Final Results from a Phase 1b Dose Escalation Study to Assess the Safety of AFM13 in Combination with Pembrolizumab in Patients with Relapsed or Refractory Classical Hodgkin Lymphoma (AFM13-103)

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On behalf of the AFM13-103 Investigators

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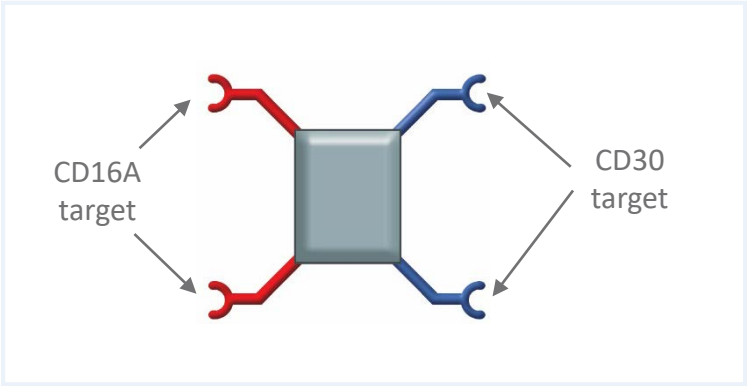
Disclosure of Conflicts of Interest

Institutional research funding for clinical trials:

- Affimed
- Bristol-Myers Squibb
- Celldex
- LAM Therapeutics
- MSD
- Seattle Genetics
- Takeda
- Regeneron
- Trillium
- Pfizer

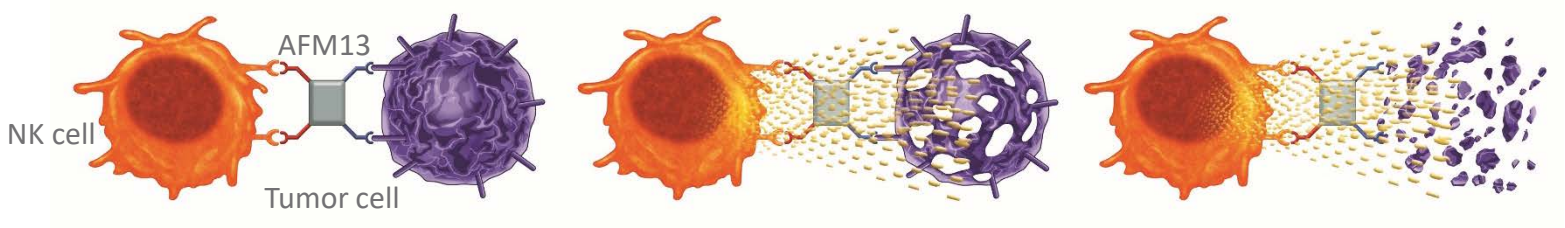
Background: AFM13

First-in-class CD30-directed innate cell engager



- Designed to activate NK cells and macrophages against CD30-expressing lymphomas
  - Potent binding of CD16A and NK cell activation
  - Enhanced antibody-dependent cellular cytotoxicity (ADCC)
- Preclinical efficacy of AFM13 in combination with anti-PD1
- Single agent activity in a Phase 1 study in patients with relapsed/refractory (R/R) Hodgkin lymphoma

Mechanism of action for AFM13

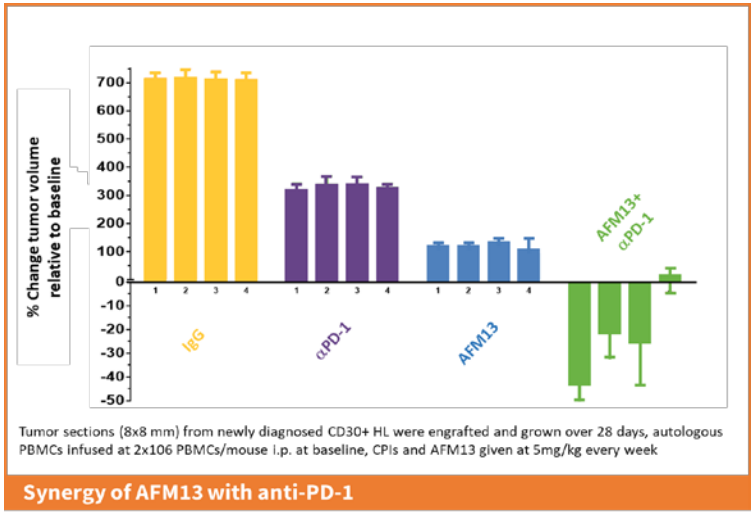


Bridging of innate and tumor cells | **Release of perforins and granzymes** | **Tumor cell lysis**

Preclinical Data Demonstrated Efficacy of AFM13 in Combination with Anti-PD1

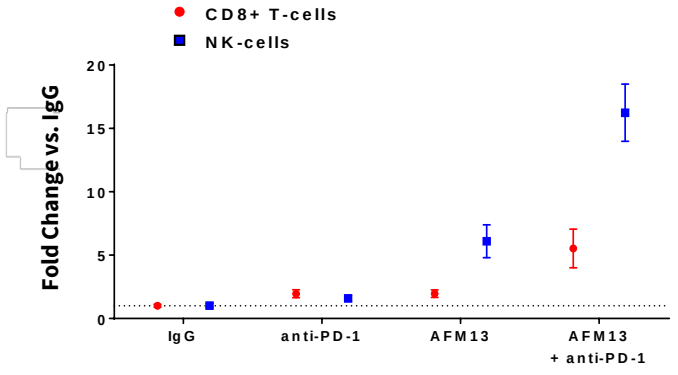
Results from a PDX model* of CD30+ HL patients provides rationale for a clinical trial

- AFM13 synergizes with αPD-1 for tumor control and lymphocyte infiltration
- AFM13 induces rapid NK cell infiltration (as early as day 2 after treatment start)



Tumor sections (8x8 mm) from newly diagnosed CD30+ HL were engrafted and grown over 28 days, autologous PBMCs infused at 2x106 PBMCs/mouse i.p. at baseline, CPIs and AFM13 given at 5mg/kg every week

Synergy of AFM13 with anti-PD-1



Lymphocyte infiltration on day 30 post treatment start

* Tumor sections (8x8 mm) from newly diagnosed CD30⁺ HL patients were engrafted and grown over 28 days, autologous PBMCs infused at $2x10^6$ PBMCs/mouse i.p. at baseline; CPIs and AFM13 given at 5mg/kg every week

Affimed ASH 2015, Zhao et al., Abstract No. 2747

Study Design

Phase 1b dose escalation study to assess the safety and preliminary efficacy of pembrolizumab* + AFM13

Patients with R/R Hodgkin lymphoma (N=30)

- Anti-PD1 naïve
- Failed ≥2 prior therapies including brentuximab vedotin (BV)

Primary objectives:

- Part 1: Maximum tolerated dose (MTD)
- Part 2: Preliminary efficacy at the chosen dose

Secondary objectives:

- Safety, tolerability, and pharmacokinetic (PK) profile

Dosing: Pembrolizumab 200 mg every 3 weeks x 52 weeks + AFM13 as below x 25 weeks:

Dose escalation schedule for AFM13

	3x/Week (W2-3)	Weekly (W4-9)	Q3W (W10-25)
Cohort 1 (N=3)	0.1 mg/kg x 3	0.5 mg/kg	0.5 mg/kg
Cohort 2 (N=3)	0.5 mg/kg x 3	1.5 mg/kg	1.5 mg/kg
Cohort 3 (n=6)	3.0 mg/kg x 3	7.0 mg/kg	7.0 mg/kg

*Keytruda (MSD)

Patient Characteristics*

Characteristic	Total patient population (N=30); N (%)
Median age in years (range)	34 (18 to 73)
Gender	Female 10 (33%); Male 20 (67%)
No. of prior therapies (median = 4)	
3	14 (47%)
4	7 (23%)
5	3 (10%)
6	4 (13%)
7	2 (7%)
Prior auto. stem cell transplant	12 (40%)
Prior brentuximab vedotin (BV)	30 (100%)
Refractory to BV	13 (43%)

*Data cutoff date: 10 May 2019

Treatment-related Adverse Events (TRAEs) for AFM13*

TRAEs, All Grades ≥10%	Safety population (N=30)
IRR	27 (90%)
Rash	9 (30%)
Nausea	7 (23%)
Pyrexia	7 (23%)
Diarrhea	6 (20%)
Fatigue	7 (23%)
Headache	5 (17%)
Elevated ALT	4 (13%)
Elevated AST	4 (13%)

TRAEs, ≥ Grade 3	Safety population (N=30)
IRR	4 (13%)
Elevated AST	2 (7%)
Neutropenia	1 (3%)
Gastritis	1 (3%)
Nausea	1 (3%)
Vomiting	1 (3%)
Hypotension	1 (3%)

*Data cutoff date: 10 May 2019

TRAEs for Pembrolizumab*

TRAEs, All Grades ≥10%	Safety population (N=30)
IRR	9 (30%)
Nausea	9 (30%)
Rash	6 (20%)
Fatigue	6 (20%)
Diarrhea	5 (17%)
Pyrexia	4 (13%)
Elevated ALT	4 (13%)
Headache	4 (13%)
Vomiting	3 (10%)
Thrombocytopenia	3 (10%)
Upper resp. infection	3 (10%)

TRAEs, ≥ Grade 3	Safety population (N=30)
Gastritis	1 (3%)
Nausea	1 (3%)
Vomiting	1 (3%)
IRR	1 (3%)

*Data cutoff date: 10 May 2019

AFM13-103: Efficacy by Investigator and Independent Assessment*

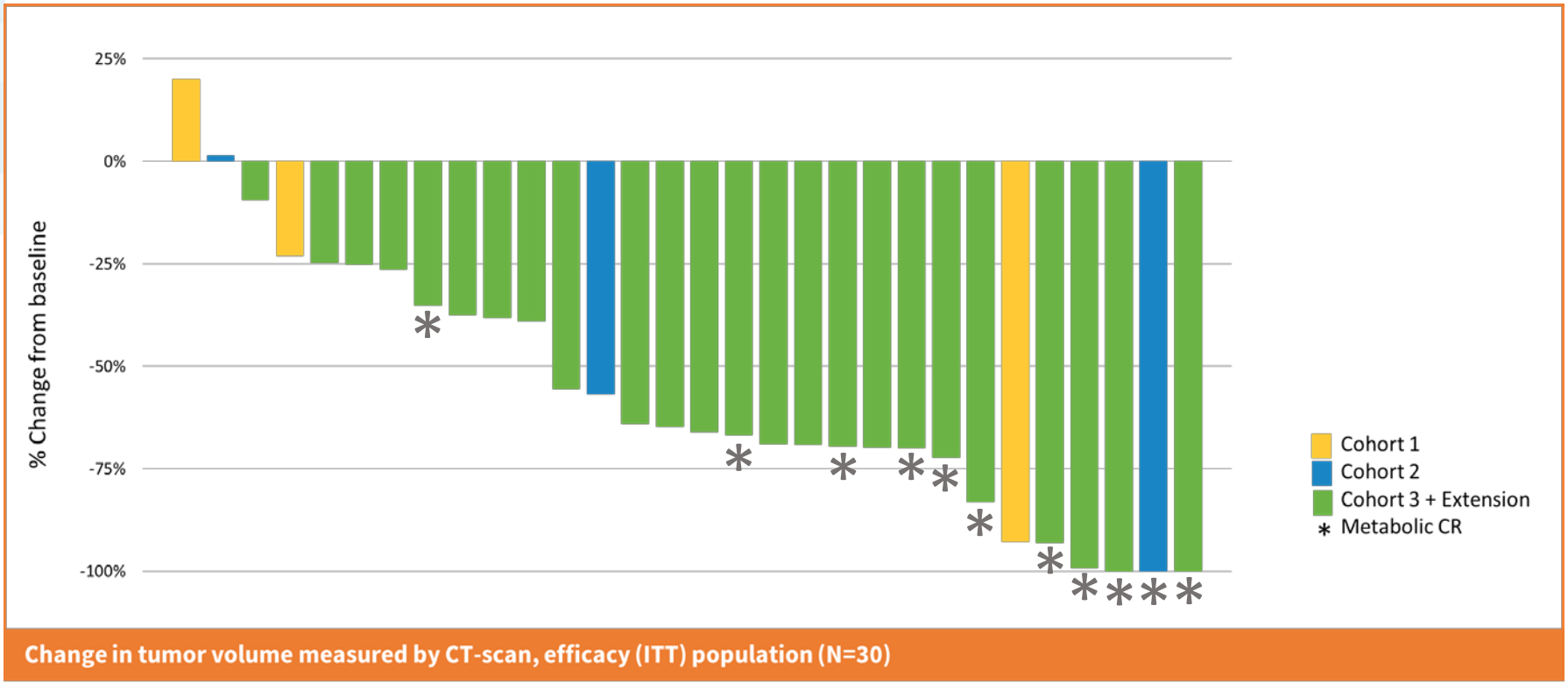
		Complete Metabolic Response (%)	Partial Metabolic Response (%)	No Metabolic Response (%)	Progressive Disease (%)	Overall Response Rate (%)
Investigator assessment	**Cohorts 1 and 2** (N=6)	1 (17%)	3 (50%)	0 (0%)	2 (33%)	4 (67%)
	Cohort 3 + Extension (N=24)	10 (42%)	11 (46%)	2 (8%)	1 (3%)	21 (88%)
	ITT (N=30)	11 (37%)	14 (47%)	2 (7%)	3 (10%)	25 (83%)#
Independent assessment	**Cohorts 1 and 2** (N=6)	1 (17%)	3 (50%)	2 (33%)	0 (0%)	4 (67%)
	Cohort 3 + Extension (N=24)	11 (46%)	10 (42%)	1 (4%)	2 (8%)	21 (88%)
	ITT (N=30)	12 (40%)	13 (43%)	3 (10%)	2 (7%)	25 (83%)

- Amongst the subgroup of patients who were primary refractory to BV, response rates were similar to those of the ITT population#, with 11 of the 13 patients achieving an objective response (85% ORR; 46% CR rate)

*Data cutoff date: 10 May 2019

AFM13-103: Efficacy: Best Response, Tumor Volume

Intent-to-treat waterfall

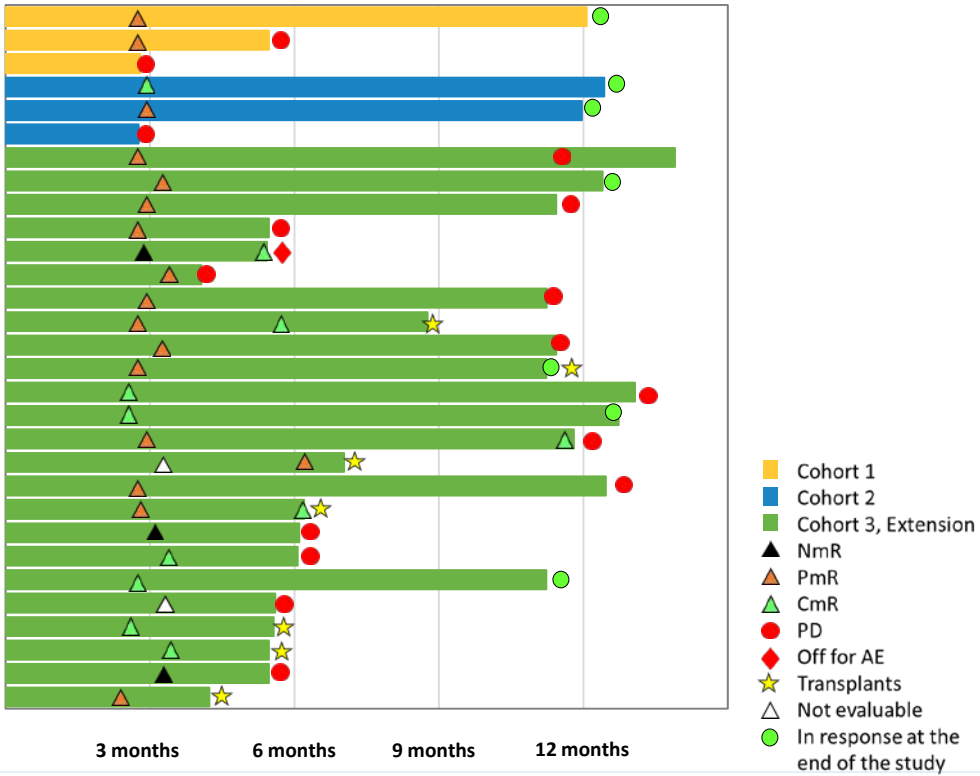


Change in tumor volume measured by CT-scan, efficacy (ITT) population (N=30)

*Data cutoff date: 10 May 2019

AFM13-103: Efficacy: Duration and Deepening of Responses*

ITT – swimmers plot



- **Deepening of response observed**
  - NmR to CmR
  - 2 cases of PmR to CmR
  - Not evaluable to PmR
- **Durable responses:**
  - Estimated 6-month PFS rate: 78%
  - Estimated 12-month PFS rate: 45%
- **Transitioned to stem cell transplantation**
  - 4 allogeneic
    - 1 patient with acute GVHD recovered with immunosuppression
  - 3 autologous

*Data cutoff date: 10 May 2019

Summary and Conclusions

- The combination of AFM13 and pembrolizumab was well tolerated, with no new or worsening safety signals observed compared to known safety profiles of each agent alone
- At the highest treated dose, the overall response rate of 88% (by both independent and investigator) and the CR rates of 42% and 46% by investigator and independent assessments, respectively, compare favorably to the historical data of monotherapy pembrolizumab in a similar patient population, with the CR rates approximately double that of pembrolizumab
- Response rates were high amongst the subgroup of patients who were primary refractory to BV, with 11 of the 13 patients achieving an objective response (ORR 85%, 46% CR rate)
- The addition of AFM13 with pembrolizumab holds promise as a novel combination worthy of further investigation for patients with relapsed/refractory Hodgkin lymphoma

Chen et al., J Clin Oncol 2017; 35:2125-2132.
Armand, et al., J Clin Oncol 2018; 36:1428-1439

AFM13-103 Investigators

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