



## HARNESSING THE POTENTIAL OF THE INNATE IMMUNE SYSTEM FOR ONCOLOGY

**NASDAQ: AFMD** 

**Webcast/Conference Call** 

**11 December 2023** 

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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, the potential of acimtamig, AFM24, AFM28 and our other product candidates, the value of our ROCK® platform, the safety and efficacy of our product candidates, the potential of the LuminICE-203 study design to support accelerated approval by the FDA, 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, 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 macroeconomic trends that may affect the industry or us, such as the instability in the banking sector experienced in the first quarter of 2023, impacts of the COVID-19 pandemic, the benefits to Affirmed of orphan drug designation, the impact on our business by political events, war, terrorism, business interruptions and other geopolitical events and uncertainties, such as the Russia-Ukraine conflict and, the risks, fact that the current clinical data of acimtamig in combination with NK cell therapy is based on acimtamig precomplexed with fresh allogeneic cord blood-derived NK cells from The University of Texas MD Anderson Cancer Center, as opposed to Artiva's AlloNK and other uncertainties and other factors described under the heading "Risk Factors" in Affirmed's filings with the Securities and Exchange Commission (the "SEC").

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### **Today's Speakers and Agenda**



### Agenda

- O Acimtamig update: Evolving HL market, Latest AFM13-104 data, LuminICE-203 progress
- O AFM24 program update: Latest data with a focus on NSCLC



Adi Hoess, MD, PhD
Chief Executive Officer



Andreas Harstrick, MD
Chief Medical Officer





### **Acimtamig**

ICE® for CD30+ Lymphomas



### **LuminICE-203: The Path Forward for Acimtamig (AFM13)**



#### Acimtamig: Unique Mechanism of Action Addressing Significant Unmet Need with Large Market Opportunity

- There is a void of viable agents for r/r HL patients due to the emergence of patients who are double refractory to BV and CPIs
- Acimtamig + AlloNK<sup>®</sup> has the potential to address a ~\$3 billion market opportunity in r/r HL & PTCL where new treatment options are needed
- Acimtamig + NK cells have shown 97% ORR, 78%
   CR, with a well manageable safety profile

# LuminICE-203 Builds on Strong Phase 1/2 Data with Accelerated Approval Potential Confirmed by FDA Interactions

- Study enrolling with dosing of first two cohorts underway
- Expect initial data update from run-in phase H1 2024
- Includes a PTCL cohort to establish POC
- FDA Fast Track Designation granted



### While Newer Agents have Improved Outcomes in HL, the Majority of R/R Patients Will Require Additional Interventions

#### DOUBLE-REFRACTORY / RELAPSED HODGKIN LYMPHOMA: TACKLING RELAPSE AFTER BV AND CPI

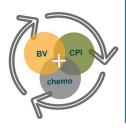


"The approval of BV and CPIs has revolutionized the management of R/R HL. In recent years, these agents have rapidly moved to earlier lines of therapy. This shift in practice means that double-refractory (i.e., refractory to both BV & CPI) HL is becoming an increasingly common clinical problem."

2021 by The American Society of Hematology DOI 10.1182/hematology.2021000256

Regardless of treatment, a majority of R/R HL patients will need multiple therapies<sup>1,2</sup>

>50% of patients receiving SCT will progress<sup>3,4</sup>



Future therapies currently being studied for R/R HL are limited

- Pembro+Lag3 limited data to-date
- > ORR 29% & CR 9%5
- Current intelligence shows no other novel drugs under clinical investigation for double R/R HL





### For HL Patients that Have Advanced Past BV and CPI, There Are No **Compelling Treatment Options Available**

History of Prior Tx, Response, PFS, with select agents with 3+ prior lines of treatment in R/R HL

