Ablynx

Nanobodies®
creating better medicines

Additional results from the Phase III HERCULES study with caplacizumab in acquired thrombotic thrombocytopenic purpura (aTTP)

Webcast – 12th December 2017

Additional results Phase III HERCULES study

Participants on the call

Dr Edwin Moses

CEO

Dr Robert K. Zeldin

CMO

Forward looking statements

Certain statements, beliefs and opinions in this presentation are forward-looking, which reflect the Company or, as appropriate, the Company directors' current expectations and projections about future events. By their nature, forward-looking statements involve a number of risks, uncertainties and assumptions that could cause actual results or events to differ materially from those expressed or implied by the forward-looking statements. These risks, uncertainties and assumptions could adversely affect the outcome and financial effects of the plans and events described herein including, without limitation, the timing for completion of certain milestones in our agreements and the amount of any milestone payments we may receive, our expected net cash burn, the progress of our key pre-clinical and clinical development programmes, the timing of the commercialization of, and the estimated market potential and projected peak sales for, our product candidates, the anticipated duration of the patent protection we receive for our product candidates, and our ability to create value from the development and commercialisation of our product candidates. A multitude of factors including, but not limited to, changes in demand, competition and technology, can cause actual events, performance or results to differ significantly from any anticipated development. Forward looking statements contained in this presentation regarding past trends or activities should not be taken as a representation that such trends or activities will continue in the future. As a result, the Company expressly disclaims any obligation or undertaking to release any update or revisions to any forward-looking statements in this presentation as a result of any change in expectations or any change in events, conditions, assumptions or circumstances on which these forward-looking statements are based. Neither the Company nor its advisers or representatives nor any of its parent or subsidiary undertakings or any such person's officers or employees guarantees that the assumptions underlying such forward-looking statements are free from errors nor does either accept any responsibility for the future accuracy of the forward-looking statements contained in this presentation or the actual occurrence of the forecasted developments. You should not place undue reliance on forward-looking statements, which speak only as of the date of this presentation.

Webcast 12th December 2017

Agenda

- Welcome and introduction
- Additional results from the Phase III HERCULES study
- Q&A

Topline results: Phase III HERCULES study

Primary endpoint and key secondary endpoints met

- *Primary endpoint*: statistically significant reduction in time to platelet count response
- *First secondary endpoint*: 74% relative reduction in patients with aTTP-related death, aTTP recurrence or a major thromboembolic event during the study drug treatment period
- *Second secondary endpoint*: 67% relative reduction in patients with aTTP recurrence during the overall study period
- *Third secondary endpoint*: no caplacizumab-treated patients had refractory disease
- *Fourth secondary endpoint*: trend to faster normalisation of organ damage markers
- Safety profile consistent with Phase II TITAN results and mechanism of action

aTTP: acquired thrombotic thrombocytopenic purpura

Other secondary endpoints

Plasma exchange parameters, duration of ICU stay and overall hospitalisation

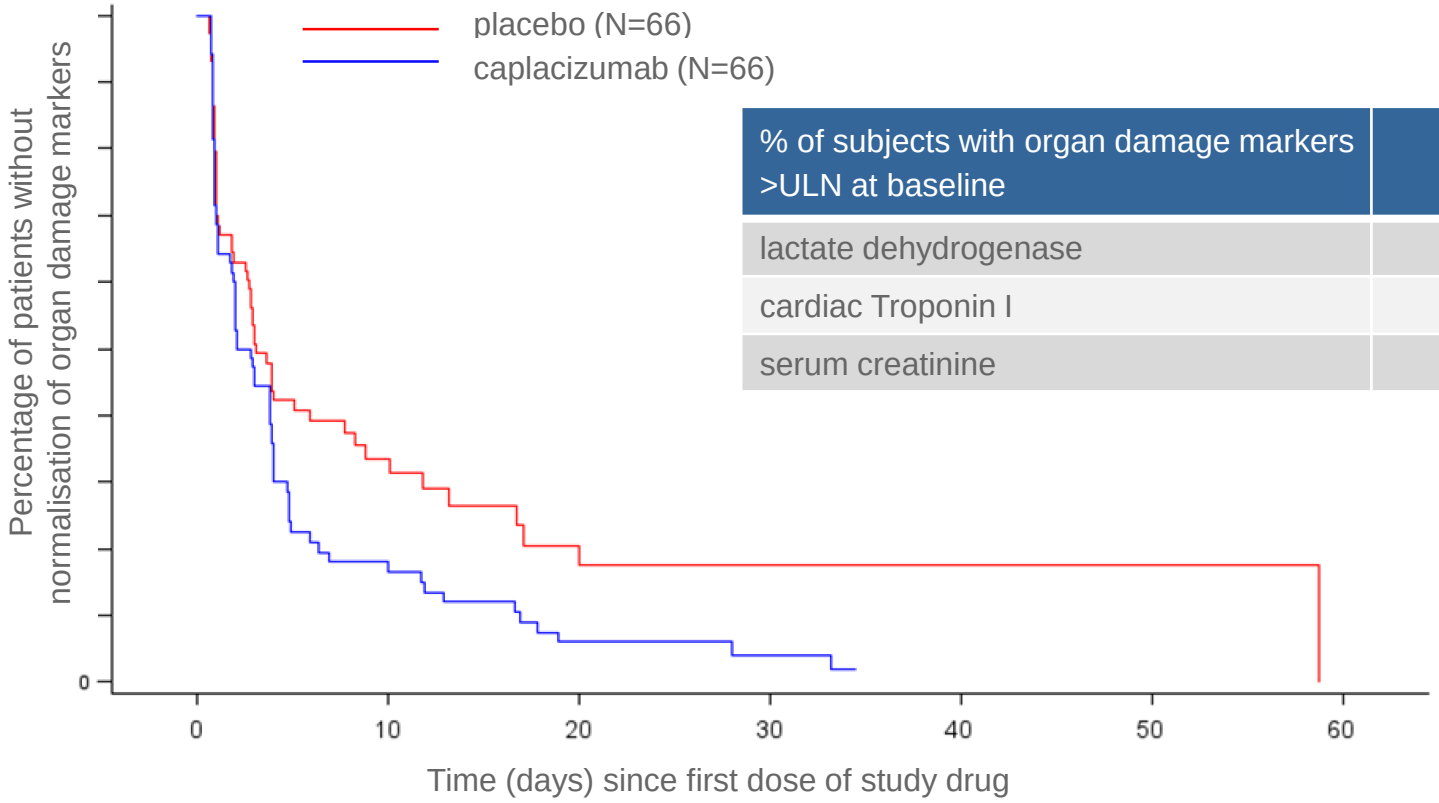
Overall study drug treatment period (mean±SE)	Placebo N=73[1]	Caplacizumab N=71	% relative reduction
Number of days of plasma exchange	9.4±0.8	5.8±0.5	↓38%
Volume of plasma (L)	35.9±4.2	21.3±1.6	↓41%
Number of days in intensive care unit	9.7±2.1 (n=27)	3.4±0.4 (n=28)	↓65%
Number of days in hospital	14.4±1.2	9.9±0.7	↓31%

