type          | Subject analysis set        | Subject analysis set        |  |  |
| Number of subjects analysed | 0 <sup>[2]</sup>            | 1                           |  |  |
| Units: percentage of events |                             |                             |  |  |
| number (not applicable)     |                             | 100                         |  |  |

Notes:

[2] - No participants were available for analysis.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time to Resolution of Acute TTP Events

|                 |                                        |
|-----------------|----------------------------------------|
| End point title | Time to Resolution of Acute TTP Events |
|-----------------|----------------------------------------|

**End point description:**

Time to resolution of acute TTP events following initiation of treatment with TAK-755 or SoC agent was assessed. Acute TTP events were considered resolved when: (a) Platelet count was >150,000 per microliter (μL) or drop of platelet count was within 25 percent (%) of baseline, whichever occurred first, and (b) Elevation of lactate dehydrogenase (LDH) <1.5 x baseline or <1.5 x upper limit of normal (ULN). As per planned analysis, data for this outcome measure were collected and reported in a combined manner irrespective of the prophylaxis treatment Periods, partitioned per treatment received (TAK-755 and SoC) for the on demand and prophylactic cohorts. '0.999' and '999' indicates that 95% confidence interval was not estimable due to censoring in the specified category. Modified FAS.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 79.6 months

| End point values                 | Prophylaxis Cohort: TAK-755 | Prophylaxis Cohort: SoC | On Demand Cohort I: TAK-755 | On Demand Cohort II: SoC |
|----------------------------------|-----------------------------|-------------------------|-----------------------------|--------------------------|
| Subject group type               | Subject analysis set        | Subject analysis set    | Subject analysis set        | Subject analysis set     |
| Number of subjects analysed      | 0 <sup>[3]</sup>            | 1                       | 1                           | 1                        |
| Units: days                      |                             |                         |                             |                          |
| median (confidence interval 95%) | ( to )                      | 14.8 (0.999 to 999)     | 3.0 (0.999 to 999)          | 1.5 (0.99999 to 99999)   |

Notes:

[3] - No participants were available for analysis.

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of Participants With Thrombocytopenia During Prophylactic Treatment**

|                 |                                                                            |
|-----------------|----------------------------------------------------------------------------|
| End point title | Number of Participants With Thrombocytopenia During Prophylactic Treatment |
|-----------------|----------------------------------------------------------------------------|

**End point description:**

Thrombocytopenia was defined as a decrease in platelet count  $\geq 25$  % of baseline or a platelet count <150,000/μL, reported by treatment arm for the prophylactic cohort. As per planned analysis, data for this outcome measure were collected and reported only for the prophylaxis cohorts, in a combined manner for Periods 1 and 2 for TAK-755 and SoC treatments respectively, and separately for Period 3 in which all participants received TAK-755. Modified FAS included all FAS participants with the exclusion of those enrolled prior to November 2017 who were treated with SoC instead of the randomized treatment of TAK-755 in period 1 because TAK-755 was not available. For participants enrolled prior to November 2017, only the first 6 months of SoC treatment in period 1 was included in the analysis. Subjects analysed indicates the number of participants with data available for analyses.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 79.6 months

| End point values            | Prophylaxis Cohort: TAK-755 (Periods 1 and 2) | Prophylaxis Cohort: TAK-755 (Period 3) | Prophylaxis Cohort: SoC (Periods 1 and 2) |  |
|-----------------------------|-----------------------------------------------|----------------------------------------|-------------------------------------------|--|
| Subject group type          | Subject analysis set                          | Subject analysis set                   | Subject analysis set                      |  |
| Number of subjects analysed | 45                                            | 45                                     | 46                                        |  |
| Units: participants         | 13                                            | 11                                     | 22                                        |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Microangiopathic Hemolytic Anemia During Prophylactic Treatment

|                 |                                                                                             |
|-----------------|---------------------------------------------------------------------------------------------|
| End point title | Number of Participants With Microangiopathic Hemolytic Anemia During Prophylactic Treatment |
|-----------------|---------------------------------------------------------------------------------------------|

End point description:

Microangiopathic hemolytic anemia was defined as an elevation of LDH  $>1.5*$  of baseline or  $>1.5*$ ULN (with a possible evidence of schistocytes on blood smear) and was reported by treatment arm for the prophylactic cohort. As per planned analysis, data for this outcome measure were collected and reported only for the prophylaxis cohorts, in a combined manner for Periods 1 and 2 for TAK-755 and SoC treatments respectively, and separately for Period 3 in which all participants received TAK-755. Modified FAS included all FAS participants with the exclusion of those enrolled prior to November 2017 who were treated with SoC instead of the randomized treatment of TAK-755 in period 1 because TAK-755 was not available. For participants enrolled prior to November 2017, only the first 6 months of SoC treatment in period 1 was included in the analysis. Subjects analysed indicates the number of participants with data available for analyses.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 79.6 months

| End point values            | Prophylaxis Cohort: TAK-755 (Periods 1 and 2) | Prophylaxis Cohort: TAK-755 (Period 3) | Prophylaxis Cohort: SoC (Periods 1 and 2) |  |
|-----------------------------|-----------------------------------------------|----------------------------------------|-------------------------------------------|--|
| Subject group type          | Subject analysis set                          | Subject analysis set                   | Subject analysis set                      |  |
| Number of subjects analysed | 45                                            | 45                                     | 46                                        |  |
| Units: participants         | 8                                             | 13                                     | 12                                        |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Neurological symptoms During Prophylactic Treatment

|                 |                                                                                 |
|-----------------|---------------------------------------------------------------------------------|
| End point title | Number of Participants With Neurological symptoms During Prophylactic Treatment |
|-----------------|---------------------------------------------------------------------------------|

End point description:

Neurological symptoms (TTP related) (e.g., confusion, dysphonia, dysarthria, focal or general motor



symptoms including seizures), were reported by treatment arm for the prophylactic cohort. As per planned analysis, data for this outcome measure were collected and reported only for the prophylaxis cohorts, in a combined manner for Periods 1 and 2 for TAK-755 and SoC treatments respectively, and separately for Period 3 in which all participants received TAK-755. Modified FAS included all FAS participants with the exclusion of those enrolled prior to November 2017 who were treated with SoC instead of the randomized treatment of TAK-755 in period 1 because TAK-755 was not available. For participants enrolled prior to November 2017, only the first 6 months of SoC treatment in period 1 was included in the analysis. Subjects analysed indicates the number of participants with data available for analyses.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Up to 79.6 months    |           |

| End point values            | Prophylaxis Cohort: TAK-755 (Periods 1 and 2) | Prophylaxis Cohort: TAK-755 (Period 3) | Prophylaxis Cohort: SoC (Periods 1 and 2) |  |
|-----------------------------|-----------------------------------------------|----------------------------------------|-------------------------------------------|--|
| Subject group type          | Subject analysis set                          | Subject analysis set                   | Subject analysis set                      |  |
| Number of subjects analysed | 45                                            | 45                                     | 46                                        |  |
| Units: participants         | 4                                             | 9                                      | 7                                         |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Renal Dysfunction During Prophylactic Treatment

|                 |                                                                             |
|-----------------|-----------------------------------------------------------------------------|
| End point title | Number of Participants With Renal Dysfunction During Prophylactic Treatment |
|-----------------|-----------------------------------------------------------------------------|

End point description:

Renal dysfunction was defined as an increase in serum creatinine  $>1.5 \times$  baseline. Number of participants with renal dysfunction were reported by treatment arm for the prophylactic cohort. As per planned analysis, data for this outcome measure were collected and reported only for the prophylaxis cohorts, in a combined manner for Periods 1 and 2 for TAK-755 and SoC treatments respectively, and separately for Period 3 in which all participants received TAK-755. Modified FAS included all FAS participants with the exclusion of those enrolled prior to November 2017 who were treated with SoC instead of the randomized treatment of TAK-755 in period 1 because TAK-755 was not available. For participants enrolled prior to November 2017, only the first 6 months of SoC treatment in period 1 was included in the analysis. Subjects analysed indicates the number of participants with data available for analyses.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Up to 79.6 months    |           |

| End point values            | Prophylaxis Cohort: TAK-755 (Periods 1 and 2) | Prophylaxis Cohort: TAK-755 (Period 3) | Prophylaxis Cohort: SoC (Periods 1 and 2) |  |
|-----------------------------|-----------------------------------------------|----------------------------------------|-------------------------------------------|--|
| Subject group type          | Subject analysis set                          | Subject analysis set                   | Subject analysis set                      |  |
| Number of subjects analysed | 45                                            | 45                                     | 46                                        |  |
| Units: participants         | 5                                             | 4                                      | 2                                         |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants With Abdominal Pain During Prophylactic Treatment

|                 |                                                                          |
|-----------------|--------------------------------------------------------------------------|
| End point title | Number of Participants With Abdominal Pain During Prophylactic Treatment |
|-----------------|--------------------------------------------------------------------------|

End point description:

Number of participants with abdominal pain (TTP related) were reported by treatment arm for the prophylaxis cohort. As per planned analysis, data for this outcome measure were collected and reported only for the prophylaxis cohorts, in a combined manner for Periods 1 and 2 for TAK-755 and SoC treatments respectively, and separately for Period 3 in which all participants received TAK-755. Modified FAS included all FAS participants with the exclusion of those enrolled prior to November 2017 who were treated with SoC instead of the randomized treatment of TAK-755 in period 1 because TAK-755 was not available. For participants enrolled prior to November 2017, only the first 6 months of SoC treatment in period 1 was included in the analysis. Subjects analysed indicates the number of participants with data available for analyses.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 79.6 months

| End point values            | Prophylaxis Cohort: TAK-755 (Periods 1 and 2) | Prophylaxis Cohort: TAK-755 (Period 3) | Prophylaxis Cohort: SoC (Periods 1 and 2) |  |
|-----------------------------|-----------------------------------------------|----------------------------------------|-------------------------------------------|--|
| Subject group type          | Subject analysis set                          | Subject analysis set                   | Subject analysis set                      |  |
| Number of subjects analysed | 45                                            | 45                                     | 46                                        |  |
| Units: participants         | 2                                             | 2                                      | 6                                         |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants With Dose Modification Not Prompted by an Acute TTP Event During Prophylactic Treatment

|                 |                                                                                                                |
|-----------------|----------------------------------------------------------------------------------------------------------------|
| End point title | Number of Participants With Dose Modification Not Prompted by an Acute TTP Event During Prophylactic Treatment |
|-----------------|----------------------------------------------------------------------------------------------------------------|

End point description:

Number of participants with dose modification not prompted by an acute TTP event were reported by treatment for the prophylactic cohort. As per planned analysis, data for this outcome measure were

collected and reported only for the prophylaxis cohorts, in a combined manner for Periods 1 and 2 for TAK-755 and SoC treatments respectively, and separately for Period 3 in which all participants received TAK-755. Modified FAS included all FAS participants with the exclusion of those enrolled prior to November 2017 who were treated with SoC instead of the randomized treatment of TAK-755 in period 1 because TAK-755 was not available. For participants enrolled prior to November 2017, only the first 6 months of SoC treatment in period 1 was included in the analysis. Subjects analysed indicates the number of participants with data available for analyses.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Up to 79.6 months    |           |

| End point values            | Prophylaxis Cohort: TAK-755 (Periods 1 and 2) | Prophylaxis Cohort: TAK-755 (Period 3) | Prophylaxis Cohort: SoC (Periods 1 and 2) |  |
|-----------------------------|-----------------------------------------------|----------------------------------------|-------------------------------------------|--|
| Subject group type          | Subject analysis set                          | Subject analysis set                   | Subject analysis set                      |  |
| Number of subjects analysed | 45                                            | 45                                     | 46                                        |  |
| Units: participants         | 0                                             | 1                                      | 3                                         |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Supplemental Doses Prompted by Subacute TTP Event During Prophylactic Treatment

|                 |                                                                                           |
|-----------------|-------------------------------------------------------------------------------------------|
| End point title | Number of Supplemental Doses Prompted by Subacute TTP Event During Prophylactic Treatment |
|-----------------|-------------------------------------------------------------------------------------------|

End point description:

Number of supplemental doses prompted by subacute TTP events were reported by treatment for the prophylactic cohort. As per planned analysis, data for this outcome measure were collected and reported only for the prophylaxis cohorts, in a combined manner for Periods 1 and 2 for TAK-755 and SoC treatments respectively, and separately for Period 3 in which all participants received TAK-755. Modified FAS included all FAS participants with the exclusion of those enrolled prior to November 2017 who were treated with SoC instead of the randomized treatment of TAK-755 in period 1 because TAK-755 was not available. For participants enrolled prior to November 2017, only the first 6 months of SoC treatment in period 1 was included in the analysis. Subjects analysed indicates the number of participants with data available for analyses.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Up to 79.6 months    |           |

| End point values            | Prophylaxis Cohort: TAK-755 (Periods 1 and 2) | Prophylaxis Cohort: TAK-755 (Period 3) | Prophylaxis Cohort: SoC (Periods 1 and 2) |  |
|-----------------------------|-----------------------------------------------|----------------------------------------|-------------------------------------------|--|
| Subject group type          | Subject analysis set                          | Subject analysis set                   | Subject analysis set                      |  |
| Number of subjects analysed | 45                                            | 45                                     | 46                                        |  |
| Units: supplemental doses   |                                               |                                        |                                           |  |
| number (not applicable)     | 0                                             | 5                                      | 9                                         |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants With Acute TTP Events on Their Final Dose

|                 |                                                                  |
|-----------------|------------------------------------------------------------------|
| End point title | Number of Participants With Acute TTP Events on Their Final Dose |
|-----------------|------------------------------------------------------------------|

End point description:

Number of participants with acute TTP events on their final dose and dosing regimen for the prophylactic cohort were reported. As per planned analysis, data for this outcome measure were collected and reported only for the prophylaxis cohorts, in a combined manner for Periods 1 and 2 for TAK-755 and SoC treatments respectively, and separately for Period 3 in which all participants received TAK-755. Modified FAS included all FAS participants with the exclusion of those enrolled prior to November 2017 who were treated with SoC instead of the randomized treatment of TAK-755 in period 1 because TAK-755 was not available. For participants enrolled prior to November 2017, only the first 6 months of SoC treatment in period 1 was included in the analysis. Subjects analysed indicates the number of participants with data available for analyses.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 79.6 months

| End point values            | Prophylaxis Cohort: TAK-755 (Periods 1 and 2) | Prophylaxis Cohort: TAK-755 (Period 3) | Prophylaxis Cohort: SoC (Periods 1 and 2) |  |
|-----------------------------|-----------------------------------------------|----------------------------------------|-------------------------------------------|--|
| Subject group type          | Subject analysis set                          | Subject analysis set                   | Subject analysis set                      |  |
| Number of subjects analysed | 45                                            | 45                                     | 46                                        |  |
| Units: participants         | 0                                             | 0                                      | 1                                         |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Treatment emergent Adverse Events (TEAEs) and Serious Treatment Emergent Adverse Events (Serious TEAEs)

|                 |                                                                                                                                     |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of Participants with Treatment emergent Adverse Events (TEAEs) and Serious Treatment Emergent Adverse Events (Serious TEAEs) |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------|

