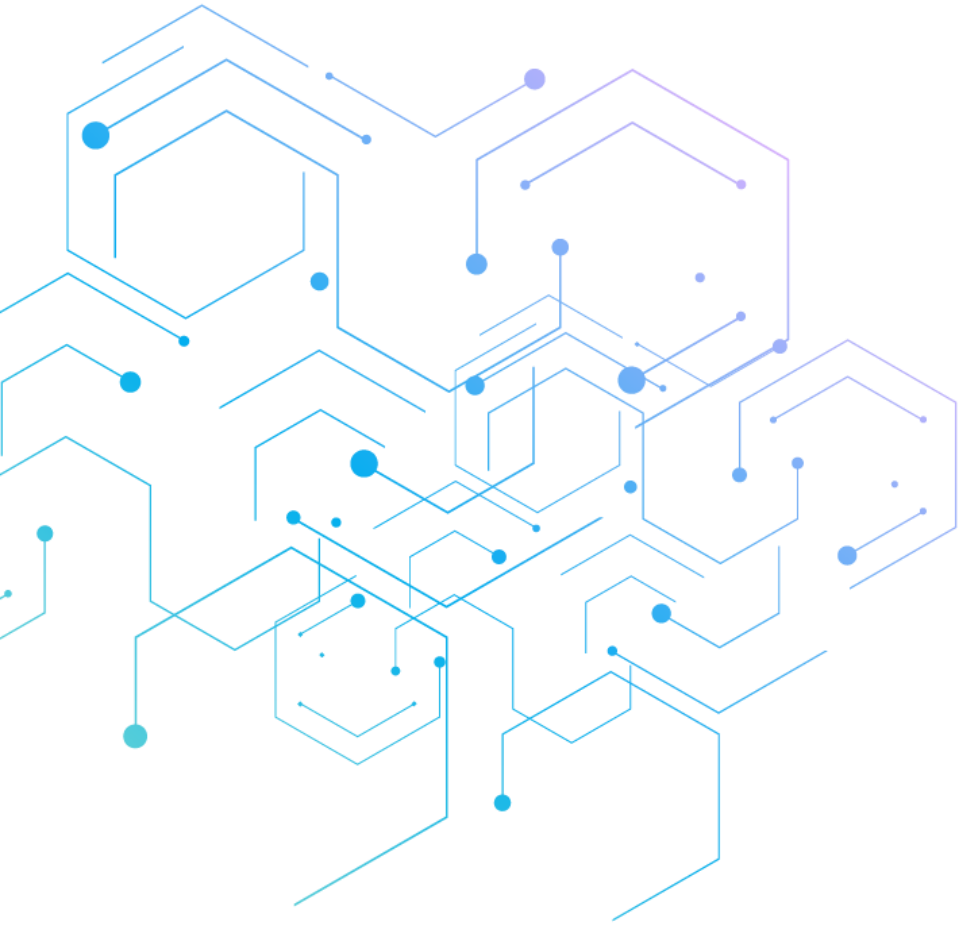
GlycoMimetics

Transforming Lives

Glycobiology-based Therapeutics

April 2024 | NASDAQ: GLYC



Forward-Looking Statements

- To the extent that statements contained in this presentation are not descriptions of historical facts, they are forward-looking statements reflecting the current beliefs and expectations of the management of GlycoMimetics, Inc. ("GlycoMimetics," "we," "us," or "our"). Forward-looking statements contained in this presentation may include, but are not limited to: (i) the expected or projected timing of events and data readout from ongoing Phase 3 clinical trials of uproleselan; (ii) the planned or potential clinical development and potential indications, benefits and impact of our drug candidates, including uproleselan and GMI-1687; (iii) the timing of receipt of clinical data; (iv) the potential safety, efficacy or clinical utility of our drug candidates; (v) the size of patient populations targeted by drug candidates we or our collaborators develop; (vi) market adoption of our potential drug candidates by payors, physicians and patients, including potential market opportunity; (vii) the likelihood and timing of regulatory filings, approvals or other anticipated interactions with regulatory authorities; (viii) our business and product development strategies, including our cash needs and expected cash runway; and (ix) any other statement containing terminology such as "may," "will," "should," "expects," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "intends," or "continue," or the negative of these terms or other comparable terminology.

- Forward-looking statements are subject to known and unknown risks, uncertainties, and other factors that may cause our or our industry's actual results, levels of activity, performance, or achievements to be materially different from those discussed, implied or otherwise anticipated by such statements. You are cautioned not to place undue reliance on such forward-looking statements, which are current only as of the date of this presentation. Examples of risks, uncertainties and factors that may cause differences between our expectations and actual results include unexpected safety or efficacy data, unexpected side effects observed during preclinical studies or in clinical trials, whether results of early clinical trials will be indicative of results from later clinical trials, changes in expected or existing competition or additional market research that may cause our expectations about market opportunity to change, changes in the regulatory environment for our drug candidates, failure of our collaborators to support or advance our collaborations or drug candidates, our need for future capital, the inability to adequately protect our intellectual property, and becoming a party to litigation or other disputes. For a further description of the risks associated with forward-looking statements, as well as other risks facing GlycoMimetics, please see the risk factors described in the Company's Annual Report on Form 10-K filed with the U.S. Securities and Exchange Commission on March 29, 2023, as well as other reports we file with the U.S. Securities and Exchange Commission from time to time, including those factors discussed under the caption "Risk Factors" in such filings. Forward-looking statements speak only as of the date of this presentation, and GlycoMimetics undertakes no obligation to update or revise these statements, except as may be required by law.

Near-Term Catalysts and Promising, Glycobiology-based Pipeline

Uproleselan: Multiple Late-Stage Clinical Trials

- **Fully enrolled Phase 3 trial** in R/R AML (n=388), time-based analysis of OS with patient data cutoff end Q1 2024; topline results expected in **Q2 2024**
- **Fully enrolled Phase 2 trial** in front-line AML (n=267) ongoing, **NCI-sponsored**
- **Ongoing IITs** in other AML populations. Preliminary data presented at ASH 2022/2023
- **Novel MOA/first-in-class** → potential **broad utility** with **Breakthrough Therapy**, **Fast Track**, and **Orphan** designations

Promising Early-Stage Pipeline

- Novel small molecules inhibit carbohydrate signaling
- Potential application in multiple inflammatory diseases
- **GMI-1687**
  - Phase 1a trial in healthy volunteers completed
  - Initial indication: treatment of sickle cell disease (SCD) vaso-occlusive crisis (VOC)
  - Being developed for self-administration at time of VOC
- **Galectins**
  - Targeting fibrotic diseases
  - First oral Galectin-3 antagonist

Targeted Operational Execution

- **Multiple Key Leadership Hires in Last Year** → purpose-driven biotechnology team
- **Deep expertise** in regulatory, technical operations, medical and commercialization across hem/onc therapies
- Cash runway through **Q4 2024**

A Portfolio of Promising Product Candidates

Program	Therapeutic Area	Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Market
SELECTINS							
UPROLESELAN (GMI-1271)*	Relapsed / Refractory AML	Time based data cutoff end Q1 2024, data in Q2 2024					
	Newly Diagnosed “Fit” AML	Fully enrolled 267 patients Dec 2021					
	Relapsed / Refractory Pediatric AML	Ph1 by NCI dosed 1st patient					
GMI-1687*	SCD Vaso-occlusive Events and Inflammatory diseases	Ph1a completed					
GALECTINS							
GMI-2093	Fibrosis and Oncology	Lead declared March 2022					

Breakthrough Therapy Designation in AML

Uproleselan (GMI-1271)

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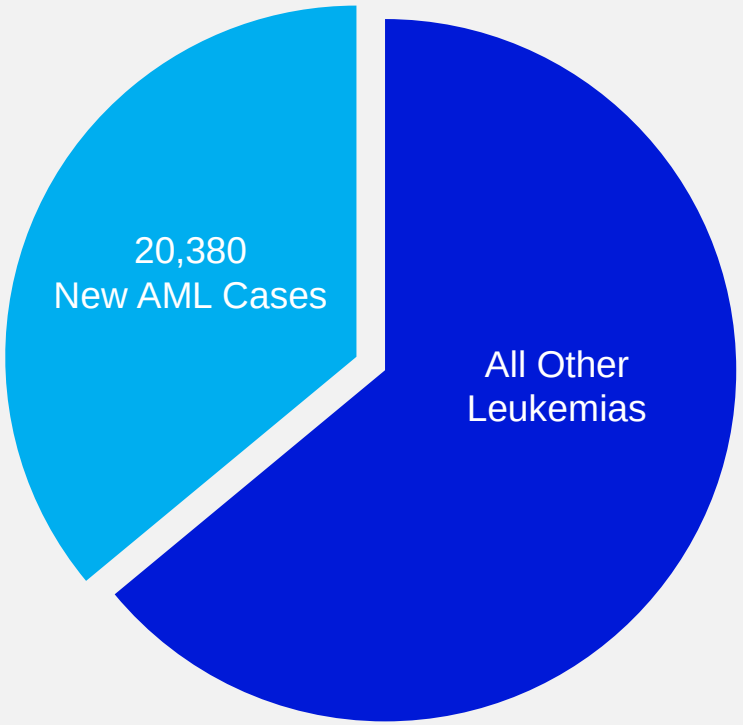
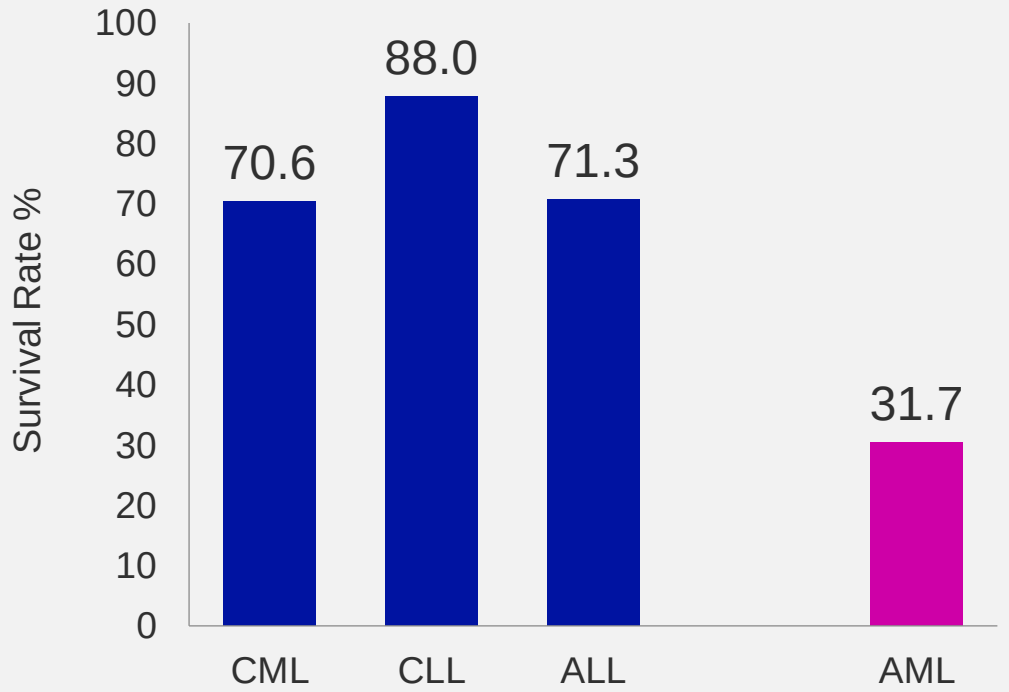
Significant Unmet Medical Need In AML[1]