	Regimen	N	Median prior lines (range)	Prior BV / CPI	ORR %	CR %	PFS, EFS Median # Months
<u></u>	Current NCCN Gui	delines: S	elected agents,	, 3+ prior lin	es of Tx in F	R/R HL (exclu	iding BV and CPI tx)
	GVD <sup>1</sup>	40	3	R/R HL studies	75%	17%	8.5
	Bendamustine <sup>2</sup>	34	4 (1-17)	were conducted	56%	34%	5.2
	Lenalidomide <sup>3</sup>	38	4 (2–9)	between 2000-2010 prior to either BV	18.4%	2.6%	4.0
	Everolimus <sup>4</sup>	19	6 (3-14)	or CPI approval	47%	5%	6.2
3		10 6 (2 14) or CPI 479/ 59/ 6 2					
	Pembro+LAG3 <sup>5</sup>	34	5	Y/Y	29%	9%	9.7

Therapies show **CRs** ranging from 5% to 34 % and **PFS** ranging from 4.0 - 9.7 months





February TA Larson S, Trinkaus K, et al. A phase 2 multicenter study of lenalidomide in relansed or refractory classical Hodgkin lymphoma. Blood 2011;118:5119-25

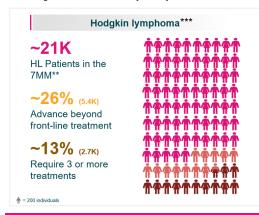
Johnston PB, Inwards DJ, Colgan JP, et al. A Phase II trial of the oral mTOR inhibitor everolimus in relapsed Hodgkin lymphoma. Am J Hematol 2010;85:320-324

Poster 1068; Presented at the EHA2023 Hybrid Congress; Frankfurt, Germany; June 8-11, 2023

## A Significant Opportunity Exists to Address R/R HL in the 7 Major Markets with Additional Potential in R/R PTCL



### Cases and Percentage of R/R CD30+ HL in the 7 Major Markets (MM)\*





#### CD30+ R/R HL

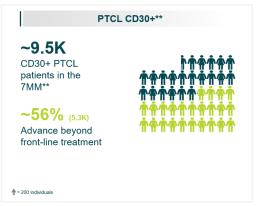
#### Acimtamig + NK cell combo:

- · Addresses the challenges of R/R HL
- Initial market value in HL is in the ≥3-line setting
- Additional HL value with earlier lines of treatment
- Market research indicating premium above CAR-T pricing

Data as of April 2023; \*7MM include US, EU5 (France, Germany, Italy, Spain, United Kingdom), and Japan \*\*Source: SEER, WHO Globocan, Global Data; Kantar; Affimed Internal Research

\*\*\* Source: SEER, WHO Globocan, Global Data; Kantar; Leukemia & Lymphoma Society; Lymphoma Research Foundation; Laribi, Oncologist. 2018 Sep; 23(9): 1039–1053.; Brossard, Blood (2014) 124 (19): 2983–2986.; Sabattini, Haematologica. 2013 Aug; 98(8): e81–e82.; Savage, Blood. 2008 Jun 15;111(12):5496-504; Affined Internal Research

### Cases and Percentage of R/R CD30+ PTCL in the 7 Major Markets (MM)\*





#### CD30+ R/R PTCL

#### Acimtamig + NK cell combo:

- Addresses R/R CD30+ PTCL
- Limited treatment options exist for R/R PTCL
- Market research indicating premium above CAR-T pricing



## Acimtamig + NK Cells Shows Unprecedented ORR and CR Rates in Double Refractory HL Patients



- All patients were heavily pre-treated and doublerefractory to BV and CPIs
- All patients were refractory to their most recent treatment





Acimtamig + NK cells is the most promising therapy being studied in HL patients who are relapsed or refractory to BV & CPIs

	AFM13-104 (NK cell combo) HL patients @ RP2D
Number Treated	32
No. Prior Lines Therapy (range)	7 (1-13)
Prior BV	100%
Prior CPI	100%
Prior SCT	63%
Response to Most Recent Treatment	0%





### AFM13-104: The First Clinical Study of an ICE® in Combination with NK Cells



#### **DESIGN**

### Active, Recruiting

 A Phase 1/2, doseescalation, proof of concept and safety study (NCT04074746; AFM13-104)

#### **PATIENTS**

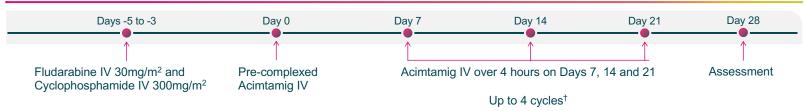
 Key Inclusion Criteria: Patients with r/r CD30+ Lymphoma aged 15 – 75 years, refractory / intolerant to BV

#### **OBJECTIVES**

- **Primary:** Safety and RP2D of NK cells pre-complexed with acimtamig, followed by IV acimtamig
- Secondary: ORR, and CR and PR rate; DOR, PFS and OS; Persistence of Acimtamig-NK cells; Immune reconstitution

### PROCEDURES





#### **PHASE 2: EFFICACY**

Cohort 3a: HL Cohort 3b: CD30+ NHL

1×10<sup>8</sup>/kg acimtamig precomplexed allo cb-NK cells 1×10<sup>8</sup>/kg acimtamig precomplexed allo cb-NK cells Acimtamig dose 200 mg Q1W





## AFM13-104: Was Well Tolerated, with No Cases of Cytokine Release Syndrome, ICANS, or GVHD



#### Safety Profile (N=42)

- There were no cases of cytokine release syndrome, immune cell associated neurotoxicity syndrome (ICANS) or GVHD
- As expected with the lymphodepleting chemotherapy, all patients had transient and reversible myelotoxicity
- There was only one case (0.9%) of grade 2 infusion-related reaction (IRR) to acimtamig-NK cells and 27 instances of IRR in 19 patients (1 grade 3, 21 grade 2 and five grade 1) to 349 infusions of acimtamig alone (7.7%)
- There were no dose limiting toxicities and the RP2D of NK cells was established at dose level 3 (108/Kg)



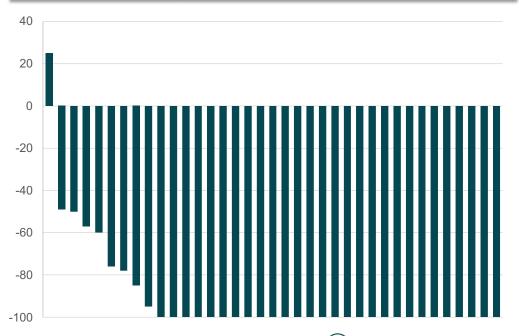


## AFM13-104: Demonstrates Unprecedented Response Rates in Heavily Pretreated Patients



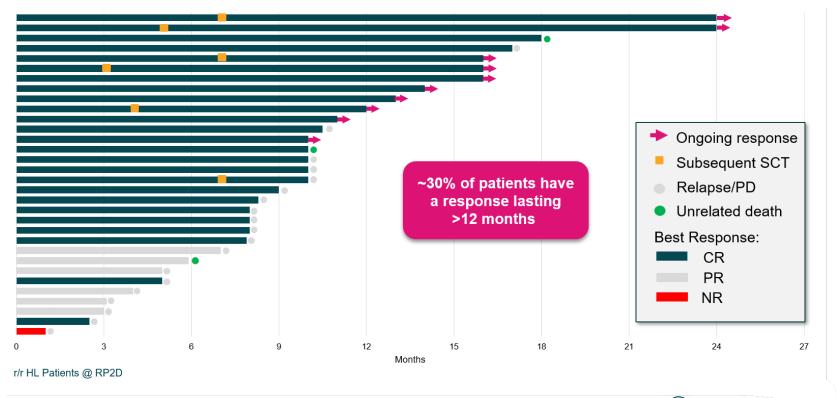
- HL patients treated at the RP2D (n=32):
  - 97% ORR (n=31)
  - 78% CR (n=25)
  - **72%** 6-month CR rate (n=23)
- CD30+ NHL patients treated at RP2D (n=4):
  - 75% ORR (n=3)
  - 25% CR (n=1)
- All 4 patients who had previously experienced PD with CAR-T had a CR

### Percent change in target lesions; HL patients, all dose levels

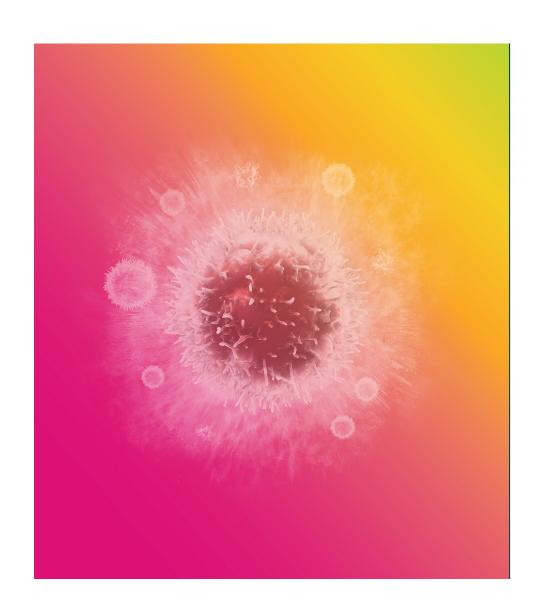




### AFM13-104: Median EFS of 9.8 Months, Median DOR of 8.8 Months and 30% of Patients Remained in Remission for More than 12 Months







### LuminICE-203 Background, Regulatory Update & Next Steps



## Recent Interactions with FDA Validated Overall Approach and Confirmed Study Could Support Registration Pending Data





Insights from **FDA Written Response** to the Type C request:

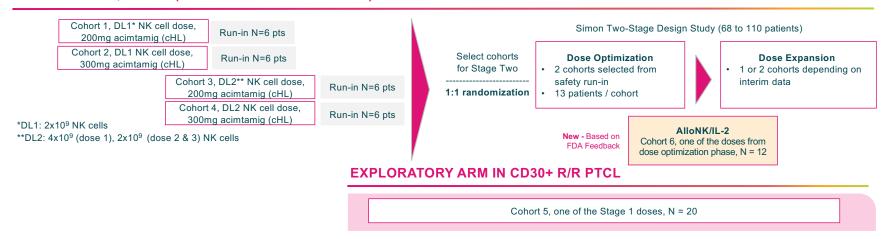
- LuminICE-203 study designed based on FDA's recommendations/ guidelines to support accelerated approval, the final alignment on the package to support regulatory approval will depend on the demonstrated magnitude of clinical benefit
- FDA is highly engaged to support the progress and design of the study combining acimtamig and AlloNK® as evidenced by the granted fast track designation and Type C feedback
- The FDA agrees with AFMD's approach to address the question of the contribution of single components activity by adding a cohort to the study evaluating the treatment with AlloNK/IL-2 only



# AlloNK® Cohort (n=12) to be Added to LuminICE-203 Study to Demonstrate Contribution of Components



#### PHASE 2 TRIAL, R/R HL (SIMON TWO-STAGE DESIGN)



#### STUDY TREATMENT REGIMEN, UP TO 3 CYCLES



## LuminICE-203 Builds on Strong Phase 1/2 Data with Accelerated Approval Potential Confirmed by FDA Interactions





**Evolving HL Landscape** with Unmet Needs

 There is a void of viable agents for r/r patients due to the emergence of patients who are double refractory to BV and CPIs



**Remarkable Efficacy** 

 Acimtamig + NK cells have shown 97% ORR, 78% CR, with a well manageable safety profile



LuminICE-203 Underway with FDA Fast Track Designation

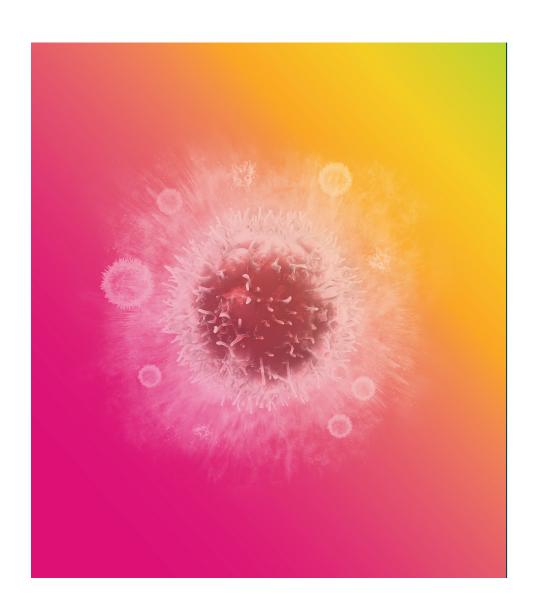
- Study enrolling with dosing of first two cohorts underway
- Expect initial data update from run-in phase H1 2024
- Includes a PTCL cohort to establish POC
- Type C meeting achieved alignment on new cohort to assess contribution of components



**Attractive Opportunity** 

Acimtamig + AlloNK® has the potential to address a ~\$3 billion market opportunity in r/r HL & PTCL where new treatment options are needed





### AFM24

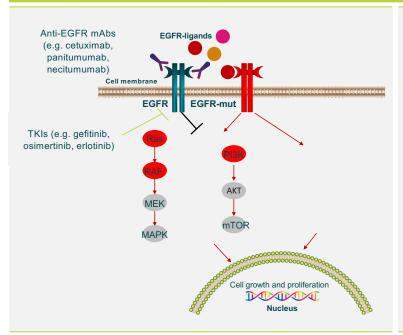
ICE® in EGFR+ Solid Tumors



# AFM24 is an EGFR/CD16A Tetravalent Bi-Specific Antibody with a Novel Approach to Treating EGFR-Expressing Solid Tumors



AFM24 with its differentiated mode of action unleashes the potential of Innate Immunity in treating EGFR-expressing solid tumor indications

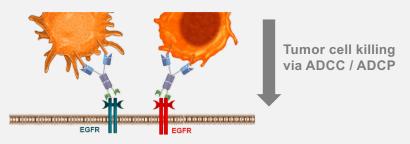


#### **Current standard of care drugs:**

- Disruption of the EGFR signaling cascade
- Resistance → activation of alternate pathways / downstream mutations
- Dose-limiting toxicities

#### The promise of AFM24's differentiated MoA\*:

- Docking to EGFR only, no dependence on EGFR signaling
- Efficacy toward cells with mutated EGFR-signaling pathway
- Activation and recruitment of both the innate and adaptive immune cells
- Differentiated safety profile



Disclaimer: The image provides an overview of selected EGFR-targeting therapeutic agents and does not represent an exhaustive summary.



<sup>\*...</sup> Based on in vitro and in vivo data in mouse, and cynomolgus monkeys and early clinical data (Wingert et al. mAbs 2021;13: 1950264). **TKI** = tyrosine kinase inhibitor.

### **AFM24 Path Forward: NSCLC in Combination with Atezolizumab**



### AFM24, a first in class ICE® for EGFR-positive solid tumors

- Early clinical program:
  - demonstrated safety as monotherapy and in combinations (NK, PD1)
  - showed anti-tumor activity as a monotherapy in combinations
  - provided clinical validation that triggering innate immunity activates adaptive immunity
- Highest efficacy seen in NSCLC across a range of indications evaluated:
  - Emerging data in NSCLC EGFRwt with AFM24 in combination atezolizumab (73% DCR including 4 objective responses) is highly encouraging
  - Monotherapy activity seen in EGFRmut NSCLC led to inclusion in AFM24-102 trial

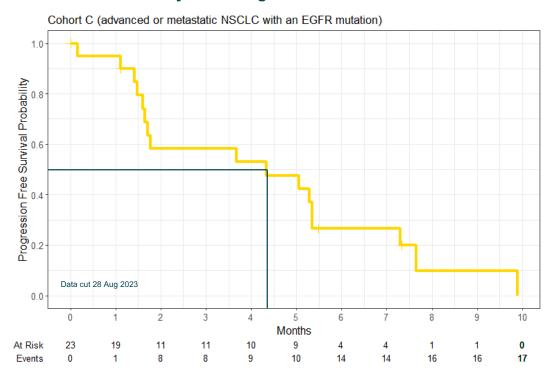
AFM24 in combination with atezolizumab has potential to demonstrate a meaningful clinical benefit with a favorable safety profile in both EGFRwt and EGFRmut NSCLC patient populations



<sup>\* 3</sup> of 4 response awaiting confirmation per RECIST 1.1

## Monotherapy: NSCLC *EGFR*mut Cohort Data Confirms Signs of Efficacy in Line with SOC Combination Chemotherapy\* (~4.5 months)

#### **Analysis of Progression Free Survival**





### **AFM24 + Atezolizumab to Focus on 2 NSCLC Cohorts**

### Building on the AFM24 monotherapy experience led to the focused development of AFM24 with atezolizumab



\* Enrollment in Gastric and HCC/PanC expansion cohorts concluded as they are unlikely to meet efficacy hurdle



NSCLC EGFRmut

NSCLC

**EGFRwt** 

\* Gastric

# AFM24-102 NSCLC *EGFR*wt Cohort Patient Characteristics & AFM24 Related Treatment-Emergent Adverse Events



Patient Characteristics NSCLC EGFRwt cohort	N=17*
Age (years) Median-Range	66 (45-75)
Sex n (%) • Male • Female	14 (82.4) 3 (17.6)
Race n (%) • White • Asian	8 (47.1) 9 (52.9)
ECOG PS (n, %)  • 0  • 1	2 (11.8) 15 (88.2)
No. Prior Lines of treatment Median (range)	2 (1-5)
Prior CPI Response to CPI Refractory to CPI**	100% 4 PR / 7 SD 6

Most Relevant AFM24 Related Treatment Emergent Adverse Events  NSCLC EGFRwt cohort	N=17
Asthenia G1	1 (1)
AST elevation G1 G2	2 (2) 1 (1)
ALT elevation G1 G2	3 (2) 2 (1)
Erythematous rash G1 G2	3 (3) 1 (1)
Infusion related reaction G1 G2 G3	3 (2) 2 (2) 1 (1)

- AFM24 has demonstrated to be safe and well-tolerated as both a monotherapy and in combination
- Combination with atezolizumab has not led to unexpected toxicity: Observed toxicity in line with toxicity profile of the individual agents



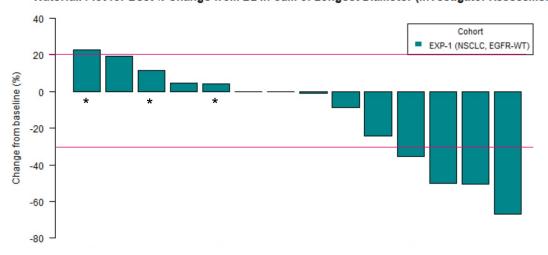
<sup>\*</sup>Overall 17 pts were recruited into the cohort, 15 pts are included in the FAS (full analysis set) for efficacy as per protocol.

<sup>\*\*</sup>All patients ultimately had progressed to previous CPI treatment

# AFM24-102 NSCLC *EGFR*wt Expansion Cohort with Tumor Shrinkage in 7 Patients (47%)



#### Waterfall Plot for Best %-Change from BL in Sum of Longest Diameter (Investigator Assessment)



Data cut: 05-Dec-2023

#### **Best Percent Change From Baseline**

- Overall, 14 of 15 patients with at least 1 efficacy scan# available
- 1 CR (unconfirmed):
  - -70% change from baseline
- 1 PR (confirmed):
  - -32% change from baseline
- 2 PR (unconfirmed):
  - -50% change from baseline
  - -50% change from baseline
- 7 SD
- 3 PD\*

According to RECIST 1.1, a subsequent second scan is required for confirmation

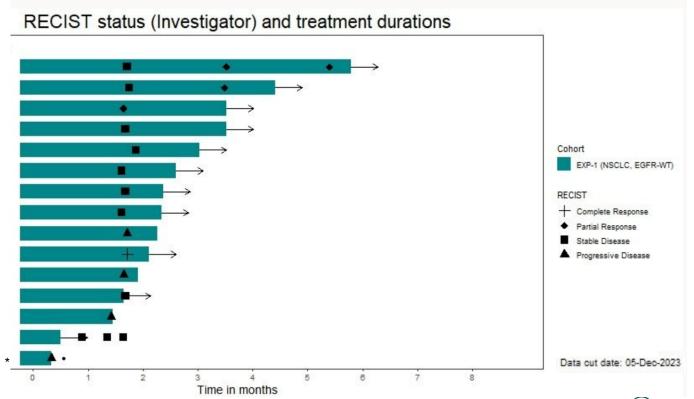
# valid post-baseline efficacy scan according to RECIST 1.1

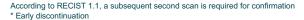


<sup>\*</sup> One additional patient (ES-002-3014 - not displayed in the waterfall plot) discontinued early and was not evaluable according to RECIST 1.1

# AFM24-102 NSCLC *EGFR*wt Expansion Cohort: Treatment Ongoing in 11 of 14 Evaluable Patients









# Based on Rechallenge Data, Atezolizumab Monotherapy has Little to No Activity After Progression on CPI



Metric	Atezo Monotherapy <sup>1</sup>	
ORR	0-7%	
) mPFS	2.9-3.9 months	



### It is unlikely the results in NSCLC EGFRwt are driven solely by atezolizumab

 <sup>&</sup>quot;Retreatment With Anti-PD-L1 Antibody in Advanced Non-small Cell Lung Cancer Previously Treated With Anti-PD-1 Antibodies", ANTICANCER RESEARCH 39: 3917-3921 (2019), "Switching administration of anti-PD-1 and anti-PD-L1antibodies as immune checkpoint inhibitor rechallenge in individuals with advanced non-small cell lung cancer: Case series and literature review," Thoracic Cancer 11 (2020) 1927–1933



# Treatment Landscape for 2L+ NSCLC *EGFR*wt Characterized by Low ORR and/or PFS





There is a significant unmet need in 2L+ NSCLC EGFRwt creating potential for AFM24+CPI in a large number of patients

	Non-Small Cell Lung Cancer ( <i>EGFR</i> wt)
1st line treatment, for Stage IV/ metastatic patients	CPI Immunotherapy +/- chemotherapy
SOC, 2L patients	CYRAMZA (ramucirumab) + docetaxel  ORR: 23%, DCR: 64%, mPFS: 4.5 months Grade 3+ TEAE: 79%, SAE: 45%
Emerging therapies	Datopotamab Deruxtecan (NSQ pts only) • ORR: 31%, mPFS: 5.6 months • Grade 3+ AE: 25%, Serious TRAE: 10%

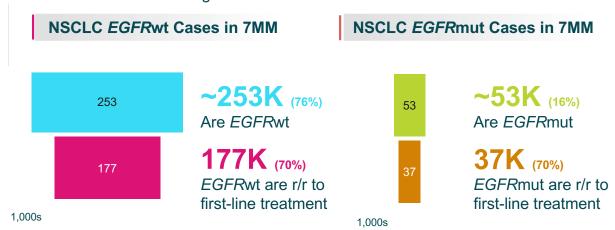


## 2L+ NSCLC *EGFR*wt and *EGFR*mut Patient Population Represents a Significant and Growing Opportunity

NSCLC Addressable Cases and Number of 2L NSCLC EGFRwt and EGFRmut in the 7 Major Markets (MM)\*\*



Stage IV metastatic NSCLC cases



Incidence = 613K NSCLC in 7MM; 331K stage IV metastatic are the addressable population; 214K 2L EGFRwt + EGFRmut

Data as of November 2023



<sup>\*7</sup>MM include US, EU5 (France, Germany, Italy, Spain, United Kingdom), and Japan

<sup>\*\*</sup>Source: SEER, WHO Globocan, Global Data; Kantar; Affimed Internal Research

## AFM24 Path Forward: NSCLC in Combination with Atezolizumab





Activity in Combination
Atezolizumab

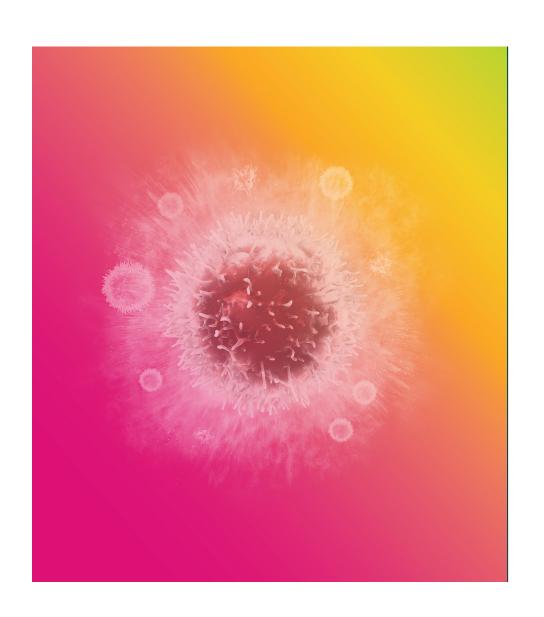
- Encouraging signals in atezo combination study in NSCLC *EGFR*wt
  - 1 confirmed PR, 3 unconfirmed responses (1 CR, 2 PR) awaiting confirmation
  - 73% DCR and 47% tumor shrinkage rate



Data Updates H1 2024

- Further updates, including PFS, for NSCLC EGFRwt cohort
- Initial data update on NSCLC EGFRmut cohort





# Summary & Upcoming Milestones



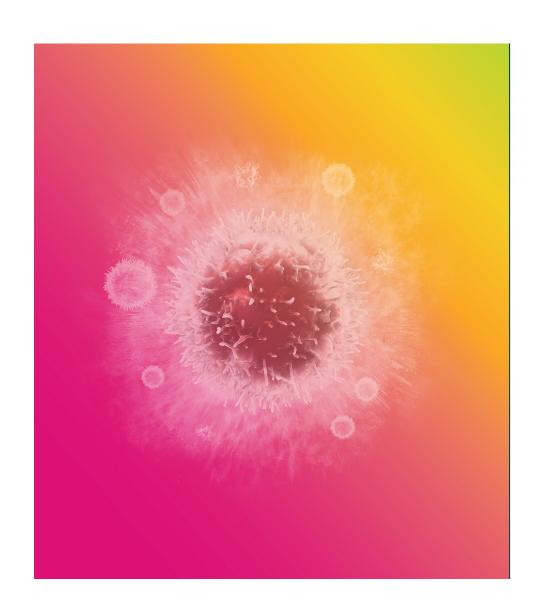
# Multiple Potential Inflection Points in H1 2024 - Cash Runway into 2025



Program	Milestone	Timing
LuminICE-203	Data update from patients treated in cohorts 1-4	H1 2024
AFM24-102	PFS data update from NSCLC EGFRwt cohort	H1 2024
AFM24-102	Data update from NSCLC EGFRmut cohort	H1 2024
AFM28-101	Progress updates from dose escalation study (safety, dose levels)	H1 2024



Confidential



### **Appendix**



### **Survival Subgroup Analysis**



	Overall (N=36)	Patients with Hodgkin (N=32)
ORR (%) (95% CI)	94.4% (86.9-100%)	96.9% (90.9-100%)
Best Overall Response		
Complete Response	72.2%	78.1%
Partial Response	22.2%	18.7%
Stable Disease	0%	0%
Progressive Disease	5.5%	3.1%
Not Evaluable	0%	0%

Suppl. Table 4. Outcomes of patients receiving the RP2D by disease and planned number of cycles.

	Overa	Overall (N=36)		Patients with Hodgkin (N=32)	
	2 cycles (N=13)	4 cycles (N=23)	2 cycles (N=12)	4 cycles (N=20)	
Median EFS, mo	8 months	10 months	8 months	10 months	
At 6 months (%) (95% CI)	61.5% (35-87.9%)	69.6% (50.8-88.4%)	66.7% (40-93.3%)	67.6% (19.9-100%)	
At 12 months (%) (95% CI)	30.8% (5.7-55.9%)	28.6% (9.3-47.9%)	33.3% (6.6-60%)	26.5% (11.7-41.3%)	
Median OS, mo	NR	NR	NR	NR	
At 6 months (%) (95% CI)	84.6% (65-100%)	86.9% (73.1-100%)	91.7% (76-100%)	85% (69.3-100%)	
At 12 months (%) (95% CI)	84.6% (65-100%)	85% (69.3-100%)	91.7% (76-100%)	82.3% (64.2-100%)	

NR: Not reached.

