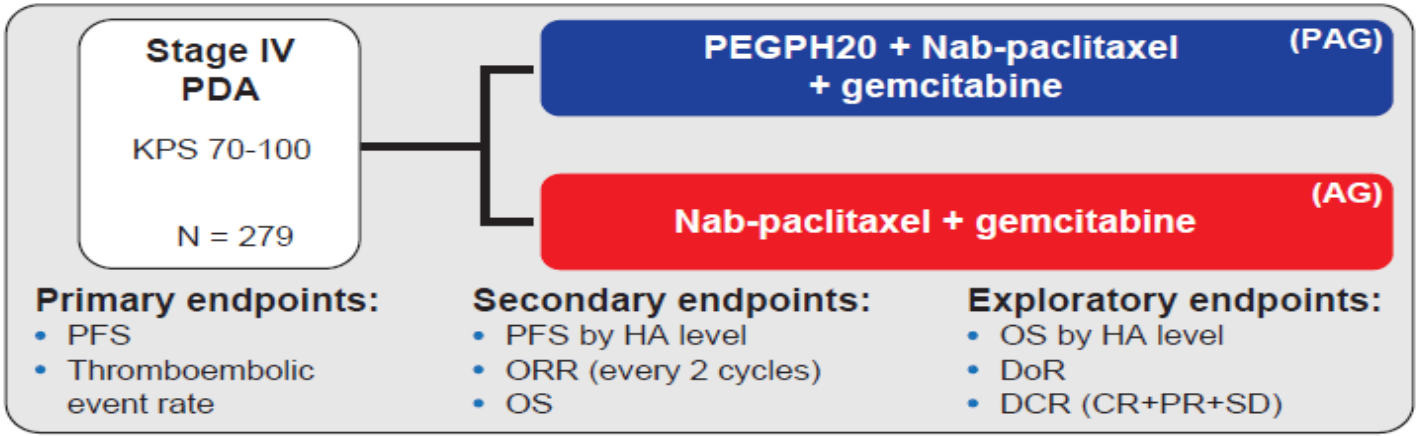
Study 202 Overall Results and Stage 2 Results

January 5, 2017

Study 202 Design Overview

- Phase 2, randomized, multicenter study
- Patients with stage IV (metastatic), previously untreated PDA
- Primary & Secondary PFS Endpoint:
  - 80% power at 2-sided alpha level of 0.1



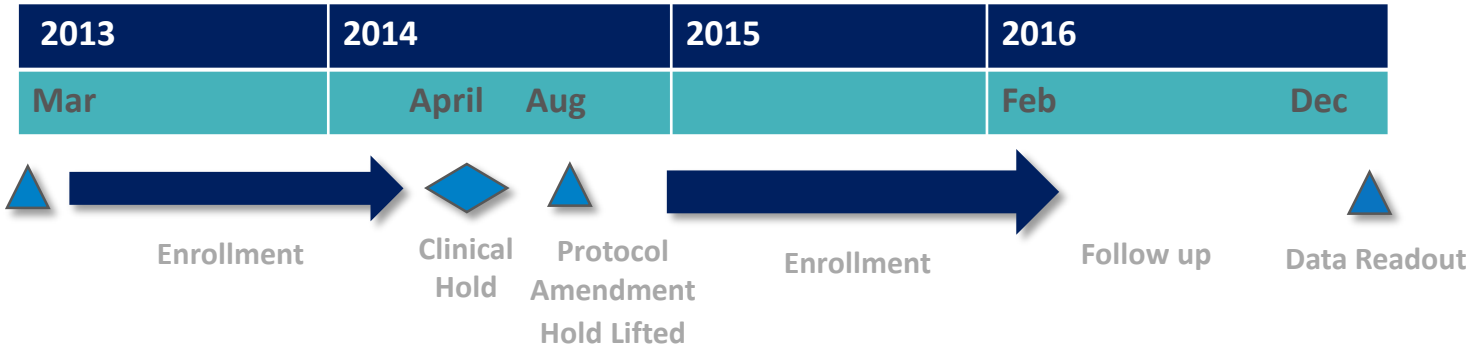
CR, complete response; DCR, disease control rate; DoR, duration of response; HA, hyaluronan; KPS, Karnofsky performance status; ORR, objective response rate; OS, overall survival; PDA, pancreatic ductal adenocarcinoma; PFS, progression-free survival; PR, partial response; SD, stable disease.

Halozyme/Ventana HA Companion Diagnostic (CDx)

Determining HA Status

- Novel CDx to identify patients with HA-High PDA tumors
- An affinity histochemistry assay with a scoring algorithm based on the HA staining pattern area in the extracellular matrix (ECM) over the entire tumor surface
- PDA tumors are HA-High when the HA score is ≥50%

Study 202 Study Timeline



Stage 1: n=146

- Training Set for CDx
- Develop Ventana HA scoring algorithm and cut-point
- ~40% HA High patients treated on PAG arm discontinued PEGPH20 at the clinical hold
- Presented at ASCO 2016

Stage 2: n=133

- Validation Set for CDx
- Prospectively validate Ventana HA scoring algorithm and cut-point used in Phase 3 study
- To be presented at Scientific Forum 2017

Study 202: Modifications Since Stage 1 Clinical Hold

Statistical Analysis Plan	Planned Analysis Populations: - Intent-to-Treat: Combined Stage 1 + Stage 2 efficacy analyses - Efficacy Evaluable (requires post baseline assessment): Primary endpoint (PFS) - Treated population: Separate analyses of Stage 1 and Stage 2 PFS event definition to include deaths occurring within 14 days of last study treatment
Protocol	Added Stage 2 Cohort: - 2:1 PAG to AG randomization - Excluded high TE risk patients - Added Low Molecular Weight Heparin prophylaxis to both arms - Added primary endpoint: rate of TE events in PAG patients