ESTIMATED NEW CASES (2023)

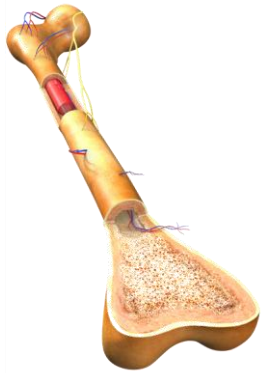


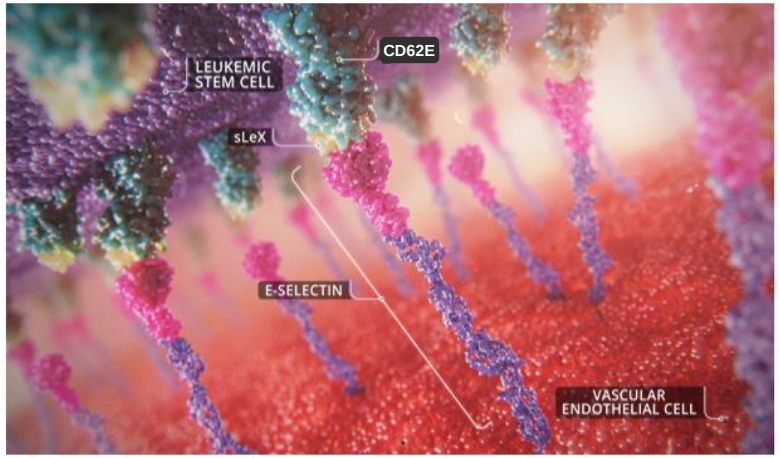
5-YEAR RELATIVE SURVIVAL (2013 – 2019)[1]

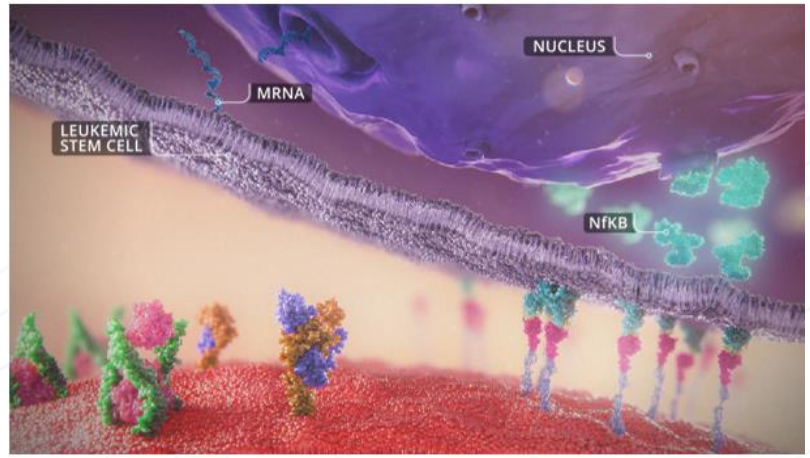


American Cancer Society. Cancer Facts and Figures 2023. Atlanta: American Cancer Society; 2023. Accessed May 10, 2023. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2023/2023-cancer-facts-and-figures.pdf.

Uproleselan: First-in-Class E-Selectin Antagonist for AML







E-selectin:

- ✓ Leukocyte adhesion molecule constitutively expressed on marrow endothelial cells, also inducibly expressed throughout vasculature by innate inflammatory mediators
- ✓ Up-regulated by AML blasts via secreted inflammatory mediators, such as TNF-alpha and IL1-beta

E-selectin/E-selectin Ligand Interaction:

- ✓ Enables AML blast and leukemia stem cell sequestration in bone marrow
- ✓ Activates pro-survival NF-kB pathways
- ✓ E-selectin ligand sLex up-regulated on AML cells via multiple distinct drug resistance mechanisms

Uproleselan, a First-in-class E-Selectin Antagonist:

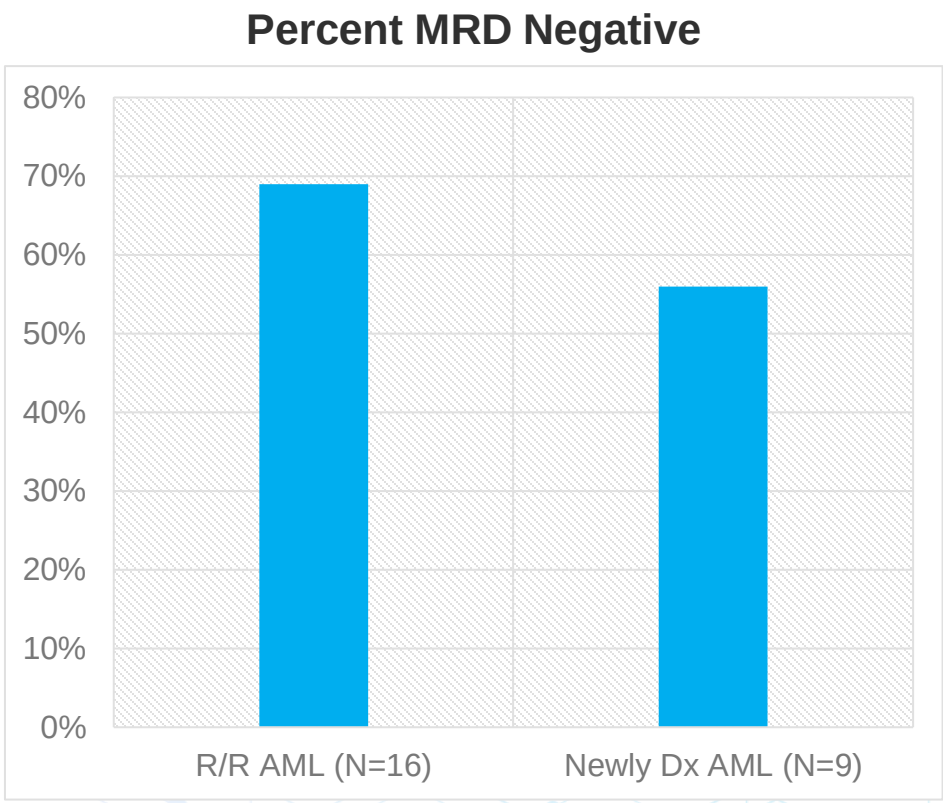
- ✓ Releases AML blasts and leukemic stem cells from vascular sequestration, agnostic to AML mutational status
- ✓ Disrupts NF-kB mediated chemoresistance pathways
- ✓ Potential broad utility across AML

Phase 1/2 Results in R/R and Newly Diagnosed AML Patients

AML population	CR	CR/CRi	Median O/S	MRD-negative
Relapsed / Refractory (n = 54)	35%	41%	8.8 mos	69%
Newly Diagnosed (n = 25) >=60yrs	52%	72%	12.6 mos	55%

E-selectin ligand expression

- Detectable in every patient tested
- Higher levels in R/R patients achieving CR/CRi, MRD- and prolonged median OS



blood® Results Published in *Blood February '22*

Potential Foundational Backbone Across Spectrum in AML

~20,380 Newly Diagnosed AML Patients in the U.S.[1]

~12K "Fit"	Patients eligible for intensive chemotherapy	~8K Unfit"
>8K PATIENTS/YEAR	**NEWLY DIAGNOSED, ELDERLY AML** **NCI-Sponsored Phase 2/3** Combination of Uproleselan + 7&3	**8K** PATIENTS/YEAR **Recent venetoclax approval**

+

8.5K
PATIENTS/YEAR

RELAPSED / REFRACTORY AML
GLYC-Sponsored Phase 3
Combination of Uproleselan + MEC/FAI