End point description:

AE: Any untoward medical occurrence in participants administered IP that does not necessarily have a causal relationship with treatment. TEAE: AE that has start date-time on/after start date-time of first dose of treatment participant is taking on that assessment/period or if it has start date-time before start date-time of first dose but increases in severity on/after start date-time of the first dose of treatment. SAE: An untoward medical occurrence that at any dose meets 1 or more of following criteria: death; initial/prolonged in-patient hospitalization; life threatening experience; persistent/significant

disability/incapacity; congenital anomaly, medically important event (may not be immediately life threatening or result in death or require hospitalization but may require medical or surgical intervention to prevent 1 of the other outcomes). Vital signs, clinical chemistry, hematology as assessed by the investigator were reported as AE.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Up to 79.6 months    |           |

| End point values            | Prophylaxis Cohort: TAK-755 | Prophylaxis Cohort: SoC | On Demand Cohort I: TAK-755 | On Demand Cohort II: SoC |
|-----------------------------|-----------------------------|-------------------------|-----------------------------|--------------------------|
| Subject group type          | Subject analysis set        | Subject analysis set    | Subject analysis set        | Subject analysis set     |
| Number of subjects analysed | 47                          | 48                      | 2                           | 4                        |
| Units: participants         |                             |                         |                             |                          |
| TEAES                       | 42                          | 44                      | 0                           | 3                        |
| Serious TEAEs               | 6                           | 8                       | 0                           | 1                        |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants With Inhibitory Antibodies to ADAMTS13

|                 |                                                               |
|-----------------|---------------------------------------------------------------|
| End point title | Number of Participants With Inhibitory Antibodies to ADAMTS13 |
|-----------------|---------------------------------------------------------------|

End point description:

Number of participants with inhibitory antibodies to ADAMTS13 were reported. As per planned analysis, data for this outcome measure were collected and reported in a combined manner irrespective of the Prophylaxis Periods and partitioned as per the treatment received during the course of the study, presented for the prophylaxis cohorts only. The Safety Analysis Set included all participants treated with at least 1 dose of TAK-755 or SoC treatment after randomization. Subjects analysed indicates the number of participants with data available for analyses.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Up to 79.6 months    |           |

| End point values            | Prophylaxis Cohort: TAK-755 | Prophylaxis Cohort: SoC |  |  |
|-----------------------------|-----------------------------|-------------------------|--|--|
| Subject group type          | Subject analysis set        | Subject analysis set    |  |  |
| Number of subjects analysed | 6                           | 4                       |  |  |
| Units: participants         | 1                           | 0                       |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Total Quantity of ADAMTS13 Administered During the Treatment of Acute TTP Events in Participants in TAK-755 Treatment Arm

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                           |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Total Quantity of ADAMTS13 Administered During the Treatment of Acute TTP Events in Participants in TAK-755 Treatment Arm |
| End point description:<br>Total quantity of ADAMTS13 administered during the treatment of acute TTP events (all acute TTP events irrespective of central lab confirmation were included) was assessed. Acute TTP events typically require 3 to 4 days of intensified treatment. As per planned analysis, data for this outcome measure were collected and reported only for the TAK-755 treatment arm of both the prophylaxis (irrespective of the prophylaxis periods) and on demand cohorts. The Safety Analysis Set. |                                                                                                                           |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Secondary                                                                                                                 |
| End point timeframe:<br>Up to 79.6 months                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                           |

| End point values                     | Prophylaxis Cohort: TAK-755 | On Demand Cohort I: TAK-755 |  |  |
|--------------------------------------|-----------------------------|-----------------------------|--|--|
| Subject group type                   | Subject analysis set        | Subject analysis set        |  |  |
| Number of subjects analysed          | 0 <sup>[4]</sup>            | 2                           |  |  |
| Units: IU                            |                             |                             |  |  |
| arithmetic mean (standard deviation) | ( )                         | 5720.25 (± 189.858)         |  |  |

Notes:

[4] - No participants were analyzed.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Incremental Recovery (IR) of ADAMTS13 Activity for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                  |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Incremental Recovery (IR) of ADAMTS13 Activity for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment |
| End point description:<br>ADAMTS13 activity measured by fluorescent resonance energy transfer (FRETs) assay. IR: body weight normalized maximum increase in plasma ADAMTS13 activity level. IR of ADAMTS13 activity for SoC agent and TAK-755 in plasma was assessed. (IU/mL)/(IU/kg) is (International units per milliliter)/(International units per kilogram). PK-I, PK-II, & PK-III denote crossover PK evaluation of a maximum of 14 days at start of Prophylaxis Treatment Period 1, end of Prophylaxis Treatment Periods 2 and 3 respectively. Per planned analysis, data for this outcome measure was collected & reported as per treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during course of study, only for prophylaxis cohorts. '9999': mean & SD were not estimable due to values below lower limit of quantification. '99999': no participants were analysed in specified category. No participants received SoC in PK-II and PK-III thus there is no data for same. |                                                                                                                  |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Secondary                                                                                                        |
| End point timeframe:<br>PK-I (Month 1: Day 1 up to 12), PK-II (Month 12: Day 1 up to 12), and PK-III (Month 19: Day 1 up to 12): Pre-infusion and at multiple timepoints post-infusion up to 288 hours                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                  |

| End point values                     | Prophylaxis Cohort: TAK-755 SIN | Prophylaxis Cohort: TAK-755 ORT | Prophylaxis Cohort: SoC |  |
|--------------------------------------|---------------------------------|---------------------------------|-------------------------|--|
| Subject group type                   | Subject analysis set            | Subject analysis set            | Subject analysis set    |  |
| Number of subjects analysed          | 23                              | 36                              | 22                      |  |
| Units: (IU/mL)/(IU/kg)               |                                 |                                 |                         |  |
| arithmetic mean (standard deviation) |                                 |                                 |                         |  |
| PK-I: ADAMTS13 Activity              | 9999 (± 9999)                   | 0.025 (± 0.00592)               | 0.0212 (± 0.0267)       |  |
| PK-II: ADAMTS13 Activity             | 0.0292 (± 0.00611)              | 0.0283 (± 0.00644)              | 99999 (± 99999)         |  |
| PK-III: ADAMTS13 Activity            | 0.0279 (± 0.00649)              | 99999 (± 99999)                 | 99999 (± 99999)         |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: IR of ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment

|                 |                                                                                          |
|-----------------|------------------------------------------------------------------------------------------|
| End point title | IR of ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment |
|-----------------|------------------------------------------------------------------------------------------|

End point description:

ADAMTS13 antigen measured using commercial ADAMTS13 enzyme-linked immunosorbent assay (ELISA) using ADAMTS13 antigen. IR: body weight normalized maximum increase in plasma ADAMTS13 antigen. IR of ADAMTS13 antigen for SoC agent & TAK-755 in plasma was assessed. ( $\mu\text{g/mL}$ )/( $\mu\text{g/kg}$ ) is (microgram per milliliter)/(microgram per kilogram). PK-I, PK-II, & PK-III denote crossover PK evaluation of a maximum of 14 days at start of Prophylaxis Treatment Period 1, end of Prophylaxis Treatment Periods 2 and 3 respectively. Per planned analysis, data for this outcome measure was collected & reported as per treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during course of study, only for prophylaxis cohorts. '9999': mean & SD were not estimable due to values below lower limit of quantification. '99999': no participants analysed in specified category. No participants received SoC in PK-II and PK-III thus there is no data for same.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

PK-I (Month 1: Day 1 up to 12), PK-II (Month 12: Day 1 up to 12), and PK-III (Month 19: Day 1 up to 12): Pre-infusion and at multiple timepoints post-infusion up to 288 hours

| End point values                                  | Prophylaxis Cohort: TAK-755 SIN | Prophylaxis Cohort: TAK-755 ORT | Prophylaxis Cohort: SoC |  |
|---------------------------------------------------|---------------------------------|---------------------------------|-------------------------|--|
| Subject group type                                | Subject analysis set            | Subject analysis set            | Subject analysis set    |  |
| Number of subjects analysed                       | 24                              | 37                              | 22                      |  |
| Units: ( $\mu\text{g/mL}$ )/ ( $\mu\text{g/kg}$ ) |                                 |                                 |                         |  |
| arithmetic mean (standard deviation)              |                                 |                                 |                         |  |
| PK-I: ADAMTS13 Antigen                            | 9999 (± 9999)                   | 0.0300 (± 0.00636)              | 0.0187 (± 0.00619)      |  |

|                          |                    |                   |                 |  |
|--------------------------|--------------------|-------------------|-----------------|--|
| PK-II: ADAMTS13 Antigen  | 0.0324 (± 0.00666) | 0.0327 (± 0.0105) | 99999 (± 99999) |  |
| PK-III: ADAMTS13 Antigen | 0.0299 (± 0.00730) | 99999 (± 99999)   | 99999 (± 99999) |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Area Under the Plasma Curve [AUC]all of ADAMTS13 Activity for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment

|                 |                                                                                                                             |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------|
| End point title | Area Under the Plasma Curve [AUC]all of ADAMTS13 Activity for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------|

End point description:

h\*IU/mL denotes for hours\*international units per milliliters. PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '99999' indicates that no participants were analysed in the specified category. PK Analysis Set. Number of subjects analysed was variable for each category.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

PK-I (Month 1:Day 1 up to 12), PK-II (Month 12:Day 1 up to 12), and PK-III (Month 19:Day 1 up to 12): Pre-infusion and at multiple timepoints post-infusion up to 288 hours

| End point values                     | Prophylaxis Cohort: TAK-755 SIN | Prophylaxis Cohort: TAK-755 ORT | Prophylaxis Cohort: SoC |  |
|--------------------------------------|---------------------------------|---------------------------------|-------------------------|--|
| Subject group type                   | Subject analysis set            | Subject analysis set            | Subject analysis set    |  |
| Number of subjects analysed          | 23                              | 33                              | 31                      |  |
| Units: h*IU/mL                       |                                 |                                 |                         |  |
| arithmetic mean (standard deviation) |                                 |                                 |                         |  |
| PK-I: ADAMTS13 Activity              | 99999 (± 99999)                 | 44.15 (± 11.197)                | 10.56 (± 8.263)         |  |
| PK-II: ADAMTS13 Activity             | 53.37 (± 13.183)                | 52.83 (± 11.940)                | 99999 (± 99999)         |  |
| PK-III: ADAMTS13 Activity            | 62.69 (± 26.763)                | 99999 (± 99999)                 | 99999 (± 99999)         |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: AUCall of ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment

|                 |                                                         |
|-----------------|---------------------------------------------------------|
| End point title | AUCall of ADAMTS13 Antigen for SoC Agent and TAK-755 in |
|-----------------|---------------------------------------------------------|



## End point description:

h\*µg/mL denotes for hours\*microgram per milliliters. PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '99999' indicates that no participants were analysed in the specified category. PK Analysis Set. Number of subjects analysed was variable for each category.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

PK-I (Month 1:Day 1 up to 12), PK-II (Month 12:Day 1 up to 12), and PK-III (Month 19:Day 1 up to 12): Pre-infusion and at multiple timepoints post-infusion up to 288 hours

| End point values                     | Prophylaxis Cohort: TAK-755 SIN | Prophylaxis Cohort: TAK-755 ORT | Prophylaxis Cohort: SoC |  |
|--------------------------------------|---------------------------------|---------------------------------|-------------------------|--|
| Subject group type                   | Subject analysis set            | Subject analysis set            | Subject analysis set    |  |
| Number of subjects analysed          | 21                              | 31                              | 28                      |  |
| Units: h*µg/mL                       |                                 |                                 |                         |  |
| arithmetic mean (standard deviation) |                                 |                                 |                         |  |
| PK-I: ADAMTS13 Antigen               | 99999 (± 99999)                 | 34.19 (± 9.953)                 | 6.899 (± 4.779)         |  |
| PK-II: ADAMTS13 Antigen              | 39.94 (± 11.569)                | 39.26 (± 8.790)                 | 99999 (± 99999)         |  |
| PK-III: ADAMTS13 Antigen             | 49.74 (± 19.147)                | 99999 (± 99999)                 | 99999 (± 99999)         |  |

## Statistical analyses

No statistical analyses for this end point

**Secondary: Terminal Half-Life (t<sub>1/2</sub>) of ADAMTS13 Activity and ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment**

|                 |                                                                                                                                                    |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Terminal Half-Life (t <sub>1/2</sub> ) of ADAMTS13 Activity and ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------|

## End point description:

PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '99999' indicates that no participants were analysed in the specified category. PK Analysis Set. Number of subjects analysed were variable for each category.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

PK-I (Month 1:Day 1 up to 12), PK-II (Month 12:Day 1 up to 12), and PK-III (Month 19:Day 1 up to 12): Pre-infusion and at multiple timepoints post-infusion up to 288 hours

| End point values                     | Prophylaxis Cohort: TAK-755 ORT | Prophylaxis Cohort: TAK-755 SIN | Prophylaxis Cohort: SoC |  |
|--------------------------------------|---------------------------------|---------------------------------|-------------------------|--|
| Subject group type                   | Subject analysis set            | Subject analysis set            | Subject analysis set    |  |
| Number of subjects analysed          | 33                              | 24                              | 22                      |  |
| Units: hours                         |                                 |                                 |                         |  |
| arithmetic mean (standard deviation) |                                 |                                 |                         |  |
| PK-I: ADAMTS13 Activity              | 47.14 (± 11.573)                | 99999 (± 99999)                 | 62.88 (± 28.927)        |  |
| PK-I: ADAMTS13 Antigen               | 53.65 (± 13.557)                | 99999 (± 99999)                 | 58.70 (± 23.575)        |  |
| PK-II: ADAMTS13 Activity             | 52.51 (± 15.579)                | 45.77 (± 9.996)                 | 99999 (± 99999)         |  |
| PK-II: ADAMTS13 Antigen              | 54.04 (± 16.899)                | 49.72 (± 15.942)                | 99999 (± 99999)         |  |
| PK-III: ADAMTS13 Activity            | 99999 (± 99999)                 | 35.38 (± 5.286)                 | 99999 (± 99999)         |  |
| PK-III: ADAMTS13 Antigen             | 99999 (± 99999)                 | 39.85 (± 3.243)                 | 99999 (± 99999)         |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Residence Time Extrapolated to Infinity (MRT0-inf) of ADAMTS13 Activity and ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment

|                 |                                                                                                                                                                     |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Mean Residence Time Extrapolated to Infinity (MRT0-inf) of ADAMTS13 Activity and ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '9999' indicates that Mean & SD were not estimable as values were below lower limit of quantification. '99999' indicates that no participants were analysed in the specified category. PK Analysis Set. Number of subjects analysed was variable for each category.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

