Affimed

Developing First-in-Class Immune Cell Engagers for Harnessing Innate and Adaptive Immunity to Fight Cancer

Corporate Presentation

December 2018

Forward-Looking Statements / Safe Harbor

Legal notices

This presentation and the accompanying oral commentary contain “forward-looking” statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this presentation and the accompanying oral commentary, including statements regarding our future financial condition, business strategy and plans and objectives of management for future operations, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “believe,” “will,” “may,” “estimate,” “continue,” “anticipate,” “intend,” “should,” “plan,” “might,” “approximately,” “expect,” “predict,” “could,” “potentially” or the negative of these terms or other similar expressions.

Forward-looking statements appear in a number of places throughout this presentation and the accompanying oral commentary and include statements regarding our intentions, beliefs, projections, outlook, analyses and current expectations concerning, among other things, the value of our ROCK® platform, the safety and efficacy of our product candidates, our ongoing and planned preclinical development and clinical trials, our collaborations and development of our products in combination with other therapies, the timing of and our ability to make regulatory filings and obtain and maintain regulatory approvals for our product candidates our intellectual property position, our collaboration activities, our ability to develop commercial functions, expectations regarding clinical trial data, our results of operations, cash needs, financial condition, liquidity, prospects, future transactions, growth and strategies, the industry in which we operate, the trends that may affect the industry or us and the risks uncertainties and other factors described under the heading “Risk Factors” in Affimed’s filings with the Securities and Exchange Commission.

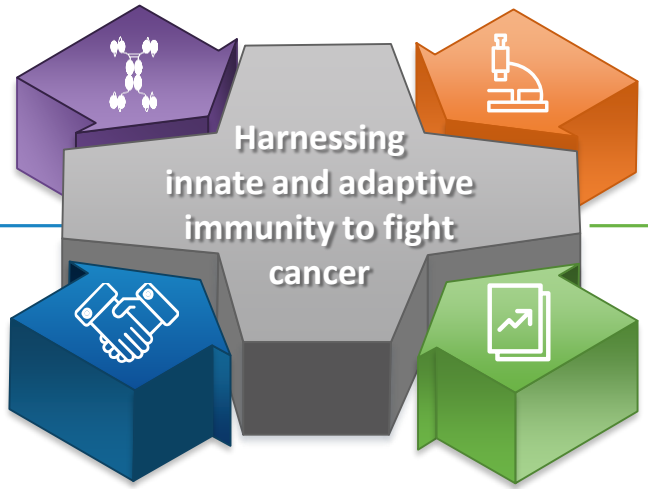
Forward-looking statements involve known and unknown risks, uncertainties, assumptions and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Forward-looking statements represent our management’s beliefs and assumptions only as of the date of this presentation. Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons why actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.

Affimed Overview

Harnessing innate and adaptive immunity to fight cancer

PRODUCTS

- Several programs in clinical and late-stage preclinical development
- Most advanced innate immune cell engager in clinic



PLATFORM

- Proprietary ROCK® platform generates highly customizable innate immune and T cell engagers
- Leader in CD16A innate immune cell targeting; broad IP protection

PARTNERSHIPS

- Pipeline acceleration through partnerships
- Genentech, Merck (MSD), Nektar Therapeutics, MD Anderson Cancer Center, Columbia University, Leukemia & Lymphoma Society

CORPORATE FACTS

- Nasdaq listed since 2014 (NASDAQ: AFMD)
- 76 employees (62 FTEs) in Heidelberg (HQ), Munich, New York
- *Pro forma* cash, equivalents, financial assets* of ~$139M (September 2018); cash runway into 2021

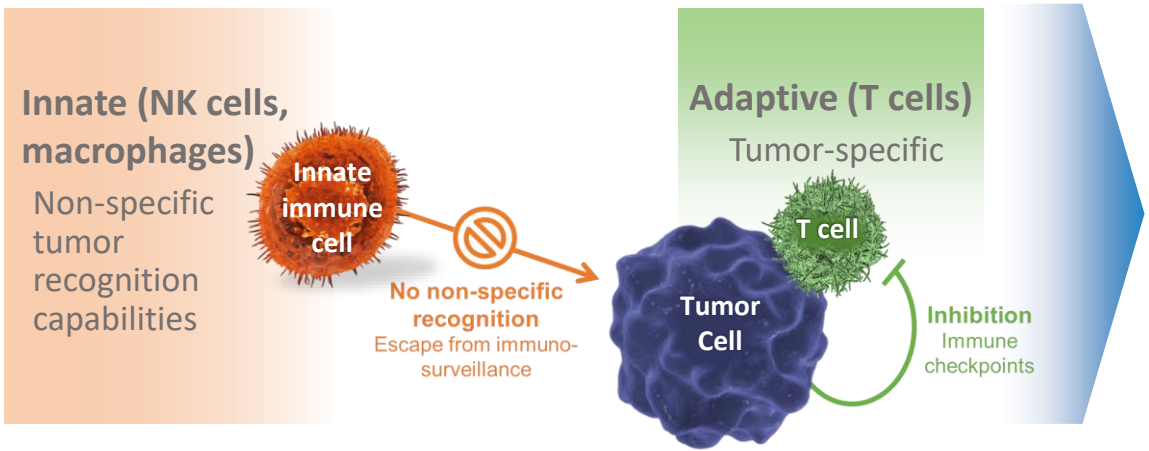
*"Pro forma" includes upfront and contractually committed received October 31 under Genentech collaboration. "Financial assets" comprises short-term deposits.