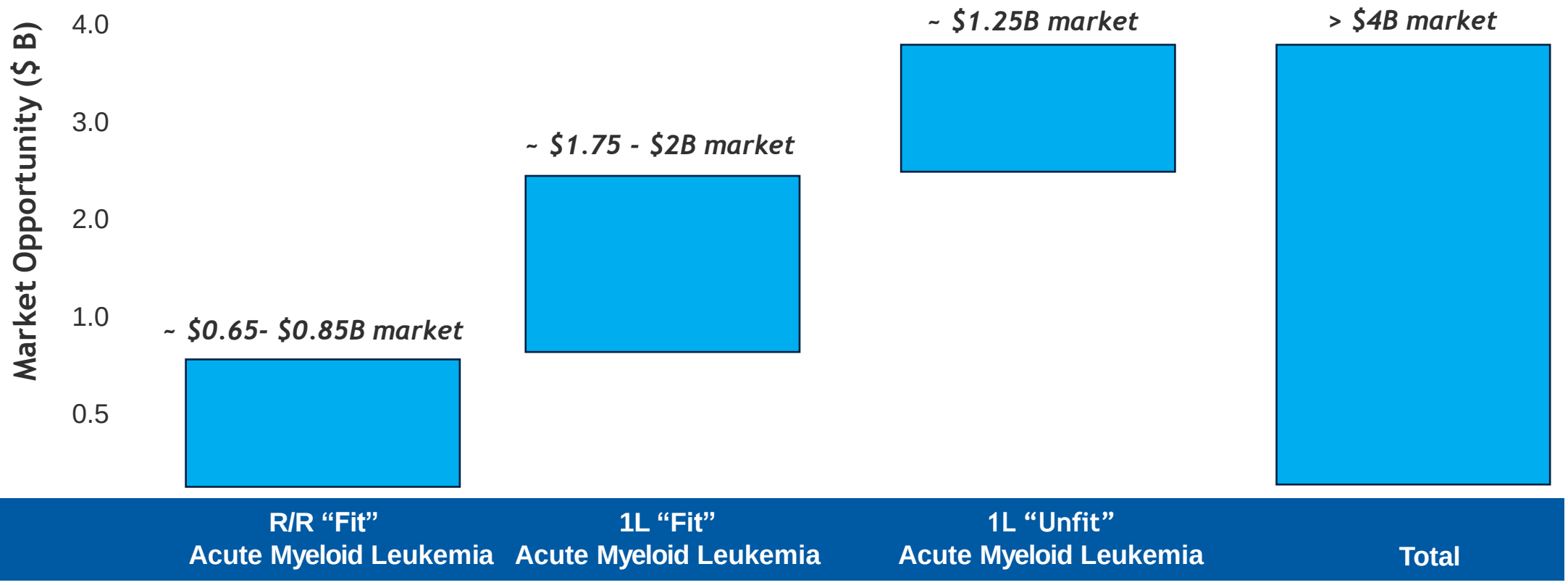
Uproleselan Value Proposition

- Improve achievement / depth of remission
- Extend overall survival
- Mitigate chemotherapy-related toxicity

1. National Cancer Institute SEER Program. Cancer Stat Facts: Acute Myeloid Leukemia.

Full realization of uproleselan's potential across AML treatment continuum could provide access to >$4B US market opportunity

Significant growth potential with indications in earlier lines of treatment



Phase 3-Uproleselan in Combination With Chemotherapy to Treat Relapsed/Refractory Acute Myeloid Leukemia (GlycoMimetics)

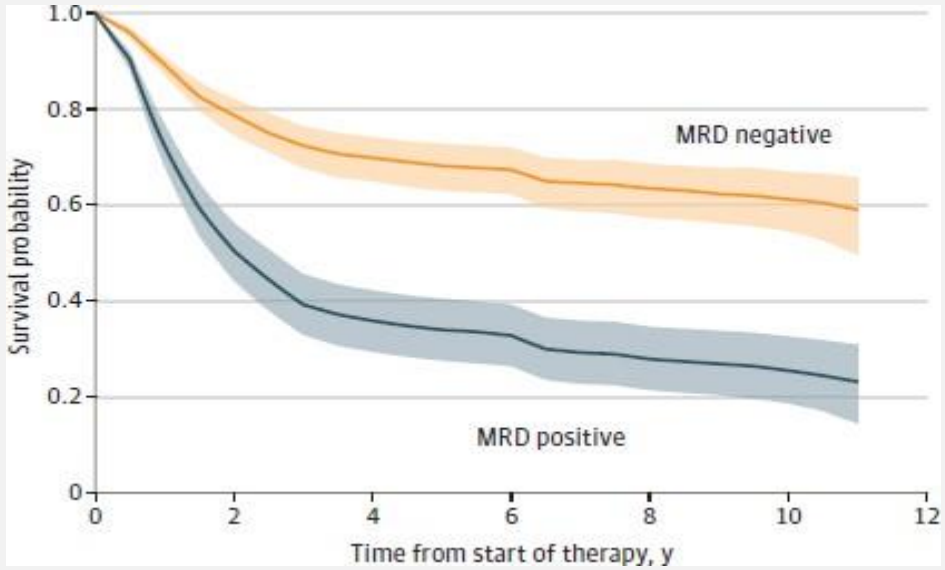
Phase 2/3-Uproleselan in Combination with 7+3 in Treating Patients With Acute Myeloid Leukemia Receiving Intensive Induction Chemotherapy (NCI)

IIT's
UC Davis Ven/Aza/Uproleselan
MDACC Cladribine/LDAC/Uproleselan

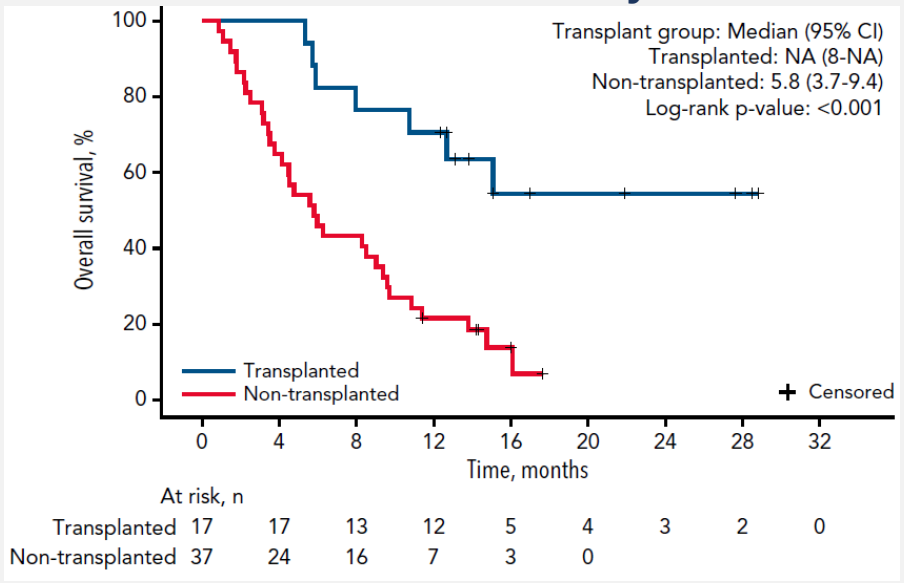
Source: Data on file; Redbook 2023

MRD Negativity and HSCT Both Favorably Prognostic

Overall Survival by MRD status[1]



Overall Survival by HSCT[2]



Meta-analysis of 81 studies (N >11,000)

- MRD negativity favorably prognostic for survival
- Effect independent of age, subtype, timing, method

Uproleselan Phase 1/2 overall survival by HSCT

- N=54 R/R AML patients at 10 mg/kg RP2D
- Overall MRD-negative: 56% 1L, 69% R/R
- 10 longest survivors all MRD-negative

1. Short, et al. JAMA Oncology 2020 6(12): 1890-1899; 2. DeAngelo et al, Blood 2022 139(8):1135-1146.

Relapsed / Refractory AML Phase 3 Trial Design

KEY ELIGIBILITY CRITERIA

- ≥18 and ≤75 years in age
- AML – primary refractory or first or second relapse
- Eligible for intensive salvage treatment
- ≤1 prior HSCT

Induction
(1 Cycle)

Consolidation
(Up to 3 Cycles)

Upro plus MEC or FAI (n=190) → Upro plus HiDAC or IDAC

1:1 Randomization
(stratified by age, disease status and backbone chemo)