PK-I (Month 1:Day 1 up to 12), PK-II (Month 12:Day 1 up to 12), and PK-III (Month 19:Day 1 up to 12): Pre-infusion and at multiple timepoints post-infusion up to 288 hours

| End point values                     | Prophylaxis Cohort: TAK-755-ORT | Prophylaxis Cohort: TAK-755 SIN | Prophylaxis Cohort: SoC |  |
|--------------------------------------|---------------------------------|---------------------------------|-------------------------|--|
| Subject group type                   | Subject analysis set            | Subject analysis set            | Subject analysis set    |  |
| Number of subjects analysed          | 31                              | 23                              | 2                       |  |
| Units: hours                         |                                 |                                 |                         |  |
| arithmetic mean (standard deviation) |                                 |                                 |                         |  |
| PK-I: ADAMTS13 Activity              | 64.35 (± 17.498)                | 99999 (± 99999)                 | 9999 (± 9999)           |  |
| PK-I: ADAMTS13 Antigen               | 71.20 (± 16.538)                | 99999 (± 99999)                 | 9999 (± 9999)           |  |
| PK-II: ADAMTS13 Activity             | 65.89 (± 13.472)                | 61.46 (± 11.488)                | 99999 (± 99999)         |  |
| PK-II: ADAMTS13 Antigen              | 72.03 (± 19.611)                | 66.30 (± 18.738)                | 99999 (± 99999)         |  |
| PK-III: ADAMTS13 Activity            | 99999 (± 99999)                 | 41.67 (± 6.171)                 | 99999 (± 99999)         |  |
| PK-III: ADAMTS13 Antigen             | 99999 (± 99999)                 | 48.63 (± 6.867)                 | 99999 (± 99999)         |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Clearance (CL) of ADAMTS13 Activity and ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment

|                 |                                                                                                                            |
|-----------------|----------------------------------------------------------------------------------------------------------------------------|
| End point title | Clearance (CL) of ADAMTS13 Activity and ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment |
|-----------------|----------------------------------------------------------------------------------------------------------------------------|

End point description:

PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '9999' indicates that Mean & SD were not estimable as values were below lower limit of quantification. '99999' indicates that no participants were analysed in the specified category. PK Analysis Set. Number of subjects analysed was variable for each category.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

PK-I (Month 1:Day 1 up to 12), PK-II (Month 12:Day 1 up to 12), and PK-III (Month 19:Day 1 up to 12): Pre-infusion and at multiple timepoints post-infusion up to 288 hours

| End point values                     | Prophylaxis Cohort: TAK-755-ORT | Prophylaxis Cohort: TAK-755 SIN | Prophylaxis Cohort: SoC |  |
|--------------------------------------|---------------------------------|---------------------------------|-------------------------|--|
| Subject group type                   | Subject analysis set            | Subject analysis set            | Subject analysis set    |  |
| Number of subjects analysed          | 31                              | 23                              | 2                       |  |
| Units: liters per hour (L/h)         |                                 |                                 |                         |  |
| arithmetic mean (standard deviation) |                                 |                                 |                         |  |

|                           |                        |                        |                      |  |
|---------------------------|------------------------|------------------------|----------------------|--|
| PK-I: ADAMTS13 Activity   | 0.0618 ( $\pm$ 0.0143) | 99999 ( $\pm$ 99999)   | 9999 ( $\pm$ 9999)   |  |
| PK-I: ADAMTS13 Antigen    | 0.0453 ( $\pm$ 0.0119) | 99999 ( $\pm$ 99999)   | 99999 ( $\pm$ 99999) |  |
| PK-II: ADAMTS13 Activity  | 0.0530 ( $\pm$ 0.0134) | 0.0553 ( $\pm$ 0.0115) | 99999 ( $\pm$ 99999) |  |
| PK-II: ADAMTS13 Antigen   | 0.0409 ( $\pm$ 0.0111) | 0.0480 ( $\pm$ 0.0133) | 99999 ( $\pm$ 99999) |  |
| PK-III: ADAMTS13 Activity | 99999 ( $\pm$ 99999)   | 0.0553 ( $\pm$ 0.0177) | 99999 ( $\pm$ 99999) |  |
| PK-III: ADAMTS13 Antigen  | 99999 ( $\pm$ 99999)   | 0.0444 ( $\pm$ 0.0108) | 99999 ( $\pm$ 99999) |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Volume at Steady State (Vss) of ADAMTS13 Activity and ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment

|                 |                                                                                                                                          |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Volume at Steady State (Vss) of ADAMTS13 Activity and ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '9999' indicates that Mean &SD were not estimable as values were below lower limit of quantification. '99999' indicates that no participants were analysed in the specified category. PK Analysis Set. Number of subjects analysed was variable for each category.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

PK-I (Month 1:Day 1 up to 12), PK-II (Month 12:Day 1 up to 12), and PK-III (Month 19:Day 1 up to 12): Pre-infusion and at multiple timepoints post-infusion up to 288 hours

| End point values                     | Prophylaxis Cohort: TAK-755-ORT | Prophylaxis Cohort: TAK-755 SIN | Prophylaxis Cohort: SoC |  |
|--------------------------------------|---------------------------------|---------------------------------|-------------------------|--|
| Subject group type                   | Subject analysis set            | Subject analysis set            | Subject analysis set    |  |
| Number of subjects analysed          | 31                              | 23                              | 2                       |  |
| Units: liters                        |                                 |                                 |                         |  |
| arithmetic mean (standard deviation) |                                 |                                 |                         |  |
| PK-I: ADAMTS13 Activity              | 3.855 ( $\pm$ 0.911)            | 99999 ( $\pm$ 99999)            | 9999 ( $\pm$ 9999)      |  |
| PK-I: ADAMTS13 Antigen               | 3.120 ( $\pm$ 0.657)            | 99999 ( $\pm$ 99999)            | 9999 ( $\pm$ 9999)      |  |
| PK-II: ADAMTS13 Activity             | 3.401 ( $\pm$ 0.715)            | 3.328 ( $\pm$ 0.631)            | 99999 ( $\pm$ 99999)    |  |
| PK-II: ADAMTS13 Antigen              | 2.791 ( $\pm$ 0.480)            | 3.009 ( $\pm$ 0.614)            | 99999 ( $\pm$ 99999)    |  |

|                           |                 |                 |                 |  |
|---------------------------|-----------------|-----------------|-----------------|--|
| PK-III: ADAMTS13 Activity | 99999 (± 99999) | 2.265 (± 0.669) | 99999 (± 99999) |  |
| PK-III: ADAMTS13 Antigen  | 99999 (± 99999) | 2.164 (± 0.625) | 99999 (± 99999) |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Maximum Concentration (Cmax) of ADAMTS13 Activity for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment

|                 |                                                                                                                     |
|-----------------|---------------------------------------------------------------------------------------------------------------------|
| End point title | Maximum Concentration (Cmax) of ADAMTS13 Activity for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment |
|-----------------|---------------------------------------------------------------------------------------------------------------------|

End point description:

IU/mL stands for International units per milliliter. PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth,Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '9999' indicates that Mean & SD were not estimable as values were below lower limit of quantification. '99999' indicates that no participants were analysed in the specified category. PK Analysis Set. Number of subjects analysed was variable for each category.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

PK-I (Month 1:Day 1 up to 12), PK-II (Month 12:Day 1 up to 12), and PK-III (Month 19:Day 1 up to 12): Pre-infusion and at multiple timepoints post-infusion up to 288 hours

| End point values                     | Prophylaxis Cohort: TAK-755-ORT | Prophylaxis Cohort: TAK-755 SIN | Prophylaxis Cohort: SoC |  |
|--------------------------------------|---------------------------------|---------------------------------|-------------------------|--|
| Subject group type                   | Subject analysis set            | Subject analysis set            | Subject analysis set    |  |
| Number of subjects analysed          | 36                              | 23                              | 41                      |  |
| Units: IU/mL                         |                                 |                                 |                         |  |
| arithmetic mean (standard deviation) |                                 |                                 |                         |  |
| PK-I: ADAMTS13 Activity              | 1.003 (± 0.235)                 | 9999 (± 9999)                   | 0.192 (± 0.102)         |  |
| PK-II: ADAMTS13 Activity             | 1.130 (± 0.253)                 | 1.167 (± 0.246)                 | 99999 (± 99999)         |  |
| PK-III: ADAMTS13 Activity            | 99999 (± 99999)                 | 1.114 (± 0.263)                 | 99999 (± 99999)         |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Cmax of ADAMTS13 Antigen for SoC Agent and TAK-755 in Plasma During Prophylactic Treatment

|                 |                                                       |
|-----------------|-------------------------------------------------------|
| End point title | Cmax of ADAMTS13 Antigen for SoC Agent and TAK-755 in |
|-----------------|-------------------------------------------------------|

## End point description:

µg/mL stands for microgram per milliliter. PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '9999' indicates that Mean & SD were not estimable as values were below lower limit of quantification. '99999' indicates that no participants were analysed in the specified category. PK Analysis Set. Number of subjects analysed was variable for each category.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

PK-I (Month 1:Day 1 up to 12), PK-II (Month 12:Day 1 up to 12), and PK-III (Month 19:Day 1 up to 12): Pre-infusion and at multiple timepoints post-infusion up to 288 hours

| End point values                     | Prophylaxis Cohort: TAK-755-ORT | Prophylaxis Cohort: TAK-755 SIN | Prophylaxis Cohort: SoC |  |
|--------------------------------------|---------------------------------|---------------------------------|-------------------------|--|
| Subject group type                   | Subject analysis set            | Subject analysis set            | Subject analysis set    |  |
| Number of subjects analysed          | 36                              | 24                              | 39                      |  |
| Units: µg/mL                         |                                 |                                 |                         |  |
| arithmetic mean (standard deviation) |                                 |                                 |                         |  |
| PK-I: ADAMTS13 Antigen               | 0.713 (± 0.147)                 | 9999 (± 9999)                   | 0.134 (± 0.0648)        |  |
| PK-II: ADAMTS13 Antigen              | 0.807 (± 0.188)                 | 0.844 (± 0.168)                 | 99999 (± 99999)         |  |
| PK-III: ADAMTS13 Antigen             | 99999 (± 99999)                 | 0.775 (± 0.202)                 | 99999 (± 99999)         |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Assessment of Von Willebrand Factor:Antigen (VWF:Ag) During Prophylactic Treatment

|                 |                                                                                                            |
|-----------------|------------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in Assessment of Von Willebrand Factor:Antigen (VWF:Ag) During Prophylactic Treatment |
|-----------------|------------------------------------------------------------------------------------------------------------|

## End point description:

VWF:Ag is a measure of total VWF protein & was assessed using a sandwich ELISA employing polyclonal anti-human-VWF antibodies. Assessments of VWF:Ag at baseline and following infusion of SoC agent and TAK-755 treatment during initial PK assessment were reported. PK-I, PK-II, and PK-III denote crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '99999' indicates that no participants were analysed in the specified category. PD Analysis Set. Number of subjects analysed was variable for each category.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

PK-I (Month 1:Day 12), PK-II (Month 12:Day 12), and PK-III (Month 19:Day 12): Post-infusion at 288 hours

| End point values                     | Prophylaxis Cohort: TAK-755-ORT | Prophylaxis Cohort: TAK-755 SIN | Prophylaxis Cohort: SoC |  |
|--------------------------------------|---------------------------------|---------------------------------|-------------------------|--|
| Subject group type                   | Subject analysis set            | Subject analysis set            | Subject analysis set    |  |
| Number of subjects analysed          | 23                              | 21                              | 19                      |  |
| Units: percentage of VWF:Ag          |                                 |                                 |                         |  |
| arithmetic mean (standard deviation) |                                 |                                 |                         |  |
| VWF:Ag : PK-I                        | -0.11 (± 17.064)                | 99999 (± 99999)                 | 3.67 (± 19.705)         |  |
| VWF:Ag : PK-II                       | 0.48 (± 34.798)                 | -1.31 (± 22.259)                | 99999 (± 99999)         |  |
| VWF:Ag : PK-III                      | 99999 (± 99999)                 | 99999 (± 99999)                 | 99999 (± 99999)         |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Assessment of Von Willebrand Factor:Ristocetin Cofactor Activity (VWF:RCo) During Prophylactic Treatment

|                 |                                                                                                                                  |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in Assessment of Von Willebrand Factor:Ristocetin Cofactor Activity (VWF:RCo) During Prophylactic Treatment |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------|

End point description:

VWF:RCo provides a measure of ability of VWF to bind platelet glycoprotein Ib. Stabilized platelets are agglutinated in presence of VWF & antibiotic Ristocetin. Assessments of VWF:RCo at baseline & following infusion of SoC agent & TAK-755 treatment during initial PK assessment was reported. PK-I, PK-II, & PK-III denote crossover PK evaluation of a maximum of 14 days at start of Prophylaxis Treatment Period 1 & end of Prophylaxis Treatment Periods 2 & 3 respectively. As per planned analysis, data for this outcome measure were collected & reported as per treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during course of study, only for prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for same. '99999' indicates that no participants were analysed in specified category. PD Analysis Set. Number of subjects analysed was variable for each category.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

PK-I (Month 1:Day 12), PK-II (Month 12:Day 12), and PK-III (Month 19:Day 12): Post-infusion at 288 hours

| End point values                     | Prophylaxis Cohort: TAK-755-ORT | Prophylaxis Cohort: TAK-755 SIN | Prophylaxis Cohort: SoC |  |
|--------------------------------------|---------------------------------|---------------------------------|-------------------------|--|
| Subject group type                   | Subject analysis set            | Subject analysis set            | Subject analysis set    |  |
| Number of subjects analysed          | 23                              | 21                              | 24                      |  |
| Units: percentage of VWF:RCo         |                                 |                                 |                         |  |
| arithmetic mean (standard deviation) |                                 |                                 |                         |  |
| VWF:RCo- PK-I                        | 3.63 (± 42.178)                 | 99999 (± 99999)                 | 9.99 (± 33.230)         |  |

|                 |                 |                 |                 |  |
|-----------------|-----------------|-----------------|-----------------|--|
| VWF:RCo- PK-II  | 7.45 (± 31.917) | 3.60 (± 30.678) | 99999 (± 99999) |  |
| VWF:RCo- PK-III | 99999 (± 99999) | 99999 (± 99999) | 99999 (± 99999) |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Assessment of ADAMTS13 Activity Expressed as Pre-Infusion ADAMTS13 Levels

|                 |                                                                           |
|-----------------|---------------------------------------------------------------------------|
| End point title | Assessment of ADAMTS13 Activity Expressed as Pre-Infusion ADAMTS13 Levels |
|-----------------|---------------------------------------------------------------------------|

End point description:

PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '9999' indicates that Mean & SD were not estimable as values were below lower limit of quantification. '99999' indicates that no participants were analysed in the specified category. PD Analysis Set. Number of subjects analysed was variable for each category.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

PK-I (Month 1:Day 1), PK-II (Month 12:Day 1), and PK-III (Month 19:Day 1): Pre-infusion (within 1 hour)

| End point values                     | Prophylaxis Cohort: TAK-755 ORT | Prophylaxis Cohort: TAK-755 SIN | Prophylaxis Cohort: SoC |  |
|--------------------------------------|---------------------------------|---------------------------------|-------------------------|--|
| Subject group type                   | Subject analysis set            | Subject analysis set            | Subject analysis set    |  |
| Number of subjects analysed          | 36                              | 22                              | 44                      |  |
| Units: IU/mL                         |                                 |                                 |                         |  |
| arithmetic mean (standard deviation) |                                 |                                 |                         |  |
| ADAMTS13 Activity: PK-I              | 9999 (± 9999)                   | 9999 (± 9999)                   | 9999 (± 9999)           |  |
| ADAMTS13 Activity: PK-II             | 9999 (± 9999)                   | 9999 (± 9999)                   | 99999 (± 99999)         |  |
| ADAMTS13 Activity: PK-III            | 99999 (± 99999)                 | 9999 (± 9999)                   | 99999 (± 99999)         |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Assessment of Select VWF Parameters Expressed as Pre-Infusion Levels of VWF:RCo

|                 |                                                       |
|-----------------|-------------------------------------------------------|
| End point title | Assessment of Select VWF Parameters Expressed as Pre- |
|-----------------|-------------------------------------------------------|



## End point description:

PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '99999' indicates that no participants were analysed in the specified category. PD Analysis Set. Number of subjects analysed was variable for each category.