FTE, full-time employees; **HQ,** headquarters; **IP**, intellectual property

Affimed's Differentiated Approach to Innate Immunity

Optimal I/O approaches build on both innate and adaptive immunity

Tumor immune evasion impairs natural function of NK cells, macrophages and T cells



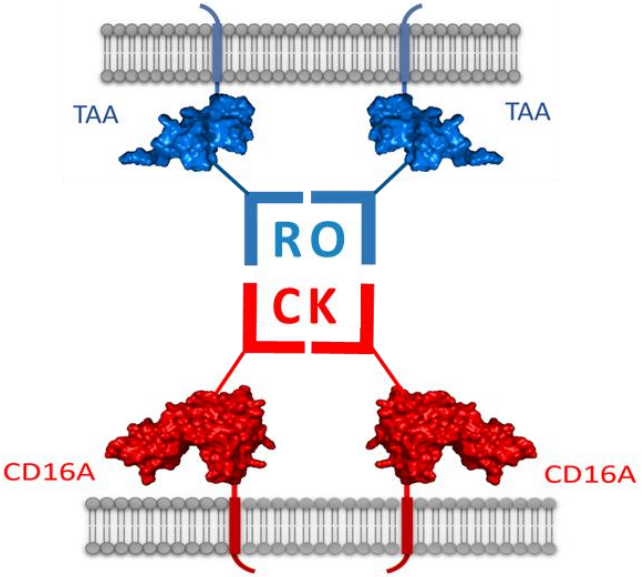
Overcome dysregulation and dysfunctionality of immune cells

- CD16A engagers re-establish recognition of tumors
- Adoptive NK cell transfer ensures sufficient numbers
- Engineered cytokines (IL2, IL15) activate immune cells
- Checkpoint inhibitors to "release the brakes" (T cells)

AFFIMED'S IMMUNE CELL ENGAGERS ARE DESIGNED TO OVERCOME THESE MECHANISMS AND REACTIVATE IMMUNE CELLS TO ATTACK TUMORS

I/O, immuno-oncology; **NK,** natural killer

Recruiting Innate Immune Cells via CD16A to Address Broad Range of Oncology Targets



Potential to address a broad range of oncology targets including argents that have failed other approaches

Unique target CD16A

- Key activating receptor capable of “arming” the NK cell and activating phagocytosis
- Affimed’s anti-CD16A binds to different epitope on CD16A than conventional mAbs
- Enables activation of tumor resident innate immune cells

Innate immune cell engagers address immune evasion

- >1000x higher affinity for CD16A than monoclonal antibodies
- Binding largely unaffected by competing IgG
- Overcome CD16A polymorphism (V/F)
- No binding to CD16B on neutrophils

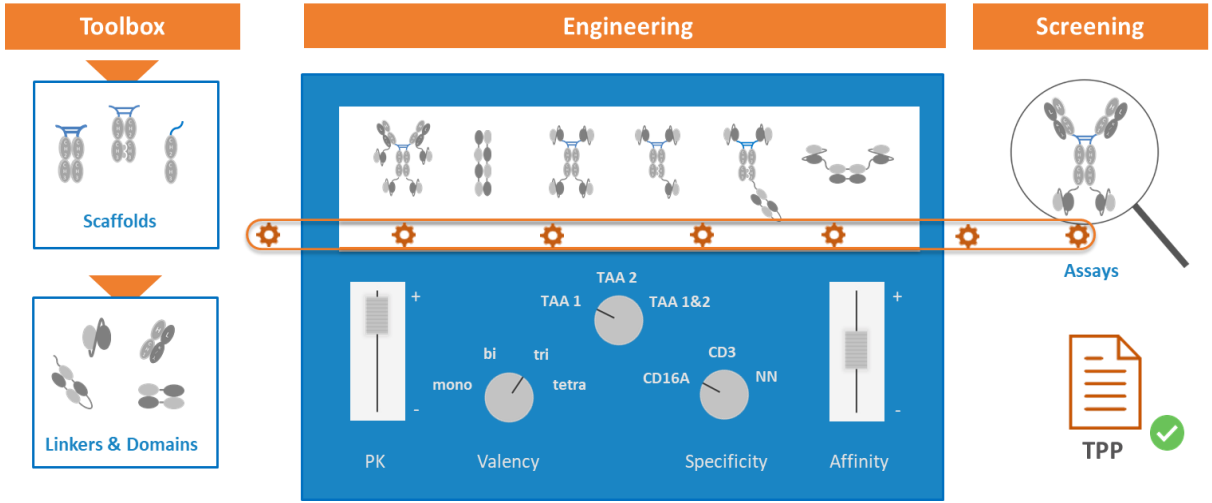
Differentiated from T cell engagement

- Similar potency but superior safety profile
- Well suited for targeting solid tumors

CAR, chimeric antigen receptor; IgG, immunoglobulin G; **NK,** natural killer; **mAb,** monoclonal antibody; **TAA,** tumor-associated antigen

ROCK® (Redirected Optimized Cell Killing) Platform Offers Unique Modularity and Versatility for Customizable Antibody Generation

