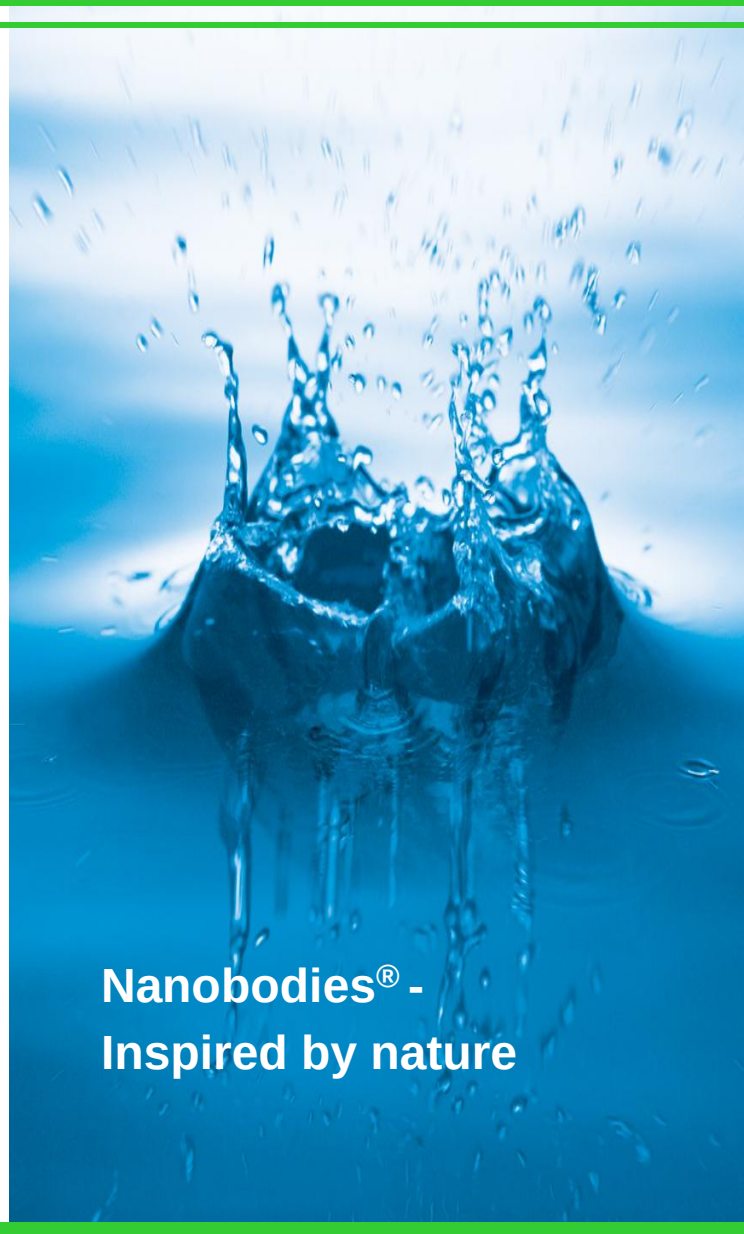
Results of the TITAN study for Caplacizumab

Webcast presentation

17th June 2014



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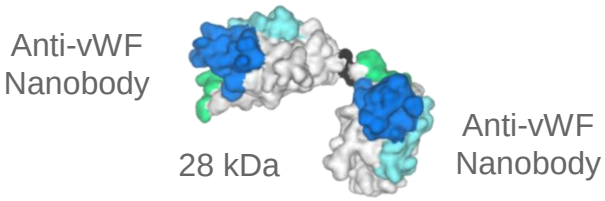
Summary

- Caplacizumab achieved clinical proof-of-concept in the TITAN trial in patients with acquired thrombotic thrombocytopenic purpura (TTP)
- Statistically significant 39% decrease in time to confirmed platelet normalisation in patients treated with caplacizumab compared to placebo for the group of patients with no plasma exchange prior to randomisation (92% of patients)
- The group of patients treated with caplacizumab in conjunction with the standard of care achieved confirmed platelet normalisation at more than twice the rate of the group receiving the standard of care plus placebo
- 81% of patients achieved complete remission in the active drug treatment arm compared to 46% in the placebo arm
- 73% fewer exacerbations in the active drug treatment arm compared to placebo
- Caplacizumab was well tolerated with a manageable increased bleeding tendency

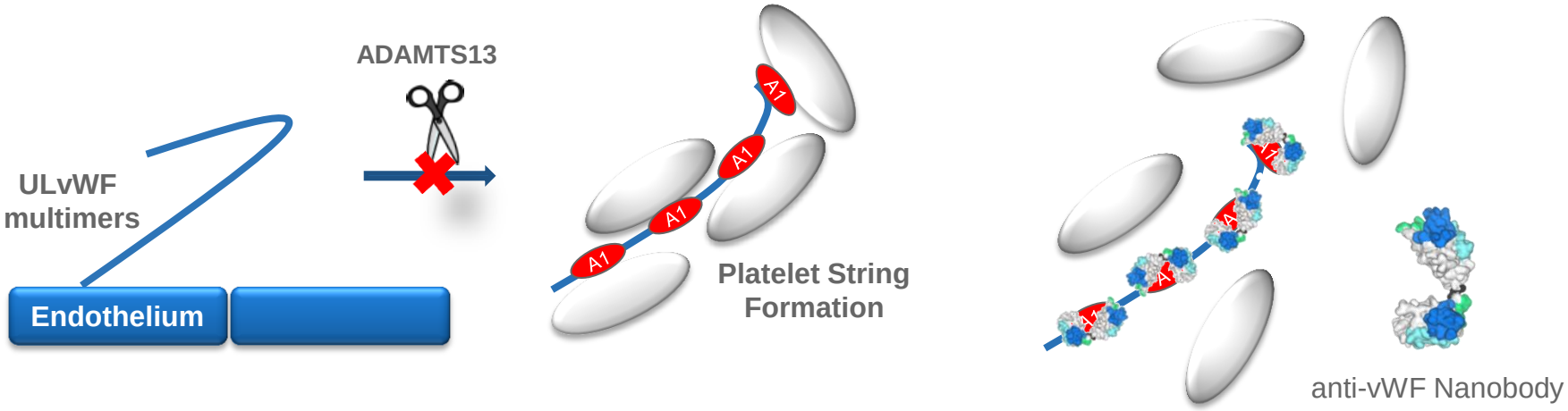
Significant unmet need in the treatment of acquired TTP

- Potentially life threatening rare disorder of the blood coagulation system
- Causes extensive microscopic thrombi in small blood vessels throughout the body
- Exists in two forms: congenital (<10%) and acquired (>90%)
- No specifically indicated therapeutic drug available
- Standard of care - multiple daily plasma exchanges
- Unmet medical need
  - lengthy hospital stays
  - potential clinical complications
  - potential relapse after recovering from a first TTP episode
- Estimated ~10,000 TTP-related events annually in US and Europe

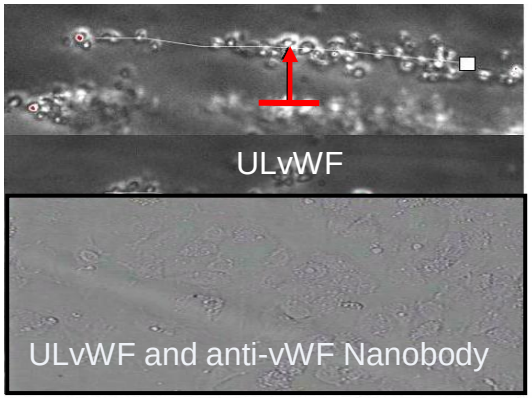


Caplacizumab – designed to prevent formation of microthrombi in TTP

anti-vWF Nanobody blocks the platelet – ULvWF interaction



***Ex vivo* platelet string formation**



Anti-vWF Nanobody inhibits platelet string formation caused by ULvWF in plasma of TTP patients

Caplacizumab in acquired TTP

Healthy active adult

Sudden onset: severe fatigue, headache, bizarre behaviour, vertigo, seizures, coma, etc.

Incidence: 11.3 per million[1]
Currently no drugs specifically approved to treat acquired TTP

Diagnosis of TTP

+ caplacizumab

Daily plasma exchanges in hospital until recovery of platelet count

Caplacizumab on top of PEX could potentially result in:

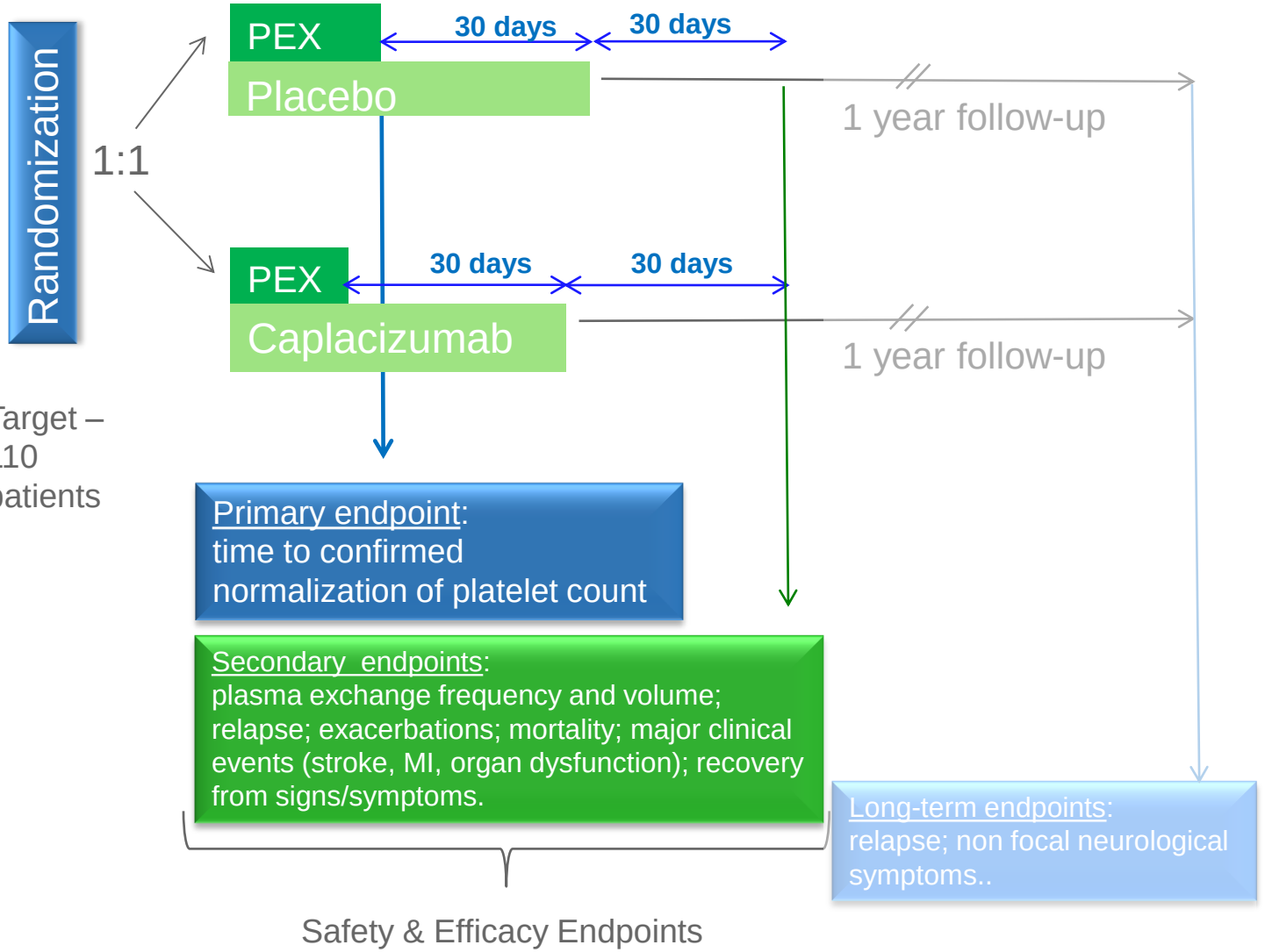
- fewer days and volume of PEX
- reduction in relapse/exacerbations
- improved longer term outcome

[1] Oklahoma Registry

Caplacizumab in acquired TTP – TITAN design and schedule

Inclusion criteria:
patients with acquired TTP requiring plasma exchange (PEX)

Exclusion criteria:
- severe infection / sepsis
- pregnancy
- bone marrow transplantation
- disseminated intravascular coagulation
- known congenital TTP



TITAN trial milestones

- January 2011: first patient recruited
- September 2013: protocol amended to allow inclusion of patients who had undergone 1 plasma exchange
- January 2014: trial stopped after 75 patients recruited to allow early analysis of data
- March 2014: last patient completes one month follow-up visit
- June 2014: initial top-line Phase II results published

Primary endpoint – time to confirmed platelet normalisation

	Caplacizumab N = 36	Placebo N = 39
Median days to confirmed platelet response – subjects with no prior plasma exchange, N = 69 (95% CI)	3.00 (2.74, 3.88)	4.92 (3.21, 6.59)
Overall Hazard Rate Ratio for Caplacizumab vs. Placebo (95% CI)	2.197 (1.278, 3.778)	
Stratified Log-rank Test p-value	0.013	

The group of patients treated with caplacizumab in conjunction with the standard of care achieved confirmed platelet normalisation at more than twice the rate of the group receiving the standard of care plus placebo

Treatment groups at baseline – demographics

		Caplacizumab N = 36	Placebo N = 39	Total N = 75
Age (years) mean ± SD		40.6 ± 12.7	42.5 ± 13.2	41.6 ± 12.9
Gender	Male	12 (33%)	19 (49%)	31 (41%)
	Female	24 (67%)	20 (51%)	44 (59%)
Ethnicity/Race	Caucasian	32 (89%)	34 (87%)	66 (88%)
	Black	4 (11%)	5 (13%)	9 (12%)
Baseline BMI (kg/m^2) mean ± SD (N=72)		28.7 ± 9.1	29.3 ± 6.7	29.1 ± 7.7

Balanced treatment groups apart from more women in the caplacizumab arm than in placebo arm – reflects gender distribution in TTP and not prognostic factor

Treatment groups at baseline – disease characteristics

	Caplacizumab N = 36	Placebo N = 39	Total N = 75
Platelets ($10^3/mm^3$) mean ± SD	21.1 ± 18.2	28.0 ± 20.0	24.6 ± 19.3
minimum, maximum	2, 70	5, 84	2, 84
LDH (U/L) mean ± SD	1277 ± 853	1270 ± 939	1274 ± 891
Initial Episode (%)	24 (66.7%)	27 (69.2%)	51 (68.0%)

Comparable disease severity in both treatment arms

Top line secondary endpoints

	Caplacizumab N = 36	Placebo N = 39
Exacerbations up to 30 days after end of daily plasma exchange for the complete population	3 (8%)	11 (28%)
Complete remission up to 30 days after end of daily plasma exchange as measured by confirmed platelet response and absence of exacerbation	29 (81%)	18 (46%)
Proportion of subjects with exacerbation and/or relapse at 1 month follow-up after study drug treatment was completed	13 (36.1%)	13 (33.3%)
Deaths	0	2

These secondary endpoints illustrate the potential protective effect of caplacizumab treatment in the acute phase of TTP

Safety profile – treatment emergent adverse events (TEAEs)

	Caplacizumab N = 35	Placebo N = 37	Total N = 72
Subjects with any TEAE	34 (97%)	37 (100%)	71 (99%)
Number of TEAEs	574	544	1118
Subjects with any TE Serious AEs	20 (57%)	19 (51%)	39 (54%)
- Subjects with TTP as TE Serious AE	13 (37%)	13 (35%)	26 (36%)
Number of TE Serious AEs	44	36	80
Subjects with TEAE leading to study drug discontinuation	4 (11%)	2 (5%)	6 (8%)

Comparable number of subjects between the two treatment arms with TE Serious AE as well as comparable number of TEAEs

Safety profile – TEAEs indicative of bleeding

	Caplacizumab N = 35	Placebo N = 37	Total N = 72
Number of bleeding related TEAEs	66	35	101
- mucosal bleeding	24	16	40
- bruising/haematoma	16	9	25
- metro/menorrhagia	9	2	11
- other	17	8	25
Number of bleeding related TE SAEs	5	2	7

Manageable increased bleeding tendency in caplacizumab arm
2 subjects in caplacizumab arm experienced 5 SAEs related to bleeding compared to 2 subjects with 2 bleeding SAEs in placebo arm

Safety profile – immune-related TEAEs

	Caplacizumab N = 35	Placebo N = 37	Total N = 72
Number of immune-related TEAEs	40	26	66
- of which injection site reactions	6	2	8
- of which hypersensitivity including transfusion reactions	11	6	17
- rash/urticaria	22 (1 SAE)	17	39
- other	1	1	2
Number of immune-related SAEs	1	0	1

Higher number of manageable immune system related TEAEs with caplacizumab of which only one serious

TITAN trial – overall conclusions on top line results

- Clinical proof-of-concept demonstrated
  - Hazard Ratio of 2.2 , p = 0.013 (95% CI [1.28, 3.78])
  - Median days to normalised platelet counts: 3.0 days for caplacizumab vs. 4.9 days for placebo
- Reduction in number of exacerbations to 3 in caplacizumab arm compared to 11 in placebo arm
- 81% of patients achieved complete remission in the active treatment arm compared to 46% in the placebo arm
- No deaths in caplacizumab arm compared to 2 deaths in placebo arm
- TEAEs and serious TEAEs consistent with serious, potentially life-threatening condition
- Increased bleeding tendency, which is manageable

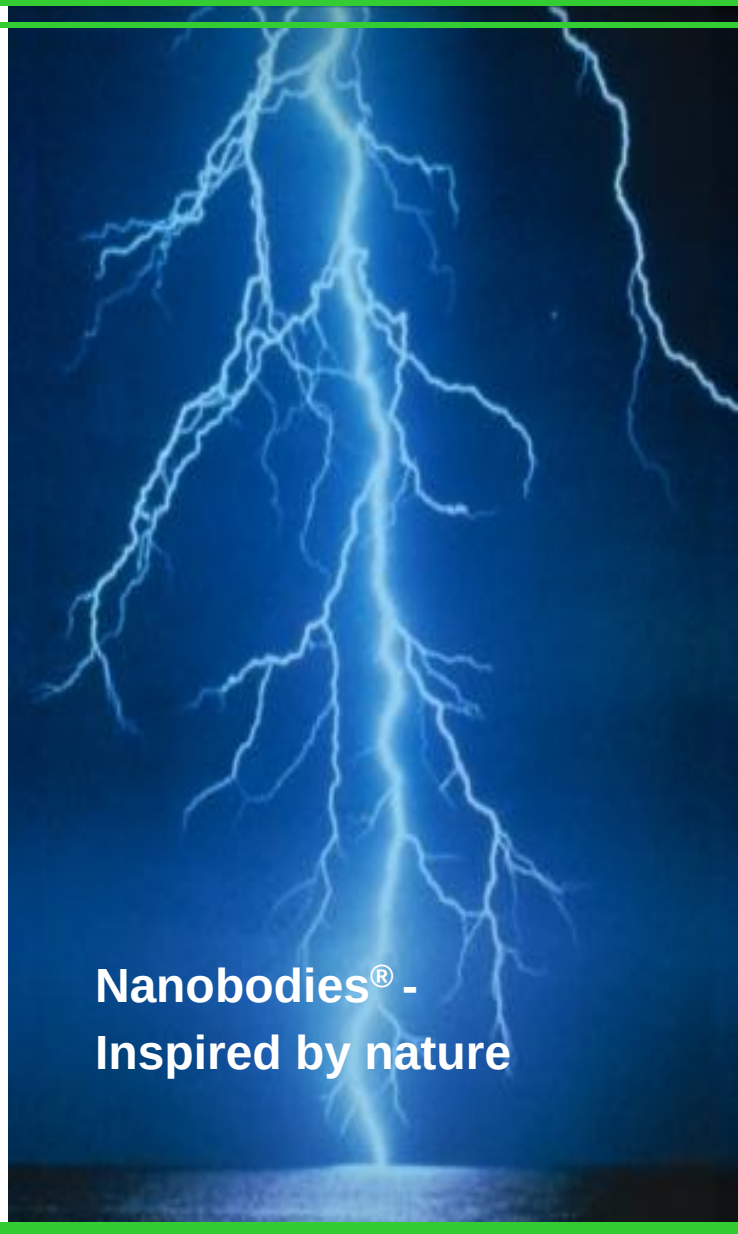
Clinical benefit demonstrated for patients with acquired TTP with acceptable safety profile

Caplacizumab – next steps

- Complete full analysis of TITAN study and consult with KOLs and regulatory authorities
- Complete a Phase I trial to demonstrate bioequivalence between the liquid and lyophilized formulations
- Continue preparations to start a Phase III study in 2015
- Discuss the programme and TITAN data with potential partners
- Continue to evaluate options to commercialize caplacizumab

Ablynx

Q&A



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