## End point type

Secondary

## End point timeframe:

PK-I (Month 1:Day 1), PK-II (Month 12:Day 1), and PK-III (Month 19:Day 1): Pre-infusion (within 1 hour)

| End point values                     | Prophylaxis Cohort: TAK-755-ORT | Prophylaxis Cohort: TAK-755-SIN | Prophylaxis Cohort: SoC |  |
|--------------------------------------|---------------------------------|---------------------------------|-------------------------|--|
| Subject group type                   | Subject analysis set            | Subject analysis set            | Subject analysis set    |  |
| Number of subjects analysed          | 36                              | 25                              | 43                      |  |
| Units: percentage of VWF:RCo         |                                 |                                 |                         |  |
| arithmetic mean (standard deviation) |                                 |                                 |                         |  |
| PK-I: VWF:RCo                        | 145.54 (± 54.698)               | 137.62 (± 52.978)               | 148.46 (± 51.415)       |  |
| PK-II: VWF:RCo                       | 155.76 (± 63.032)               | 154.98 (± 74.444)               | 99999 (± 99999)         |  |
| PK-III: VWF:RCo                      | 99999 (± 99999)                 | 99999 (± 99999)                 | 99999 (± 99999)         |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Assessment of Select VWF Parameters Expressed as Pre-Infusion Levels of VWF:Ag

## End point title

Assessment of Select VWF Parameters Expressed as Pre-Infusion Levels of VWF:Ag

## End point description:

PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '9999' indicates that Mean &SD were not estimable as values were below lower limit of quantification. '99999' indicates that no participants were analysed in the specified category. PD Analysis Set. Number of subjects analysed was variable for each category.

## End point type

Secondary

## End point timeframe:

PK-I (Month 1:Day 1), PK-II (Month 12:Day 1), and PK-III (Month 19:Day 1): Pre-infusion (within 1 hour)

| End point values                     | Prophylaxis Cohort: TAK-755-ORT | Prophylaxis Cohort: TAK-755-SIN | Prophylaxis Cohort: SoC |  |
|--------------------------------------|---------------------------------|---------------------------------|-------------------------|--|
| Subject group type                   | Subject analysis set            | Subject analysis set            | Subject analysis set    |  |
| Number of subjects analysed          | 37                              | 25                              | 35                      |  |
| Units: percentage of VWF:Ag          |                                 |                                 |                         |  |
| arithmetic mean (standard deviation) |                                 |                                 |                         |  |
| PK-I: VWF:Ag                         | 110.38 (± 45.205)               | 9999 (± 9999)                   | 105.07 (± 40.539)       |  |
| PK-II: VWF:Ag                        | 120.48 (± 49.224)               | 116.66 (± 60.338)               | 99999 (± 99999)         |  |
| PK-III: VWF:Ag                       | 99999 (± 99999)                 | 99999 (± 99999)                 | 99999 (± 99999)         |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Assessment of Select VWF Parameters Expressed as Pre-Infusion Levels of VWF:mm Low Resolution (Res.) Intermediate

|                 |                                                                                                                   |
|-----------------|-------------------------------------------------------------------------------------------------------------------|
| End point title | Assessment of Select VWF Parameters Expressed as Pre-Infusion Levels of VWF:mm Low Resolution (Res.) Intermediate |
|-----------------|-------------------------------------------------------------------------------------------------------------------|

End point description:

PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '9999' indicates that Mean &SD were not estimable as values were below lower limit of quantification. '99999' indicates that no participants were analysed in the specified category. PD Analysis Set. Number of subjects analysed was variable for each category.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

PK-I (Month 1:Day 1), PK-II (Month 12:Day 1), and PK-III (Month 19:Day 1): Pre-infusion (within 1 hour)

| End point values                        | Prophylaxis Cohort: TAK-755-ORT | Prophylaxis Cohort: TAK-755-SIN | Prophylaxis Cohort: SoC |  |
|-----------------------------------------|---------------------------------|---------------------------------|-------------------------|--|
| Subject group type                      | Subject analysis set            | Subject analysis set            | Subject analysis set    |  |
| Number of subjects analysed             | 38                              | 25                              | 39                      |  |
| Units: % of VWF:mm Low Res.Intermediate |                                 |                                 |                         |  |
| arithmetic mean (standard deviation)    |                                 |                                 |                         |  |
| PK-I: VWF:mm Low Res. Intermediate      | 32.14 (± 3.375)                 | 9999 (± 9999)                   | 31.22 (± 2.955)         |  |

|                                      |                      |                      |                      |  |
|--------------------------------------|----------------------|----------------------|----------------------|--|
| PK-II: VWF:mm Low Res. Intermediate  | 30.87 ( $\pm$ 3.754) | 31.10 ( $\pm$ 3.616) | 99999 ( $\pm$ 99999) |  |
| PK-III: VWF:mm Low Res. Intermediate | 99999 ( $\pm$ 99999) | 99999 ( $\pm$ 99999) | 99999 ( $\pm$ 99999) |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Assessment of Select VWF Parameters Expressed as Pre-Infusion Levels of VWF:mm Low Res. Large

|                 |                                                                                               |
|-----------------|-----------------------------------------------------------------------------------------------|
| End point title | Assessment of Select VWF Parameters Expressed as Pre-Infusion Levels of VWF:mm Low Res. Large |
|-----------------|-----------------------------------------------------------------------------------------------|

End point description:

PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '9999' indicates that Mean &SD were not estimable as values were below lower limit of quantification. '99999' indicates that no participants were analysed in the specified category. PD Analysis Set. Number of subjects analysed was variable for each category.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

PK-I (Month 1:Day 1), PK-II (Month 12:Day 1), and PK-III (Month 19:Day 1): Pre-infusion (within 1 hour)

| End point values                     | Prophylaxis Cohort: TAK-755-ORT | Prophylaxis Cohort: TAK-755-SIN | Prophylaxis Cohort: SoC |  |
|--------------------------------------|---------------------------------|---------------------------------|-------------------------|--|
| Subject group type                   | Subject analysis set            | Subject analysis set            | Subject analysis set    |  |
| Number of subjects analysed          | 38                              | 25                              | 39                      |  |
| Units: % of VWF:mm Low Res. Large    |                                 |                                 |                         |  |
| arithmetic mean (standard deviation) |                                 |                                 |                         |  |
| PK-I: VWF:mm Low Res. Large          | 45.98 ( $\pm$ 5.920)            | 9999 ( $\pm$ 9999)              | 46.03 ( $\pm$ 5.043)    |  |
| PK-II: VWF:mm Low Res. Large         | 46.17 ( $\pm$ 5.670)            | 44.93 ( $\pm$ 7.319)            | 99999 ( $\pm$ 99999)    |  |
| PK-III: VWF:mm Low Res. Large        | 99999 ( $\pm$ 99999)            | 99999 ( $\pm$ 99999)            | 99999 ( $\pm$ 99999)    |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Assessment of Select VWF Parameters Expressed as Pre-Infusion Levels of VWF:mm Low Res. Small

|                 |                                                       |
|-----------------|-------------------------------------------------------|
| End point title | Assessment of Select VWF Parameters Expressed as Pre- |
|-----------------|-------------------------------------------------------|

## End point description:

PK-I, PK-II, and PK-III denote the crossover PK evaluation of a maximum of 14 days at the start of Prophylaxis Treatment Period 1 and end of Prophylaxis Treatment Periods 2 and 3 respectively. As per planned analysis, data for this outcome measure were collected and reported as per the treatment (intervention) received (rADAMTS13 manufactured in Orth, Austria [TAK-755 ORT], rADAMTS13 manufactured in Singapore [TAK-755 SIN], or SoC) during the course of the study, only for the prophylaxis cohorts. No participants received SoC in PK-II and PK-III thus there is no data for the same. '9999' indicates that Mean & SD were not estimable as values were below lower limit of quantification. '99999' indicates that no participants were analysed in the specified category. PD Analysis Set. Number of subjects analysed was variable for each category.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

PK-I (Month 1:Day 1), PK-II (Month 12:Day 1), and PK-III (Month 19:Day 1): Pre-infusion (within 1 hour)

| End point values                     | Prophylaxis Cohort: TAK-755-ORT | Prophylaxis Cohort: TAK-755-SIN | Prophylaxis Cohort: SoC |  |
|--------------------------------------|---------------------------------|---------------------------------|-------------------------|--|
| Subject group type                   | Subject analysis set            | Subject analysis set            | Subject analysis set    |  |
| Number of subjects analysed          | 38                              | 25                              | 39                      |  |
| Units: % of VWF:mm Low Res. Small    |                                 |                                 |                         |  |
| arithmetic mean (standard deviation) |                                 |                                 |                         |  |
| PK-I: VWF:mm Low Res. Small          | 21.66 (± 4.230)                 | 9999 (± 9999)                   | 22.77 (± 5.161)         |  |
| PK-II: VWF:mm Low Res. Small         | 22.96 (± 3.047)                 | 23.96 (± 5.320)                 | 99999 (± 99999)         |  |
| PK-III: VWF:mm Low Res. Small        | 99999 (± 99999)                 | 99999 (± 99999)                 | 99999 (± 99999)         |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants With Total Binding Antibodies to ADAMTS13 During Prophylactic Treatment

|                 |                                                                                                |
|-----------------|------------------------------------------------------------------------------------------------|
| End point title | Number of Participants With Total Binding Antibodies to ADAMTS13 During Prophylactic Treatment |
|-----------------|------------------------------------------------------------------------------------------------|

## End point description:

Total binding antibodies to ADAMTS13 were measured by an ELISA-based assay, detecting total immunoglobulins (IgG, IgA, and IgM). As per planned analysis, data for this outcome measure were collected and reported per sequence (Prophylaxis Cohort I: TAK-755 Then SoC and Prophylaxis Cohort II: SoC Then TAK-755) for the prophylaxis cohorts only. The Safety Analysis Set.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

Up to 79.6 months

| End point values            | Prophylaxis Cohort I: TAK-755 Then SoC | Prophylaxis Cohort II: SoC Then TAK-755 |  |  |
|-----------------------------|----------------------------------------|-----------------------------------------|--|--|
| Subject group type          | Subject analysis set                   | Subject analysis set                    |  |  |
| Number of subjects analysed | 21                                     | 27                                      |  |  |
| Units: participants         | 0                                      | 2                                       |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants With Neutralizing Antibodies to ADAMTS13 During Prophylactic Treatment

|                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                               |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                 | Number of Participants With Neutralizing Antibodies to ADAMTS13 During Prophylactic Treatment |
| End point description:<br>Neutralizing antibodies were measured by a Bethesda method with Nijmegen modification using the ADAMTS13 FRETs-VWF73 activity assay. As per planned analysis, data for this outcome measure were collected and reported per sequence (Prophylaxis Cohort I: TAK-755 Then SoC and Prophylaxis Cohort II: SoC Then TAK-755) for the prophylaxis cohorts only.. The Safety Analysis Set. |                                                                                               |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                  | Secondary                                                                                     |
| End point timeframe:<br>Up to 79.6 months                                                                                                                                                                                                                                                                                                                                                                       |                                                                                               |

| End point values            | Prophylaxis Cohort I: TAK-755 Then SoC | Prophylaxis Cohort II: SoC Then TAK-755 |  |  |
|-----------------------------|----------------------------------------|-----------------------------------------|--|--|
| Subject group type          | Subject analysis set                   | Subject analysis set                    |  |  |
| Number of subjects analysed | 21                                     | 27                                      |  |  |
| Units: participants         | 0                                      | 1                                       |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants With Anti-Chinese Hamster Ovary (Anti-CHO) Protein Antibodies During Prophylactic Treatment

|                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                    |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                               | Number of Participants With Anti-Chinese Hamster Ovary (Anti-CHO) Protein Antibodies During Prophylactic Treatment |
| End point description:<br>Total immunoglobulin antibodies (Immunoglobulin G [IgG], A [IgA], and M [IgM]) against CHO protein were analyzed using ELISA assay. As per planned analysis, data for this outcome measure were collected and reported per sequence (Prophylaxis Cohort I: TAK-755 Then SoC and Prophylaxis Cohort II: SoC Then TAK-755) for the prophylaxis cohorts only. The Safety Analysis Set. |                                                                                                                    |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                | Secondary                                                                                                          |
| End point timeframe:<br>Up to 79.6 months                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                    |

| End point values            | Prophylaxis Cohort I: TAK-755 Then SoC | Prophylaxis Cohort II: SoC Then TAK-755 |  |  |
|-----------------------------|----------------------------------------|-----------------------------------------|--|--|
| Subject group type          | Subject analysis set                   | Subject analysis set                    |  |  |
| Number of subjects analysed | 21                                     | 27                                      |  |  |
| Units: participants         | 0                                      | 2                                       |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Health Related Quality of Life (HRQoL) Assessed as Change From Baseline in cTTP-Patient Experience Questionnaire (cTTP-PEQ) Total Score

|                 |                                                                                                                                         |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Health Related Quality of Life (HRQoL) Assessed as Change From Baseline in cTTP-Patient Experience Questionnaire (cTTP-PEQ) Total Score |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------|

End point description:

cTTP-PEQ has 26 questions that assess participant's experience of fatigue, joint, muscle, abdominal & chest pain in previous 24 hours, neurologic manifestations, bruising, feelings of depression & mood alterations, & activity limitation in past 7 days, & participant's attitudes, experienced side effects, work/school absences & travel impact associated with treatment received for TTP during previous 2 weeks. cTTP PEQ is focused on measuring symptoms & impacts of disease. Total scores range: 0 to 162. Higher score indicates greater burden & poor quality of life. Per planned analysis, for prophylaxis cohorts data for this outcome measure was collected & reported by categorizing as per Prophylaxis Periods and per age groups,  $\geq 12$  years, 12-18 years,  $\geq 18$  years for both on demand & prophylaxis cohorts. '999999': SD was not estimable for a single participant. '999999': no participants were analysed in specified category. No participants in OD Cohorts had cTTP-PEQ data available for analysis at scheduled