[1] 26 of 73 placebo treated patients had an exacerbation and were switched to open-label caplacizumab, potentially reducing the mean values on plasma exchange parameters and duration of ICU stay and overall hospitalisation during the study drug treatment period

ICU: intensive care unit

Fourth key secondary endpoint

Time to normalisation of organ damage markers[1]



% of subjects with organ damage markers >ULN at baseline	all subjects N=145
lactate dehydrogenase	87.1%
cardiac Troponin I	53.8%
serum creatinine	22.7%

[1] *time to LDH ≤ 1 x ULN and cardiac Troponin I ≤ 1 x ULN and serum creatinine ≤ 1 x ULN*

LDH: lactate dehydrogenase; **ULN:** upper limit of normal

Safety profile

Treatment emergent adverse events (TEAEs)

Number of subjects (%) with TEAE	Placebo N=73	Caplacizumab N=71
At least one TEAE	71 (97.3)	69 (97.2)
At least one study drug-related TEAE	32 (43.8)	41 (57.7)
At least one TEAE leading to study drug discontinuation	9 (12.3)	5 (7.0)
At least one SAE	39 (53.4)	28 (39.4)
At least one study drug-related SAE	4 (5.5)	10 (14.1)
At least one SAE leading to death	3 (4.1)	1 (1.4)[1]

[1] *adverse event occurred during the follow-up period of the study and was assessed by the investigator as not related to study drug treatment*

Safety data consistent with Phase II TITAN study

Safety profile

Bleeding-related TEAEs*

Number of subjects (%) with TEAE	Placebo N (%)	Caplacizumab N (%)
Bleeding-related TEAEs (by SMQ)[1]	**17 (23.3)**	**33 (45.6)**
Epistaxis	1 (1.4)	17 (23.9)
Gingival bleeding	0	8 (11.3)
Bruising	3 (4.1)	5 (7.0)
Hematuria	1 (1.4)	4 (5.6)
Vaginal hemorrhage	1 (1.4)	3 (4.2)
Menorrhagia	1 (1.4)	2 (2.8)
Catheter site hemorrhage	3 (4.1)	2 (2.8)
Injection site bruising	2 (2.7)	2 (2.8)
Hematochezia	0	2 (2.8)
Hematoma	0	2 (2.8)

** Treatment emergent adverse events occurring in at least 2 subjects in either group*

[1] Standardised MeDRA Query "Hemorrhage"

Caplacizumab Phase III HERCULES study

Conclusions

Caplacizumab addresses the pathophysiological platelet aggregation that leads to the formation of microthrombi and the resultant mortality and morbidity seen in aTTP

- Faster resolution of an aTTP episode with significantly shorter time to platelet count response
- Clinically relevant reduction in aTTP-related death, exacerbation of aTTP, or a major thromboembolic event
- Prevention of aTTP relapses when treatment is extended until resolution of underlying disease
- Potential to prevent refractory disease and speed normalisation of markers of organ damage
- Striking reduction in use of plasma exchange and length of stay in the ICU and hospital, potentially providing considerable cost savings
- Safety profile in line with previous study results and mechanism of action

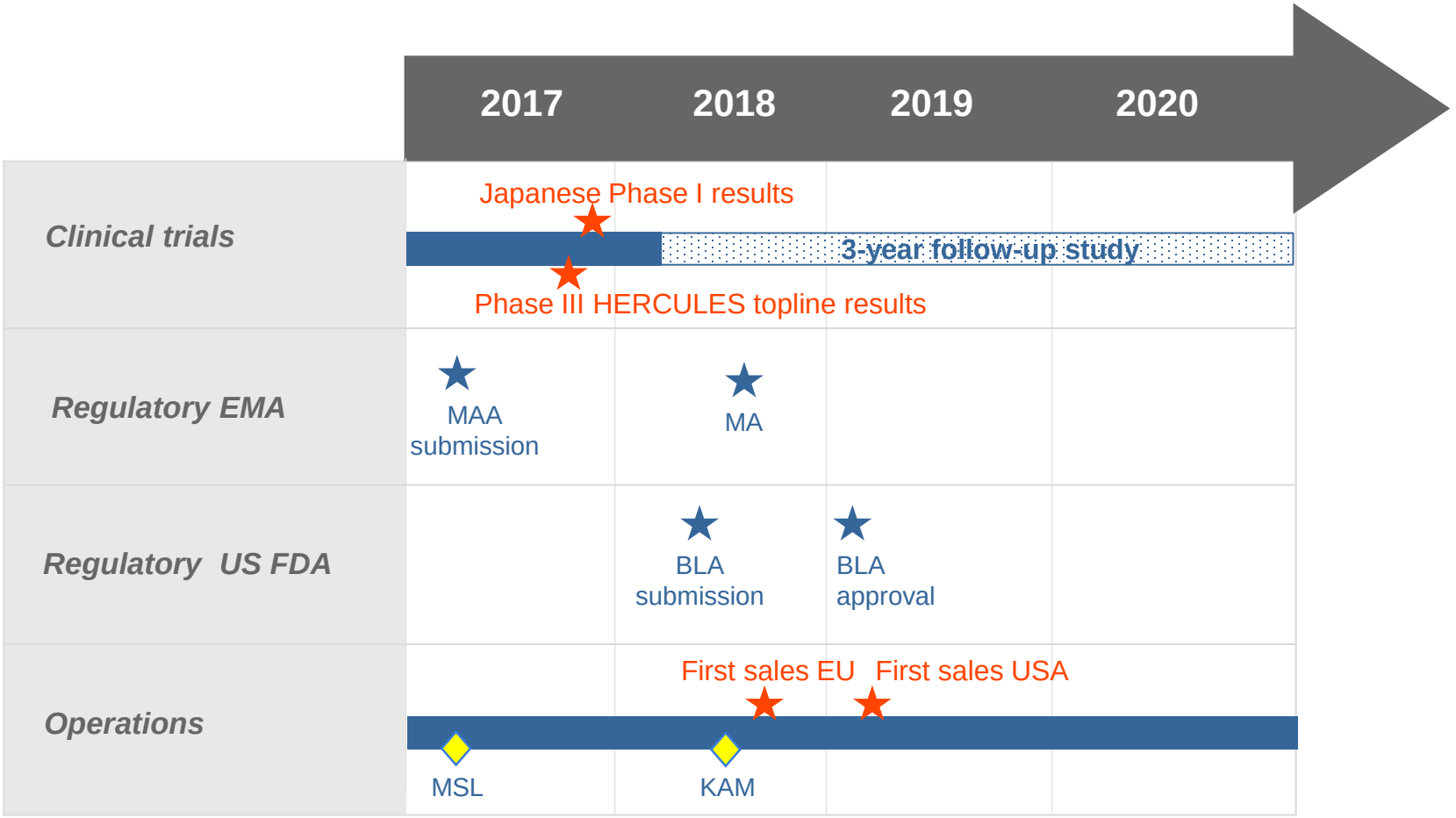
Next steps

All communicated timelines remain on track

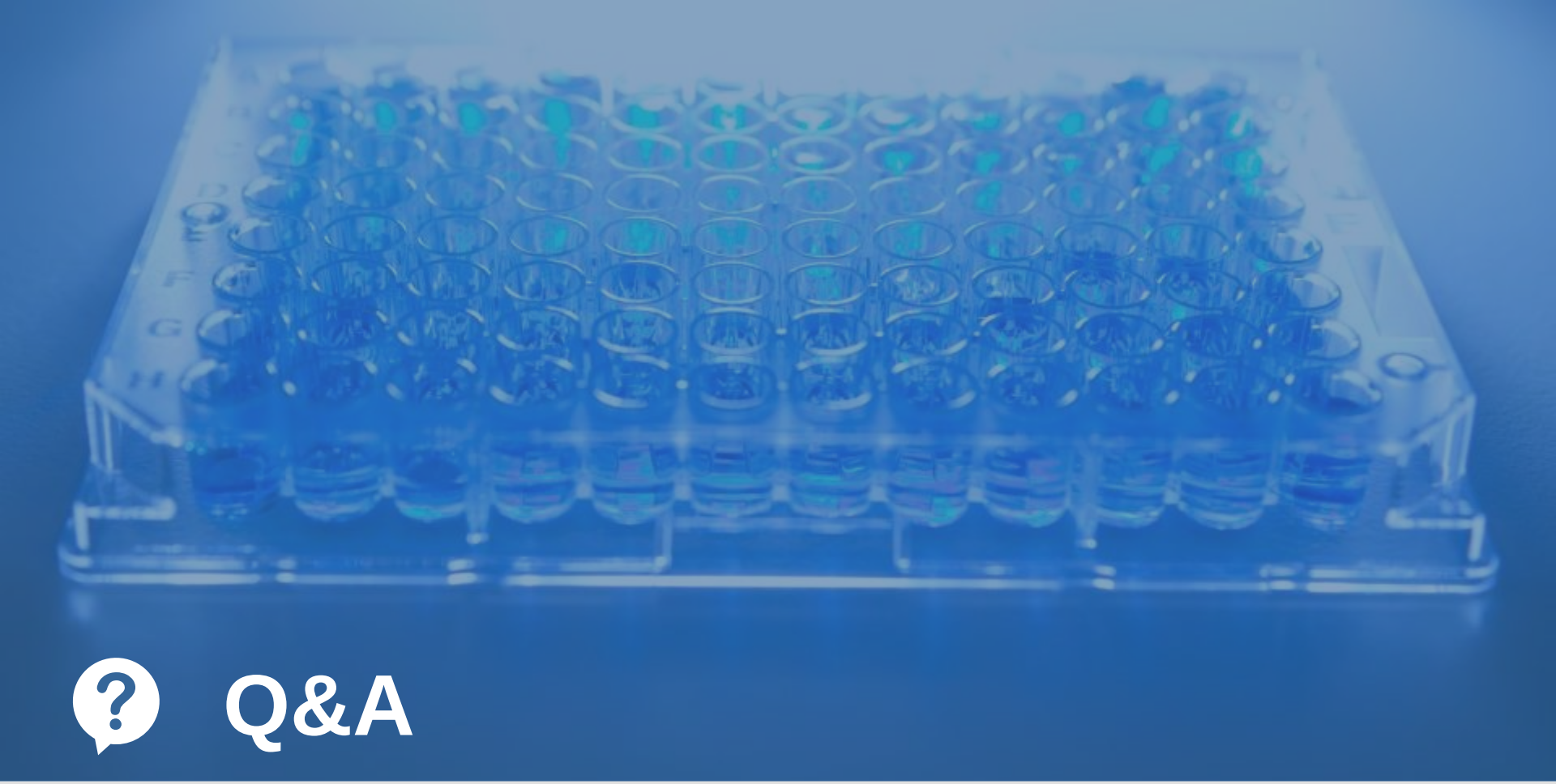
- Complete full analysis of Phase III HERCULES results and present at a key scientific conference ✓ and submit to a peer-reviewed journal
- Submit Phase III HERCULES results to EMA to support the MAA filed in February 2017 ✓
- Prepare BLA for USA FDA, filing planned in H1 2018
- Continue the 3-year follow-up study for eligible patients who participated in the Phase III HERCULES study
- Continue preparations for commercialisation of caplacizumab which is wholly-owned