Study 202 Study Populations: December 2016

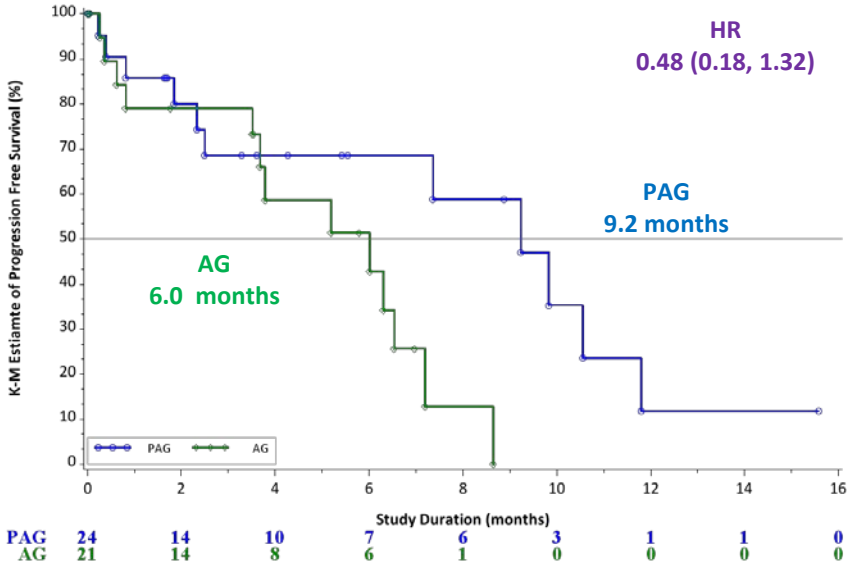
Population	Stage 1 (n)	Stage 2 (n)	Total Phase 2 (Stage 1 & Stage 2) (n)
Intent-To-Treat (Total) Intent-to-Treat (HA High)	146 HA-High: 47	133 HA-High: 37	279 HA-High: 84 (PFS Secondary Endpoint)
Treated Population (Total) Treated Population (HA High)	135 HA-High: 45*	125 HA-High: 35	260 HA-High: 80
Data Maturity: HA High Median Follow-Up Off Treatment Off Study	 8.8 months (0.3, 39.8) 100% 98%	 8.7 months (0.6, 27.9) 92% 80%	 8.5 (0.0, 39.8) 96% 90%

*Updated from ASCO 2016 where number of patients was 43 HA High; December 2016. Analysis includes 2 additional HA high patients (PAG arm), 2 PFS events reclassified upon data reconciliation, PFS analysis per revised definition. Updated Stage 1 data: medians unchanged; HR 0.48 (0.18, 1.32)