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Urgent Treatment Period: Day 7, End of Period 1 (Month 6), End of Period 2 (Month 12), and End of Period 3. Modified FAS. Number of subjects analysed was variable for each category.

| End point values                               | Prophylaxis Cohort: TAK-755 | Prophylaxis Cohort: SoC | On Demand Cohort I: TAK-755 | On Demand Cohort II: SoC |
|------------------------------------------------|-----------------------------|-------------------------|-----------------------------|--------------------------|
| Subject group type                             | Subject analysis set        | Subject analysis set    | Subject analysis set        | Subject analysis set     |
| Number of subjects analysed                    | 23                          | 13                      | 0 <sup>[5]</sup>            | 0 <sup>[6]</sup>         |
| Units: score on a scale                        |                             |                         |                             |                          |
| arithmetic mean (standard deviation)           |                             |                         |                             |                          |
| $\geq 12$ years: Total Score, End of Period 1  | -2.6 ( $\pm$ 24.17)         | -1.8 ( $\pm$ 12.00)     | ()                          | ()                       |
| $\geq 12$ years: Total Score, End of Period 2  | -9.4 ( $\pm$ 17.75)         | -1.4 ( $\pm$ 18.38)     | ()                          | ()                       |
| $\geq 12$ years: Total Score, End of Period 3  | -10.0 ( $\pm$ 13.14)        | 99999 ( $\pm$ 99999)    | ()                          | ()                       |
| 12 to < 18 years: Total Score, End of Period 1 | 99999 ( $\pm$ 99999)        | 12.0 ( $\pm$ 999999)    | ()                          | ()                       |
| 12 to < 18 years: Total Score, End of Period 2 | 13.0 ( $\pm$ 999999)        | 99999 ( $\pm$ 99999)    | ()                          | ()                       |

|                                                    |                 |                 |    |    |
|----------------------------------------------------|-----------------|-----------------|----|----|
| 12 to < 18 years: Total Score, End of Period 3     | -6.0 (± 996999) | 99999 (± 99999) | () | () |
| ≥18 years: Total Score, End of Period 1            | -2.6 (± 24.17)  | -3.0 (± 11.76)  | () | () |
| ≥18 years: Total Score, End of Period 2            | -11.3 (± 17.16) | -1.4 (± 18.38)  | () | () |
| ≥18 years: Total Score, End of Period 3            | -10.2 (± 13.42) | 99999 (± 99999) | () | () |
| ≥12 years: Total Score, Urgent Treatment Period Da | 99999 (± 99999) | 99999 (± 99999) | () | () |
| ≥18years:Total Score,Urgent Treatment Period Day7  | 99999 (± 99999) | 99999 (± 99999) | () | () |
| 12 to < 18 years: Total Score, Urgent Treatment D7 | 99999 (± 99999) | 99999 (± 99999) | () | () |

Notes:

[5] - No participants in the on demand cohorts had post-baseline data.

[6] - No participants in the on demand cohorts had post-baseline data.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Health Related Quality of Life (HRQoL) Assessed as Change From Baseline in Physical and Mental Component Scores of the 36-Item Short Form Health Survey Version 2 (SF-36v2)

|                 |                                                                                                                                                                             |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Health Related Quality of Life (HRQoL) Assessed as Change From Baseline in Physical and Mental Component Scores of the 36-Item Short Form Health Survey Version 2 (SF-36v2) |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

SF-36v2:questionnaire to evaluate participant's health related quality of life,has 36 questions related to 8 health dimensions:physical functioning,role-physical(role limitations due to physical health problems),bodily pain,general health,vitality(energy/fatigue),social functioning,role-emotional(role limitations due to emotional problems),&mental health.Physical component score(between 0 &100)was generated using physical functioning,role-physical,bodily pain,general health scales.Higher scores=better quality of life.Mental component score(between 0-100)was generated using vitality,social functioning,role-emotional,&mental health scales.Higher scores=better quality of life.Per planned analysis,prophylaxis cohorts data was collected&reported by categorizing as per Prophylaxis Periods&per component scores for both on demand&prophylaxis cohorts.'99999':no participants analysed in specified category.Modified FAS.No post-baseline SF-36v2 data was available for OD Cohort participants.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Urgent Treatment Period: Day 7, End of Period 1 (Month 6), End of Period 2 (Month 12), and End of Period 3 (Month 19)

| End point values                          | Prophylaxis Cohort I: TAK-755 Then SoC | Prophylaxis Cohort II: SoC Then TAK-755 | On Demand Cohort I: TAK-755 | On Demand Cohort II: SoC |
|-------------------------------------------|----------------------------------------|-----------------------------------------|-----------------------------|--------------------------|
| Subject group type                        | Reporting group                        | Reporting group                         | Subject analysis set        | Subject analysis set     |
| Number of subjects analysed               | 22                                     | 12                                      | 0 <sup>[7]</sup>            | 0 <sup>[8]</sup>         |
| Units: score on a scale                   |                                        |                                         |                             |                          |
| arithmetic mean (standard deviation)      |                                        |                                         |                             |                          |
| Physical Component Score: End of Period 1 | 3.934 (± 10.1098)                      | -0.197 (± 5.2511)                       | ()                          | ()                       |
| Physical Component Score: End of Period 2 | 3.112 (± 6.0506)                       | 2.625 (± 6.4219)                        | ()                          | ()                       |
| Physical Component Score: End of Period 3 | 0.715 (± 4.9878)                       | 99999 (± 99999)                         | ()                          | ()                       |

|                                               |                        |                        |    |    |
|-----------------------------------------------|------------------------|------------------------|----|----|
| Mental Component Score: End of Period 1       | -7.263 ( $\pm$ 7.4244) | 5.001 ( $\pm$ 5.0039)  | () | () |
| Mental Component Score: End of Period 2       | 1.481 ( $\pm$ 7.1315)  | -4.853 ( $\pm$ 9.9302) | () | () |
| Mental Component Score: End of Period 3       | 3.766 ( $\pm$ 7.2392)  | 99999 ( $\pm$ 99999)   | () | () |
| Physical Component Score: Urgent Treatment D7 | 99999 ( $\pm$ 99999)   | 99999 ( $\pm$ 99999)   | () | () |
| Mental Component Score: Urgent Treatment D7   | 99999 ( $\pm$ 99999)   | 99999 ( $\pm$ 99999)   | () | () |

Notes:

[7] - No participants in the on demand cohorts had post-baseline data.

[8] - No participants in the on demand cohorts had post-baseline data.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Health Related Quality of Life (HRQoL) Assessed as Change From Baseline in Abbreviated 9-item Treatment Satisfaction Questionnaire for Medication (TSQM-9) Domain Scores

|                 |                                                                                                                                                                          |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Health Related Quality of Life (HRQoL) Assessed as Change From Baseline in Abbreviated 9-item Treatment Satisfaction Questionnaire for Medication (TSQM-9) Domain Scores |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

TSQM is a treatment satisfaction measure used to assess the overall level of participant's satisfaction or dissatisfaction with their medications. TSQM-9 is a 9-item, validated, self-administered instrument used to assess participant's satisfaction with medication. The three domains assessed are treatment effectiveness, convenience, and global satisfaction. The score of each of the 3 domains is based on an algorithm to create a score of 0 to 100. Higher score indicates greater satisfaction in that domain. As per planned analysis, for the prophylaxis cohorts data for this outcome measure were collected and reported by categorizing as per Prophylaxis Periods and per domain scores for both on demand and prophylaxis cohorts. '99999' indicates that no participants were analysed in the specified category. Modified FAS. Number of subjects analysed was variable for each category. No participants in the OD Cohorts had TSQM-9 data available for analysis at scheduled post-baseline visits.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Urgent Treatment Period: Day 7, End of Period 1 (Month 6), End of Period 2 (Month 12), and End of Period 3 (Month 19)

| End point values                               | Prophylaxis Cohort I: TAK-755 Then SoC | Prophylaxis Cohort: SoC   | On Demand Cohort I: TAK-755 | On Demand Cohort II: SoC |
|------------------------------------------------|----------------------------------------|---------------------------|-----------------------------|--------------------------|
| Subject group type                             | Reporting group                        | Subject analysis set      | Subject analysis set        | Subject analysis set     |
| Number of subjects analysed                    | 20                                     | 11                        | 0 <sup>[9]</sup>            | 0 <sup>[10]</sup>        |
| Units: score on a scale                        |                                        |                           |                             |                          |
| arithmetic mean (standard deviation)           |                                        |                           |                             |                          |
| Treatment Effectiveness Score: End of Period 1 | 26.8519 ( $\pm$ 36.07548)              | 3.5354 ( $\pm$ 13.21072)  | ()                          | ()                       |
| Treatment Effectiveness Score: End of Period 2 | 23.2323 ( $\pm$ 17.53624)              | 12.9630 ( $\pm$ 17.09330) | ()                          | ()                       |
| Treatment Effectiveness Score: End of Period 3 | 21.6667 ( $\pm$ 19.73673)              | 99999 ( $\pm$ 99999)      | ()                          | ()                       |
| Convenience Score: End of Period 1             | 36.1111 ( $\pm$ 16.75900)              | 1.5152 ( $\pm$ 10.85565)  | ()                          | ()                       |



|                                                    |                           |                           |    |    |
|----------------------------------------------------|---------------------------|---------------------------|----|----|
| Convenience Score: End of Period 2                 | 27.2727 ( $\pm$ 14.58363) | 14.8148 ( $\pm$ 27.81479) | () | () |
| Convenience Score: End of Period 3                 | 21.3889 ( $\pm$ 28.74204) | 99999 ( $\pm$ 99999)      | () | () |
| Global Satisfaction Score: End of Period 1         | 28.5714 ( $\pm$ 9.03508)  | 4.5455 ( $\pm$ 16.05880)  | () | () |
| Global Satisfaction Score: End of Period 2         | 22.0779 ( $\pm$ 16.73763) | 14.2857 ( $\pm$ 21.66536) | () | () |
| Global Satisfaction Score: End of Period 3         | 22.5000 ( $\pm$ 15.76462) | 99999 ( $\pm$ 99999)      | () | () |
| Treatment Effectiveness Score: Urgent Treatment D7 | 99999 ( $\pm$ 99999)      | 99999 ( $\pm$ 99999)      | () | () |
| Convenience Score: Urgent Treatment Period Day 7   | 99999 ( $\pm$ 99999)      | 99999 ( $\pm$ 99999)      | () | () |
| Global Satisfaction Score: Urgent Treatment D7     | 99999 ( $\pm$ 99999)      | 99999 ( $\pm$ 99999)      | () | () |

Notes:

[9] - No participants in the on demand cohorts had post-baseline data.

[10] - No participants in the on demand cohorts had post-baseline data.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Health Related Quality of Life (HRQoL) Assessed as Change From Baseline in EuroQoL 5 Dimensions Questionnaire 3-Level (EQ-5D-3L) Domain Scores

|                 |                                                                                                                                                |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Health Related Quality of Life (HRQoL) Assessed as Change From Baseline in EuroQoL 5 Dimensions Questionnaire 3-Level (EQ-5D-3L) Domain Scores |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

EQ-5D-3L health questionnaire is a participant-answered questionnaire scoring 5 dimensions(domains) - mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension is scored on an ordinal scale with 3 available levels of response and scores ranging from 1 to 3, "no problems," "some problems," and "extreme problems," respectively. Lower scores for the domains in the EQ-5D-3L indicate improvement. As per planned analysis, for the prophylaxis cohorts data for this outcome measure were collected and reported by categorizing as per Prophylaxis Periods and per domain scores for both on demand and prophylaxis cohorts. '99999' indicates that no participants were analysed in the specified category. Modified FAS. Number of subjects analysed was variable for each category. No participants in the OD Cohorts had EQ-5D-3L data available for analysis at scheduled post-baseline visits.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Urgent Treatment Period: Day 7, End of Period 1 (Month 6), End of Period 2 (Month 12), and End of Period 3 (Month 19)

| End point values                     | Prophylaxis Cohort I: TAK-755 Then SoC | Prophylaxis Cohort: SoC | On Demand Cohort I: TAK-755 | On Demand Cohort II: SoC |
|--------------------------------------|----------------------------------------|-------------------------|-----------------------------|--------------------------|
| Subject group type                   | Reporting group                        | Subject analysis set    | Subject analysis set        | Subject analysis set     |
| Number of subjects analysed          | 20                                     | 11                      | 0 <sup>[11]</sup>           | 0 <sup>[12]</sup>        |
| Units: score on a scale              |                                        |                         |                             |                          |
| arithmetic mean (standard deviation) |                                        |                         |                             |                          |
| Mobility: End of Period 1            | 0.3 ( $\pm$ 0.46)                      | -0.1 ( $\pm$ 0.30)      | ()                          | ()                       |
| Mobility: End of Period 2            | -0.1 ( $\pm$ 0.29)                     | 0.0 ( $\pm$ 0.00)       | ()                          | ()                       |

|                                                   |                 |                 |    |    |
|---------------------------------------------------|-----------------|-----------------|----|----|
| Mobility: End of Period 3                         | -0.1 (± 0.22)   | 99999 (± 99999) | () | () |
| Self-Care: End of Period 1                        | 0.1 (± 0.35)    | 0.0 (± 0.00)    | () | () |
| Self-Care: End of Period 2                        | 0.0 (± 0.00)    | 0.0 (± 0.00)    | () | () |
| Self-Care: End of Period 3                        | -0.1 (± 0.22)   | 99999 (± 99999) | () | () |
| Usual Activities: End of Period 1                 | 0.0 (± 0.53)    | -0.2 (± 0.40)   | () | () |
| Usual Activities: End of Period 2                 | 0.0 (± 0.43)    | 0.0 (± 0.63)    | () | () |
| Usual Activities: End of Period 3                 | -0.1 (± 0.39)   | 99999 (± 99999) | () | () |
| Pain/Discomfort: End of Period 1                  | 0.3 (± 0.46)    | -0.1 (± 0.70)   | () | () |
| Pain/Discomfort: End of Period 2                  | -0.3 (± 0.62)   | 0.2 (± 0.41)    | () | () |
| Pain/Discomfort: End of Period 3                  | -0.2 (± 0.59)   | 99999 (± 99999) | () | () |
| Anxiety/Depression: End of Period 1               | 0.1 (± 0.64)    | 0.0 (± 0.00)    | () | () |
| Anxiety/Depression: End of Period 2               | -0.1 (± 0.29)   | 0.0 (± 0.00)    | () | () |
| Anxiety/Depression: End of Period 3               | -0.1 (± 0.45)   | 99999 (± 99999) | () | () |
| Mobility: Urgent Treatment Period Day 7           | 99999 (± 99999) | 99999 (± 99999) | () | () |
| Self-Care: Urgent Treatment Period Day 7          | 99999 (± 99999) | 99999 (± 99999) | () | () |
| Usual Activities: Urgent Treatment Period Day 7   | 99999 (± 99999) | 99999 (± 99999) | () | () |
| Pain/Discomfort: Urgent Treatment Period Day 7    | 99999 (± 99999) | 99999 (± 99999) | () | () |
| Anxiety/Depression: Urgent Treatment Period Day 7 | 99999 (± 99999) | 99999 (± 99999) | () | () |

Notes:

[11] - No participants in the on demand cohorts had post-baseline data.