Caplacizumab in aTTP

Key anticipated milestones



MAA: marketing authorisation application; **MA**: marketing authorisation; **BLA**: biologic license application; **MSL:** medical science liaison; **KAM**: key account manager



Q&A

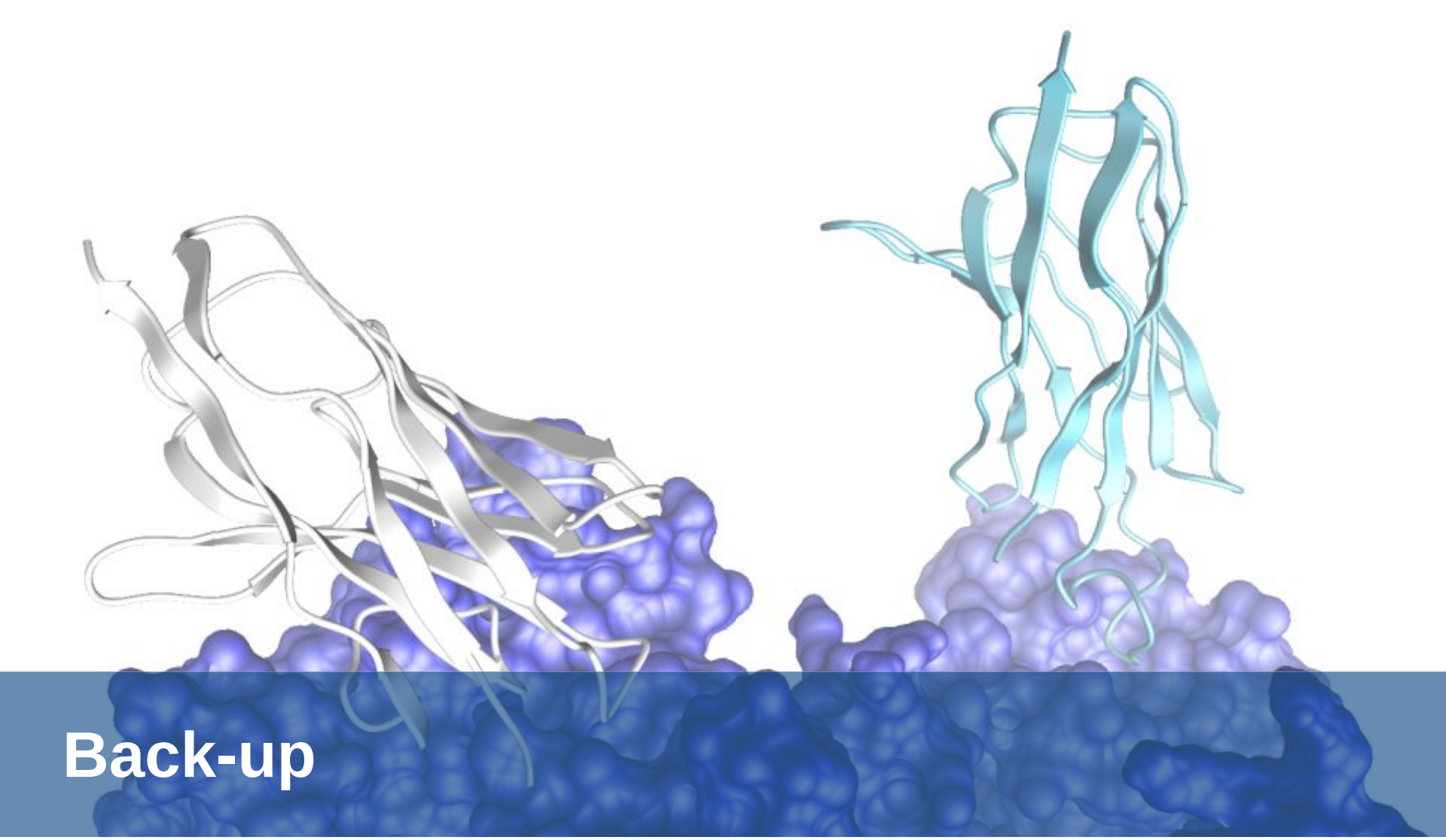
CONTACT DETAILS

+32 9 262 00 00

investors@ablynx.com

www.ablynx.com

Ablynx

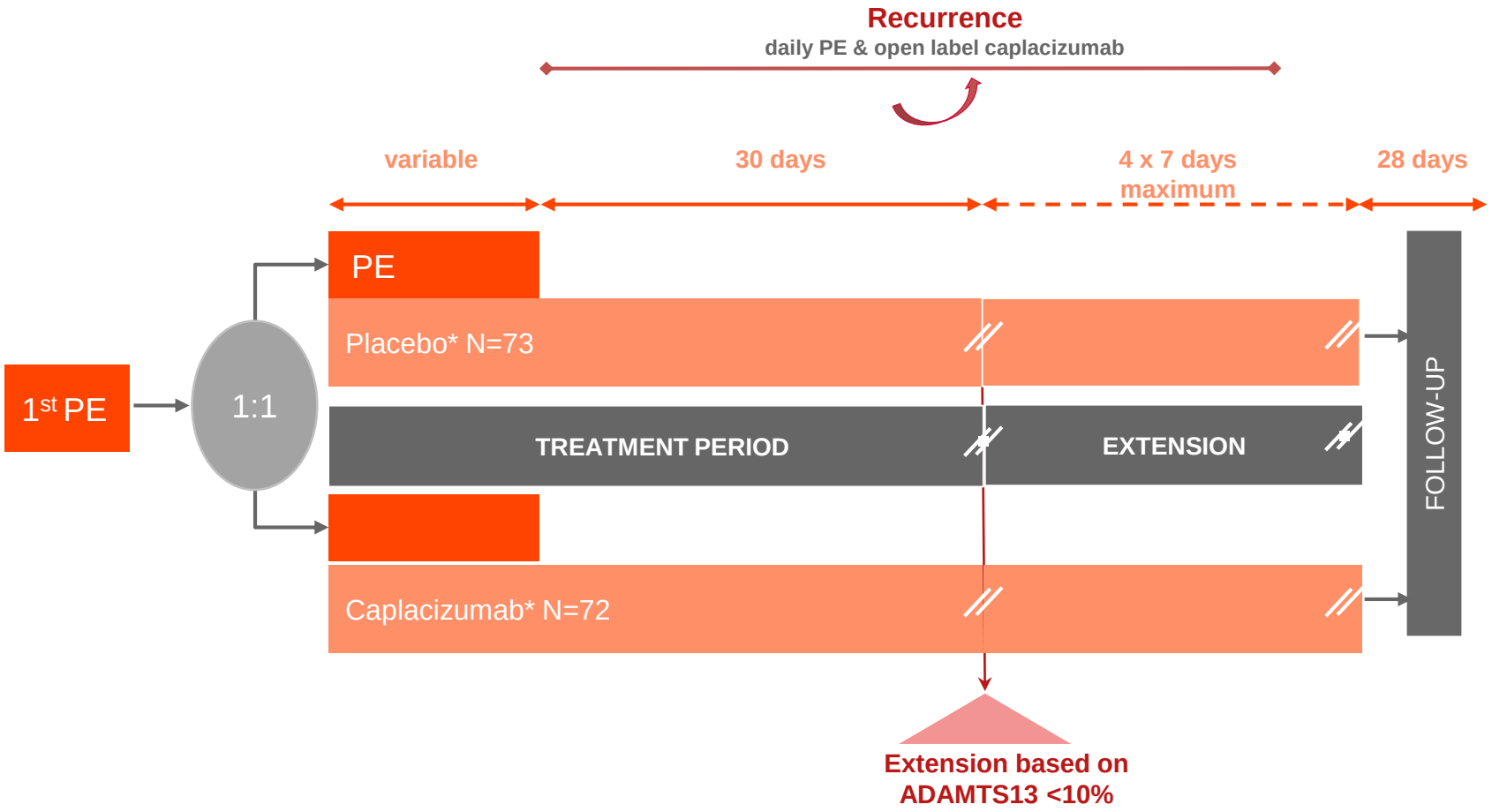


Back-up

Ablynx

Phase III HERCULES study design

Randomised, double-blind, placebo-controlled, multi-national study



** i.v. bolus (10mg) followed by daily s.c. dose (10mg)*

PE: plasma exchange

Key study endpoints

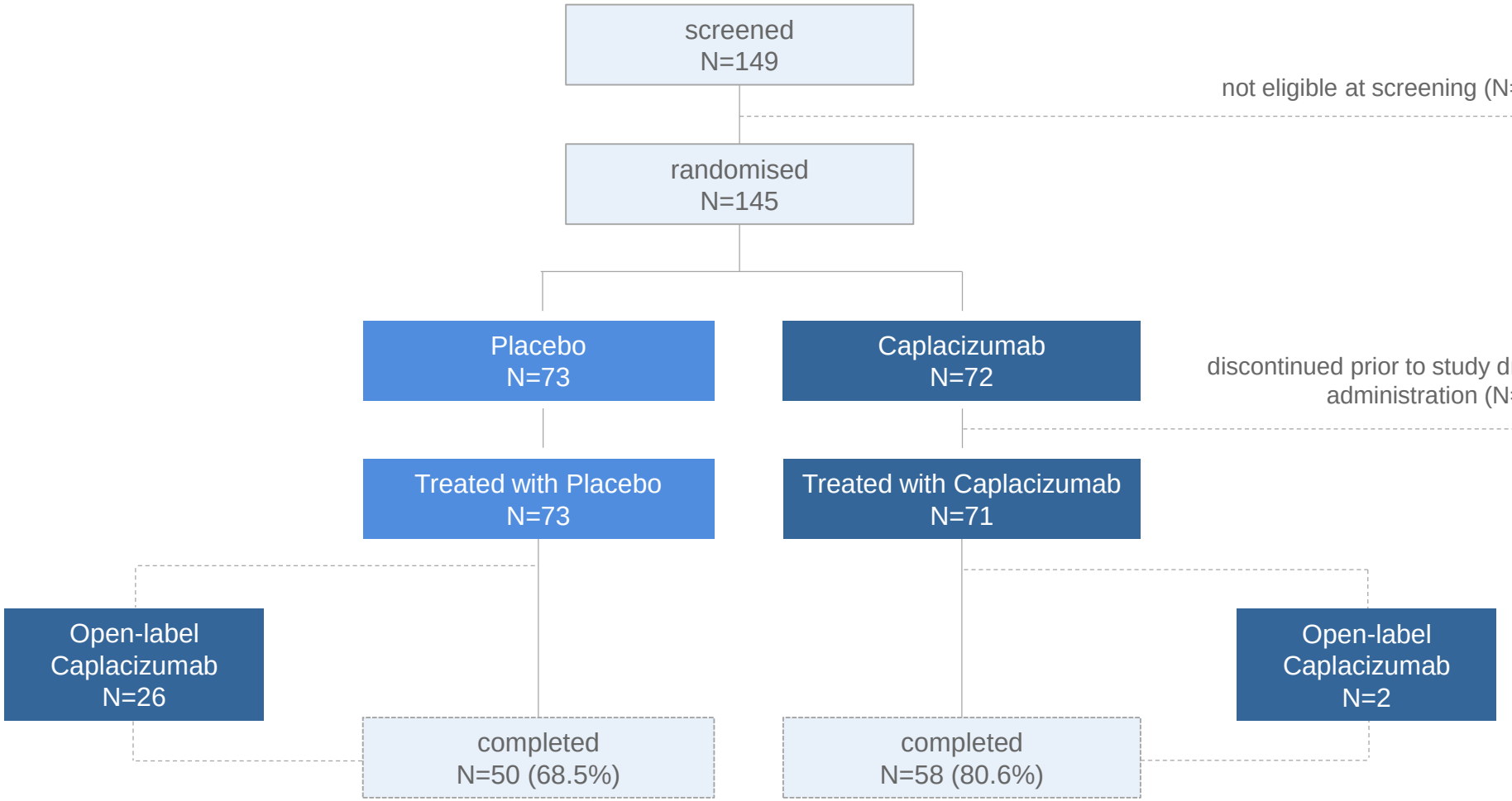
- Primary endpoint: time to confirmed platelet count response[1]
- Key secondary endpoints (hierarchically tested)
    1. aTTP-related death, recurrence of aTTP, or at least one major thromboembolic event during the study drug treatment period
    2. recurrence of aTTP in the overall study period
    3. refractoriness to treatment
    4. time to normalization of 3 organ damage markers
- Safety
- PK/PD and anti-drug antibodies[2]

[1] platelet count response was defined as initial platelet count ≥ 150×10^9/L with subsequent stop of daily PE within 5 days

[2] data not yet available

Phase III HERCULES study

Recruitment flow



Patient demographics and baseline disease characteristics

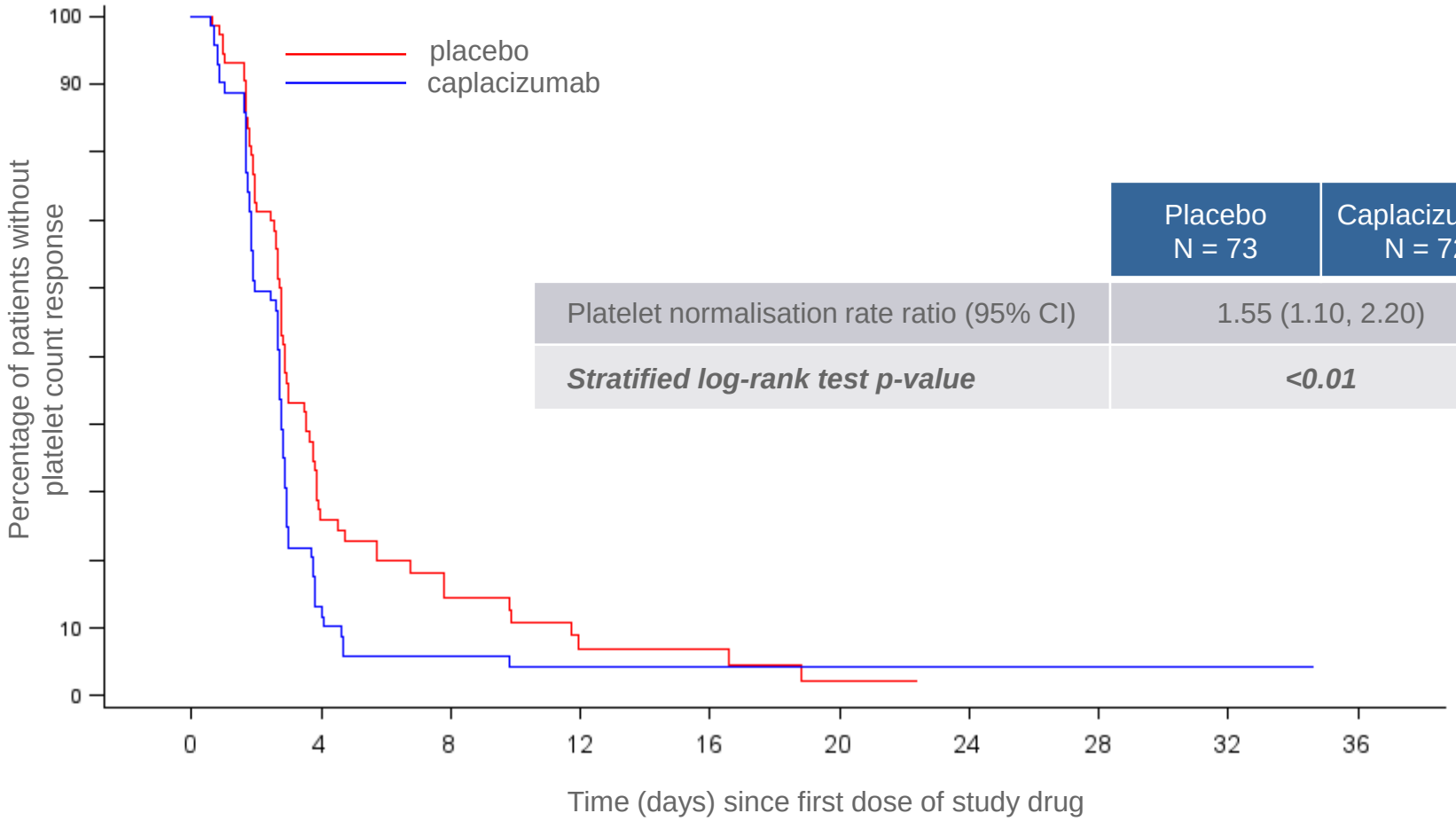
Groups generally well balanced

	Placebo N=73	Caplacizumab N=72
Mean age (SD)	47.3 (14.1)	44.9 (13.5)
Females – N (%)	51 (69.9)	49 (68.1)
Baseline platelet count (10^9/L) – mean (SD)	39.1 (29.1)	32.0 (27.2)
Previous aTTP episode(s) – N (%) - initial - recurrent	 34 (46.6) 39 (53.4)	 48 (66.7) 24 (33.3)
ADAMTS13 activity at baseline – N (%) - <10% - ≥10%	 65 (90.3) 7 (9.7)	 58 (81.7) 13 (18.3)
Disease severity at baseline – N (%)* - less severe - very severe	 48 (65.8) 7 (34.2)	 42 (58.3) 30 (41.7)

** very severe was defined as: French severity score ≥3 (cerebral involvement: yes=1 / no=0, LDH: >10xULN=1 / ≤10xULN=0, age: >60 years=2 / >40 and ≤60 years=1 / ≤40 years=0), or severe neurological involvement at baseline, or cardiac involvement (cTnI > 2.5 x upper limit of normal*

Primary endpoint

Statistically significant reduction in time to platelet count response*



	Placebo N = 73	Caplacizumab N = 72
Platelet normalisation rate ratio (95% CI)	1.55 (1.10, 2.20)	
Stratified log-rank test p-value	***<0.01***	

** platelet count response was defined as initial platelet count ≥ 150×10^9/L with subsequent stop of daily PE within 5 days*

First key secondary endpoint

Subjects with aTTP-related death, aTTP recurrence or at least one major thromboembolic event during the study drug treatment period

Number of subjects (%)	Placebo N=73	Caplacizumab N=72*
Total number of subjects with at least one of the events below[1]	**36 (49.3)**	**9 (12.7)**
aTTP-related death[2]	3 (4.1)	0
recurrence[3] of aTTP	28 (38.4)	3 (4.2)
at least one treatment emergent major thromboembolic event[2]:	6 (8.2)[4]	6 (8.5)
- cerebrovascular accident	*3 (4.1)*	*2 (2.8)*
- myocardial infarction	*1 (1.4)*	*1 (1.4)*
- pulmonary embolism	*0*	*1 (1.4)*
- deep venous thrombosis (spontaneous)	*1 (1.4)*	*0*
- deep venous thrombosis (catheter-associated)	*2 (2.7)*	*3 (4.2)*
p-value	***<0.0001***	

** percentages are based on 71 subjects entering the study drug treatment period*

[1] patients could have more than 1 event
[2] adjudication of aTTP-related death and major thromboembolic events by a blinded independent committee
[3] recurrence = recurrent thrombocytopenia after initial recovery of platelet count, requiring re-initiation of daily PEX
[4] 26 of 73 placebo treated patients had an exacerbation and were switched to open-label caplacizumab, potentially preventing additional treatment emergent major thromboembolic events during the study drug treatment period

Second key secondary endpoint

Subjects with aTTP recurrence during the overall study period

Number of subjects (%)	Placebo N=73	Caplacizumab N=72*
aTTP recurrence[1]	**28 (38.4)**	**9 (12.7)**
during the study drug treatment period	28 (38.4)	3 (4.2)
during the follow-up period	0	6 (9.1)[2]
p-value	***<0.001***	

** percentages are based on 71 subjects entering the study drug treatment period and 66 subjects in the follow-up period*

[1] recurrence = recurrent thrombocytopenia after initial recovery of platelet count, requiring re-initiation of daily PEX

[2] ADAMTS-13 activity levels were <10% at the end of the study drug treatment period in all of these patients

Third key secondary endpoint

Percentage of subjects with refractory aTTP

- Protocol-specified key secondary endpoint (Benhamou *et al.*, 2015)

Number of subjects (%)	Placebo N=73*	Caplacizumab N=72
Refractory aTTP[1]	3 (4.2)	0
p-value	*0.057*	

[1] refractory TTP = absence of platelet count doubling after 4 days of standard treatment and LDH > ULN

- International TTP working group consensus definition (Scully *et al.*, 2017)

Number of subjects (%)	Placebo N=73*	Caplacizumab N=72
Refractory aTTP[2]	5 (7.0)	0
p-value	*0.018*	

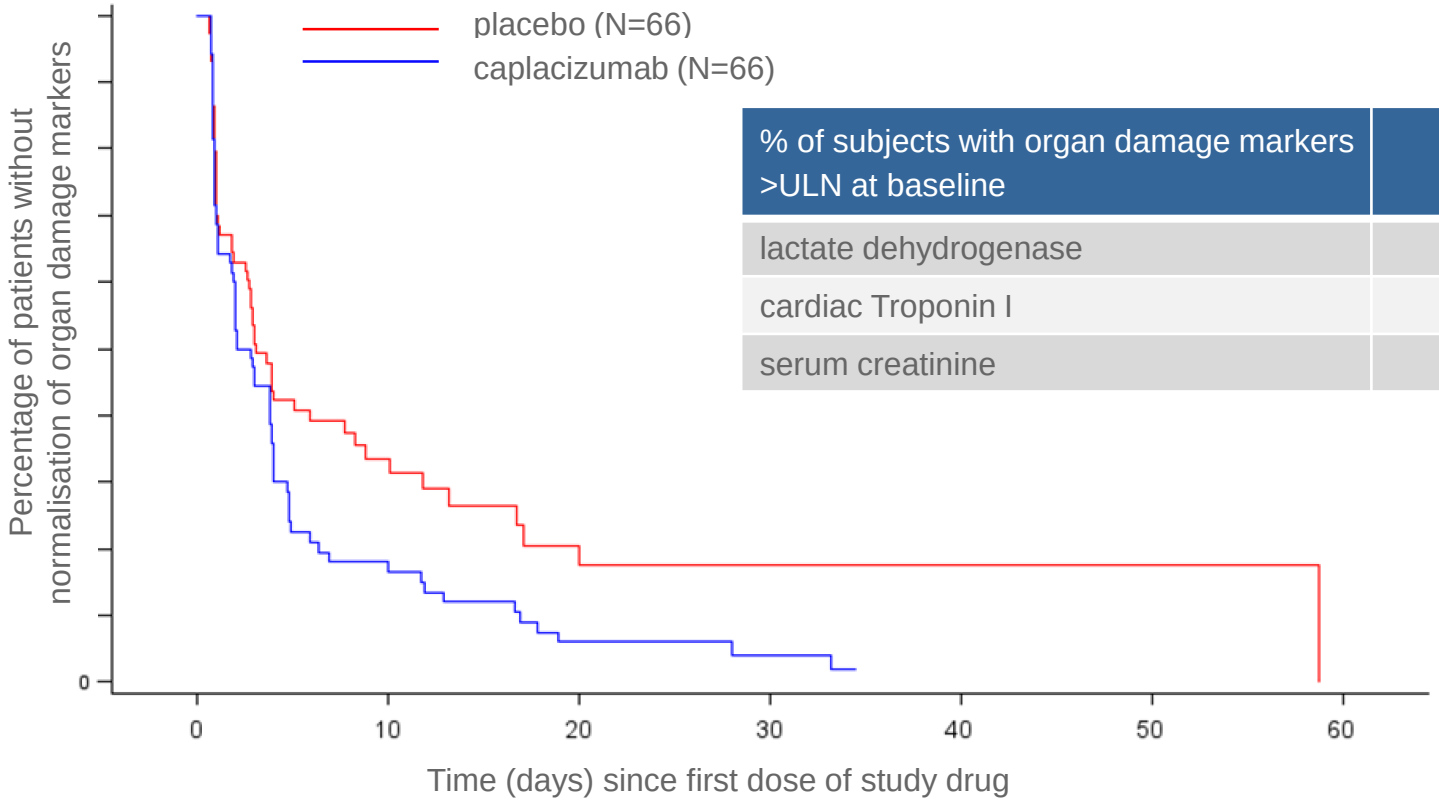
[2] refractory TTP = persistent thrombocyopenia, lack of a sustained platelet count increment or platelet counts of <50 x 10^9 L-1 and a persistently raised LDH level (> 1.5 ULN) despite five plasma exchanges and steroid treatment

** one subject discontinued prior to day 5 and is not included in the analysis*

LDH: lactate dehydrogenase; **ULN:** upper limit of normal

Fourth key secondary endpoint

Time to normalisation of organ damage markers[1]



% of subjects with organ damage markers >ULN at baseline	all subjects N=145
lactate dehydrogenase	87.1%
cardiac Troponin I	53.8%
serum creatinine	22.7%

[1] *time to LDH ≤ 1 x ULN and cardiac Troponin I ≤ 1 x ULN and serum creatinine ≤ 1 x ULN*

LDH: lactate dehydrogenase; **ULN:** upper limit of normal

Other secondary endpoints

Plasma exchange parameters, duration of ICU stay and overall hospitalisation

Overall study drug treatment period (mean±SE)	Placebo N=73[1]	Caplacizumab N=71	% relative reduction
Number of days of plasma exchange	9.4±0.8	5.8±0.5	↓38%
Volume of plasma (L)	35.9±4.2	21.3±1.6	↓41%
Number of days in intensive care unit	9.7±2.1 (n=27)	3.4±0.4	↓65%
Number of days in hospital	14.4±1.2	9.9±0.7	↓31%

[1] 26 of 73 placebo treated patients had an exacerbation and were switched to open-label caplacizumab, potentially reducing the mean values on plasma exchange parameters and duration of ICU stay and overall hospitalisation during the study drug treatment period

Safety profile

Treatment emergent adverse events (TEAEs)

Number of subjects (%) with TEAE	Placebo N=73	Caplacizumab N=71
At least one TEAE	71 (97.3)	69 (97.2)
At least one study drug-related TEAE	32 (43.8)	41 (57.7)
At least one TEAE leading to study drug discontinuation	9 (12.3)	5 (7.0)
At least one SAE	39 (53.4)	28 (39.4)
At least one study drug-related SAE	4 (5.5)	10 (14.1)
At least one SAE leading to death	3 (4.1)	1 (1.4)[1]

[1] adverse event occurred during the follow-up period of the study and was assessed by the investigator as not related to study drug treatment

Safety data consistent with Phase II TITAN study

Safety profile

Bleeding-related TEAEs*

Number of subjects (%) with TEAE	Placebo N (%)	Caplacizumab N (%)
Bleeding-related TEAEs (by SMQ)[1]	**17 (23.3)**	**33 (45.6)**
Epistaxis	1 (1.4)	17 (23.9)
Gingival bleeding	0	8 (11.3)
Bruising	3 (4.1)	5 (7.0)
Hematuria	1 (1.4)	4 (5.6)
Vaginal hemorrhage	1 (1.4)	3 (4.2)
Menorrhagia	1 (1.4)	2 (2.8)
Catheter site hemorrhage	3 (4.1)	2 (2.8)
Injection site bruising	2 (2.7)	2 (2.8)
Hematochezia	0	2 (2.8)
Hematoma	0	2 (2.8)

** Treatment emergent adverse events occurring in at least 2 subjects in either group*

[1] Standardised MeDRA Query "Hemorrhage"