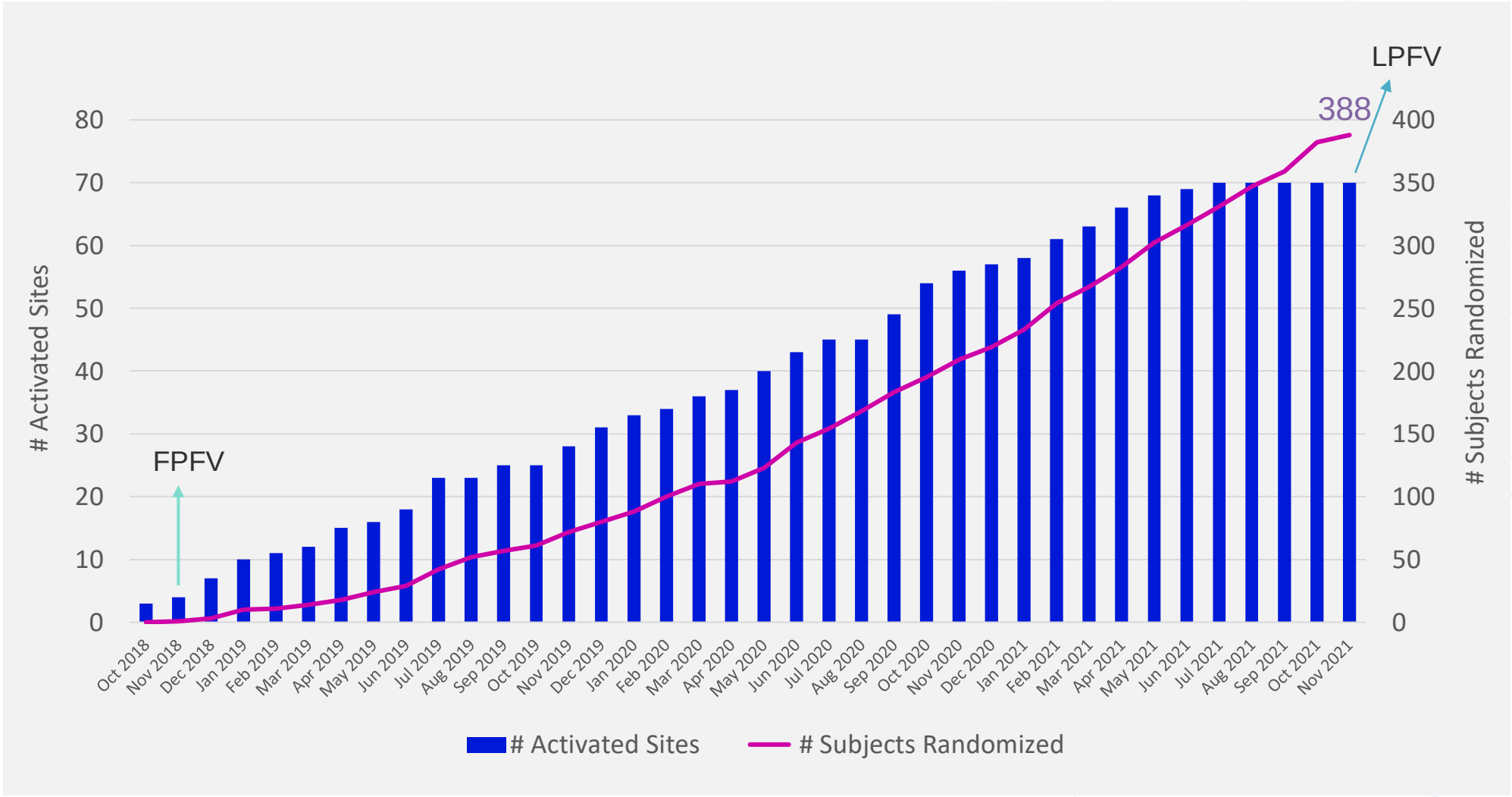
Placebo plus MEC or FAI (n=190) → Placebo plus HiDAC or IDAC

Follow-Up for Overall Survival not censored for transplant.

MEC: Mitoxantrone, etoposide and cytarabine
FAI: Fludarabine, cytarabine and idarubicin
HiDAC/IDAC: High-dose or Intermediate-dose cytarabine

Enrollment of 388 Patients Completed in November 2021; Data cutoff end Q1-2024, Topline Results to be Reported in Q2 2024

Trial GMI-1271-301 Enrollment



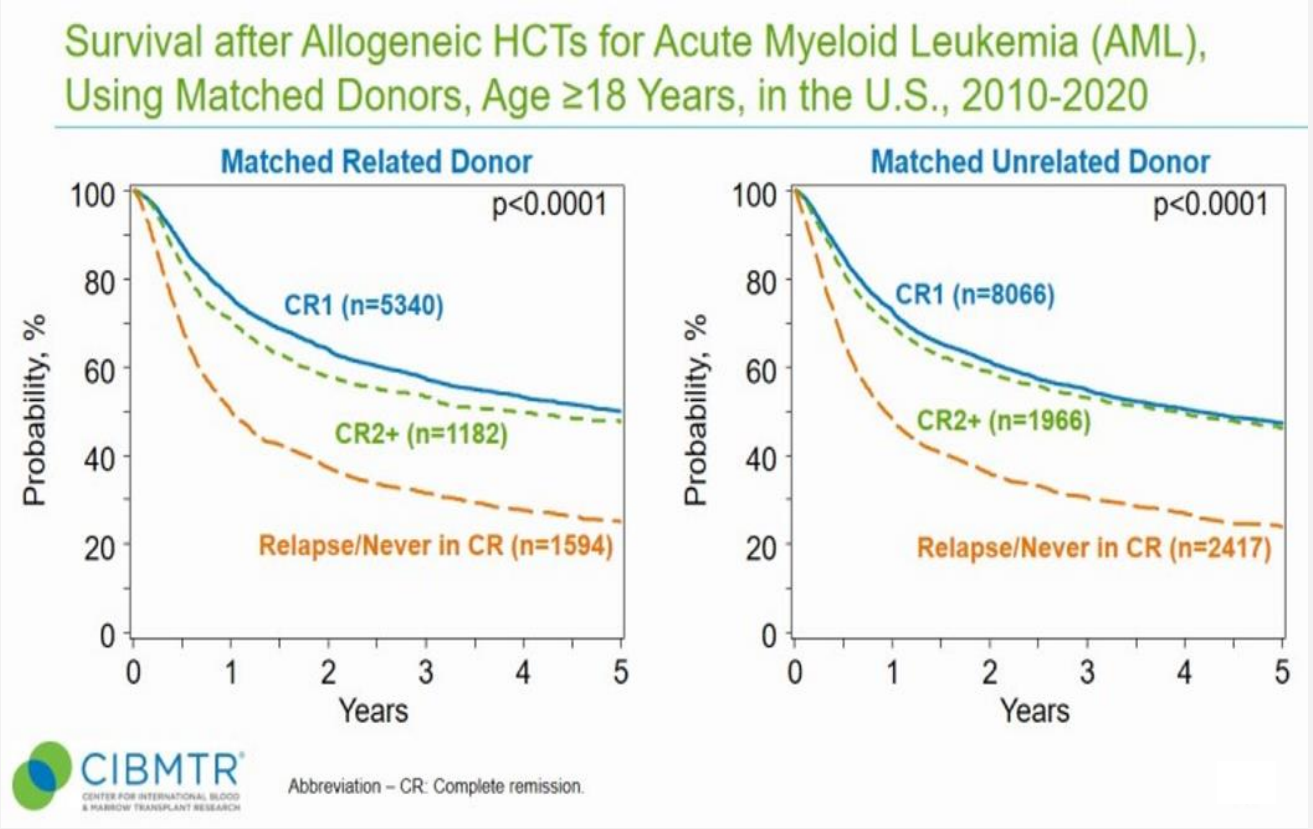
- 380 patients planned, 388 patients enrolled
- 12 patients (3%) lost to follow- up/ withdrew consent

Phase 3 Patient Characteristics Broadly Similar to Phase 2

	301 Study | N=388	201 Study | N=66
Relapsed/Refractory Patient Demographics		
Age, median (range)	58 (20-75)	59 (26-84)
Refractory, n (%)	129 (33%)	22 (33%)
Relapsed, n (%)	259 (67%)	44 (67%)
Duration of prior remission ≤6 mos	56 (22%)	18 (41%)
Prior Therapies		
HSCT	70 (18%)	12 (18%)
≥2 Induction Regimens	63 (16%)	22 (33%)
ELN Risk Category		
Adverse	42%	50%
Intermediate	23%	17%
Favorable	21%	11%
Unknown	14%	22%

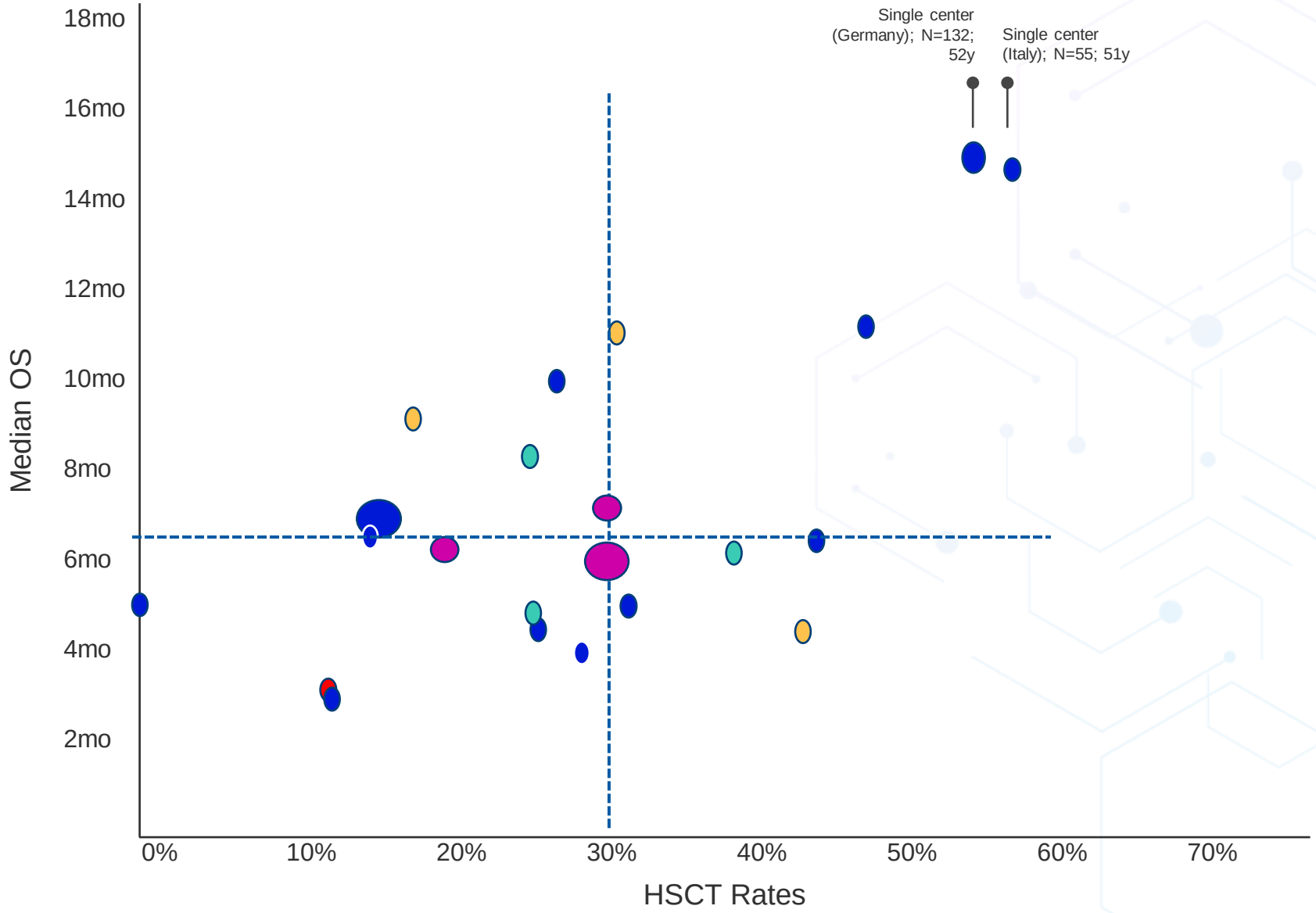
FDA Clears Time-Based Analysis to Phase 3 Trial Protocol

- June 2023 FDA clears Phase 3 time-based OS analysis after defined cutoff if 295 events not reached by that date
- Clinically mature data in Q2 2024 will reflect > 3 years median follow-up and > 2 years post-transplant follow-up for the substantial majority of remaining patients that received stem cell transplants
- After 2 years post-transplant, AML relapse becomes infrequent



Bolon YT, Atshan R, Allbee-Johnson M, Estrada-Merly N, Lee SJ. Current use and outcome of hematopoietic stem cell transplantation: CIBMTR summary slides (slide 79), 2022.