[12] - No participants in the on demand cohorts had post-baseline data.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Health Related Quality of Life (HRQoL) Assessed as Change From Baseline in EQ-5D-youth (EQ-5D-Y) Domain Scores

|                 |                                                                                                                |
|-----------------|----------------------------------------------------------------------------------------------------------------|
| End point title | Health Related Quality of Life (HRQoL) Assessed as Change From Baseline in EQ-5D-youth (EQ-5D-Y) Domain Scores |
|-----------------|----------------------------------------------------------------------------------------------------------------|

End point description:

EQ-5D-Y:health questionnaire;participant aged from 8 to 16 years answered on 5 dimensions (domains)-mobility,self-care,usual activities,pain/discomfort&anxiety/depression.EQ-5D-Y:includes 5 descriptive items:Mobility,self-care,doing usual activities,having pain/discomfort,& feeling anxiety/depressed.Each dimension is scored at 3 levels:1=No problems,2=some problems,&3=a lot of problems.Lower scores indicate improvement.As per planned analysis,for prophylaxis cohorts data for this outcome measure was collected&reported by categorizing as per Prophylaxis Periods per domain scores for both on demand&prophylaxis cohorts.'999999':SD was not estimable for a single participant.'99999':no participants were analysed in specified category.Modified FAS.Number of subjects analysed was variable for each category.No participants in OD Cohorts had EQ-5D-Y data available for analysis at scheduled post-baseline visits.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Urgent Treatment Period: Day 7, End of Period 1 (Month 6), End of Period 2 (Month 12), and End of Period 3 (Month 19)

| End point values                                  | Prophylaxis Cohort I: TAK-755 Then SoC | Prophylaxis Cohort: SoC | On Demand Cohort I: TAK-755 | On Demand Cohort II: SoC |
|---------------------------------------------------|----------------------------------------|-------------------------|-----------------------------|--------------------------|
| Subject group type                                | Reporting group                        | Subject analysis set    | Subject analysis set        | Subject analysis set     |
| Number of subjects analysed                       | 4                                      | 3                       | 0 <sup>[13]</sup>           | 0 <sup>[14]</sup>        |
| Units: score on a scale                           |                                        |                         |                             |                          |
| arithmetic mean (standard deviation)              |                                        |                         |                             |                          |
| Mobility: End of Period 1                         | 0.0 (± 999999)                         | 0.0 (± 0.00)            | ()                          | ()                       |
| Mobility: End of Period 2                         | 0.0 (± 0.00)                           | 0.0 (± 999999)          | ()                          | ()                       |
| Mobility: End of Period 3                         | 0.0 (± 0.00)                           | 99999 (± 99999)         | ()                          | ()                       |
| Self-Care: End of Period 1                        | 0.0 (± 999999)                         | 0.0 (± 0.00)            | ()                          | ()                       |
| Self-Care: End of Period 2                        | 0.0 (± 0.00)                           | 0.0 (± 999999)          | ()                          | ()                       |
| Self-Care: End of Period 3                        | 0.0 (± 0.00)                           | 99999 (± 99999)         | ()                          | ()                       |
| Usual Activities: End of Period 1                 | 0.0 (± 999999)                         | 0.0 (± 0.00)            | ()                          | ()                       |
| Usual Activities: End of Period 2                 | 0.0 (± 0.00)                           | 0.0 (± 999999)          | ()                          | ()                       |
| Usual Activities: End of Period 3                 | 0.0 (± 0.00)                           | 99999 (± 99999)         | ()                          | ()                       |
| Pain/Discomfort: End of Period 1                  | 1.0 (± 999999)                         | -0.7 (± 0.58)           | ()                          | ()                       |
| Pain/Discomfort: End of Period 2                  | -0.7 (± 0.58)                          | 0.0 (± 999999)          | ()                          | ()                       |
| Pain/Discomfort: End of Period 3                  | -0.3 (± 0.96)                          | 99999 (± 99999)         | ()                          | ()                       |
| Anxiety/Depression: End of Period 1               | 0.0 (± 999999)                         | 0.0 (± 0.00)            | ()                          | ()                       |
| Anxiety/Depression: End of Period 2               | 0.3 (± 0.58)                           | 0.0 (± 999999)          | ()                          | ()                       |
| Anxiety/Depression: End of Period 3               | 0.0 (± 0.00)                           | 99999 (± 99999)         | ()                          | ()                       |
| Mobility: Urgent Treatment Period Day 7           | 99999 (± 99999)                        | 99999 (± 99999)         | ()                          | ()                       |
| Self-Care: Urgent Treatment Period Day 7          | 99999 (± 99999)                        | 99999 (± 99999)         | ()                          | ()                       |
| Usual Activities: Urgent Treatment Period Day 7   | 99999 (± 99999)                        | 99999 (± 99999)         | ()                          | ()                       |
| Pain/Discomfort: Urgent Treatment Period Day 7    | 99999 (± 99999)                        | 99999 (± 99999)         | ()                          | ()                       |
| Anxiety/Depression: Urgent Treatment Period Day 7 | 99999 (± 99999)                        | 99999 (± 99999)         | ()                          | ()                       |

Notes:

[13] - No participants in the on demand cohorts had post-baseline data.

[14] - No participants in the on demand cohorts had post-baseline data.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Health Related Quality of Life (HRQoL) Assessed as Change From Baseline in Pediatric Quality of Life Inventory (Peds QL) Scale Total Scores

|                 |                                                                                                                                             |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Health Related Quality of Life (HRQoL) Assessed as Change From Baseline in Pediatric Quality of Life Inventory (Peds QL) Scale Total Scores |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

PedsQL: generic health related quality of life instrument designed specifically for pediatric population & captures domains like physical functioning, emotional functioning, social functioning, school functioning, psychosocial summary, physical health & total score. Peds-QL total score consists 23 items of all domains. This modular instrument uses 5-point scale: 0 (never) - 4 (almost always). Items are reversed scored & linearly transformed to 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0. Higher scores: better quality of life. Per planned analysis, prophylaxis cohorts data for this outcome measure were collected & reported by categorizing as per Prophylaxis Periods & per age groups, 2-<5 years, 5-<8 years, 8-

<13years,&13-<18years,for both on demand&prophylaxis cohorts.'999999':SD was not estimable for a single participant.'99999':no participants were analysed in specified category.No participants in OD Cohorts had Peds QL data available for analysis at scheduled post-baseline visits.

|                                                                                                                                 |           |
|---------------------------------------------------------------------------------------------------------------------------------|-----------|
| End point type                                                                                                                  | Secondary |
| End point timeframe:                                                                                                            |           |
| Baseline, Urgent Treatment Period: Day 7, End of Period 1 (Month 6), End of Period 2 (Month 12), and End of Period 3 (Month 19) |           |

| End point values                               | Prophylaxis Cohort I: TAK-755 Then SoC | Prophylaxis Cohort: SoC | On Demand Cohort I: TAK-755 | On Demand Cohort II: SoC |
|------------------------------------------------|----------------------------------------|-------------------------|-----------------------------|--------------------------|
| Subject group type                             | Reporting group                        | Subject analysis set    | Subject analysis set        | Subject analysis set     |
| Number of subjects analysed                    | 7                                      | 5                       | 0 <sup>[15]</sup>           | 0 <sup>[16]</sup>        |
| Units: score on a scale                        |                                        |                         |                             |                          |
| arithmetic mean (standard deviation)           |                                        |                         |                             |                          |
| 2 to< 5 years,End of Period 1                  | 25.0000 (± 47.14045)                   | 99999 (± 99999)         | ()                          | ()                       |
| 2 to< 5 years, End of Period 2                 | 99999 (± 99999)                        | 27.3810 (± 47.14045)    | ()                          | ()                       |
| 2 to< 5 years, End of Period 3                 | 24.4048 (± 49.66583)                   | 99999 (± 99999)         | ()                          | ()                       |
| 5 to< 8 years, End of Period 1                 | 29.3478 (± 999999)                     | -16.3043 (± 999999)     | ()                          | ()                       |
| 5 to< 8 years, End of Period 2                 | -6.5217 (± 999999)                     | 32.6087 (± 999999)      | ()                          | ()                       |
| 5 to< 8 years, End of Period 3                 | 17.9348 (± 19.21486)                   | 99999 (± 99999)         | ()                          | ()                       |
| 8 to< 13 years, End of Period 1                | -2.1739 (± 999999)                     | 15.2174 (± 13.83470)    | ()                          | ()                       |
| 8 to < 13 years, End of Period 2               | 8.6957 (± 23.05783)                    | 1.0870 (± 999999)       | ()                          | ()                       |
| 8 to< 13 years, End of Period 3                | 5.7971 (± 7.39876)                     | 99999 (± 99999)         | ()                          | ()                       |
| 13 to< 18 years, End of Period 1               | 99999 (± 99999)                        | 99999 (± 99999)         | ()                          | ()                       |
| 13 to< 18 years, End of Period 2               | 99999 (± 99999)                        | 99999 (± 99999)         | ()                          | ()                       |
| 13 to< 18 years, End of Period 3               | 99999 (± 99999)                        | 99999 (± 99999)         | ()                          | ()                       |
| 2 to < 5 years: Urgent Treatment Period Day 7  | 99999 (± 99999)                        | 99999 (± 99999)         | ()                          | ()                       |
| 5 to< 8 years: Urgent Treatment Period Day 7   | 99999 (± 99999)                        | 99999 (± 99999)         | ()                          | ()                       |
| 8 to < 13 years: Urgent Treatment Period Day 7 | 99999 (± 99999)                        | 99999 (± 99999)         | ()                          | ()                       |

Notes:

[15] - No participants in the on demand cohorts had post-baseline data.

[16] - No participants in the on demand cohorts had post-baseline data.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Resource Utilization: Annualized Length of Hospital Stay for Acute TTP Events for Prophylaxis Cohorts

|                 |                                                              |
|-----------------|--------------------------------------------------------------|
| End point title | Resource Utilization: Annualized Length of Hospital Stay for |
|-----------------|--------------------------------------------------------------|

## End point description:

The annualized number of days participants stayed in hospital for acute TTP events were assessed. As per planned analysis, data for this outcome measure were collected and reported only for the prophylaxis cohorts in a combined manner for Periods 1 and 2 for SoC treatment and for Periods 1, 2, and 3 for TAK-755 treatment respectively. Modified FAS.

## End point type

Secondary

## End point timeframe:

Up to 79.6 months

| End point values              | Prophylaxis Cohort: TAK-755 | Prophylaxis Cohort: SoC |  |  |
|-------------------------------|-----------------------------|-------------------------|--|--|
| Subject group type            | Subject analysis set        | Subject analysis set    |  |  |
| Number of subjects analysed   | 45                          | 46                      |  |  |
| Units: days/year              |                             |                         |  |  |
| median (full range (min-max)) | 0.00 (0.0 to 0.0)           | 0.00 (0.0 to 3.4)       |  |  |

## Statistical analyses

No statistical analyses for this end point

**Secondary: Resource Utilization: Annualized Number of Acute Care Visits for Prophylaxis Cohorts**

## End point title

Resource Utilization: Annualized Number of Acute Care Visits for Prophylaxis Cohorts

## End point description:

Annualized number of acute care visits was calculated as the number of acute care visits  $\times$  365.25/(End date - treatment start date + 1). As per planned analysis, data for this outcome measure were collected and reported only for the prophylaxis cohorts in a combined manner for Periods 1 and 2 for SoC treatment and for Periods 1, 2, and 3 for TAK-755 treatment respectively. Modified FAS.

## End point type

Secondary

## End point timeframe:

Up to 79.6 months

| End point values                     | Prophylaxis Cohort: TAK-755 | Prophylaxis Cohort: SoC |  |  |
|--------------------------------------|-----------------------------|-------------------------|--|--|
| Subject group type                   | Subject analysis set        | Subject analysis set    |  |  |
| Number of subjects analysed          | 45                          | 46                      |  |  |
| Units: acute care visits per year    |                             |                         |  |  |
| arithmetic mean (standard deviation) | 0.59 ( $\pm$ 1.378)         | 0.14 ( $\pm$ 0.493)     |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Resource Utilization: Annualized Number of Days Missed From School or Work for Prophylaxis Cohorts

|                 |                                                                                                    |
|-----------------|----------------------------------------------------------------------------------------------------|
| End point title | Resource Utilization: Annualized Number of Days Missed From School or Work for Prophylaxis Cohorts |
|-----------------|----------------------------------------------------------------------------------------------------|

End point description:

Annualized number of days missed from school or work were assessed. As per planned analysis, data for this outcome measure were collected and reported only for the prophylaxis cohorts in a combined manner for Periods 1 and 2 for SoC treatment and for Periods 1, 2, and 3 for TAK-755 treatment respectively. Modified FAS.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 79.6 months

| End point values              | Prophylaxis Cohort: TAK-755 | Prophylaxis Cohort: SoC |  |  |
|-------------------------------|-----------------------------|-------------------------|--|--|
| Subject group type            | Subject analysis set        | Subject analysis set    |  |  |
| Number of subjects analysed   | 45                          | 46                      |  |  |
| Units: days/year              |                             |                         |  |  |
| median (full range (min-max)) | 0.00 (0.0 to 180.3)         | 0.00 (0.0 to 294.5)     |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug up to end of study (79.6 months)

Adverse event reporting additional description:

Safety Analysis Set=all participants treated with at least 1 dose of TAK-755/SoC treatment after randomization.As per planned analysis,data for AEs were collected & reported in a combined manner irrespective of Prophylaxis Periods & partitioned as per treatment received during course of study,presented for on demand & prophylaxis cohorts.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 26.1 |
|--------------------|------|

### Reporting groups

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | Prophylaxis Cohort: TAK-755 |
|-----------------------|-----------------------------|

Reporting group description:

Participants received a single IV infusion of 40 IU/kg TAK-755 ORT Q2W for 6 months in either Period 1 or Period 2. Thereafter participants received TAK-755 SIN dose of IV infusions of 40 IU/kg Q2W for another 6 months in Period 3. TAK-755 ORT could be replaced with TAK-755 SIN and vice versa depending on availability and other criteria.

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Prophylaxis Cohort: SoC |
|-----------------------|-------------------------|

Reporting group description:

Participants received SoC for 6 months in either Period 1 or Period 2.