Affimed's ROCK® platform



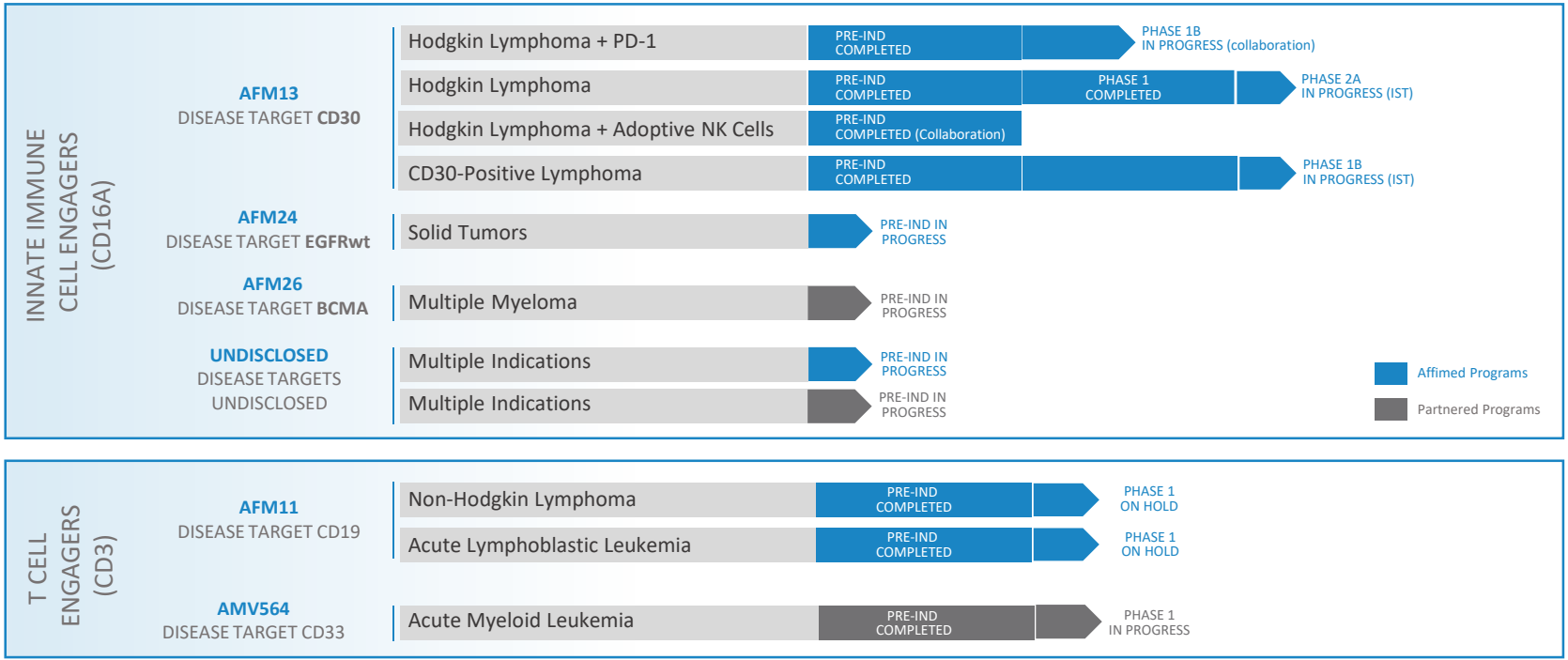
ROCK® generates antibodies that:

- Target different tumor-associated antigens
- Use the avidity effect
- Possess long cell retention time
- Recruit innate immune cells through anti-CD16A-specific epitopes and T cells through anti-CD3-specific epitopes
- Offer different PK profiles
- Show excellent stability and manufacturing features

ROCK® IS PROTECTED BY A BROAD IP PORTFOLIO

PK, pharmacokinetics; **TAA,** tumor-associated antigen
TPP, target product profile

Differentiated Pipeline of Innate and Adaptive Immunity Engagers Provides Future Growth Opportunities



BCMA, B-cell maturation antigen; **EGFR,** epidermal growth factor receptor; **IND,** investigational new drug; **IST,** investigator-sponsored trial; **NK,** natural killer

Genentech's Oncology Leadership Combined With Affimed's Expertise in Innate Immunity in NK Cell Engager Collaboration

Genentech
A Member of the Roche Group

affimed

$96M
upfront and near-term committed funding

$5B
in potential milestones, plus tiered royalties

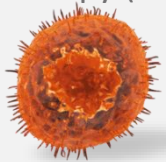
- Strategic collaboration covers CD16A bispecific antibody generation and preclinical programs for multiple cancer targets based on Affimed's ROCK® platform
- Target-by-target exclusivity on CD16A engagers in both solid and hematologic malignancies; Affimed retains rights for same target with other immune cell engagers (e.g. T cells)
- Affimed retains all rights to clinical assets AFM13, AFM11, key preclinical programs
- Affimed's current human resources sufficient to support collaboration and to further advance own programs without further investment

NK, natural killer

Affimed's Key Product Candidates

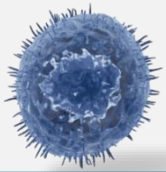
AFM13

- Lead innate immune cell engager targeting CD30/CD16A
- In Phase 1/2 clinical development as monotherapy and combination therapy (HL, CD30+ NHL)