Intensive Chemotherapy (IC) in R/R AML



Typical ~6-7 months mOS and HSCT rates ~25-30%

- Phase III, RCT
- Prospective cohort study
- Retrospective study
- Phase I or II study

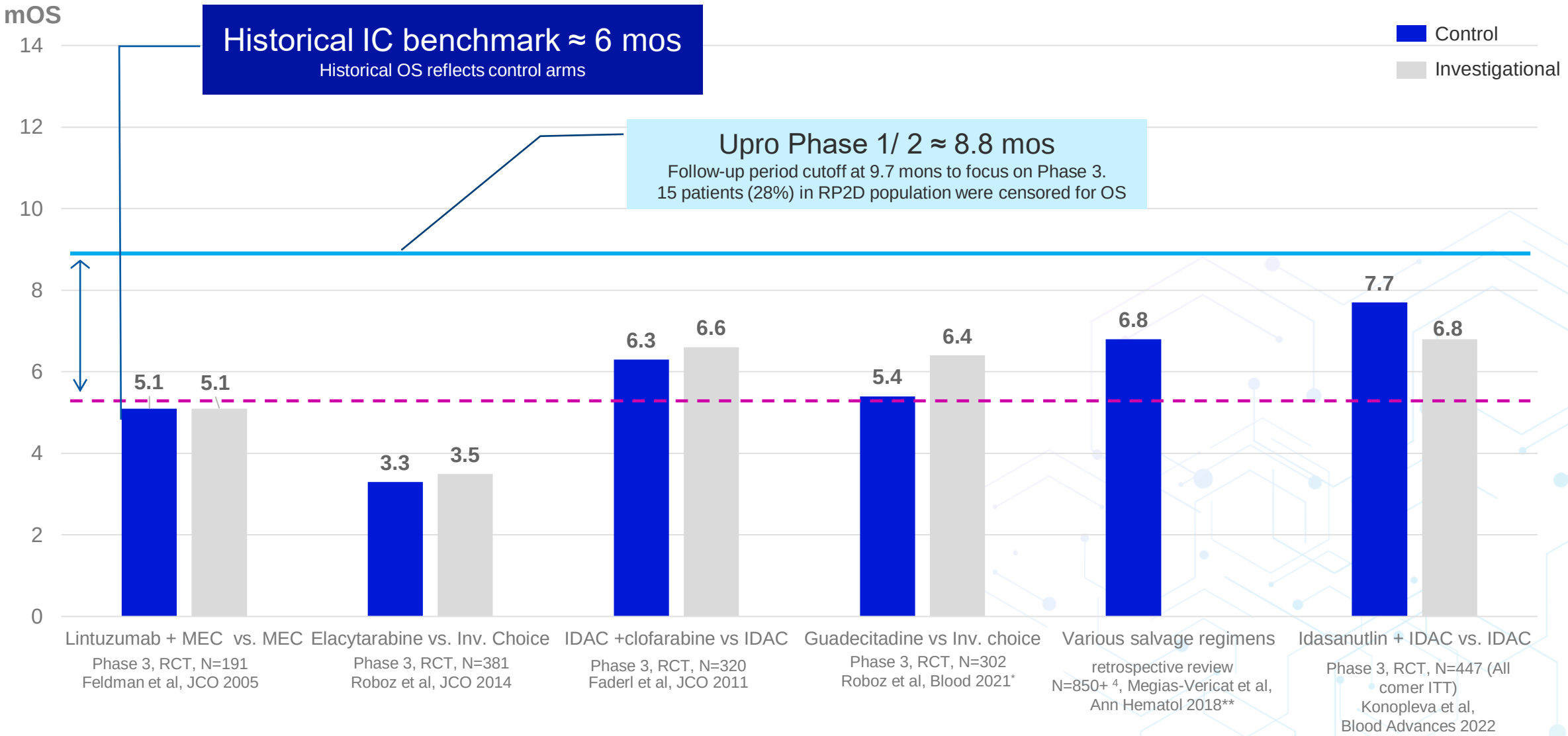
NOTES

Scatter plot is not exhaustive but includes trials with similar populations to Phase 3 trial of uproleselan.

Outcomes with intensive chemotherapy may be heavily impacted by patient. characteristics including age, ELN risk, disease status and prior therapy, and that patient numbers are small for some of the data shown.

Size of bubble is proportional to sample size.

Historical Intensive Chemotherapy benchmarks for mOS are ~6 months

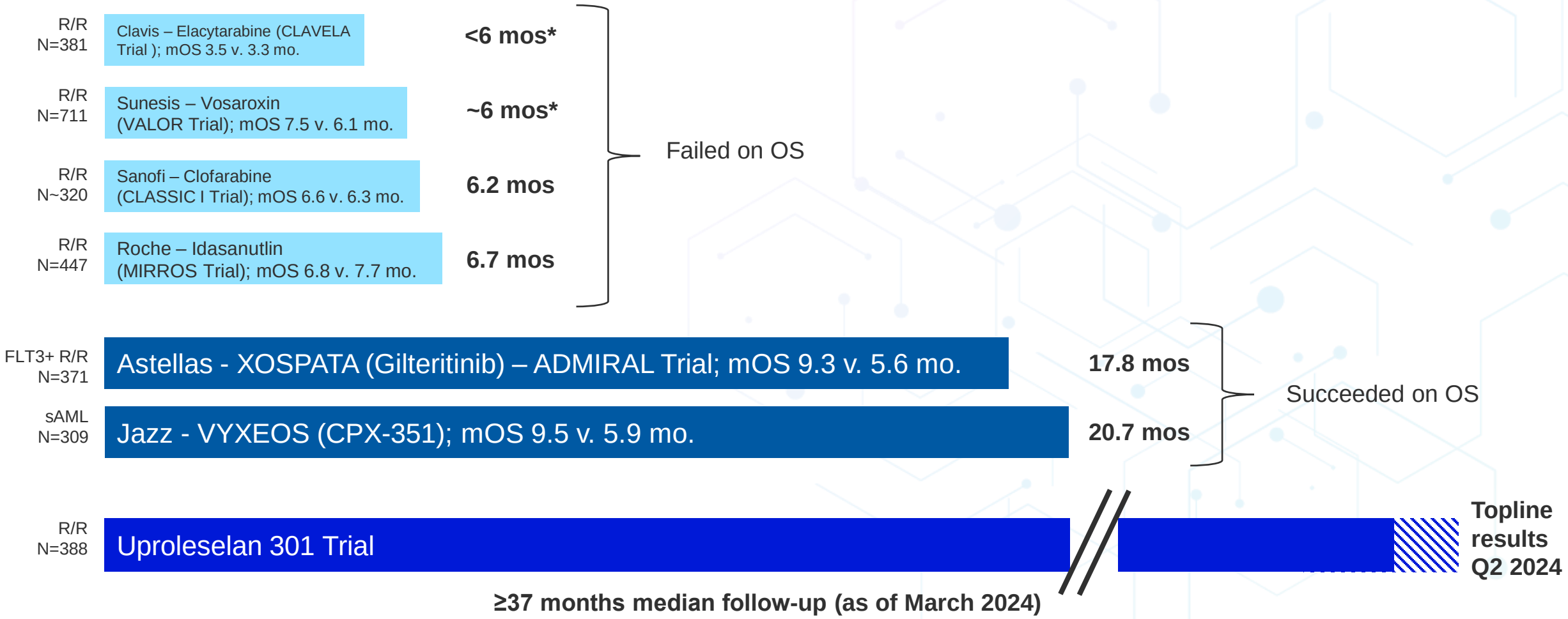


Note: patient outcomes for IC eligible populations often vary depending upon patient and disease characteristics

* Control group includes patients on MEC and FLAG-IDA

** All patients in this analysis received MEC

Duration of Follow-Up and Outcomes in Key AML Trials



*Median follow-up at time of event trigger for CLAVELA and VALOR estimated from protocol and/or final results as it was not included in the publication

Follow-Up Versus Outcome in Select AML Trials

Trial	Median Survival (mos)	Median Follow-up (mos)	Enrolled (N)	Events	OS HR	P-value
CLAVELA	3.5 vs 3.3 mos	< 6*	381	302	0.97	0.96
VALOR	7.5 vs 6.1 mos	~ 6*	711	562	0.87	0.0610
CLASSIC I	6.6 vs 6.3 mos	6.2	320	258	1.00	1.00
MIRROS	6.8 vs 7.7 mos	6.7	436	296	1.09	0.52
VIALE-A	15 vs 10 mos	20.5	433	270	0.66	**< 0.001**
VYXEOS	9.6 vs 6.0 mos	20.7	309	236	0.69	**0.003**
ADMIRAL	9.3 vs 5.6 mos	17.8	371	258	0.64	**< 0.001**
Uproleselan	TBD	>37 (Mar '24)	388	295	TBD	TBD