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | On Demand Cohort I: TAK-755 |
|-----------------------|-----------------------------|

Reporting group description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the TAK-755 cohort of the Urgent Treatment Period received initial dose of IV infusions 40 IU/kg [ $\pm$  4 IU/kg] TAK-755 ORT or TAK-755 SIN infusion on Day 1 followed by a subsequent dose IV infusions of 20 IU/kg [ $\pm$  2 IU/kg] TAK-755 ORT or TAK-755 SIN on Day 2 and an additional daily dose IV infusions of 15 IU/kg [ $\pm$  1.5 IU/kg] TAK-755 on Day 3 until 2 days after the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.

|                       |                          |
|-----------------------|--------------------------|
| Reporting group title | On Demand Cohort II: SoC |
|-----------------------|--------------------------|

Reporting group description:

Participants experiencing an acute TTP event who met all other inclusion criteria and entered the study through the SoC cohort of the Urgent Treatment Period received the investigator-recommended SoC and dosing regimen until the acute event was resolved. Upon resolution of the acute TTP event, participants had the option to either move to the prophylaxis cohort of the study or discontinue entirely.

| Serious adverse events                            | Prophylaxis Cohort: TAK-755 | Prophylaxis Cohort: SoC | On Demand Cohort I: TAK-755 |
|---------------------------------------------------|-----------------------------|-------------------------|-----------------------------|
| Total subjects affected by serious adverse events |                             |                         |                             |
| subjects affected / exposed                       | 6 / 47 (12.77%)             | 8 / 48 (16.67%)         | 0 / 2 (0.00%)               |
| number of deaths (all causes)                     | 0                           | 0                       | 0                           |
| number of deaths resulting from adverse events    | 0                           | 0                       | 0                           |
| Investigations                                    |                             |                         |                             |
| Platelet count decreased                          |                             |                         |                             |

|                                                      |                |                |               |
|------------------------------------------------------|----------------|----------------|---------------|
| subjects affected / exposed                          | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0         |
| Injury, poisoning and procedural complications       |                |                |               |
| Shoulder fracture                                    |                |                |               |
| subjects affected / exposed                          | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0         |
| Road traffic accident                                |                |                |               |
| subjects affected / exposed                          | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0         |
| Cardiac disorders                                    |                |                |               |
| Tachycardia                                          |                |                |               |
| subjects affected / exposed                          | 1 / 47 (2.13%) | 0 / 48 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0         |
| Nervous system disorders                             |                |                |               |
| Headache                                             |                |                |               |
| subjects affected / exposed                          | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0         |
| Blood and lymphatic system disorders                 |                |                |               |
| Thrombocytopenia                                     |                |                |               |
| subjects affected / exposed                          | 0 / 47 (0.00%) | 2 / 48 (4.17%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 2          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0         |
| Thrombotic thrombocytopenic purpura                  |                |                |               |
| subjects affected / exposed                          | 1 / 47 (2.13%) | 0 / 48 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0         |
| General disorders and administration site conditions |                |                |               |
| Pyrexia                                              |                |                |               |



|                                                 |                |                |               |
|-------------------------------------------------|----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Immune system disorders                         |                |                |               |
| Seasonal allergy                                |                |                |               |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Gastrointestinal disorders                      |                |                |               |
| Abdominal pain                                  |                |                |               |
| subjects affected / exposed                     | 1 / 47 (2.13%) | 0 / 48 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Reproductive system and breast disorders        |                |                |               |
| Ovarian cyst                                    |                |                |               |
| subjects affected / exposed                     | 1 / 47 (2.13%) | 0 / 48 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Adnexal torsion                                 |                |                |               |
| subjects affected / exposed                     | 1 / 47 (2.13%) | 0 / 48 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Respiratory, thoracic and mediastinal disorders |                |                |               |
| Sinus disorder                                  |                |                |               |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 1 / 48 (2.08%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Endocrine disorders                             |                |                |               |
| Hyperthyroidism                                 |                |                |               |
| subjects affected / exposed                     | 1 / 47 (2.13%) | 0 / 48 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Infections and infestations                     |                |                |               |
| Pneumonia                                       |                |                |               |

|                                                 |                |                |               |
|-------------------------------------------------|----------------|----------------|---------------|
| subjects affected / exposed                     | 1 / 47 (2.13%) | 0 / 48 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Gastroenteritis clostridial                     |                |                |               |
| subjects affected / exposed                     | 1 / 47 (2.13%) | 0 / 48 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |

|                                                   |                             |  |  |
|---------------------------------------------------|-----------------------------|--|--|
| <b>Serious adverse events</b>                     | On Demand Cohort<br>II: SoC |  |  |
| Total subjects affected by serious adverse events |                             |  |  |
| subjects affected / exposed                       | 1 / 4 (25.00%)              |  |  |
| number of deaths (all causes)                     | 0                           |  |  |
| number of deaths resulting from adverse events    | 0                           |  |  |
| Investigations                                    |                             |  |  |
| Platelet count decreased                          |                             |  |  |
| subjects affected / exposed                       | 0 / 4 (0.00%)               |  |  |
| occurrences causally related to treatment / all   | 0 / 0                       |  |  |
| deaths causally related to treatment / all        | 0 / 0                       |  |  |
| Injury, poisoning and procedural complications    |                             |  |  |
| Shoulder fracture                                 |                             |  |  |
| subjects affected / exposed                       | 0 / 4 (0.00%)               |  |  |
| occurrences causally related to treatment / all   | 0 / 0                       |  |  |
| deaths causally related to treatment / all        | 0 / 0                       |  |  |
| Road traffic accident                             |                             |  |  |
| subjects affected / exposed                       | 0 / 4 (0.00%)               |  |  |
| occurrences causally related to treatment / all   | 0 / 0                       |  |  |
| deaths causally related to treatment / all        | 0 / 0                       |  |  |
| Cardiac disorders                                 |                             |  |  |
| Tachycardia                                       |                             |  |  |
| subjects affected / exposed                       | 0 / 4 (0.00%)               |  |  |
| occurrences causally related to treatment / all   | 0 / 0                       |  |  |
| deaths causally related to treatment / all        | 0 / 0                       |  |  |
| Nervous system disorders                          |                             |  |  |
| Headache                                          |                             |  |  |

|                                                      |                |  |  |
|------------------------------------------------------|----------------|--|--|
| subjects affected / exposed                          | 0 / 4 (0.00%)  |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Blood and lymphatic system disorders                 |                |  |  |
| Thrombocytopenia                                     |                |  |  |
| subjects affected / exposed                          | 1 / 4 (25.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Thrombotic thrombocytopenic purpura                  |                |  |  |
| subjects affected / exposed                          | 0 / 4 (0.00%)  |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| General disorders and administration site conditions |                |  |  |
| Pyrexia                                              |                |  |  |
| subjects affected / exposed                          | 0 / 4 (0.00%)  |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Immune system disorders                              |                |  |  |
| Seasonal allergy                                     |                |  |  |
| subjects affected / exposed                          | 0 / 4 (0.00%)  |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Gastrointestinal disorders                           |                |  |  |
| Abdominal pain                                       |                |  |  |
| subjects affected / exposed                          | 0 / 4 (0.00%)  |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Reproductive system and breast disorders             |                |  |  |
| Ovarian cyst                                         |                |  |  |
| subjects affected / exposed                          | 0 / 4 (0.00%)  |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Adnexal torsion                                      |                |  |  |

|                                                 |               |  |  |
|-------------------------------------------------|---------------|--|--|
| subjects affected / exposed                     | 0 / 4 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Respiratory, thoracic and mediastinal disorders |               |  |  |
| Sinus disorder                                  |               |  |  |
| subjects affected / exposed                     | 0 / 4 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Endocrine disorders                             |               |  |  |
| Hyperthyroidism                                 |               |  |  |
| subjects affected / exposed                     | 0 / 4 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Infections and infestations                     |               |  |  |
| Pneumonia                                       |               |  |  |
| subjects affected / exposed                     | 0 / 4 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Gastroenteritis clostridial                     |               |  |  |
| subjects affected / exposed                     | 0 / 4 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |

Frequency threshold for reporting non-serious adverse events: 5 %

| <b>Non-serious adverse events</b>                     | Prophylaxis Cohort:<br>TAK-755 | Prophylaxis Cohort:<br>SoC | On Demand Cohort<br>I: TAK-755 |
|-------------------------------------------------------|--------------------------------|----------------------------|--------------------------------|
| Total subjects affected by non-serious adverse events |                                |                            |                                |
| subjects affected / exposed                           | 39 / 47 (82.98%)               | 37 / 48 (77.08%)           | 0 / 2 (0.00%)                  |
| Vascular disorders                                    |                                |                            |                                |
| Hypertension                                          |                                |                            |                                |
| subjects affected / exposed                           | 3 / 47 (6.38%)                 | 0 / 48 (0.00%)             | 0 / 2 (0.00%)                  |
| occurrences (all)                                     | 3                              | 0                          | 0                              |
| Haematoma                                             |                                |                            |                                |

|                                                         |                     |                     |                    |
|---------------------------------------------------------|---------------------|---------------------|--------------------|
| subjects affected / exposed<br>occurrences (all)        | 3 / 47 (6.38%)<br>4 | 2 / 48 (4.17%)<br>3 | 0 / 2 (0.00%)<br>0 |
| General disorders and administration<br>site conditions |                     |                     |                    |
| Asthenia                                                |                     |                     |                    |
| subjects affected / exposed                             | 3 / 47 (6.38%)      | 1 / 48 (2.08%)      | 0 / 2 (0.00%)      |
| occurrences (all)                                       | 3                   | 1                   | 0                  |
| Fatigue                                                 |                     |                     |                    |
| subjects affected / exposed                             | 5 / 47 (10.64%)     | 7 / 48 (14.58%)     | 0 / 2 (0.00%)      |
| occurrences (all)                                       | 5                   | 10                  | 0                  |
| Malaise                                                 |                     |                     |                    |
| subjects affected / exposed                             | 3 / 47 (6.38%)      | 2 / 48 (4.17%)      | 0 / 2 (0.00%)      |
| occurrences (all)                                       | 3                   | 2                   | 0                  |
| Pyrexia                                                 |                     |                     |                    |
| subjects affected / exposed                             | 6 / 47 (12.77%)     | 2 / 48 (4.17%)      | 0 / 2 (0.00%)      |
| occurrences (all)                                       | 11                  | 4                   | 0                  |
| Immune system disorders                                 |                     |                     |                    |
| Seasonal allergy                                        |                     |                     |                    |
| subjects affected / exposed                             | 3 / 47 (6.38%)      | 1 / 48 (2.08%)      | 0 / 2 (0.00%)      |
| occurrences (all)                                       | 4                   | 1                   | 0                  |
| Respiratory, thoracic and mediastinal<br>disorders      |                     |                     |                    |
| Oropharyngeal pain                                      |                     |                     |                    |
| subjects affected / exposed                             | 5 / 47 (10.64%)     | 4 / 48 (8.33%)      | 0 / 2 (0.00%)      |
| occurrences (all)                                       | 8                   | 6                   | 0                  |
| Rhinorrhoea                                             |                     |                     |                    |
| subjects affected / exposed                             | 5 / 47 (10.64%)     | 0 / 48 (0.00%)      | 0 / 2 (0.00%)      |
| occurrences (all)                                       | 5                   | 0                   | 0                  |
| Cough                                                   |                     |                     |                    |
| subjects affected / exposed                             | 8 / 47 (17.02%)     | 3 / 48 (6.25%)      | 0 / 2 (0.00%)      |
| occurrences (all)                                       | 10                  | 3                   | 0                  |
| Epistaxis                                               |                     |                     |                    |
| subjects affected / exposed                             | 3 / 47 (6.38%)      | 4 / 48 (8.33%)      | 0 / 2 (0.00%)      |
| occurrences (all)                                       | 4                   | 8                   | 0                  |
| Investigations                                          |                     |                     |                    |
| Platelet count decreased                                |                     |                     |                    |
| subjects affected / exposed                             | 4 / 47 (8.51%)      | 5 / 48 (10.42%)     | 0 / 2 (0.00%)      |
| occurrences (all)                                       | 7                   | 8                   | 0                  |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                 |                                                                                                                                                                                          |                                                                                                                                                      |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------|
| Blood lactate dehydrogenase increased<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                                                                                                                                                                                                                                                 | 4 / 47 (8.51%)<br>4                                                                                                                                                                             | 1 / 48 (2.08%)<br>1                                                                                                                                                                      | 0 / 2 (0.00%)<br>0                                                                                                                                   |
| Injury, poisoning and procedural complications<br>Immunisation reaction<br>subjects affected / exposed<br>occurrences (all)<br><br>Allergic transfusion reaction<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                                                                                                                      | 3 / 47 (6.38%)<br>4<br><br>0 / 47 (0.00%)<br>0                                                                                                                                                  | 1 / 48 (2.08%)<br>2<br><br>7 / 48 (14.58%)<br>8                                                                                                                                          | 0 / 2 (0.00%)<br>0<br><br>0 / 2 (0.00%)<br>0                                                                                                         |
| Cardiac disorders<br>Tachycardia<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                                                                                                                                                                                                                                                      | 1 / 47 (2.13%)<br>1                                                                                                                                                                             | 3 / 48 (6.25%)<br>3                                                                                                                                                                      | 0 / 2 (0.00%)<br>0                                                                                                                                   |
| Nervous system disorders<br>Dizziness<br>subjects affected / exposed<br>occurrences (all)<br><br>Headache<br>subjects affected / exposed<br>occurrences (all)<br><br>Hypoaesthesia<br>subjects affected / exposed<br>occurrences (all)<br><br>Lethargy<br>subjects affected / exposed<br>occurrences (all)<br><br>Migraine<br>subjects affected / exposed<br>occurrences (all)<br><br>Paraesthesia<br>subjects affected / exposed<br>occurrences (all)<br><br>Syncope<br>subjects affected / exposed<br>occurrences (all) | 5 / 47 (10.64%)<br>13<br><br>15 / 47 (31.91%)<br>106<br><br>4 / 47 (8.51%)<br>4<br><br>5 / 47 (10.64%)<br>12<br><br>7 / 47 (14.89%)<br>18<br><br>1 / 47 (2.13%)<br>1<br><br>4 / 47 (8.51%)<br>4 | 0 / 48 (0.00%)<br>0<br><br>10 / 48 (20.83%)<br>70<br><br>0 / 48 (0.00%)<br>0<br><br>3 / 48 (6.25%)<br>6<br><br>2 / 48 (4.17%)<br>4<br><br>2 / 48 (4.17%)<br>4<br><br>1 / 48 (2.08%)<br>1 | 0 / 2 (0.00%)<br>0<br><br>0 / 2 (0.00%)<br>0<br><br>0 / 2 (0.00%)<br>0<br><br>0 / 2 (0.00%)<br>0<br><br>0 / 2 (0.00%)<br>0<br><br>0 / 2 (0.00%)<br>0 |