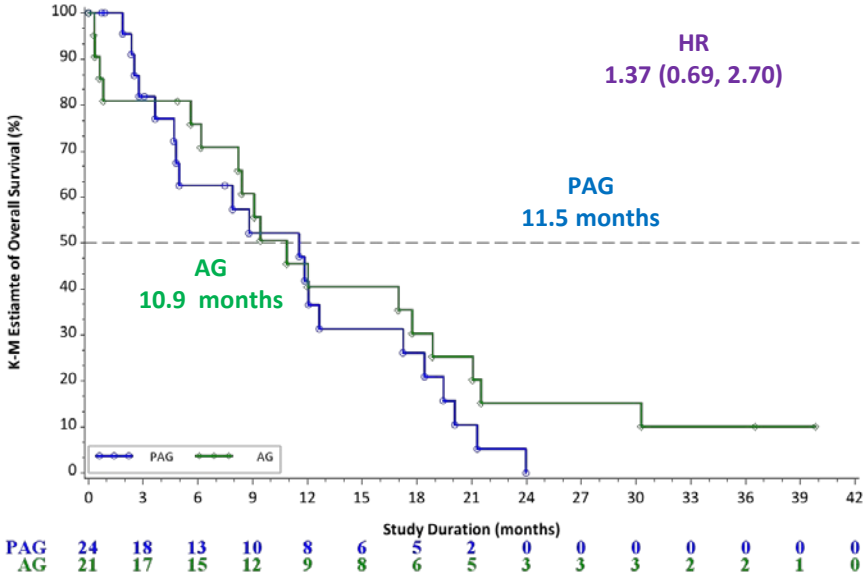
Study 202 Efficacy Summary

Stage 1 Secondary Endpoint PFS and Exploratory Endpoint OS in HA-High Patients

Progression Free Survival



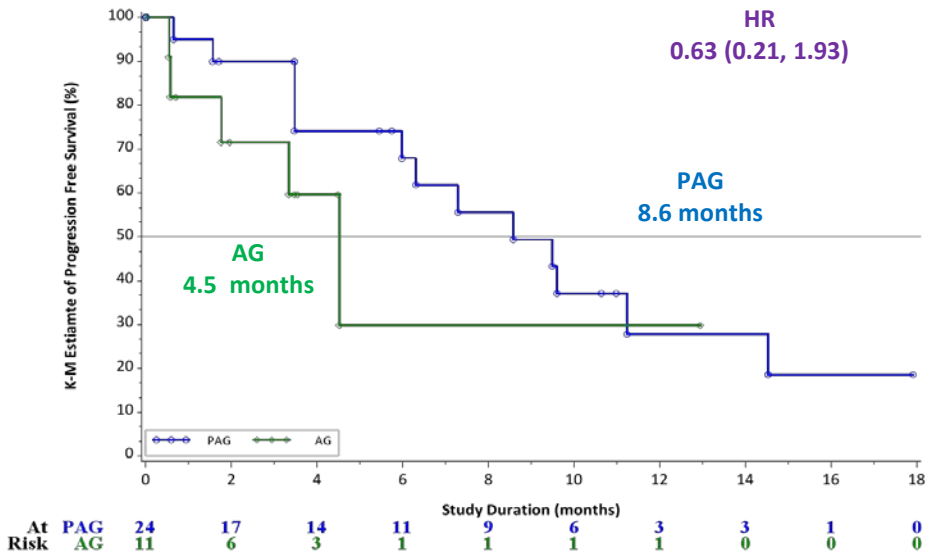
Overall Survival



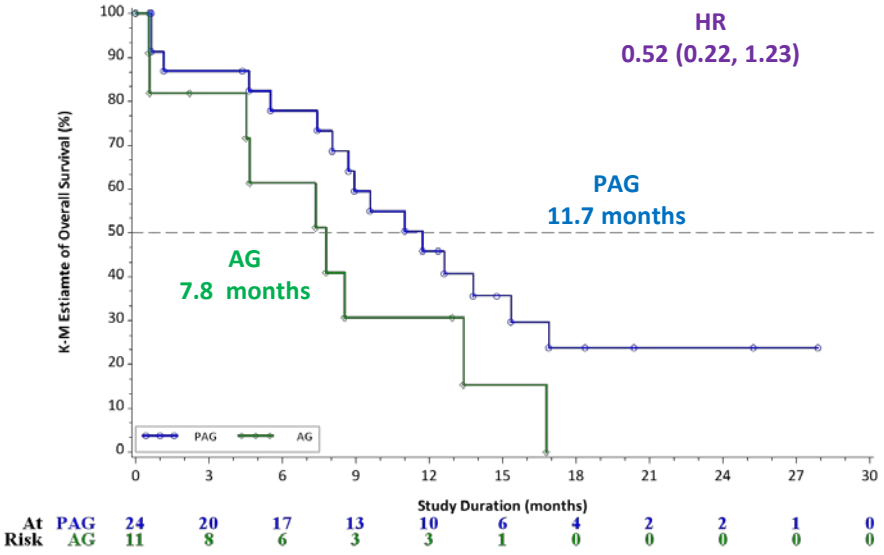
Treated Population

Stage 2 Secondary Endpoint PFS and Exploratory Endpoint OS in HA-High Patients

Progression Free Survival



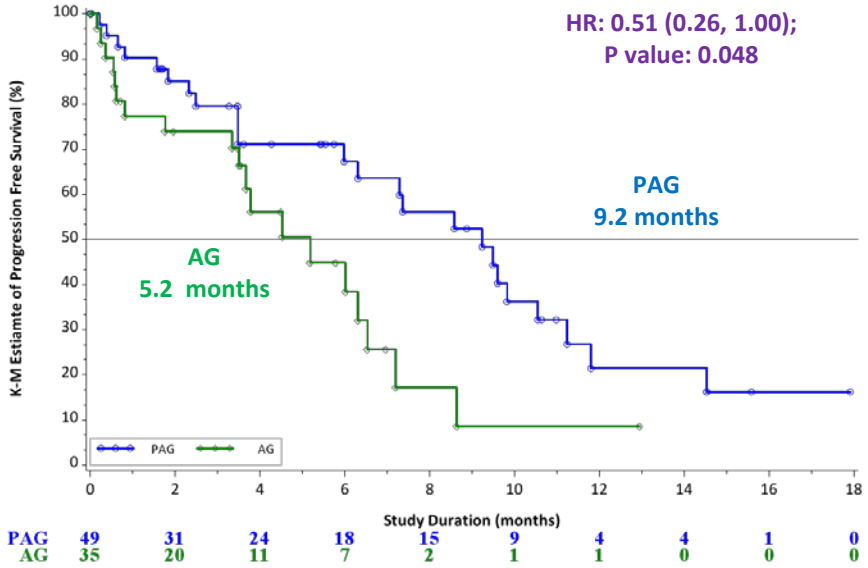
Overall Survival



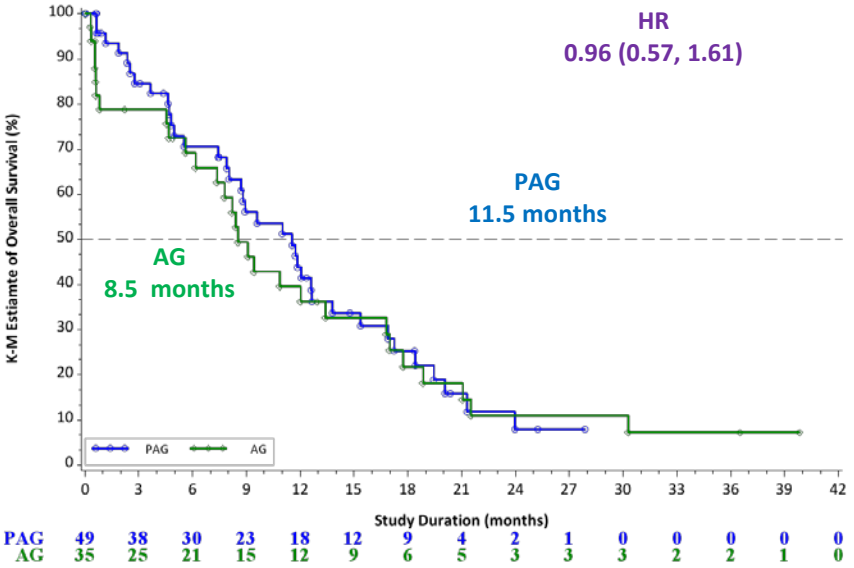
Treated Population

Study 202 (Stage 1 + Stage 2) Secondary Endpoint PFS and Exploratory Endpoint OS in HA-High Patients

Progression Free Survival



Overall Survival



ITT Population

Stage 2 Data

Stage 2 Patient Population

Populations (n)	PAG	AG
Treated Population N=125	86	39
Treated with HA available data N=111	77	34
• **Treated (HA High)** **N=35 (32%)**	**24**	**11**
• Treated (HA Low) N=76 (68%)	53	23

Baseline characteristics balanced across all groups

Stage 2 Secondary Endpoint PFS in HA High Patients

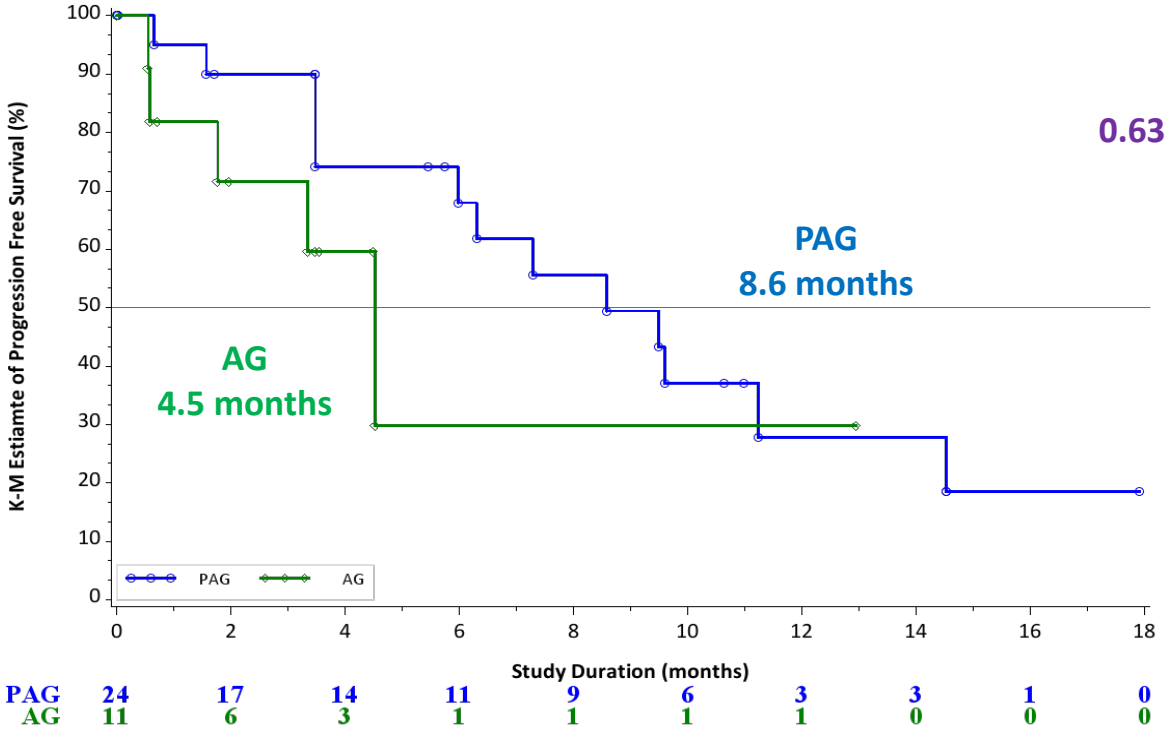
- **In 35 HA high patients, the PAG arm had a 91% improvement in median PFS over the AG arm; HR 0.63**

Populations	Events/Total (n); Median PFS, months		HR (95% CI)
	PAG	AG	
All treated	57/86; 6.4	23/39; 5.8	0.87 (0.53-1.42)
All treated with HA data	53/77; 6.4	20/34; 5.8	0.90 (0.53-1.52)
HA-Low	40/53; 6.0	15/23; 7.2	1.21 (0.63-2.30)
HA-High	**13/24; 8.6**	**5/11; 4.5**	**0.63 (0.21-1.93)**
6-month PFS Rate	68%	30%	
12-month PFS Rate	28%	30%	

Differences in PFS between treatment arms did not reach statistical significance
CI, confidence interval; HR, hazard ratio

Treated Population

Stage 2 Secondary Endpoint PFS in HA-High Patients



PAG
8.6 months

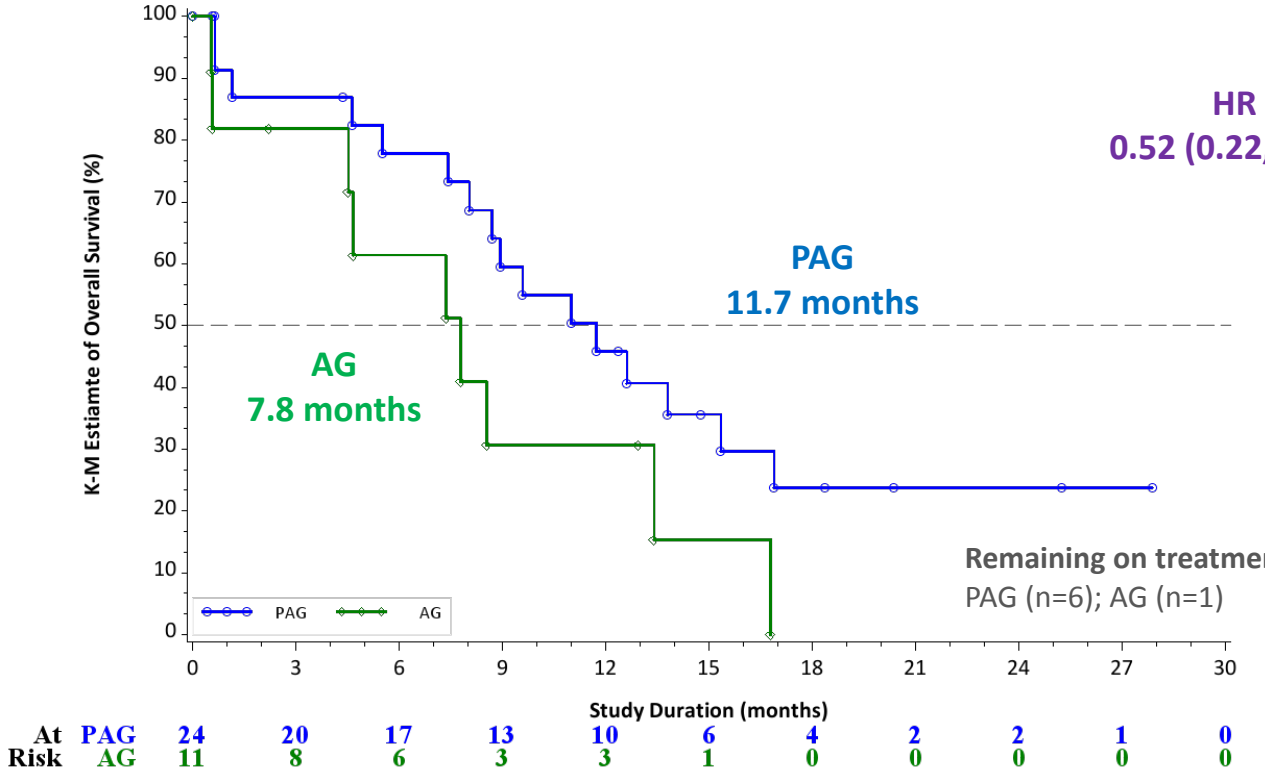
AG
4.5 months

HR:
0.63 (0.21, 1.93)

Remaining on treatment:
PAG (n=2); AG (n=1)

Treated Population

Stage 2 Exploratory Endpoint Overall Survival in HA-High Patients



HR
0.52 (0.22, 1.23)

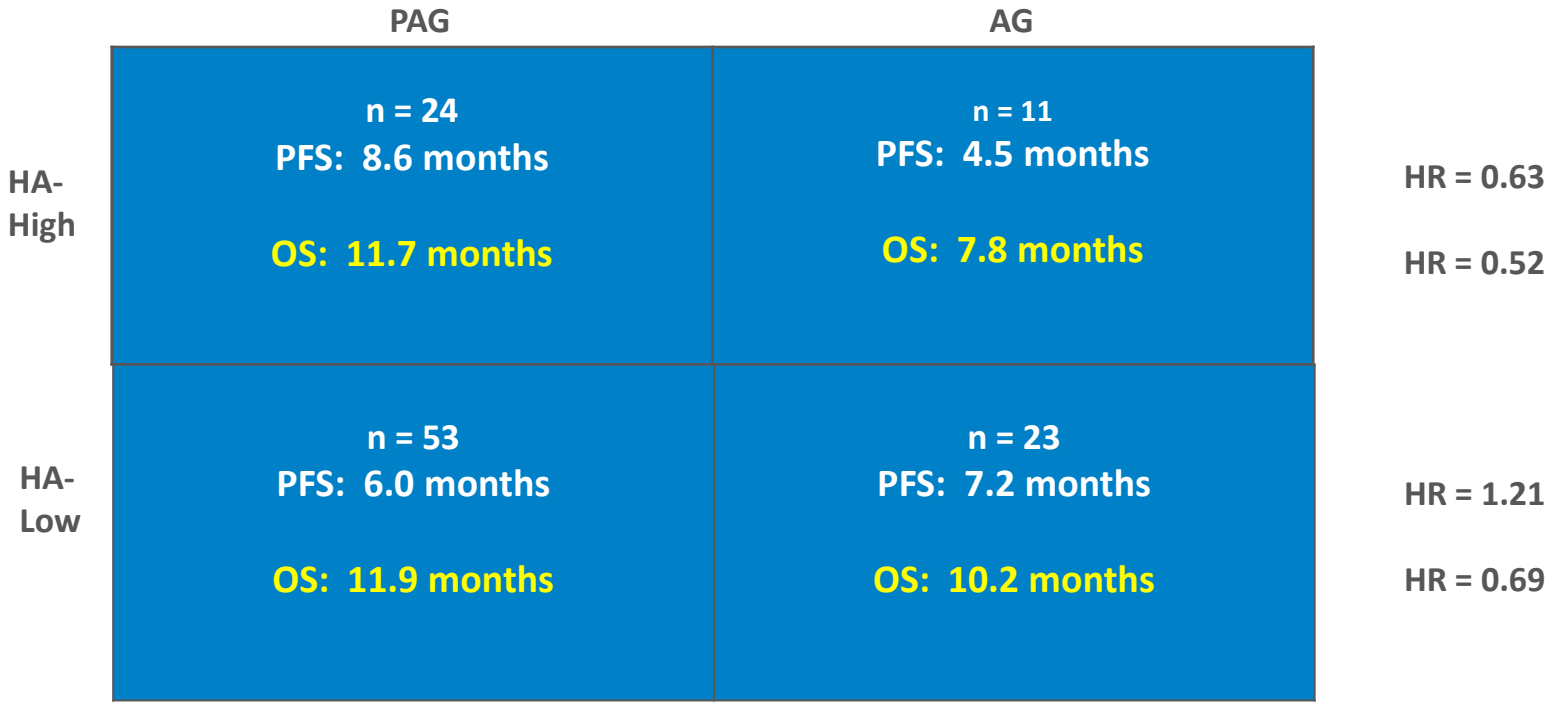
PAG
11.7 months

AG
7.8 months

Remaining on treatment and/or follow up:
PAG (n=6); AG (n=1)

Treated Population

Stage 2 PFS and OS Results Support HA High As A Potential Predictive and Prognostic Biomarker



Treated Population

Stage 2 Treatment Exposure*

Populations, n	PAG	AG
Treated population (n=125)	86	39
Treated population with HA data (n=111) (HA-High/HA-Low)	77 (24/53)	34 (11/23)
Treated population with HA data duration of treatment, months Median (range)	5.6 (0.1-18.2)	3.2 (0.03-12.9)
Treated subjects (HA-High) Duration of treatment, months median (range)*	**n = 24 5.9 (0.1-18.2)**	**n = 11 2.3 (0.03-12.9)**
≥ 6 months, n (%)	11 (46)	1 (9)
≥ 12 months, n (%)	5 (21)	1 (9)

*Exposure: first to last dose of any study medication

Treated Population

Stage 2 Treatment-Related Adverse Events (AEs) in ≥ 25% of Patients

Preferred Term	PAG (n = 86) Patients, n (%)		AG (n = 39) Patients, n (%)	
	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
Any AE	84 (97.7)	74 (86.0)	37 (94.9)	30 (76.9)
Fatigue	63 (73.3)	18 (20.9)	24 (61.5)	5 (12.8)
Peripheral edema	57 (66.3)	6 (7.0)	7 (17.9)	0 (0.0)
Muscle spasms	48 (55.8)	14 (16.3)	2 (5.1)	1 (2.6)
Alopecia	36 (41.9)	1 (1.2)	14 (35.9)	0 (0.0)
Anemia	36 (41.9)	12 (14.0)	14 (35.9)	10 (25.6)
Nausea	36 (41.9)	3 (3.5)	16 (41.0)	2 (5.1)
Diarrhea	33 (38.4)	5 (5.8)	15 (38.5)	3 (7.7)
Decreased appetite	32 (37.2)	3 (3.5)	11 (28.2)	0 (0.0)
Neutropenia	32 (37.2)	28 (32.6)	10 (25.6)	9 (23.1)
Neuropathy peripheral	30 (34.9)	6 (7.0)	13 (33.3)	3 (7.7)
Thrombocytopenia	28 (32.6)	16 (18.6)	7 (17.9)	2 (5.1)
ALT increased	25 (29.1)	16 (18.6)	3 (7.7)	3 (7.7)
Dysgeusia	25 (29.1)	0	9 (23.1)	0
Myalgia	23 (26.7)	5 (5.8)	2 (5.1)	0
Platelet Count Decreased	23 (26.7)	5 (5.8)	3 (7.7)	2 (5.1)
Vomiting	22 (25.6)	1 (1.2)	11 (28.2)	2 (5.1)

Stage 2 Select Grade 3+ Laboratory Abnormalities: September 2016

Hematologic Laboratory Abnormalities	PAG n = 86 n (%)	AG n = 39 n (%)
Anemia	20 (23)	11 (28)
Thrombocytopenia	14 (16)	5 (13)
Neutropenia	42 (49)	17 (44)

Hepatic Laboratory Abnormalities	PAG n = 86 n (%)	AG n = 39 n (%)
ALT increased	13 (15)	3 (8)
AST increased	6 (7)	5 (13)
Total Bilirubin increased	3 (4)	4 (10)

Stage 2 Incidence of Thromboembolic (TE) Events

	Enoxaparin Prophylaxis Dose	TE Rate	
		PAG	AG
Stage 1* (Dec 2016)	N/A	43% (32/74)	25% (15/61)
		HA^{high}: 42% (10/24)	HA^{high}: 24% (5/21)
		HA^{low}: 46% (21/46)	HA^{low}: 28% (9/32)
Stage 2** (Dec 2016)	Started with 40 mg/day	28% (5/18)	29% (2/7)
	Started on 1 mg/kg/day	**10% (7/68)**	**6% (2/32)**

*Stage 1 data reflects additional biopsies collected: 2 HA-High (2 PAG); and 3 HA-Low (2 PAG; 1 AG)

****TE rates for all stage 2 patients are 14% (12/86) in PAG arm and 10% (4/39) in AG arm**

Treated Population

Study 202 (Stage 1 and Stage 2 Data)

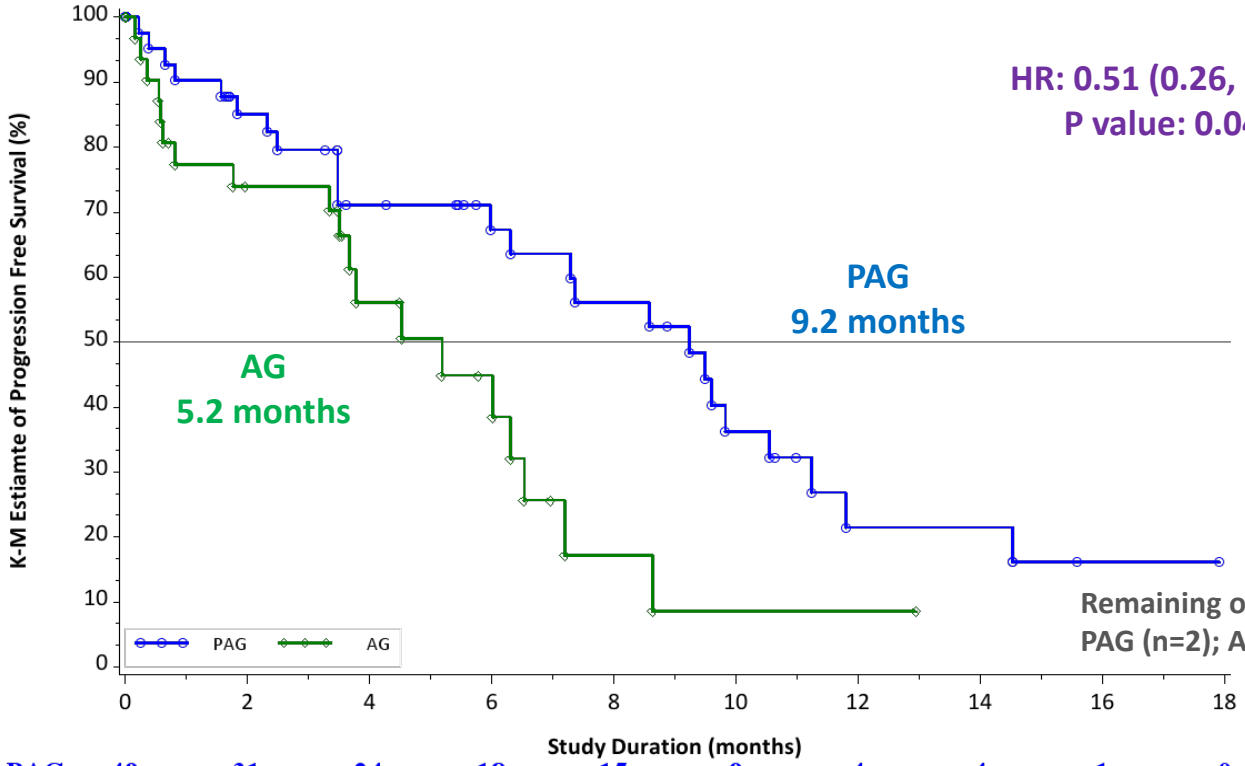
Study 202 (Stage 1 + Stage 2): Progression Free Survival

Populations	Events/Total (n); Median PFS, months		HR (95% CI)	P value
	PAG	AG		
Efficacy Evaluable	100/139; 6.0	65/92; 5.3	0.73 (0.53, 1.00)	0.048
Intent-to-Treat	102/166; 6.0	67/113; 5.3	0.73 (0.53-0.99)	0.045
Intent-to-Treat with HA data	95/153; 6.0	57/93; 5.3	0.74 (0.53-1.04)	NS
HA-Low	71/104; 5.6	38/58; 5.3	0.88 (0.59-1.32)	NS
HA-High	**24/49; 9.2**	**19/35; 5.2**	**0.51 (0.26-1.00)**	**0.048**
6-month PFS Rate	67%	45%		
12-month PFS Rate	22%	9%		

NS, not significant; CI, confidence interval; HR, hazard ratio.

ITT Population

Study 202 (Stage 1 + Stage 2) Secondary Endpoint: PFS in HA-High Patients



ITT Population

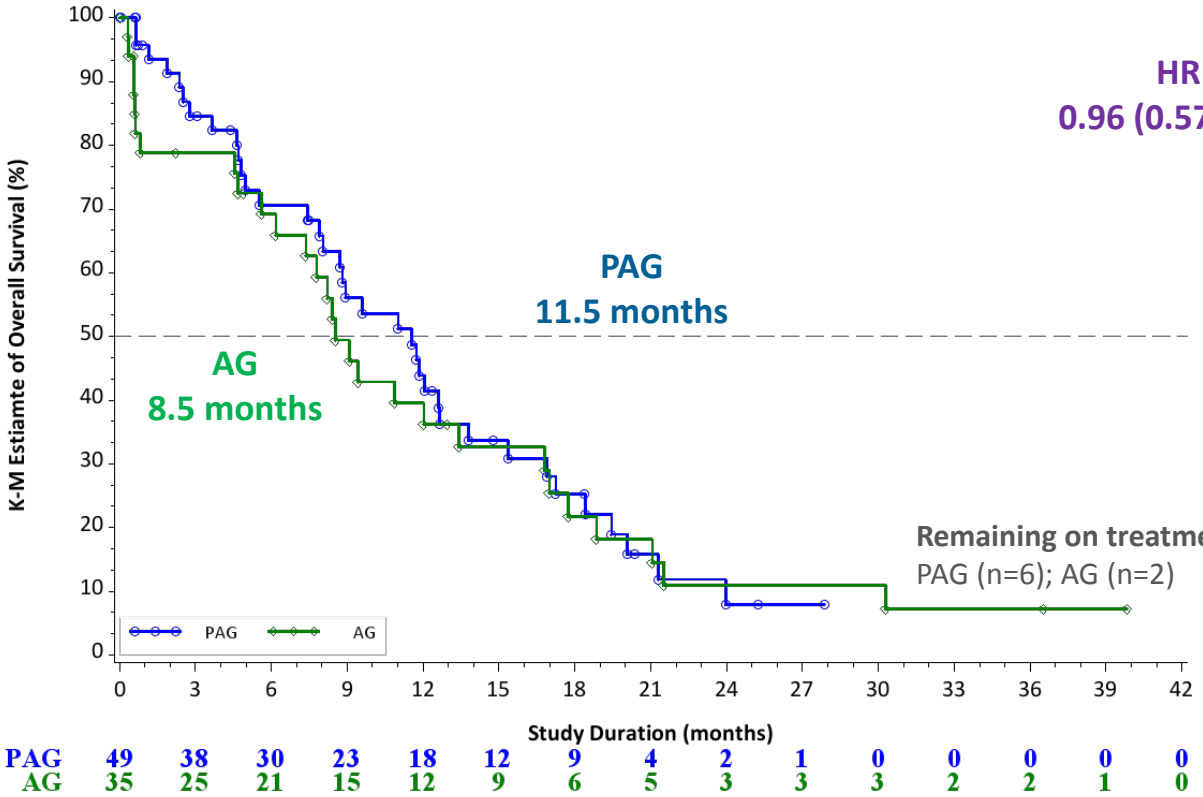
Study 202 (Stage 1 + Stage 2) PFS by HA Cut-point Using Ventana Assay

50% HA High Cutoff Shows Robust Signal

HA cutoff level Ventana Assay	Combined Study 202 Data PAG arm Events/Patients Median	Combined Study 202 Data AG arm Events/Patients Median
≥75%	9/18 9.2 months	10/15 3.8 months
≥ 50%	**24/49** **9.2 months**	**19/35** **5.2 months**
<50%	71/104 5.6 months	38/58 5.3 months

ITT Population

Study 202 (Stage 1 + Stage 2) Exploratory Endpoint: Overall Survival in HA High Patients



HR:
0.96 (0.57, 1.61)

Remaining on treatment and/or follow up:
PAG (n=6); AG (n=2)

ITT Population

Study 202 (Stage 1 + Stage 2): Treatment Exposure*

Populations, n	PAG	AG
Treated Population (n=260)	160	100
Treated Population with HA data (n=234) (HA-High/HA-Low)	147 (48/99)	87 (32/55)
Treated subjects (HA-High) Duration of treatment, months median (range)	**n = 48 3.3 (0.1-18.2)**	**n = 32 3.2 (0.03-12.9)**
≥ 6 months, n (%)	19 (40)	3 (9)
≥ 12 months, n (%)	6 (13)	1 (3)

*Exposure: first to last dose of any study medication

Treated Population

Study 202 (Stage 1 + Stage 2) Treatment-Related Adverse Events (AEs) in ≥ 25% of Patients

	PAG (n = 160) Patients, n (%)		AG (n = 100) Patients, n (%)	
Preferred Term	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
Any AE	157 (98.1)	138 (86.3)	93 (93.0)	75 (75.0)
Fatigue	115 (71.9)	33 (20.6)	66 (66.0)	16 (16.0)
Peripheral edema	101 (63.1)	8 (5.0)	26 (26.0)	4 (4.0)
Muscle spasms	89 (55.6)	20 (12.5)	3 (3.0)	1 (1.0)
Nausea	79 (49.4)	8 (5.0)	47 (47.0)	4 (4.0)
Diarrhea	64 (40.0)	11 (6.9)	39 (39.0)	5 (5.0)
Anemia	62 (38.8)	27 (16.9)	38 (38.0)	20 (20.0)
Alopecia	60 (37.5)	1 (0.6)	39 (39.0)	0 (0.0)
Decreased appetite	59 (36.9)	7 (4.4)	25 (25.0)	2 (2.0)
Neutropenia	54 (33.8)	47 (29.4)	19 (19.0)	18 (18.0)
Neuropathy peripheral	47 (29.4)	10 (6.3)	31 (31.0)	8 (8.0)
Vomiting	46 (28.8)	5 (3.1)	27 (27.0)	2 (2.0)
Dysgeusia	45 (28.1)	0	19 (19.0)	0
Myalgia	41 (25.6)	8 (5.0)	7 (7.0)	0 (0.0)
Thrombocytopenia	41 (25.6)	26 (16.3)	17 (17.0)	9 (9.0)

Treated Population

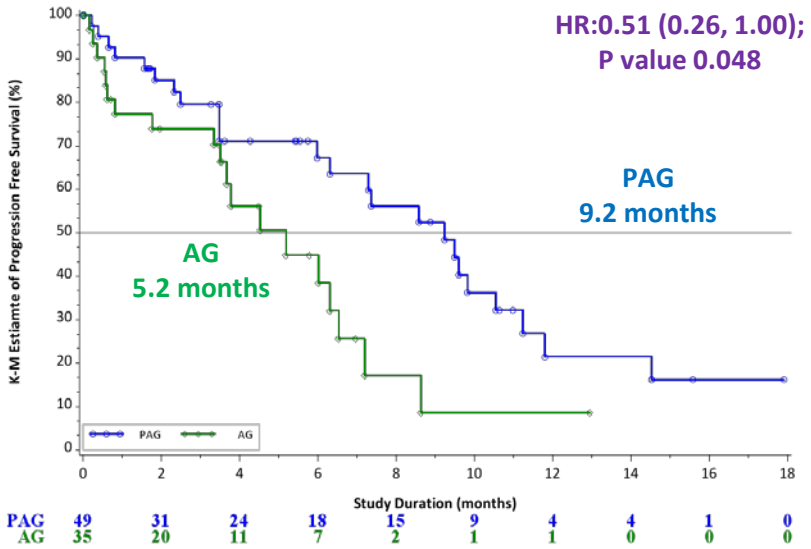
Halozyme

Summary & Conclusions

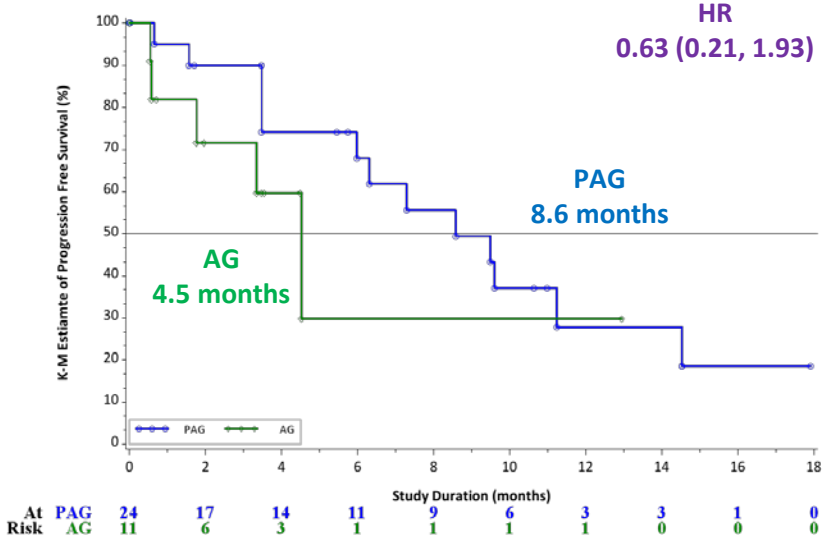
Study 202: Consistent Improvement in PFS in PEGPH20 Treatment Arm

Secondary Endpoint PFS in HA-High Patients

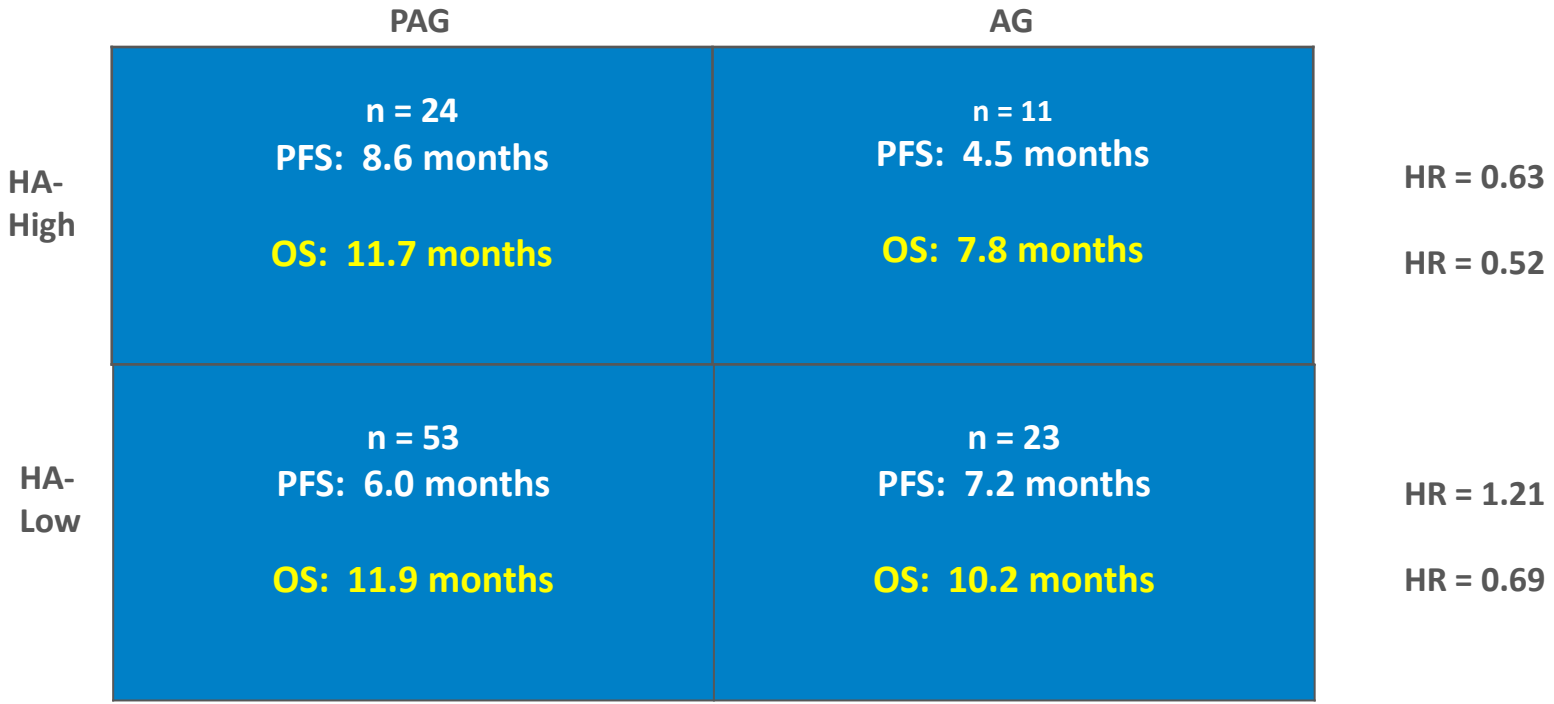
Study 202 (Stage 1 & Stage 2)



Stage 2



Stage 2 PFS and OS Results Support HA High As A Potential Predictive and Prognostic Biomarker



Treated Population

Study 202 Conclusions

1. **Randomized Phase 2 Study 202 met multiple key study objectives**
   - Primary Endpoint (PFS) achieved
   - Secondary Endpoint (PFS in HA High patients) achieved

2. **Stage 2 of Study 202 met primary safety endpoint & shows consistent improvement across PFS and OS in HA High patients**
   - Primary Safety Endpoint achieved: Decreased TE events with protocol modifications & LMWH prophylaxis
   - Secondary Endpoint: 91% improvement in median PFS
   - Exploratory Endpoint: 50% improvement in median OS
   - HA algorithm and cut-point of ≥ 50% validated

3. **Randomized Phase 2 Study 202 results continue to support the Phase 3 HALO 301 trial**
   - Same patient population as Stage 2 with LMWH prophylaxis
   - Same CDx cutoff as Phase 2 study
   - Two primary endpoints: PFS (Phase 2 statistically significant); and OS (Stage 2 signal)

Study 202 Overall Results and Stage 2 Results

January 5, 2017