Longer median follow-up at time of primary analysis correlates with trials being positive

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*Median follow-up at time of event trigger for CLAVELA and VALOR estimated from protocol and/or final results as it was not included in the publication

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Uproleselan Value Proposition

- Improve achievement / depth of remission
- Extend overall survival
- Mitigate chemotherapy-related toxicity

1. National Cancer Institute SEER Program. Cancer Stat Facts: Acute Myeloid Leukemia.

NCI / Alliance Frontline “Fit” AML Phase 2/3 Trial Design

KEY ELIGIBILITY CRITERIA

- ≥ 60 years in age
- AML and fit for 7+3
  - Includes sAML
  - Excludes FLT3+

Induction
(1 Cycle)

Consolidation
(Up to 3 Cycles)

Upro plus 7&3
(n=131)

Upro plus
IDAC

7&3
(n=131)

IDAC

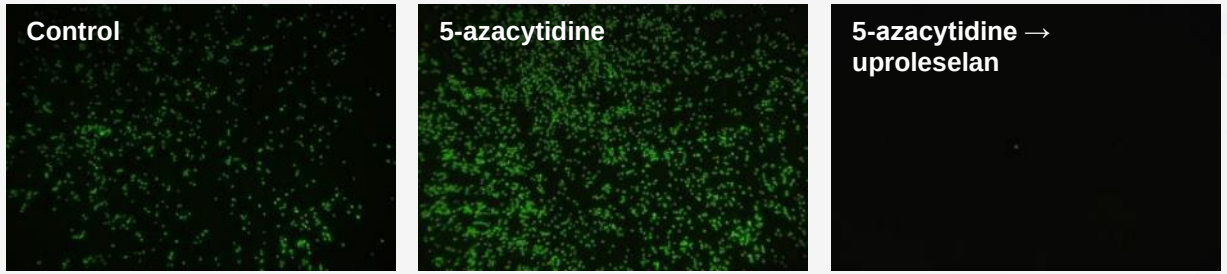
Follow-Up for EFS & Phase 3 Go/No-Go

7&3: Cytarabine and daunorubicin
IDAC: Intermediate-dose cytarabine

Enrollment of 267 Patients in Phase 2 Portion Completed in December 2021

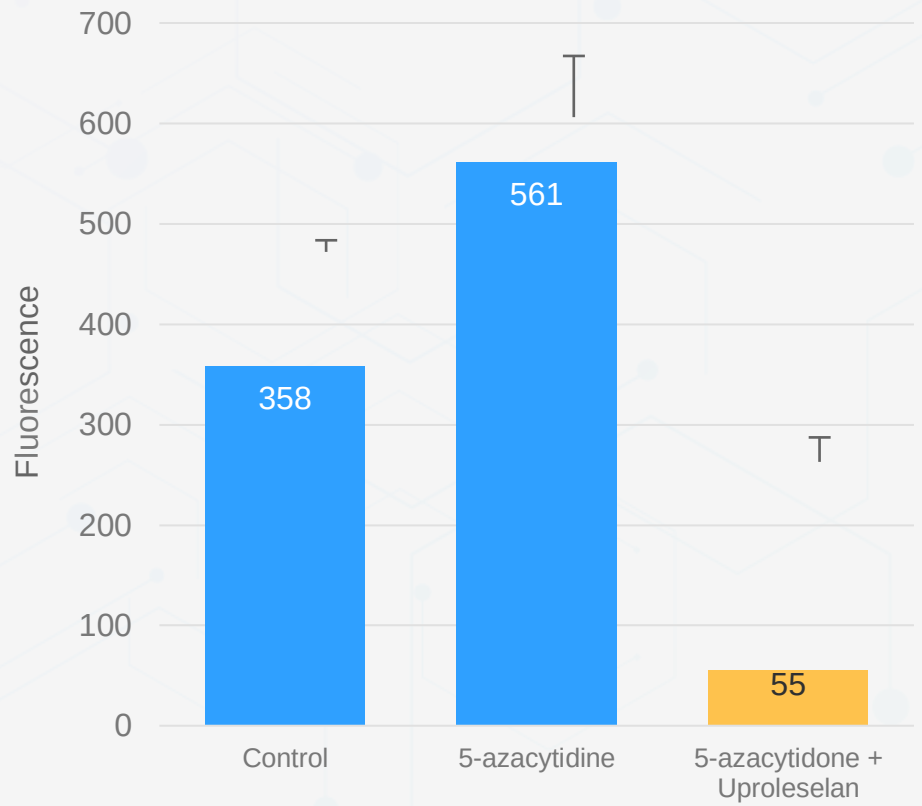
HMA Resistance is Driven by E-selectin, Broken by Uproleselan

UPROLESELAN INHIBITS BINDING OF BLASTS



KG1 AML cells were incubated for 96 hours in the absence or presence of 100 nM 5-azacytidine, labeled with calcein and allowed to adhere to E-selectin coated plates (control and 5-azacytidine above). After 45 minutes of adhesion, Uproleselan was added to the wells and fluorescence determined after 30 minutes

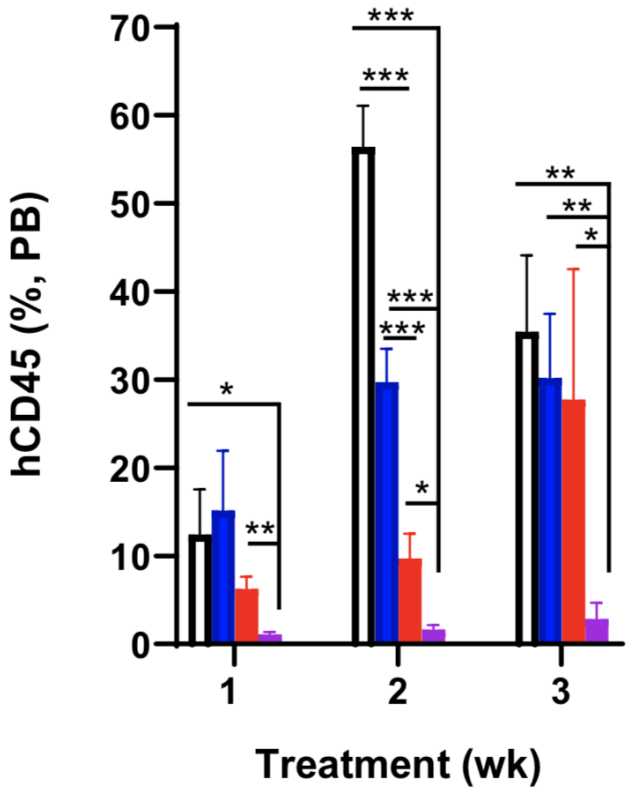
(5-azacytidine → Uproleselan above).

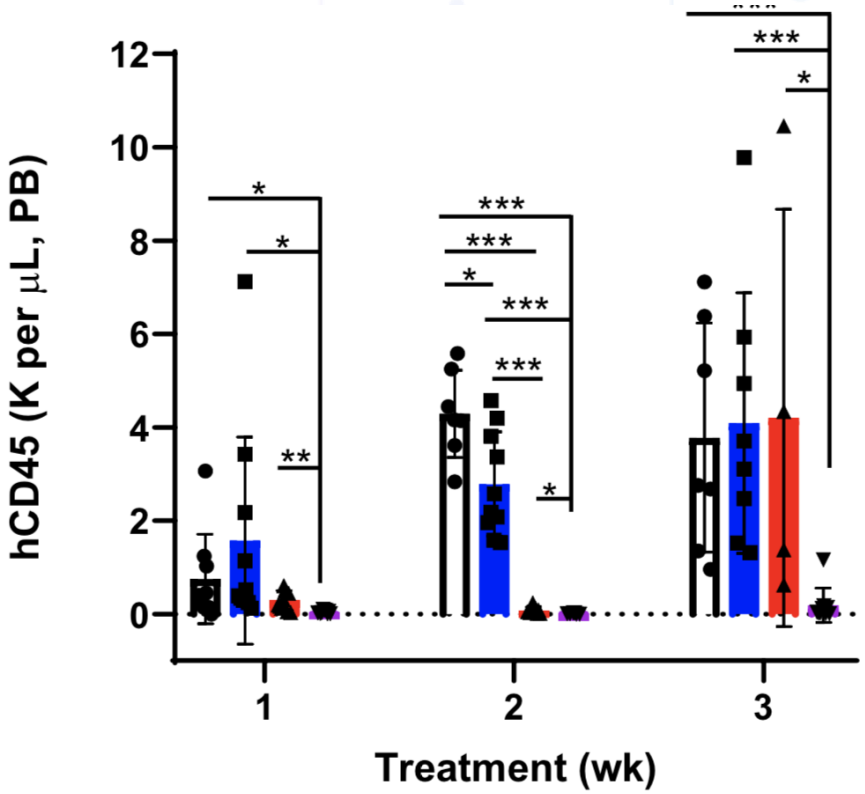


Targeting E-selection with GMI-1271 Overcomes Microenvironment-mediated Resistance to Venetoclax/HMA Therapy K.H. Chang, M. Muftuoglu, W. Zhang, M. Basyal, L. Ostermann, W.E. Fogler, J.L. Magnani, M. Andreeff, 2020

Uproleselan/ Venetoclax/ HMA Combination Significantly Reduces Leukemia Burden, Compared to Ven+5Aza Alone[1]

AML-PDX FROM A VENETOCLAX / HMA RESISTANT PATIENT





Venetoclax
Uproleselan
Ven+5Aza
Combination

*p< 0.05; **p<0.01; ***p<0.001, Student's t-test for experiments that compare two groups.

ASH 2022/2023: First Clinical Uproleselan Data Generated Outside of GLYC-Sponsored Trials

Uproleselan data from two investigator-initiated trials presented at ASH in December 2022/2023

A Phase I Study of Uproleselan Combined with Azacitidine and Venetoclax for the Treatment of Older or Unfit Patients with Treatment Naïve Myeloid Leukemia B.A. Jonas, J.L. Welborn, N.S. Esteghamat, R.T. Hoeg, A.S. Rosenberg, L. Molnar, A. Linh Dang-Chu, S.L. steward, and J.M. Tuscano, 2022

Publication Number: 2764

Encouraging safety and evidence of disease activity

- **8 evaluable patients with poor prognosis**
  - 6/8 (75%) were ELN 2017 adverse risk disease
  - 3/8 (38%) had complex cytogenetics
- **Data outcomes**
  - 6/8 (75%) CR/CRi
    - 5/8 (63%) full CR
    - 1/8 (13%) CRi
      - 5/8 (63%) CR/CRi responses occurred with cycle 1
  - 4 CR/CRi MFC MRD negative
    - 50% overall MRD negative rate
    - 67% among CR/CRi responders

Uproleselan added to Cladribine Plus Low Dose Cytarabine (LDAC) in Patients with Treated Secondary Myeloid Leukemia (TS-AML) E.A. Huante, H. Kantarjian, K.S. Chien, C.D. DiNardo, N. Short, A. Maiti, G. Montalban, N. Daver, J.D. Kawedia, K. Bowie, S.A. Pierce, F. Ravandi, M. Konopleva, G. Garcia Manero, and T. M. Kadia, 2023

Publication Number: 2992

39% ORR in very high-risk patient population

- **18 evaluable patients**
  - All patients had unfavorable cytogenetics and had previously received treatment with a hypomethylating agent.
  - 11 patients (55%) had received prior treatment with venetoclax, and five (25%) had undergone stem cell transplantation.
- **Data outcomes**
  - Combination of Cladribine + LDAC with uproleselan overall well tolerated with few treatment-related AEs
  - Combination reduced bone marrow blasts in 13 (72%) patients
  - Three patients went on to receive a potentially curative hematopoietic cell transplantation (HCT)
  - Study investigators concluded data support this low-risk approach to marrow blast reduction and disease control in preparation for HCT

Treatment of Vaso-occlusive Crisis (VOC) in Patients with Sickle Cell Disease

GMI-1687

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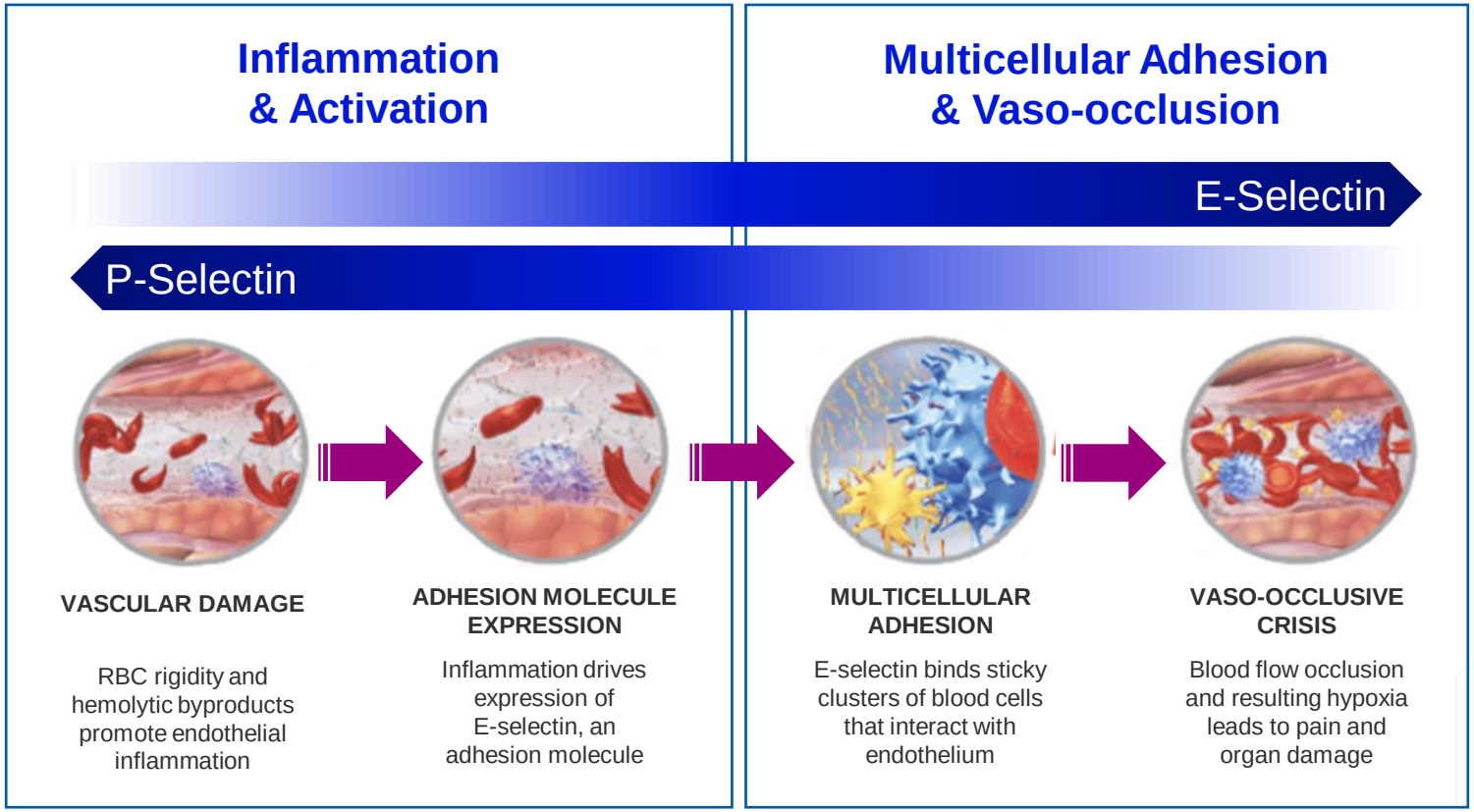
E-Selectin Mediates Multicellular Adhesion and Vaso-Occlusion



Data Supporting E-Selectin Role in Cellular Adhesion and Clotting

Preclinical

- E-selectin leads to rolling and cell arrest
- Blocking E-selectin inhibits leukocyte adhesion
- Blocking E-selectin restores blood flow in animal models of vessel occlusion in sickle cell disease

Clinical

- sE-selectin correlates with frequency of VOC
- sE-selectin correlates with poor survival
- Reduced sE-selectin correlated with clinical benefit in RESET trial (time to discharge)

E-selectin Antagonism Provides a Unique Therapeutic Target to Interrupt VOC in SCD patients

Front. Immunol., 28 April 2021Sec. https://doi.org/10.3389/fimmu.2021.663886; Clin Hemorheol Microcirc. 2018; 68(2-3): 263–299.; Image adapted from https://www.rethinkscd.com

Even with Prophylactic and Gene Therapy Approaches, VOC Will Remain A Significant Unmet Medical Need

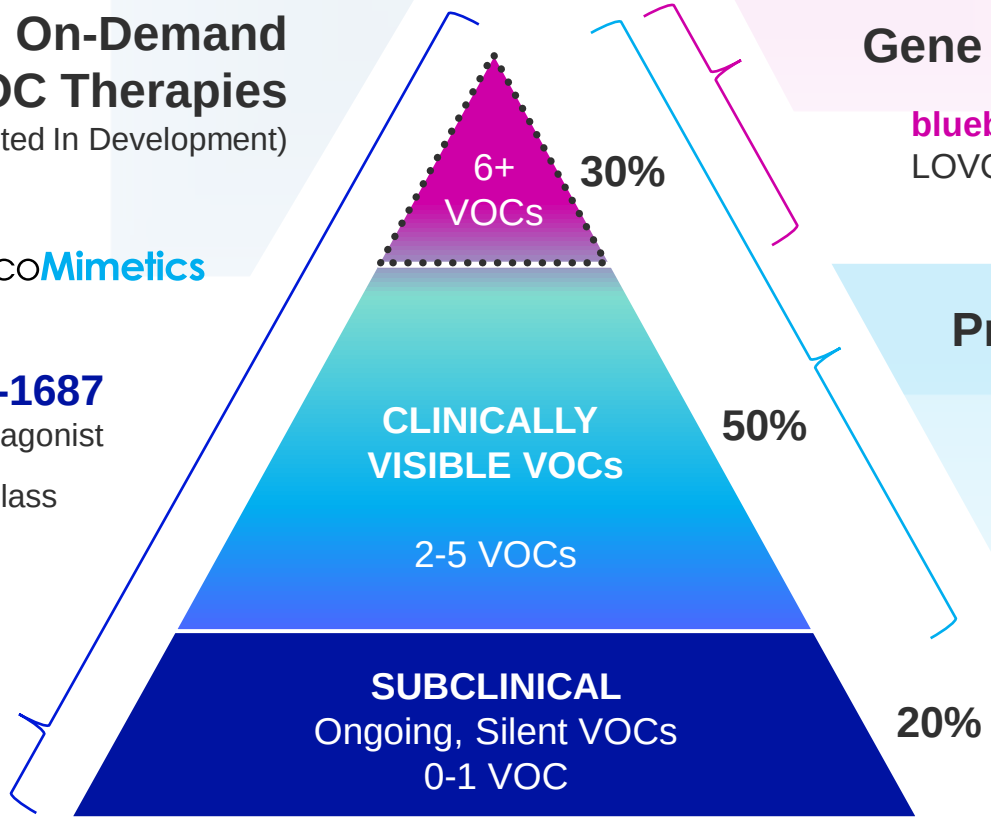
On-Demand VOC Therapies
(Selected In Development)

GlycoMimetics

GMI-1687
E-selectin antagonist

First-in-class

Novel MoA



Gene Therapies (In Development)

bluebird bio	**Editas Med.**	**Vertex/CRISPR**	**Beam Ther.**
LOVO-CEL	EDIT-301	EXA-CEL	BEAM-101

Prophylactic Therapies

APPROVED

Multiple (generic)	**Pfizer**	**Novartis**
Hydroxyurea	Voxeletor	Crizanlizumab-tmca*

PHASE 3

Pfizer	**Novo Nordisk**	**Agios Pharma**
Inclacumab; GBT021601	Etavopivat	Mitapivat

220,000 – 450,000 VOCs/year (in the era of prophylactic therapies)

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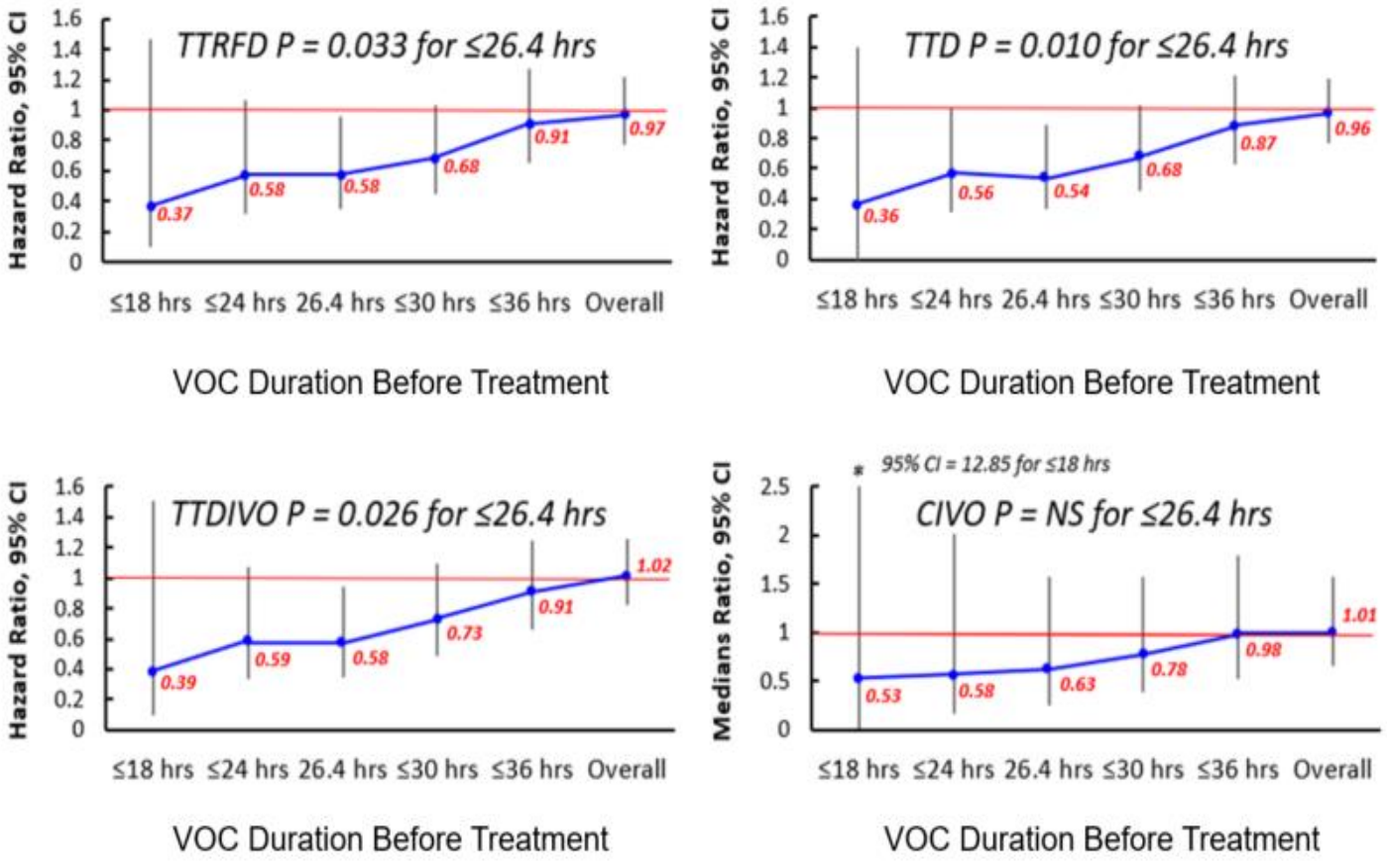
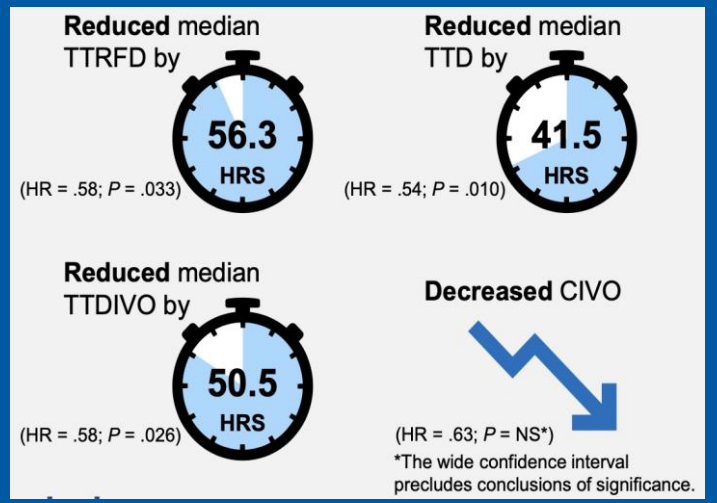
*Authorization revoked in EU

Dampier et al. 2017 American Society of Hematology Annual Meeting. Abstract# 4660.
N Engl J Med 2019; 381:509-51; N Engl J Med 2017; 376:429-439

Early Treatment Resulted in Clinical Benefit



For patients treated within first quartile of treatment (≤26.4hrs), a meaningful, statistically significant benefit was seen across study endpoints



TTRD = time to readiness for discharge; TTD = time to discharge;
TTDIVO = time to discontinuation of IV opioids; CIVO = cumulative IV opioid use
Dampier et al, Blood 2023

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GMI-1687 Seeks to Empower Patients to Take Control

Potentially **revolutionizing the treatment paradigm** to on-demand disease modifying therapy

Lessons Learned	GMI-1687
E-selectin drives VOC[1]	• **Fast-acting**, small molecule E-selectin antagonist to eliminate vaso-occlusion
Early treatment in VOC is critical	• Potential **self-administration** of GMI-1687 after patient recognizes VOC episode • 100% bioavailable in preclinical models following subcutaneous administration
Deliver full dose to stop VOC	• **Optimize dose and regimen** based on reductions in sE-selectin • Agreed to as part of FDA Pre-IND Meeting

Phase 1a Study Completed

1 Morikis et al, Frontiers in Immunology, April 2021, Vol. 12, Article 663886

Potential Treatments in Oncology, Inflammation and Fibrosis

GALECTIN-3 INHIBITORS

GlycoMimetics

The Promise of Targeting Galectins

Potential to modulate the immune and inflammatory response to cancer and fibrosis

Target
Galectin-3 carbohydrate-binding protein

Chemistry
Rationally designed with proprietary platform

Differentiation
Compounds have high binding affinity and specificity for Galectin-3

Relevance
Central role in fibrosis and cancer

- Inflammation, aberrant cell activation/proliferation, fibrogenesis
- Blockade may prevent/reverse fibrosis following organ damage
- Antifibrotic/antitumor activity in various disease models

Orally Bioavailable

Recent Accomplishments and Expected News Flow*

- FDA cleared addition of time-based final analysis to Phase 3 trial
- Boston Children's Hospital initiation of pediatric Phase 1/2 trial (uproleselan, busulfan, clofarabine, fludarabine) in chemotherapy resistant AML
- GMI-1687 Phase 1a completed

NEXT 12 MONTHS

- Data from ongoing IITs
- GMI-1687 Phase 1a data readout; Phase 1b/2 trial initiation
- NCI Phase 2 EFS interim analysis readout in frontline AML fit for chemo trial
- NCI Phase 1 uproleselan in pediatric AML
- Uproleselan R/R pivotal Phase 3 final analysis; topline results in Q2 2024

* Subject to enrollment and acceptances of abstract submissions

Near-Term Catalysts and Promising, Glycobiology-based Pipeline

Uproleselan: Multiple Late-Stage Clinical Trials

- **Fully enrolled Phase 3 trial** in R/R AML (n=388), time-based analysis of OS with patient data cutoff end Q1 2024; topline results expected in **Q2 2024**
- **Fully enrolled Phase 2 trial** in front-line AML (n=267) ongoing, **NCI-sponsored**
- **Ongoing IITs** in other AML populations. Preliminary data presented at ASH 2022/2023
- **Novel MOA/first-in-class** → potential **broad utility** with **Breakthrough Therapy**, **Fast Track**, and **Orphan** designations

Promising Early-Stage Pipeline

- Novel small molecules inhibit carbohydrate signaling
- Potential application in multiple inflammatory diseases
- **GMI-1687**
  - Phase 1a trial in healthy volunteers completed
  - Initial indication: treatment of sickle cell disease (SCD) vaso-occlusive crisis (VOC)
  - Being developed for self-administration at time of VOC
- **Galectins**
  - Targeting fibrotic diseases
  - First oral Galectin-3 antagonist

Targeted Operational Execution

- **Multiple Key Leadership Hires in Last Year** → purpose-driven biotechnology team
- **Deep expertise** in regulatory, technical operations, medical and commercialization across hem/onc therapies
- Cash runway through **Q4 2024**

Thank You

www.glycomimetics.com | NASDAQ: GLYC

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