|                                        |                 |                 |               |
|----------------------------------------|-----------------|-----------------|---------------|
| Blood and lymphatic system disorders   |                 |                 |               |
| Anaemia                                |                 |                 |               |
| subjects affected / exposed            | 3 / 47 (6.38%)  | 2 / 48 (4.17%)  | 0 / 2 (0.00%) |
| occurrences (all)                      | 3               | 2               | 0             |
| Thrombocytopenia                       |                 |                 |               |
| subjects affected / exposed            | 3 / 47 (6.38%)  | 3 / 48 (6.25%)  | 0 / 2 (0.00%) |
| occurrences (all)                      | 5               | 9               | 0             |
| Ear and labyrinth disorders            |                 |                 |               |
| Ear pain                               |                 |                 |               |
| subjects affected / exposed            | 3 / 47 (6.38%)  | 0 / 48 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)                      | 3               | 0               | 0             |
| Gastrointestinal disorders             |                 |                 |               |
| Abdominal pain                         |                 |                 |               |
| subjects affected / exposed            | 8 / 47 (17.02%) | 6 / 48 (12.50%) | 0 / 2 (0.00%) |
| occurrences (all)                      | 16              | 7               | 0             |
| Vomiting                               |                 |                 |               |
| subjects affected / exposed            | 8 / 47 (17.02%) | 6 / 48 (12.50%) | 0 / 2 (0.00%) |
| occurrences (all)                      | 8               | 8               | 0             |
| Nausea                                 |                 |                 |               |
| subjects affected / exposed            | 8 / 47 (17.02%) | 2 / 48 (4.17%)  | 0 / 2 (0.00%) |
| occurrences (all)                      | 15              | 4               | 0             |
| Diarrhoea                              |                 |                 |               |
| subjects affected / exposed            | 9 / 47 (19.15%) | 2 / 48 (4.17%)  | 0 / 2 (0.00%) |
| occurrences (all)                      | 14              | 3               | 0             |
| Skin and subcutaneous tissue disorders |                 |                 |               |
| Petechiae                              |                 |                 |               |
| subjects affected / exposed            | 0 / 47 (0.00%)  | 0 / 48 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)                      | 0               | 0               | 0             |
| Rash                                   |                 |                 |               |
| subjects affected / exposed            | 2 / 47 (4.26%)  | 4 / 48 (8.33%)  | 0 / 2 (0.00%) |
| occurrences (all)                      | 2               | 5               | 0             |
| Pruritus                               |                 |                 |               |
| subjects affected / exposed            | 2 / 47 (4.26%)  | 3 / 48 (6.25%)  | 0 / 2 (0.00%) |
| occurrences (all)                      | 3               | 5               | 0             |
| Urticaria                              |                 |                 |               |
| subjects affected / exposed            | 2 / 47 (4.26%)  | 7 / 48 (14.58%) | 0 / 2 (0.00%) |
| occurrences (all)                      | 2               | 9               | 0             |

|                                                 |                 |                 |               |
|-------------------------------------------------|-----------------|-----------------|---------------|
| Musculoskeletal and connective tissue disorders |                 |                 |               |
| Myalgia                                         |                 |                 |               |
| subjects affected / exposed                     | 2 / 47 (4.26%)  | 3 / 48 (6.25%)  | 0 / 2 (0.00%) |
| occurrences (all)                               | 2               | 3               | 0             |
| Arthralgia                                      |                 |                 |               |
| subjects affected / exposed                     | 3 / 47 (6.38%)  | 3 / 48 (6.25%)  | 0 / 2 (0.00%) |
| occurrences (all)                               | 5               | 4               | 0             |
| Infections and infestations                     |                 |                 |               |
| COVID-19                                        |                 |                 |               |
| subjects affected / exposed                     | 8 / 47 (17.02%) | 3 / 48 (6.25%)  | 0 / 2 (0.00%) |
| occurrences (all)                               | 8               | 3               | 0             |
| Influenza                                       |                 |                 |               |
| subjects affected / exposed                     | 3 / 47 (6.38%)  | 0 / 48 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)                               | 5               | 0               | 0             |
| Nasopharyngitis                                 |                 |                 |               |
| subjects affected / exposed                     | 8 / 47 (17.02%) | 6 / 48 (12.50%) | 0 / 2 (0.00%) |
| occurrences (all)                               | 18              | 13              | 0             |
| Upper respiratory tract infection               |                 |                 |               |
| subjects affected / exposed                     | 6 / 47 (12.77%) | 3 / 48 (6.25%)  | 0 / 2 (0.00%) |
| occurrences (all)                               | 7               | 3               | 0             |
| Tooth abscess                                   |                 |                 |               |
| subjects affected / exposed                     | 1 / 47 (2.13%)  | 0 / 48 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)                               | 1               | 0               | 0             |
| Rhinitis                                        |                 |                 |               |
| subjects affected / exposed                     | 7 / 47 (14.89%) | 2 / 48 (4.17%)  | 0 / 2 (0.00%) |
| occurrences (all)                               | 8               | 2               | 0             |
| Pharyngitis                                     |                 |                 |               |
| subjects affected / exposed                     | 3 / 47 (6.38%)  | 0 / 48 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)                               | 3               | 0               | 0             |
| Oral herpes                                     |                 |                 |               |
| subjects affected / exposed                     | 3 / 47 (6.38%)  | 1 / 48 (2.08%)  | 0 / 2 (0.00%) |
| occurrences (all)                               | 5               | 1               | 0             |
| Viral infection                                 |                 |                 |               |
| subjects affected / exposed                     | 4 / 47 (8.51%)  | 2 / 48 (4.17%)  | 0 / 2 (0.00%) |
| occurrences (all)                               | 5               | 2               | 0             |
| Metabolism and nutrition disorders              |                 |                 |               |



|                                                                                                                              |                             |                     |                    |
|------------------------------------------------------------------------------------------------------------------------------|-----------------------------|---------------------|--------------------|
| Iron deficiency<br>subjects affected / exposed<br>occurrences (all)                                                          | 3 / 47 (6.38%)<br>3         | 2 / 48 (4.17%)<br>2 | 0 / 2 (0.00%)<br>0 |
| <b>Non-serious adverse events</b>                                                                                            | On Demand Cohort<br>II: SoC |                     |                    |
| Total subjects affected by non-serious<br>adverse events<br>subjects affected / exposed                                      | 3 / 4 (75.00%)              |                     |                    |
| Vascular disorders<br>Hypertension<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 4 (0.00%)<br>0          |                     |                    |
| Haematoma<br>subjects affected / exposed<br>occurrences (all)                                                                | 0 / 4 (0.00%)<br>0          |                     |                    |
| General disorders and administration<br>site conditions<br>Asthenia<br>subjects affected / exposed<br>occurrences (all)      | 0 / 4 (0.00%)<br>0          |                     |                    |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)                                                                  | 0 / 4 (0.00%)<br>0          |                     |                    |
| Malaise<br>subjects affected / exposed<br>occurrences (all)                                                                  | 0 / 4 (0.00%)<br>0          |                     |                    |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)                                                                  | 0 / 4 (0.00%)<br>0          |                     |                    |
| Immune system disorders<br>Seasonal allergy<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 4 (0.00%)<br>0          |                     |                    |
| Respiratory, thoracic and mediastinal<br>disorders<br>Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all) | 0 / 4 (0.00%)<br>0          |                     |                    |
| Rhinorrhoea                                                                                                                  |                             |                     |                    |

|                                                                                                                                |                     |  |  |
|--------------------------------------------------------------------------------------------------------------------------------|---------------------|--|--|
| subjects affected / exposed<br>occurrences (all)                                                                               | 0 / 4 (0.00%)<br>0  |  |  |
| Cough<br>subjects affected / exposed<br>occurrences (all)                                                                      | 0 / 4 (0.00%)<br>0  |  |  |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)                                                                  | 0 / 4 (0.00%)<br>0  |  |  |
| Investigations<br>Platelet count decreased<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 4 (0.00%)<br>0  |  |  |
| Blood lactate dehydrogenase<br>increased<br>subjects affected / exposed<br>occurrences (all)                                   | 1 / 4 (25.00%)<br>2 |  |  |
| Injury, poisoning and procedural<br>complications<br>Immunisation reaction<br>subjects affected / exposed<br>occurrences (all) | 0 / 4 (0.00%)<br>0  |  |  |
| Allergic transfusion reaction<br>subjects affected / exposed<br>occurrences (all)                                              | 1 / 4 (25.00%)<br>1 |  |  |
| Cardiac disorders<br>Tachycardia<br>subjects affected / exposed<br>occurrences (all)                                           | 0 / 4 (0.00%)<br>0  |  |  |
| Nervous system disorders<br>Dizziness<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 4 (0.00%)<br>0  |  |  |
| Headache<br>subjects affected / exposed<br>occurrences (all)                                                                   | 1 / 4 (25.00%)<br>1 |  |  |
| Hypoaesthesia<br>subjects affected / exposed<br>occurrences (all)                                                              | 1 / 4 (25.00%)<br>1 |  |  |

|                                                                                                     |                     |  |  |
|-----------------------------------------------------------------------------------------------------|---------------------|--|--|
| Lethargy<br>subjects affected / exposed<br>occurrences (all)                                        | 0 / 4 (0.00%)<br>0  |  |  |
| Migraine<br>subjects affected / exposed<br>occurrences (all)                                        | 0 / 4 (0.00%)<br>0  |  |  |
| Paraesthesia<br>subjects affected / exposed<br>occurrences (all)                                    | 1 / 4 (25.00%)<br>1 |  |  |
| Syncope<br>subjects affected / exposed<br>occurrences (all)                                         | 0 / 4 (0.00%)<br>0  |  |  |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all) | 0 / 4 (0.00%)<br>0  |  |  |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)                                | 1 / 4 (25.00%)<br>1 |  |  |
| Ear and labyrinth disorders<br>Ear pain<br>subjects affected / exposed<br>occurrences (all)         | 0 / 4 (0.00%)<br>0  |  |  |
| Gastrointestinal disorders<br>Abdominal pain<br>subjects affected / exposed<br>occurrences (all)    | 0 / 4 (0.00%)<br>0  |  |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                                        | 0 / 4 (0.00%)<br>0  |  |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)                                          | 1 / 4 (25.00%)<br>1 |  |  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 4 (0.00%)<br>0  |  |  |
| Skin and subcutaneous tissue disorders                                                              |                     |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| Petechiae                                       |                |  |  |
| subjects affected / exposed                     | 1 / 4 (25.00%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Rash                                            |                |  |  |
| subjects affected / exposed                     | 0 / 4 (0.00%)  |  |  |
| occurrences (all)                               | 0              |  |  |
| Pruritus                                        |                |  |  |
| subjects affected / exposed                     | 1 / 4 (25.00%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Urticaria                                       |                |  |  |
| subjects affected / exposed                     | 0 / 4 (0.00%)  |  |  |
| occurrences (all)                               | 0              |  |  |
| Musculoskeletal and connective tissue disorders |                |  |  |
| Myalgia                                         |                |  |  |
| subjects affected / exposed                     | 0 / 4 (0.00%)  |  |  |
| occurrences (all)                               | 0              |  |  |
| Arthralgia                                      |                |  |  |
| subjects affected / exposed                     | 0 / 4 (0.00%)  |  |  |
| occurrences (all)                               | 0              |  |  |
| Infections and infestations                     |                |  |  |
| COVID-19                                        |                |  |  |
| subjects affected / exposed                     | 0 / 4 (0.00%)  |  |  |
| occurrences (all)                               | 0              |  |  |
| Influenza                                       |                |  |  |
| subjects affected / exposed                     | 0 / 4 (0.00%)  |  |  |
| occurrences (all)                               | 0              |  |  |
| Nasopharyngitis                                 |                |  |  |
| subjects affected / exposed                     | 0 / 4 (0.00%)  |  |  |
| occurrences (all)                               | 0              |  |  |
| Upper respiratory tract infection               |                |  |  |
| subjects affected / exposed                     | 0 / 4 (0.00%)  |  |  |
| occurrences (all)                               | 0              |  |  |
| Tooth abscess                                   |                |  |  |
| subjects affected / exposed                     | 1 / 4 (25.00%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Rhinitis                                        |                |  |  |

|                                    |               |  |  |
|------------------------------------|---------------|--|--|
| subjects affected / exposed        | 0 / 4 (0.00%) |  |  |
| occurrences (all)                  | 0             |  |  |
| Pharyngitis                        |               |  |  |
| subjects affected / exposed        | 0 / 4 (0.00%) |  |  |
| occurrences (all)                  | 0             |  |  |
| Oral herpes                        |               |  |  |
| subjects affected / exposed        | 0 / 4 (0.00%) |  |  |
| occurrences (all)                  | 0             |  |  |
| Viral infection                    |               |  |  |
| subjects affected / exposed        | 0 / 4 (0.00%) |  |  |
| occurrences (all)                  | 0             |  |  |
| Metabolism and nutrition disorders |               |  |  |
| Iron deficiency                    |               |  |  |
| subjects affected / exposed        | 0 / 4 (0.00%) |  |  |
| occurrences (all)                  | 0             |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 15 March 2017    | The following changes were made as per Amendment 1: 1. Replaced hereditary thrombotic thrombocytopenic purpura (hTTP) with congenital thrombotic thrombocytopenic purpura (cTTP). 2. Adapted pharmacokinetic (PK) infusion numbers. 3. Removed PK test from dosing visits.                                                                                                                                                                                                                                                 |
| 09 May 2017      | The following changes were made as per Amendment 2: 1. ADAMTS13 trough levels were re-defined as pre-infusion ADAMTS13. 2. Defined severe TTP signs. 3. Specified that participants enrolling in the on-demand cohort and moving to the prophylaxis cohort were analysed separately and were not counted towards the 40 participants cap on the prophylaxis cohort. 4. Updated criteria for enrolling adolescent participants.                                                                                             |
| 06 December 2018 | The following changes were made as per Amendment 5: 1. Changed hereditary TTP to congenital TTP. 2. Added SHP655, as the new name given to BAX 930. 3. Numbers of participants for planned enrolment (i.e., sample size changed from 60 to 62), enrolment of pediatric participants, duration of time for participants in the prophylaxis cohort, and planned study period dates and study duration were amended. 4. PK/PD points were added to reflect the PK comparability study. 5. Period 3 treatment phase was added. |
| 06 March 2020    | The following changes were made as per Amendment 9: 1. Added TAK-755, as the new name given to SHP655. 2. 6 more participants were added to the study, in the prophylaxis cohort. 3. Health Related Quality of Life and Resource Utilization were included under secondary objectives.                                                                                                                                                                                                                                     |
| 23 February 2021 | The following changes were made as per Amendment 11: 1. The estimated study completion date was changed from June 2023 to January 2024. 2. The total duration of the study was increased from 60 months to 70 months. 3. After 30 September 2021, screened participants in the prophylactic cohort could initiate the study with TAK-755 SIN. 4. Secondary efficacy outcome measures text was changed from "number and incidence of acute TTP episodes..." to "proportion of acute TTP episodes...".                       |
| 18 April 2021    | The following changes were made as per Amendment 13: 1. Participants receiving a COVID-19 vaccination during the study period were monitored frequently by telephonic health checks and for thrombocytopenia for 14 consecutive days following vaccination, as deemed appropriate by the investigator.                                                                                                                                                                                                                     |
| 18 November 2021 | The following changes were made as per Amendment 15: 1. Study completion dates were updated as: Study Primary Completion date changed from Feb 2023 to Nov 2023 and Study Completion from Jan 2024 to Mar 2024. 2. Sentence was removed: "Participants who switch from the on-demand to the prophylaxis cohort upon resolution of the acute event will be excluded from the primary efficacy analysis." 3. Secondary outcome measure 8 was revised to "Incidence of supplemental doses prompted by subacute TTP events".   |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported