



# Transforming Immuno-Oncology: Harnessing the power of innate and adaptive immunity

Corporate Presentation  
March 20, 2018

# Forward-looking statements / safe harbor

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 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.

### Approach

- Eliminating tumor cells by engaging NK cells or T cells

### Pipeline

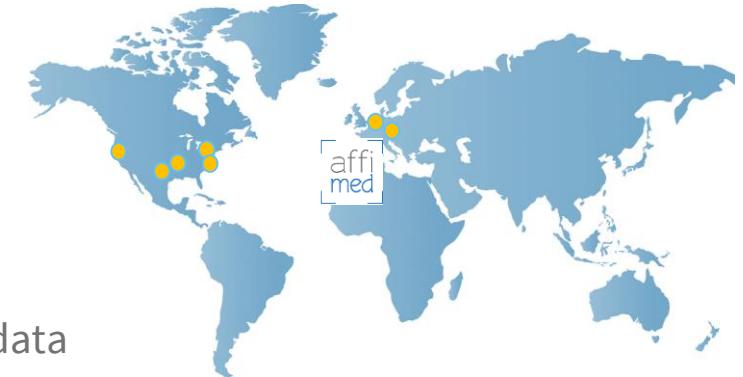
- Clinical and preclinical assets based on tetravalent bispecific antibody formats

### Harnessing the power of innate and adaptive immunity

- AFM13 is the most advanced NK cell engager with favorable safety and efficacy data
- Suitable for combinations with checkpoint inhibitors (CPIs), adoptive NK cell transfer or cytokines (IL-2, IL-15)
- Differentiated T cell-based approach
- Two molecules in clinical development based on AFMD platform

### Partnerships with industry, academia, and advocacy groups

- Merck (MSD), MD Anderson Cancer Center (MDACC), Leukemia & Lymphoma Society (LLS)



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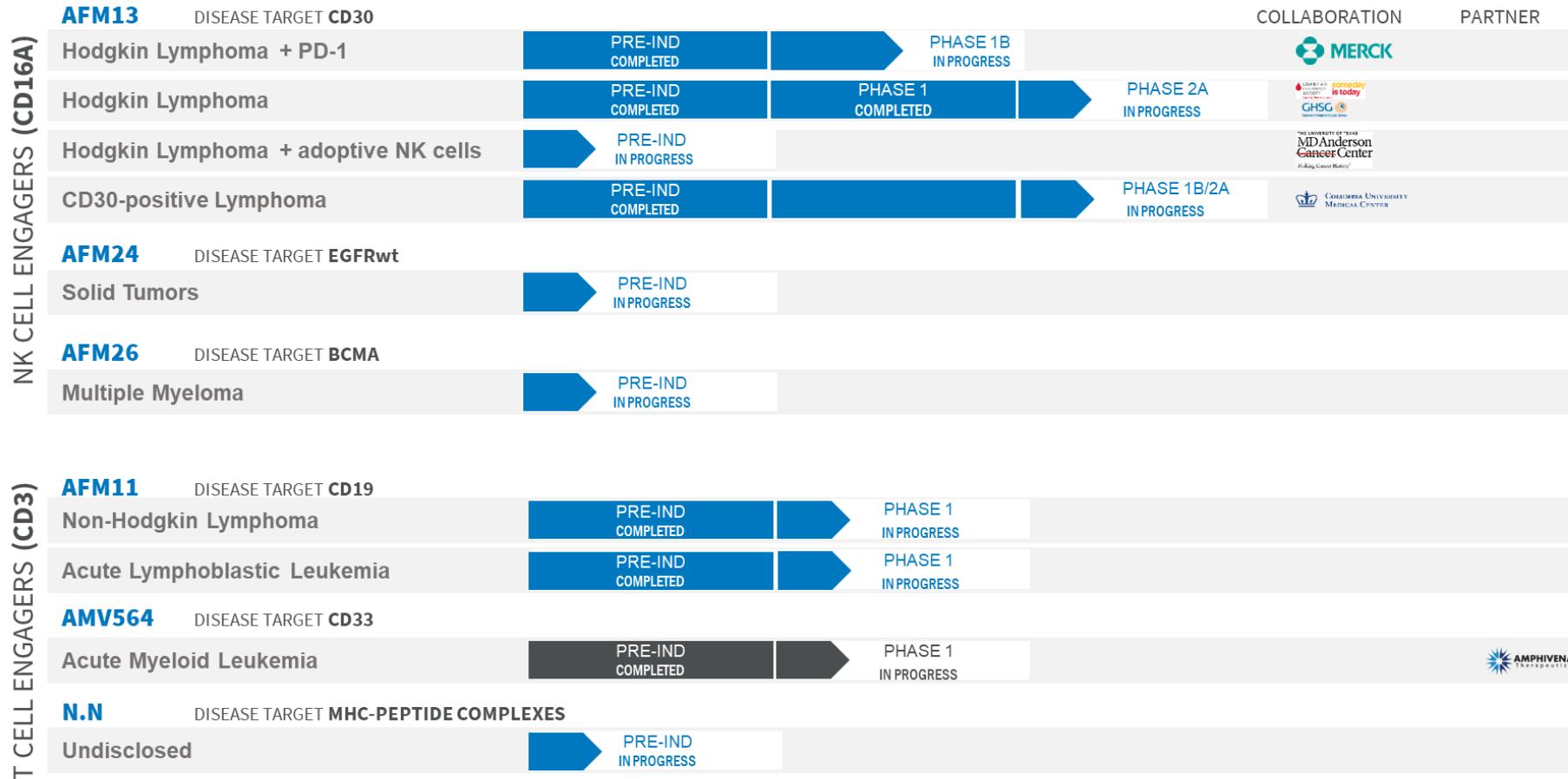


Washington  
University in St. Louis

LEUKEMIA &  
LYMPHOMA  
SOCIETY®  
fighting blood cancers

# Affimed's pipeline

Pipeline of differentiated and versatile engagers to activate innate and adaptive immunity



Partnered program \* Affimed has 18,5% equity ownership

# AFMD's pipeline opportunities

Pipeline of differentiated and versatile engagers to activate innate and adaptive immunity

## AFM13: Most advanced NK cell engager in clinical development

- Positive efficacy data as monotherapy in HL and in CD30-positive lymphoma
- CD30+ lymphoma represents a novel opportunity with limited competition (e.g. ALCL, PTCL)
- Encouraging efficacy in combination with Keytruda® (best response preliminary data: ORR of 89% and CR rate of 44%)

## AFM26: Leveraging BCMA as target in autologous stem cell transplant (ASCT)-eligible patients

- Addressing MRD in MM due to its ability to eliminate MM cells with very low BCMA expression

## AFM24: Potential to widen therapeutic window and address patients resistant to EGFR-targeting agents

- First-in-class NK cell engager in solid tumors
- Opportunity to improve efficacy of CPIs

## AFM11: Well-differentiated approach for CD19+ malignancies

- Positioned for treatment of DLBCL and MCL
- Opportunity: Potential to pave path for fast market approval

# Q4&YE/2017 updates (1)

Key hires made to strengthen Management team and expand U.S. presence; offering completed

## Corporate Updates

- Underwritten public offering on Nasdaq Global Market completed (Feb 2018)
  - Total of ~US \$24.5 million (€19.7 million) in net proceeds
  - Proceeds from transaction together with existing cash expected to fund operations, including clinical development and early development activities, at least until Q4/2019
- Appointed Dr. Leila Alland as CMO (joining March 2018)
  - Seasoned immuno-oncology expert with broad experience developing oncology products for solid and hematological malignancies, including Opdivo®, Tagrisso® and Tasigna®
  - Previous leadership at Tarveda Therapeutics, AstraZeneca, Bristol-Myers Squibb and Novartis
  - Based in Affimed's NYC location along with Dr. C. Choe-Juliak (Clinical U.S.) and D. Mueller (Commercial Strategy and BD)
- Appointed Dr. Wolfgang Fischer as COO (joined Sep 2017)
  - Former Global Head of Program and Project Management of Sandoz Biopharmaceuticals (Novartis Group)
  - > 20 years of R&D experience in oncology, immunology and pharmacology and a proven track record in drug development

# Experienced Management Team

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

## Adi Hoess, Ph.D., CEO

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

- CEO since 2011, joined 2010 from Jerini/Jenowis,
- Led AFMD IPO in 2014
- CCO at Jerini, instrumental in IPO, M&A with Shire
- GM and VP Molecular Medicine at Carl-Zeiss
- Co-founded MorphoSys; VP Licensing and BD

## Florian Fischer, Ph.D., CFO

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

- AFMD full-time CFO since 2014, joined in 2005 from MedVenture Partners, a company he founded
- Led AFMD IPO in 2014
- CFO of Activaero GmbH and of Vivendy
- Deutsche Bank and KPMG (Biotech/Healthcare)

## Wolfgang Fischer, Ph.D, COO

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

- Joined in 2017 from Sandoz Biopharmaceuticals
- Global Head of Program & Project Management at Sandoz Biopharmaceuticals
- Regional Medical Director Hematology at Novartis Oncology
- Medical Director Oncology at Novartis Switzerland

## Leila Alland, M.D., CMO\*

*Seasoned immuno-oncology expert with broad experience developing oncology products*

- Joined in 2018 from Tarveda Therapeutics
- Was instrumental in developing oncology products for solid and hematological malignancies, including Opdivo®, Tagrisso® and Tasigna®
- Previous leadership positions at AstraZeneca, Bristol-Myers Squibb and Novartis

## Martin Treder, Ph.D., CSO

*Broad experience in the field of biotherapeutics R&D in I/O discovery and pre-clinical development*

- Joined in 2015 from CT Atlantic AG, a Swiss I/O company he co-founded
- Co-founder of U3 Pharma (targeted cancer therapeutics)
- Responsible for U3's innovative anti-HER3 therapeutic antibodies portfolio

## Denise Mueller, Head Comm. Strat/ BD

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

- Joined in 2016 from Pfizer
- Previous leadership roles in U.S. & global marketing and Wyeth and Pfizer
- Responsible for launch of new products and line extensions in-line and globally
- Led two of Pfizer's largest alliances and was BD lead for Pfizer's rare disease business unit

\*effective March 26, 2018

## Q4&YE/2017 updates (2)

AFM13 is clinically active and well-tolerated as mono- and combination therapy

### Clinical NK cell engager program AFM13

- Phase 2 monotherapy in r/r HL (IST led by the German Hodgkin Study Group)
  - Showed ORR or 29% (2/7) in r/r patients post B.V. but naïve to anti-PD-1
  - Open and recruiting under new study design (patients r/r to B.V. and anti-PD-1)
- Phase 1b/2a study in CD30+ lymphoma (IST led by Columbia University) including serial biopsies
  - Assessment of cohort 1 (3 patients) showed ORR of 66% (1 CR, 1 PR and 1 SD)
  - Enrollment completed into second cohort, ongoing into third cohort
- AFM13 (CD30/CD16A) Phase 1b combination study with Merck's Keytruda® in r/r HL
  - Enrollment completed in expansion cohort
  - Assessment of 9 patients showed ORR of 89% and CR of 44%
  - Potential to achieve durable responses through improving both overall and complete response rates

## Q4&YE/2017 updates (3)

Preclinical NK cell and clinical T cell engager programs are progressing

### Preclinical NK cell engager programs

- Testing combination of NK cell engagers with adoptive NK cell product at MD Anderson Cancer Center
- NK cell engager sensitizes NK cells to IL-2- or IL-15, potentially achieving deeper clinical responses (published in *Cancer Immunol Res*, March 7, 2018)
- Advancing candidates AFM26 (BCMA/CD16A) and AFM24 (EGFR/CD16A)

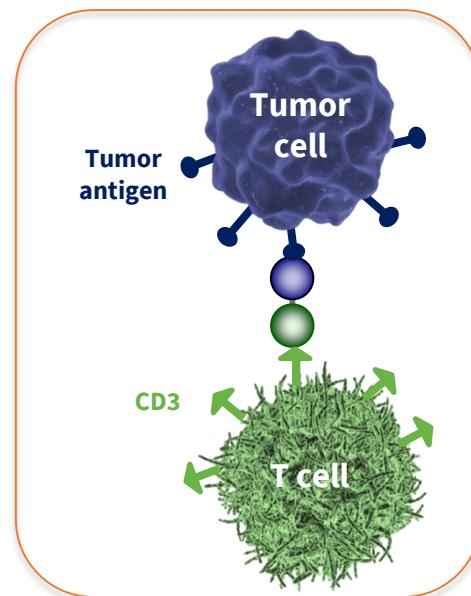
### Clinical T cell engager programs

- Differentiation: Proprietary formats with unique PK/PD profiles and without non-specific activation of T cells
- Competitor programs with low ORRs or stopped
- Phase 1 dose-escalation trials of AFM11 (CD19/CD3):
  - NHL: 3<sup>rd</sup> dose cohort completed
  - ALL: Recruiting into 5<sup>th</sup> dose cohort
- Amphivena's AMV564 (CD33/CD3) based on AFMD' platform; Phase 1 study ongoing and recruiting in AML and planned in MDS; Potential to address MDSCs in solid tumors

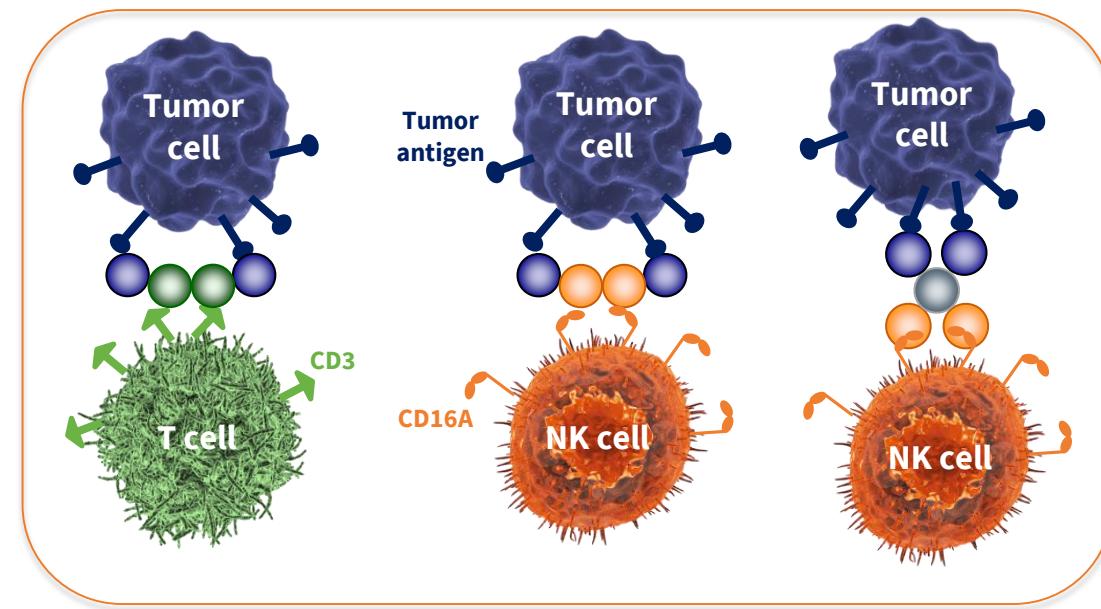
# Affimed's tetravalent bispecific antibody formats

Versatile immune cell engager formats designed for avidity, high specificity and tailored PK

Most competitors  
Bivalent, T cell focus



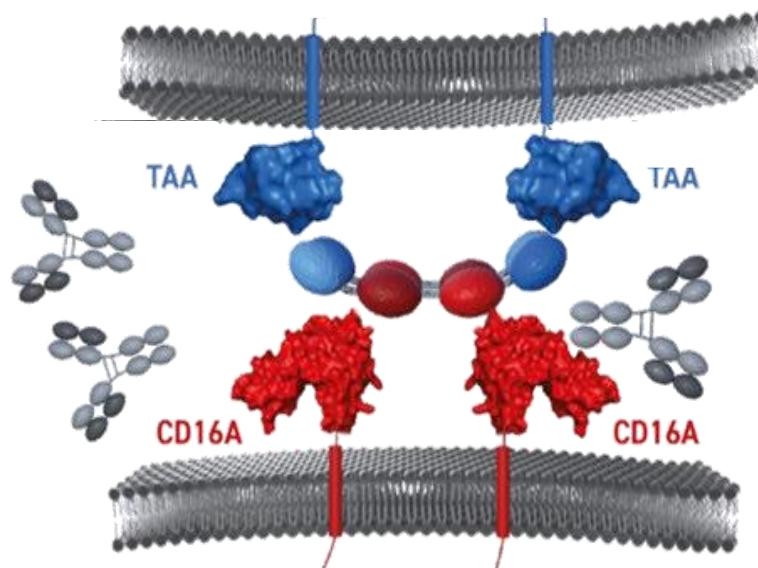
AFMD engager formats  
Tetravalent, NK and T cells



Avidity, high specificity, tailored PK

# Targeting NK cells through high affinity binding to CD16A

Addressing need of targeting malignant cells that escape elimination by current therapeutics



## NK cells

- Crucial in the body's defense against pathogens and malignantly transformed cells
- NK cell engagers can address immune evasion, which prevents immune cell activation

## Unique target CD16A

- Key activating receptor capable of “arming” the NK cell
- Constitutively expressed on ~95% of NK cells

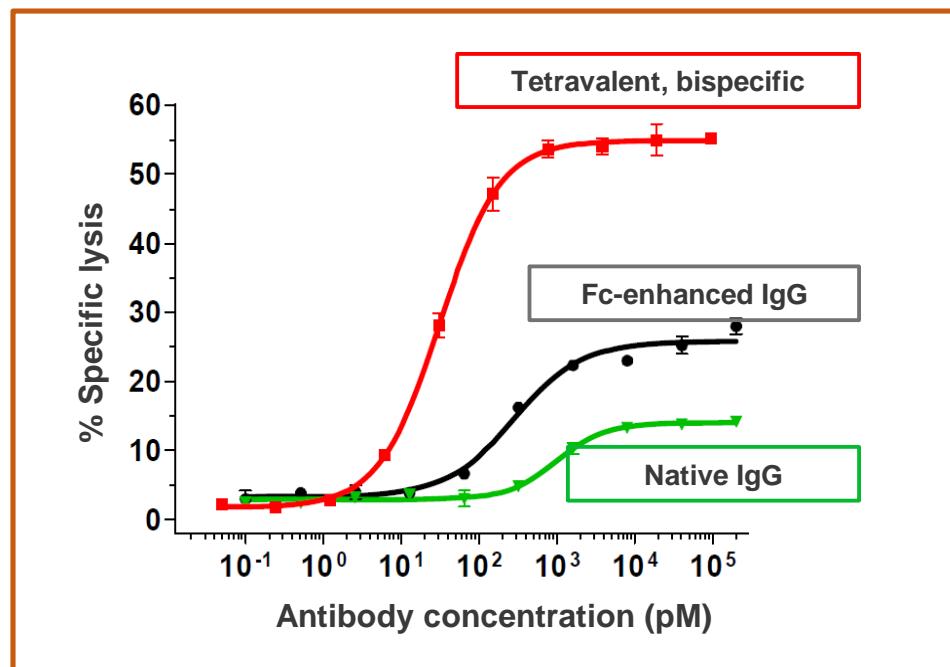
## Tetravalent bispecific NK cells engagers

- Up to 1000x higher affinity for CD16A than monoclonal antibodies
- Binding largely unaffected by competing IgG
- High potency independent of whether NK cells express high or low affinity CD16A (V/F)
- No binding to CD16B

# NK cell engager efficacy

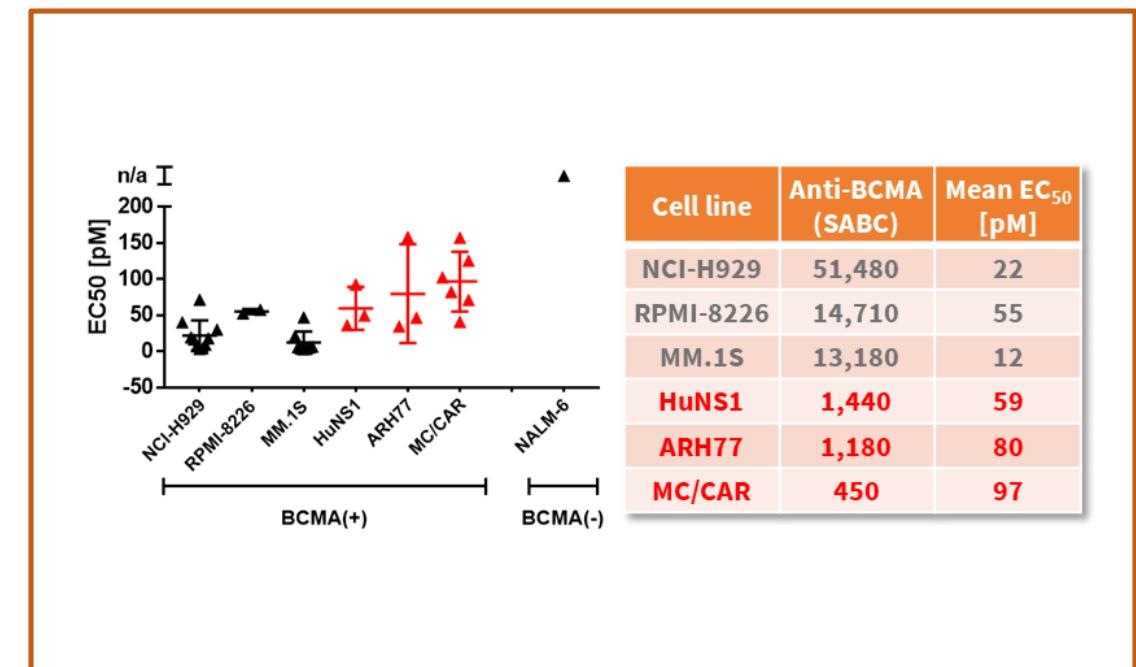
Designed to elicit more potent and effective tumor cell lysis compared to monoclonal antibodies even in cells with very low target expression

Superior potency and efficacy



CD30

Tumor cell lysis at a few hundred receptors



BCMA

# AFM13 (CD30/CD16A) clinical development (1)

Favorable safety profile and single agent clinical activity demonstrated in Hodgkin lymphoma

## Phase 1: Safety and clinical activity demonstrated in heavily pre-treated HL patients

- Dose escalation study: 0.01 – 7.0 mg/kg
- No MTD, favorable safety profile determined
- Tumor shrinkage in 62 % (8/13) and PRs in 23% (3/13) of patients at doses of at least 1.5 mg/kg

## Phase 2a: Monotherapy in r/r HL (IST by GHSG, ongoing) demonstrates single agent activity

- Favorable safety profile confirmed
- ORR of 29% (2/7) in patients failing standard treatments including B.V. and who were anti-PD1 naïve
- Data set important for combination studies

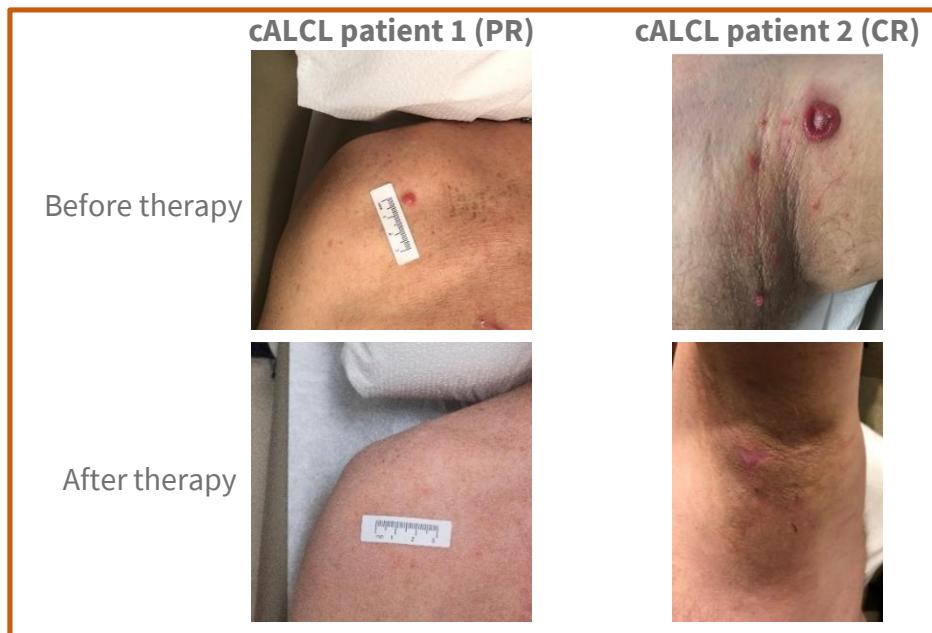
# AFM13 (CD30/CD16A) clinical development (2)

CD30-positive lymphoma represents a novel opportunity (e.g. ALCL, PTCL)

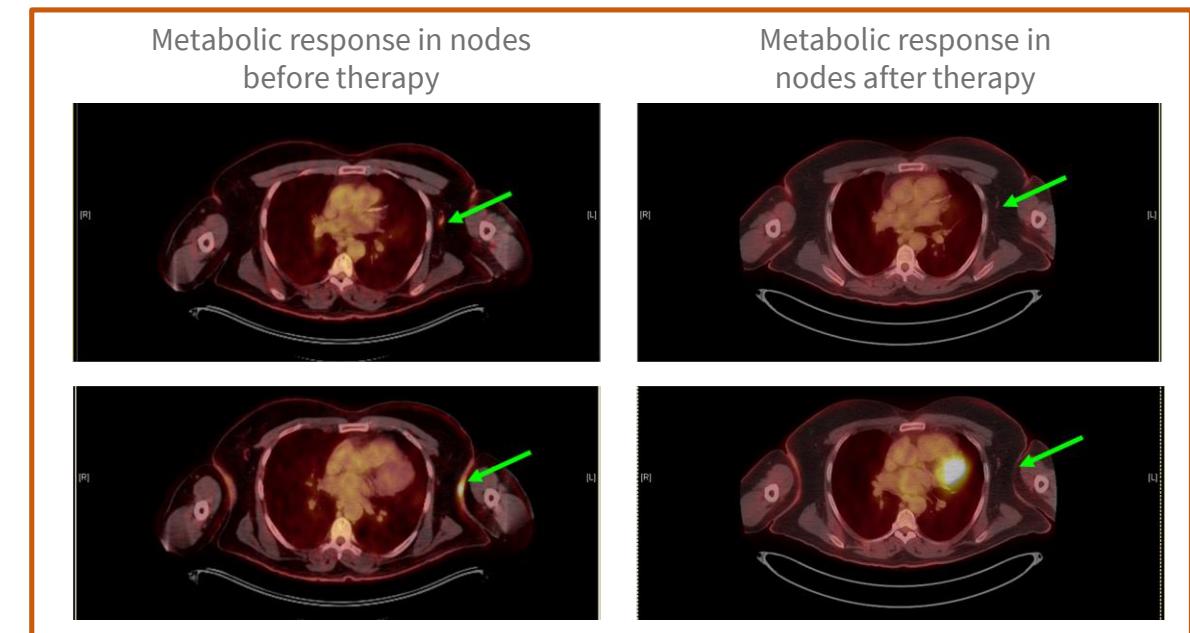
## Phase 1b/2a study in r/r CD30+ lymphoma (IST by Columbia University, ongoing)

- Response data from first cohort by global response score (3 patients treated at 1.5 mg/kg)
  - 1 CR, 1 PR (both cALCL) and 1 SD (TMF)
- Recruitment into 2<sup>nd</sup> cohort completed, 3<sup>rd</sup> cohort ongoing

### Cutaneous lesions

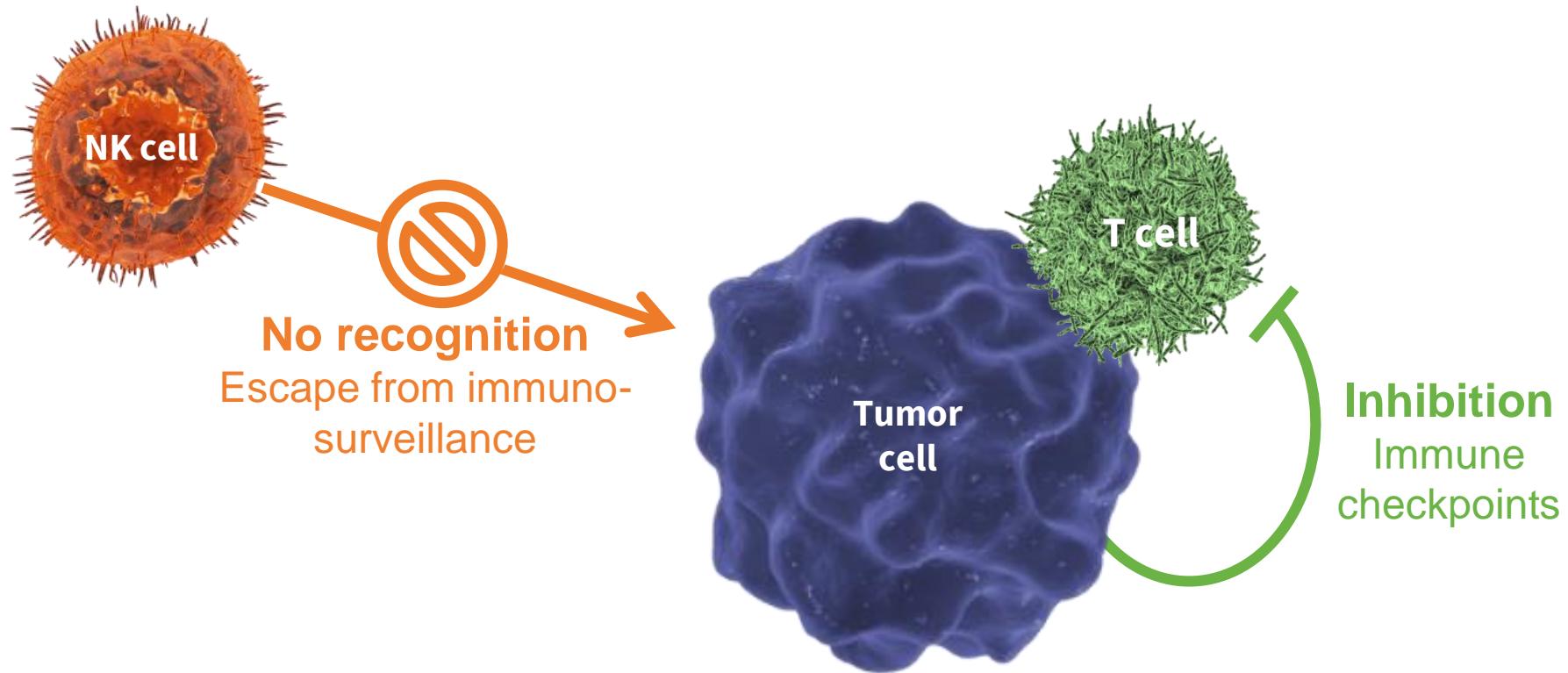


### PET CT results - cALCL Patient 2 (CR)



# Tumor immune evasion impairs both NK and T cell function

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



# AFM13 (CD30/CD16A) clinical development (3)

NK cell engagement shows synergy with PD-1 blocking antibodies *in vivo* and in patients

Synergy between AFM13 and anti-PD-1 in PDX model provides rationale for combination of AFM13 with CPIs

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

**Phase 1b in r/r HL in combination with Merck's Keytruda® (ongoing)**

- Patients with a minimum of three prior lines of treatments: High-dose chemotherapy, ASCT, B.V.
- Favorable safety profile: Well-tolerated with most of the adverse events observed mild to moderate in nature and manageable with standard of care
- Best response preliminary data for 9 patients
  - ORR of 89% (8/9) in patients failing standard treatments including B.V. (vs. 58-63% with anti-PD-1 monotherapy)
  - CR rate of 44% (4/9) in patients failing standard treatments including B.V. (vs. 9-22% with anti-PD-1 monotherapy)
- Both ORR and CRs compare favorably to historical data of anti-PD-1 monotherapy alone in a similar patient population
- Recruitment completed into dose expansion cohort; total of 24 patients to be treated at highest AFM13 dose

# AFM13 (CD30/CD16A) further upside potential

Enhancing NK cell efficacy by combining NK cell-engagers with adoptive NK cell transfer or cytokines

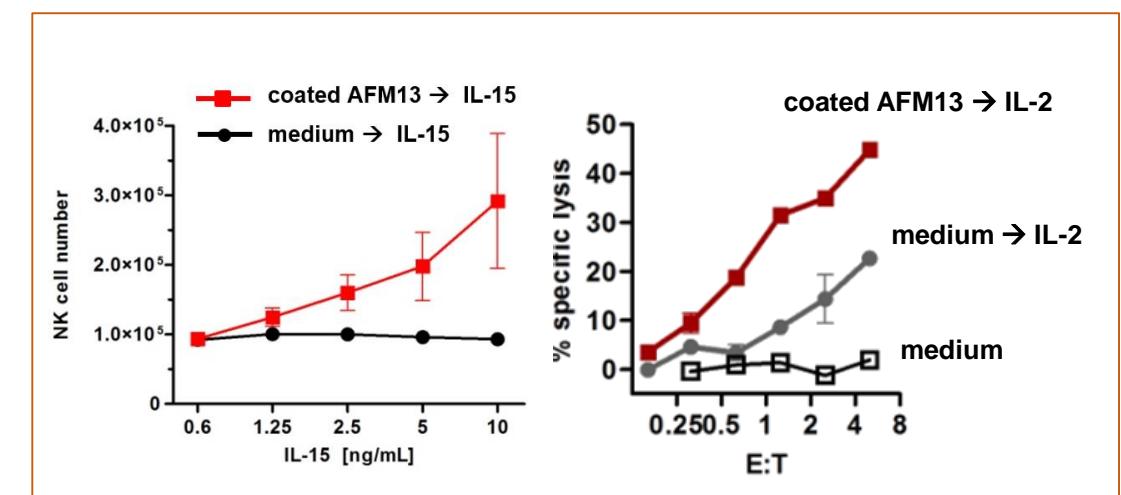
## Combination with adoptive NK cell transfer

- Higher NK cell numbers show increased efficacy (*in vitro*)
- MDACC collaboration investigates AFMD's NK cell engagers in combination with cord blood derived NK cells
- Initially focused on AFM13
- Approach independent of a patient's endogenous NK cell count
- May pave way for combinations in further indications, e.g. multiple myeloma

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## Combination with cytokines

- Cytokines show strong activation of immune cells
- Preclinical data suggest that AFM13 sensitizes NK cells to IL-2 and IL-15 stimulation and proliferation
- Potential to achieve deeper clinical responses



AFM13-induced sensitization for cytokine-stimulated NK cell cytotoxicity

# AFM26 (BCMA/CD16A) treatment of multiple myeloma

Leveraging BCMA as target in autologous stem cell transplant (ASCT)-eligible patients

## Medical need for a novel approach to treat multiple myeloma

- Treatment at or shortly after ASCT to eliminate minimal residual disease (MRD), avoiding relapse

## Targeting BCMA

- BCMA is a highly promising target for therapeutic intervention based on early clinical data (CAR-T and ADCs)
- Low expression of BCMA is a significant hurdle to eliminate malignant cells
- NKs are the first population of lymphocytes to recover post transplant; opportunity to exploit AFM26 in ASCT setting
- Unique opportunity for combination of AFM26 with adoptive NK cell transfer

## AFM26: Final candidate selected

- Differentiated MOA: High affinity engagement of NK cells
  - Efficacy (*in vitro*) against cells expressing very low levels of BCMA
  - NK cell binding largely unaffected by IgG competition
- Safety: Lower cytokine release vs. BiTE
- Convenience: Novel NK cell format selected with prolonged half life

# AFM24 (EGFR/CD16A) treatment of solid tumors

Targeting EGFR: NK cell engagement offers a new mode of action

Medical need for a novel approach to treat EGFR+ solid tumors

- Widen therapeutic window and address resistant patient population

Targeting EGFR

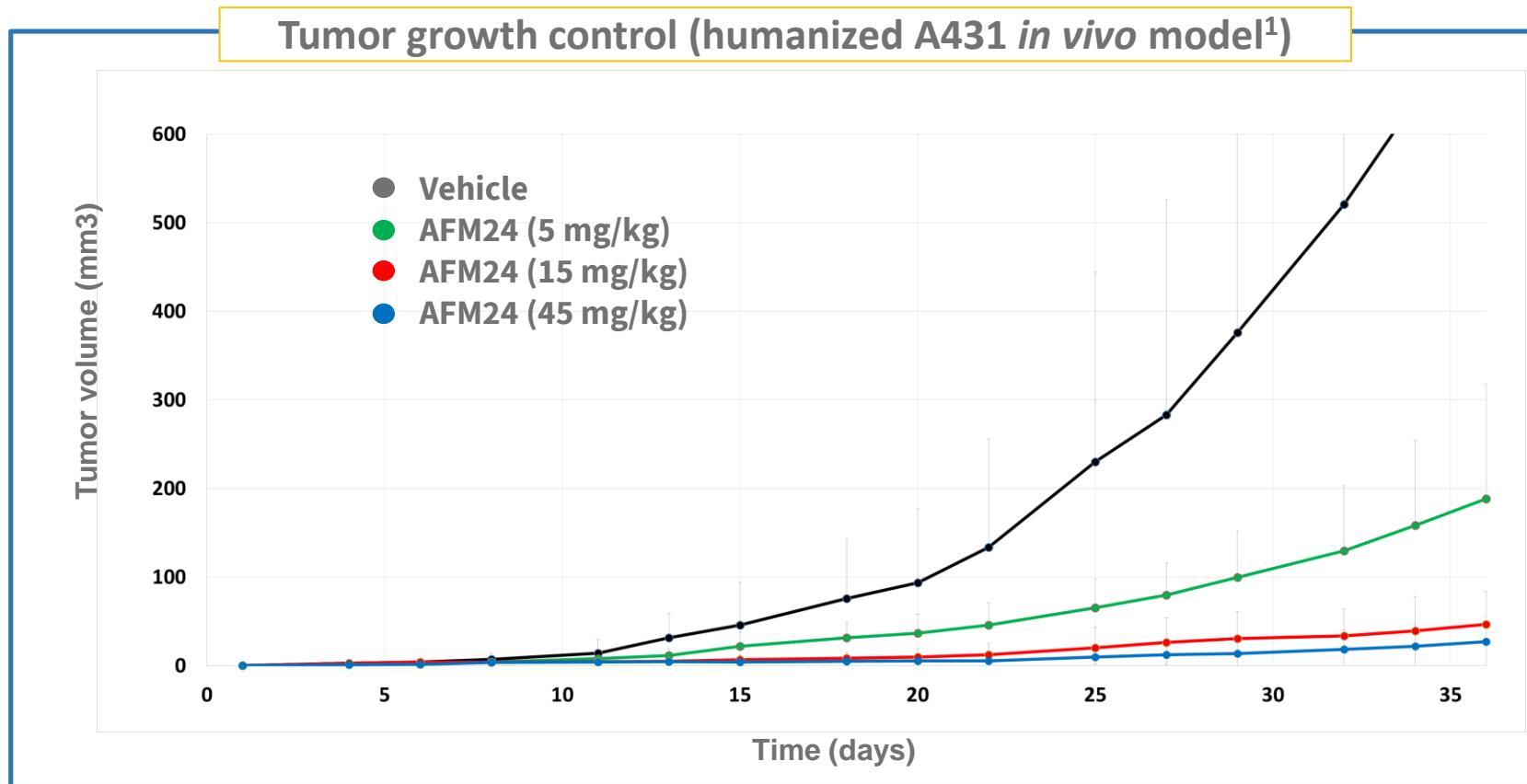
- EGFR as validated target in solid tumors, however side effects negatively impact market potential (skin toxicity)
- Receptor blocking (e.g. cetuximab) cannot address activating mutations (K-RAS)

AFM24: IND-enabling studies anticipated to be completed by mid-year 2019

- Two development candidates selected: AFM24\_T and AFM24\_I
- CMC: GMP cell line generation initiated, RCB available (both, \_T and \_I)
- Convenience: Novel antibody format selected with prolonged half-life (\_I > \_T)
- Differentiated MOA: NK cell activation vs. solely receptor inhibition
  - Increased potency compared to cetuximab enabling NK cell-mediated killing of EGFR low cells
  - *In vivo* efficacy through NK cell killing
  - Efficacy against *Ras*-mutated, cetuximab-resistant HCT-116 cells in a humanized mouse model
  - Reduced/no blocking of EGF-induced signal transduction-aimed at improving safety

# AFM24 (EGFR/CD16A) treatment of solid tumors

NK cell killing can induce complete tumor growth control in *in vivo* model



<sup>1</sup> NOG mice humanized with CD34+ humor cord blood stem cells were boosted for NK cells by hIL-15 transient/temporal expression on d-7. A431 human epidermoid carcinoma cells were inoculated (s.c.,  $1 \times 10^6$  cells/mouse) at d0. The animals received vehicle or AFM24 (i.v.) on days 1, 7, 14, and 21 (3 days before termination of the study the animals received a last dosage). Group size n=7, tumor size determined by caliper measurement.

# T cell-based therapies

CAR-Ts in the lead, however, antibody-based platforms can address weaknesses

## T cell-based anti-tumor therapies

- Clinically validated for CD19 and BCMA
- Limited by significant associated toxicities (CRS, neurotoxicity), high COGS and accessibility (CAR-Ts)

## Immune cell engagers

- Different platforms in development
- Short-lived molecules (BiTE, DART) with evidence of good efficacy
- Long-lived platforms with setbacks (stopped trials, low ORRs)

## Affimed's tetravalent bispecific antibody platform

- Differentiating features
- Two programs in clinical development with the potential for fast development timelines
  - AFM11 (CD19/CD3), developed by AFMD
  - AMV564 (CD33/CD3) developed by Amphivena

# Affimed's T cell-targeting platform

Well-differentiated approach designed to optimize T cell engagement

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

- No unspecific 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 CD19/CD3 TandAb

- Determining best dose: Two Phase 1 dose-escalation trials ongoing in patients with r/r ALL and with r/r NHL, respectively
- Trial status: 3<sup>rd</sup> cohort completed (NHL); recruiting into 5<sup>th</sup> dose cohort (ALL)
- Opportunity: Potential to pave path to fast market approval in indications such as DLBCL and MCL

### AMV564 (Amphivena): a CD33/CD3 TandAb

- Phase 1 ongoing in r/r acute myeloid leukemia (AML)
- ASH 2017: Treatment with AMV564 selectively depletes myeloid-derived suppressor cells (MDSCs) in bone marrow cells from patients with myelodysplastic syndrome (MDS) with resultant reactivation of T lymphocytes
- Amphivena plans to launch a Phase 1 clinical study in patients with MDS

# YE 2017 Cash flow statement and pro forma cash position

	For the twelve months ended December 31, 2017 (thousands of €)	For the twelve months ended December 31, 2017 (thousands of \$) <sup>1)</sup>
<b>Cash and cash equivalents and financial assets<sup>2)</sup> beginning of period</b>	<b>44,894</b>	<b>46,982</b>
<b>Cash and cash equivalents at the beginning of the period</b>	<b>35,407</b>	
<b>Net cash used in operating activities</b>	<b>(25,549)</b>	
<b>Cash Flow from investing activities</b>	<b>8,050</b>	
<b>Cash Flow from financing activities</b>	<b>23,797</b>	
<b>FX related changes to Cash and Cash equivalents</b>	<b>(1,867)</b>	
<b>Cash and cash equivalents at the end of the period</b>	<b>39,837</b>	<b>47,777</b>
<b>Cash and cash equivalents at the end of the period (pro forma)<sup>3)</sup></b>	<b>64,156</b>	<b>76,942</b>

1) Unaudited US dollar amounts (\$/€ exchange rates of 1.0465 and 1.1993 as of January 2, 2017 and December 31, 2017, respectively)

2) Short-term deposits

3) Unaudited estimate, reflects Affimed's receipt of approximately \$29.3m (€24.3m) in net proceeds from February 2018 public offering and ATM usage following December 31, 2017

- Runway at least until Q4/2019

# Milestones 2018

## Maximize value from pipeline and technologies

### Expand NK cell engagement leadership

- Develop AFM13 (CD30/CD16A) to market as monotherapy in CD30+ lymphoma & in combination with Keytruda® in r/r HL
- Explore NK cell engager combinations with CPIs, adoptive NK cells or immune activating agents (IL-2, IL-15)
- Advance AFM24 (EGFRwt/CD16A) and AFM26 (BCMA/CD16A)

### Focus on DLBCL, MCL and AML in T cell engagement

- Generate POC for AFM11 (CD19/CD3) in NHL
- Prepare for follow-on trial for AFM11
- Additional POC through AMV564 (CD33/CD3) in AML

### Broaden engager platforms

- Continue to develop and advance novel tetravalent bispecific molecules with the potential to tailor immune-engaging therapy to different indications and settings

### Use pipeline and technologies to create value through both next-generation products and partnership opportunities