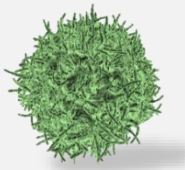
AFM24

- Innate immune cell engager targeting EGFR/CD16A
- In IND-enabling studies (solid tumor indications)



AFM11

- T cell engager targeting CD19/CD3
- In Phase 1 proof-of-concept studies (ALL, NHL)



ALL, acute lymphocytic leukemia; **EGFR,** epidermal growth factor receptor;
IND, investigational new drug; **HL,** Hodgkin lymphoma; **NHL,** non-Hodgkin lymphoma

AFM13: The Only Clinical Stage Innate Immune Cell Engager Targeting CD30

Designed to improve outcomes for patients with relapsed/refractory Hodgkin and non-Hodgkin (T cell) lymphoma

Mechanism of Action	▪ Redirects cytotoxic effector cells (NK cells and macrophages) against CD30-expressing target tumor cells via activation of CD16A
Indications	▪ CD30+ peripheral T cell lymphoma (Phase 1b/2a) ▪ CD30+ cutaneous T cell lymphoma (Phase 1b/2a) ▪ Hodgkin lymphoma + pembrolizumab (Phase 1b)
Current Status	▪ Favorable safety profile and promising signs of efficacy demonstrated as monotherapy and in combination with pembrolizumab ▪ Data on monotherapy and combination therapies presented at ASH 2018

Getting the tumor cell engaged with natural killer cells and T cells at the same time might be a further way in which we can move beyond immune checkpoint therapy.

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Stephen Ansell, MD, PhD[1]

1. Mayo Clinic, Rochester, ASCO Post, August 25, 2018

NK, natural killer; **PD1,** programmed cell death protein 1

AFM13 Opportunity: Relapsed and Refractory Lymphoma Remains Difficult to Treat With Limited Options

Peripheral T Cell Lymphoma (pTCL)	Cutaneous T Cell Lymphoma (cTCL)	Hodgkin Lymphoma (HL)
Remission is not achievable for most patients Without transplantation, median overall survival for most relapsed/refractory patients is 6 months	Limited therapeutic options for advanced stages Disfiguring lesions have significant negative impact on quality of life High risk for complications due to frequent infections	Anti-PD1 agents are not curative; most, if not all, patients will progress No definitive SOC in ASCT ineligible or failure patients

ASCT, adoptive stem cell transplant; **PD1,** programmed cell death protein 1; **SOC,** standard of care

In Clinical Studies, AFM13 Has Shown Preliminary Efficacy in Difficult to Treat Patients With CD30 Positive Lymphoma

CD30-Positive Lymphoma

Treatment:

- AFM13 monotherapy

Total of 9 patients treated to date:

- Investigator-sponsored*, translational study to evaluate immunological effects and preliminary efficacy of AFM13 in R/R CD30+ lymphoma with cutaneous presentation

Preliminary efficacy data:**

- 9 patients treated in 3 dose cohorts
- 44% ORR including 1 CR and 3 PRs
- Biomarker data: possible correlation between response and tumor NK cell infiltration pre-therapy

R/R Hodgkin Lymphoma

Treatment:

- AFM13 in combination with Merck's Keytruda® (pembrolizumab)

Total of 30 patients treated to date:

- MTD not reached in Part 1; highest dose employed in Part 2/Extension

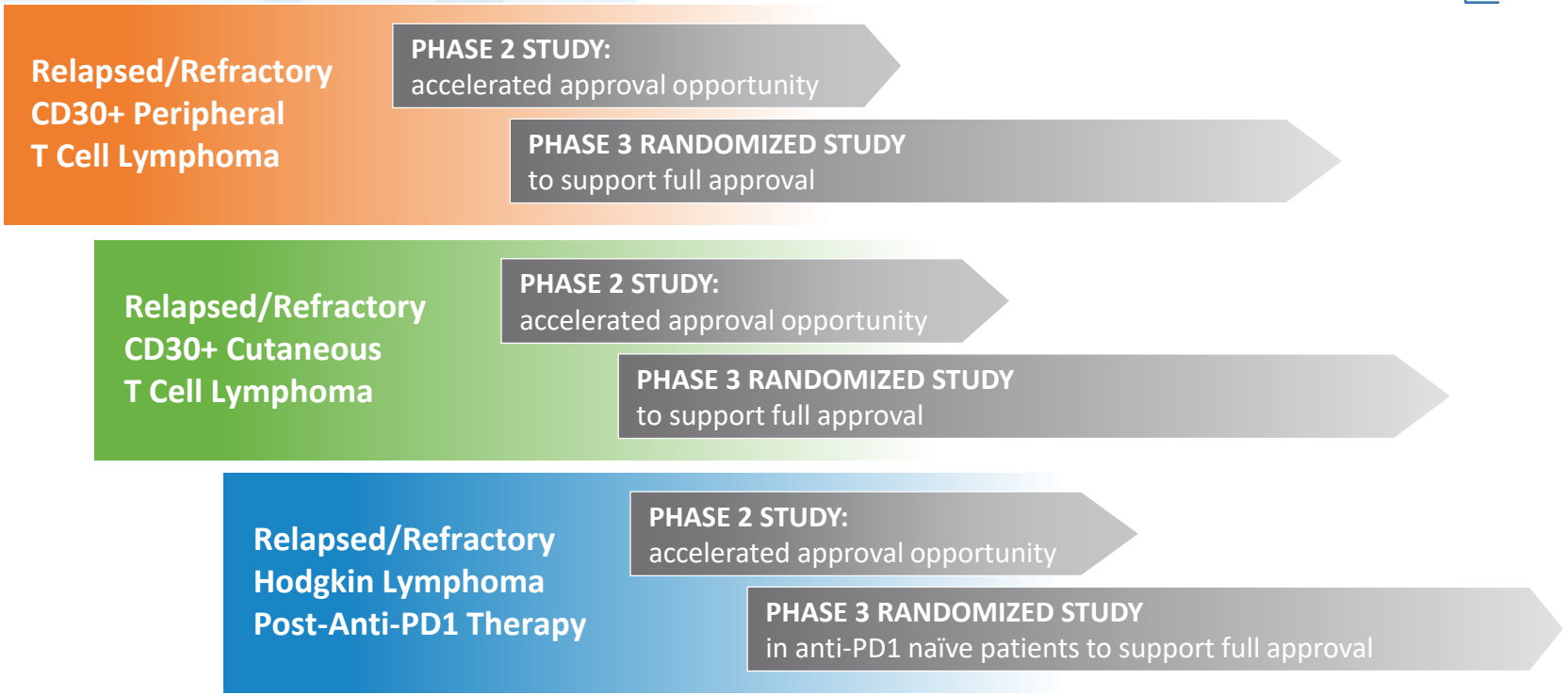
Efficacy data#:

- 24 patients evaluable in highest dose cohort
- 88% ORR, 42-46% CR rate (local/central read)
- Deepening of responses over time in multiple patients
- Patients previously transplant ineligible transitioned to transplant after achieving an objective response

*Principal Investigator: Ahmed Sawas, MD, Columbia University Medical Center, New York, NY
**A Sawas et al., ASH 2018 Abstract 2908; #NL Bartlett et al., ASH 2018 Abstract 1620

CR, complete response; **MTD,** maximum-tolerated dose; **ORR,** objective response rate; **PR,** partial response; **R/R,** relapsed/refractory

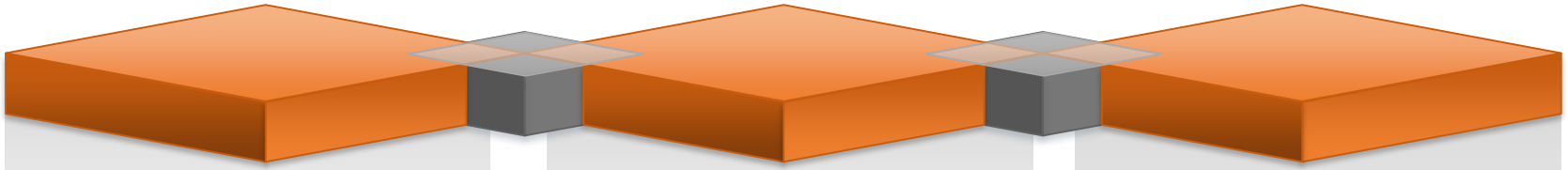
Multiple Potential Development Paths to Accelerated and Full Approval for AFM13*



* Slide is for illustrative purposes only and does not reflect Affimed's current development status or planned paths.

PD1, programmed cell death protein 1

Rational Combinations With Innate Immune Cell Engagers to Further Enhance Immunotherapy



AFM13 + Anti-PD1

Combination of AFM13 with Merck's Keytruda® (pembrolizumab) is currently being investigated in Phase 1b study salvage therapy in relapsed/refractory Hodgkin lymphoma

AFM13 + Adoptive NK Cell Transfer

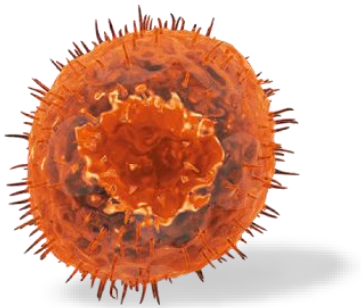
Combining AFM13 with an allogeneic NK cell product (cord blood-derived and activated NK cells) developed at MD Anderson Cancer Center to enhance the therapeutic effect of NK cells

CD16A Engagers + Cytokine-Based Products

Combining Affimed's innate immune cell engagers with cytokine-based products NKTR-214 and NKTR-255 (Nektar Therapeutics) to enhance immune cell proliferation, potentially achieving deeper clinical responses

NK, natural killer; **PD1,** programmed cell death protein 1

Numerous Longer-Term Development Opportunities for AFM13



AFM13 potential future indications

CD30-POSITIVE LYMPHOMA

TREATMENT SETTING	TCL	HL	BCL
First-line	AFM13 + chemo		
Second-line (SCT)	AFM13 + aNK	AFM13 + aNK	AFM13 + aNK
Salvage	AFM13 mono	AFM13 + anti-PD1	

aNK, activated natural killer; **BCL,** B-cell lymphoma; **HL,** Hodgkin lymphoma; **PD1,** programmed cell death protein 1; **SCT,** stem cell transplant; **TCL,** T cell lymphoma

AFM24 (EGFR/CD16A) Designed to Address Current Treatment Limitations

IND-enabling studies expected to be completed by mid-2019

The Importance of EGFR in Solid Tumors

- Overexpression in several solid tumor types (CRC, HNSCC, NSCLC, GBM, TNBC, etc)
- EGFR-mediated signaling is frequently affected by mutations in various cancer types leading to uncontrolled proliferation and increased tumor neo-angiogenesis
- Infiltration with TILs and/or with NK cells is associated with a beneficial prognosis
- K-RAS mutations prevent antitumor activity of EGFR-signaling inhibiting therapeutics

Current EGFR Target Therapies Have Limitations

Currently approved mAbs and TKIs rely primarily on signal inhibition for antitumor activity

- Associated with toxicities (skin, diarrhea, nausea), resulting in dose interruption and discontinuation
- Resistance described
- Limited activation of antitumor immune response

AFM24 Novel Mode of Action

Antitumor activity via redirected innate immune cells with potential for activation of broad immune response

- Minimized toxicity (preclinical data)
- Could address resistance to mAbs and TKIs
- Strong ADCC-mediated activity offering combinations with other I/O agents to further enhance responses

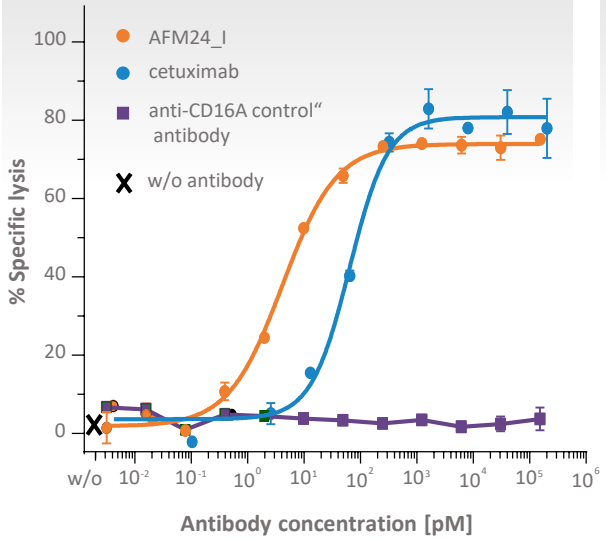
ADCC; antibody-dependent cellular cytotoxicity; **CRC,** colorectal cancer; **EGFR,** epidermal growth factor receptor; **IL,** interleukin; **I/O,** immuno-oncology; **mAbs,** monoclonal antibodies; **GBM,** glioblastoma multiforme; **HNSCC,** head and neck squamous cell cancer; **NSCLC,** non-small cell lung cancer; **PD1,** programmed cell death protein 1; **TIL,** tumor-infiltrating lymphocytes; **TKI,** tyrosine kinase inhibitor; **TNBC,** triple-negative breast cancer.

AFM24 (EGFR/CD16A): Potent *in vitro* and *in vivo* Killing

AFM24 shows potent killing of target cells in an *in vitro* cytotoxicity assay

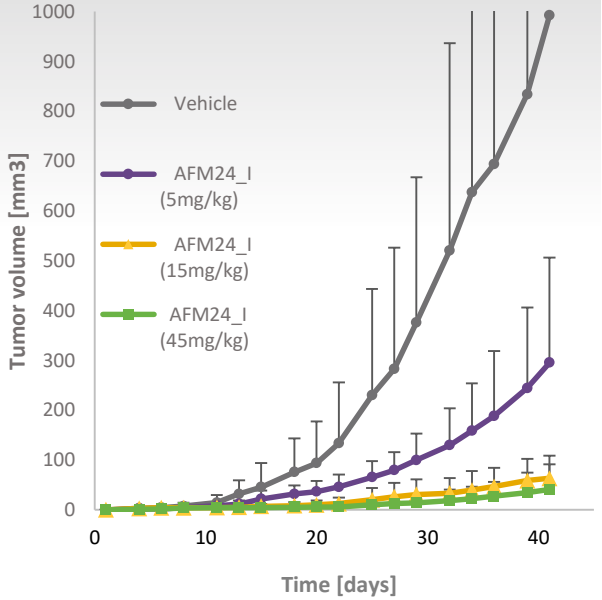
In vitro

Cytotoxicity assay with A-431 targets and NK cells as effector cells



AFM24 demonstrates dose-dependent tumor growth inhibition in a *in vivo* mouse model

In vivo

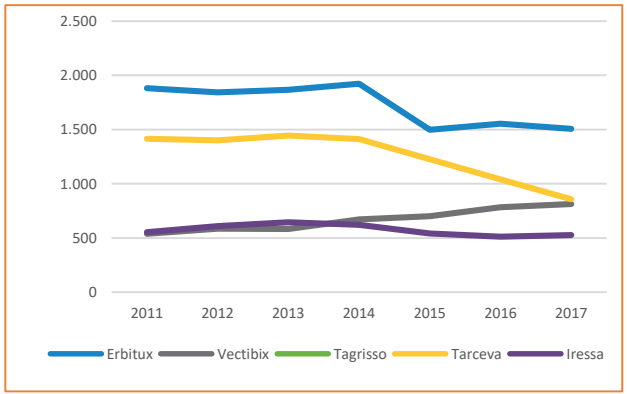


- IND-enabling studies expected to be completed by mid-2019
- Broad clinical development plan with potential to provide significant benefit to cancer patients with high unmet need (e.g. colorectal, head and neck, lung)

IND, investigtional new drug

AFM24's Novel Innate Mechanism Could Address Unmet Need Among EGFR-Targeted Therapies

Current Therapies



In 2017, sales of EGFR-targeted therapies totaled $4.7B globally[1]

AFM24 Market Opportunity

NSCLC

Actively Treated **Stage IV** Patients, US[2]	
1L	19,731
2L	14,861
3L+	11,088

Colorectal Cancer

Actively Treated **Stage IV** Patients, US[2]	
1L	22,827
2L	13,513
3L+	11,355

TNBC

Actively Treated **Stage IV** Patients, US[2]	
1L	2,839
2L	2,205
3L+	2,343

Head and Neck Cancer

Actively Treated **Stage IV** Patients, US[2]	
1L	6,567
2L	4,026
3L+	2,627

- AFM24 profile to aimed to address multiple indications by either improving safety or efficacy of SOC
- Strong activation of innate immunity by AFM24 may offer novel combinations with anti-EGFR-mAbs, CPIs, or chemotherapy and novel agents in development such as IL-2 or IL-15 (NKTR)

1. Source: Company reports
2. Source: Datamonitor Healthcare survey, 2016

1L, first line; **2L,** second line; **3L,** third line; **CPI,** checkpoint inhibitor; **EGFR,** epidermal growth factor receptor; **IL,** interleukin; **mAbs,** monoclonal antibodies; **NSCLC,** non-small cell lung cancer; **SOC,** standard of care; **TNBC,** triple-negative breast cancer; **US,** United States

Affimed's T Cell-targeting Platform: Status and Study Data

Well-differentiated approach designed to optimize T cell engagement

Platform: Potential to overcome challenge to find the optimal therapeutic window

- No non-specific activation of T cells in absence of target cells
- Targeting tumor cells with very low target expression; lysis of tumor cells independent of number of T cells
- Significantly improved PK vs. BiTEs

AFM11 – a T cell engager targeting CD19

- Designed to address (i) limitations of Blincyto and (ii) accessibility - benefit/risk profile of CAR-T
- Limited competition: Other candidates based on different antibody formats have reported difficulties
- Phase 1 dose-escalation trials currently on HOLD in r/r ALL and NHL after occurrence of SAEs in three patients
- Affimed assessing all AFM11 program data and working with global health authorities to determine next steps; update to be provided upon completion of the evaluation

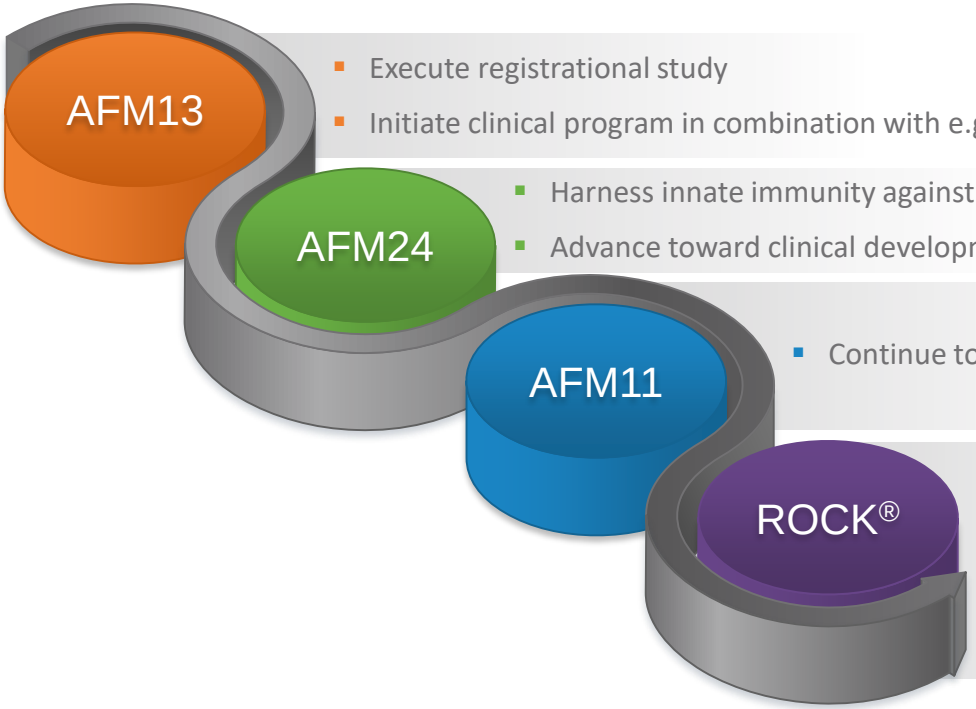
ASH 2018 data presentation: AFM11 monotherapy in r/r ALL*

- Phase 1 dose-escalation study with 17 patients treated in 6 dose cohorts
- Preliminary efficacy data: Responses include 3 CRs (2 CRs, 1 CRi), with one patient achieving MRD negativity

*G Salogub et al., ASH 2018 Abstract 3969

ALL, Acute lymphoblastic leukemia**; CR,** complete response; **MRD,** minimal residual disease
NHL, Non-Hodgkin lymphoma; **PK,** pharmacokinetics; **BiTE,** bispecific T cell engager

Affimed Positioned to Pursue Multiple Strategic Options



- Execute registrational study
- Initiate clinical program in combination with e.g. with adoptive NK cell transfer

- Harness innate immunity against solid tumors
- Advance toward clinical development with planned IND mid-2019

- Continue to advance to proof-of-concept

- Advance internal novel innate immune cell engagers toward clinical development
- Investigate rational combinations (eg, IL-2/IL-15, macrophages)

IL, interleukin; **I/O,** immuno-oncology; **NK,** natural killer

Recent Highlights and Upcoming Milestones

Highlights

ASH2018

- Update on AFM13 Phase 1b combination study with Keytruda® (pembrolizumab) in HL
- Data from AFM13 monotherapy Phase 1b/2a study in R/R CD30-positive lymphoma with cutaneous presentation (CUMC)
- Preclinical data on combination with adoptive NK cells (MDACC), ROCK® engager-based activation of macrophages, and AFM26 (partnered)
- Data from AFM11 Phase 1 dose escalation study in ALL

CD16A ENGAGER COLLABORATIONS

- New collaborations with Genentech and Nektar

Upcoming Anticipated Milestones

AFM13

- R&D Day December 7: Clinical development strategy
- 2019: Initiate registration study

AFM24

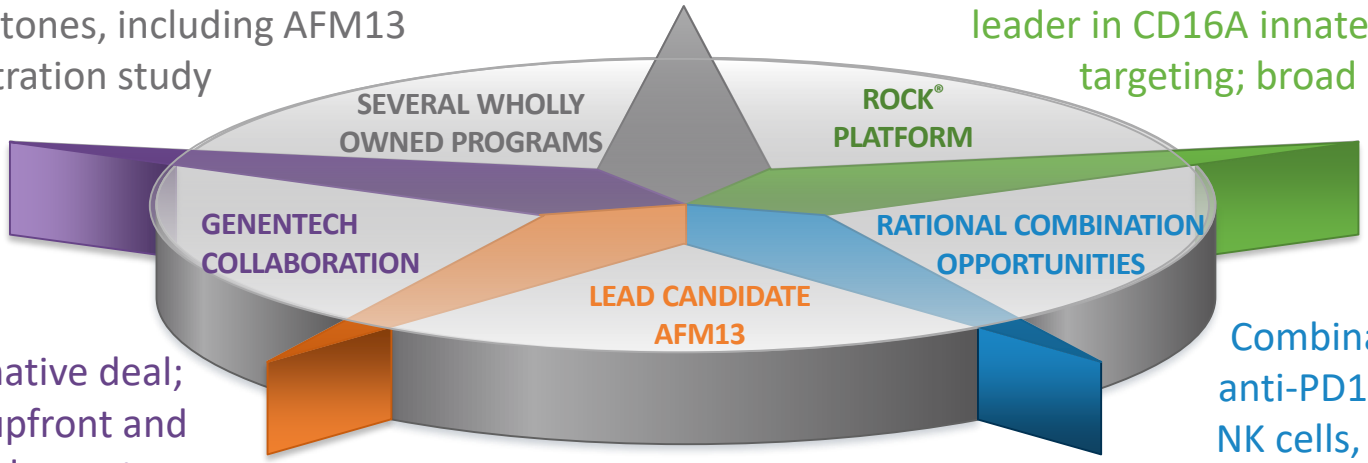
- Mid-2019: IND filing

AACR, American Association for Cancer Research; **ALL,** acute lymphocytic leukemia; **EHA,** European Hematology Association; **IND,** investigational new drug; **MDACC,** MD Anderson Cancer Center; **NHL,** non-Hodgkin lymphoma; **R/R,** relapsed/refractory

Affimed: Growing Leadership in Innate Immunity

Multiple upcoming anticipated milestones, including AFM13 registration study

Foundation for internal pipeline and partnerships; leader in CD16A innate immune cell targeting; broad IP protection



Transformative deal; $96M in upfront and committed near-term payments strengthen balance sheet

Differentiated safety profile and single agent efficacy in CD30+ lymphoma → registration study to be initiated

Combination with anti-PD1, adoptive NK cells, IL-2, IL-15

IL, interleukin; **IP,** intellectual property; **NK,** natural killer; **PD1,** programmed cell death protein 1;

Experienced Management Team

Proven track record in biotech, pharma, product development, and finance

Adi Hoess, PhD, CEO

Extensive background in general management, product commercialization, fundraising and M&A

Florian Fischer, PhD, CFO

Strong financial background, lead advisor in a variety of transactions & financings life sciences/healthcare

Wolfgang Fischer, PhD, COO

In-depth expertise in R&D with a focus on oncology, immunology and pharmacology

Leila Alland, MD, CMO

Seasoned immuno-oncology expert with broad experience developing oncology products

Martin Treder, PhD, CSO

Broad experience in the field of biotherapeutics R&D in I/O discovery and preclinical development

Denise Mueller, Head Comm Strat/BD

Strong background in commercialization and global marketing including launch of new products

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