



# MOLECULIN

November 14, 2024  
Corporate Presentation



# Disclaimer



All statements contained herein other than statements of historical fact, including statements regarding our future results of operations and financial position, our business strategy and plans, and our objectives for future operations, are forward-looking statements. The words “believe,” “may,” “will,” “estimate,” “continue,” “anticipate,” “intend,” “expect,” and similar expressions are intended to identify forward-looking statements. We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy, short-term and long-term business operations and objectives, and financial needs. Our potential to sustain our relationship with MD Anderson revolves around the continued collaboration and capitalizing on intellectual property resulting from sponsored research. The feasibility and promptness of our clinical trials are influenced by regulatory stipulations from entities like the US Food & Drug Administration (FDA) and their global counterparts. As such, all of our trials, including the MIRACLE trial, are subject to timely, future filings with and feedback, allowance, approvals, etc. from the FDA and their global counterparts. The implications of global events, such as the conflict in Ukraine, the COVID-19 pandemic, and prevalent supply chain challenges, play a role in our forward-looking statements. Additionally, our ongoing need for financing, fueling our clinical trial and product development initiatives, securing regulatory approvals in essential markets, and sourcing cost-effective drug solutions are core to our forward-looking statements. Furthermore, our commitments concerning intellectual property licenses, the potential efficacy of our drug candidates, market reception, potential product liabilities, and the emerging competitive landscape are also fundamental to our forward-looking statements. Any reference related to cardiotoxicity or the lack thereof concerning Annamycin is based on our expert’s opinion as detailed in our filings, from time to time, with the SEC. Our dependencies on third-party manufacturers, strategies for establishing business collaborations, the defense of our intellectual property rights, our plans for fostering company growth, and the imperative to retain key executive personnel also guide our projections. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties, and assumptions, the future events and trends discussed in this presentation may not occur, and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. More detailed information about Moleculin is set forth in our filings with the Securities and Exchange Commission. Investors and security holders are urged to read these documents free of charge on the SEC’s website at <http://www.sec.gov>. Data related to currently active trials of Moleculin are preliminary and subject to change until a final Clinical Study Report is published.

# Recent Developments

- Accelerates Planned Unblinding Data Readout for MB-108 MIRACLE Phase 3 Pivotal Trial for Annamycin in Combination with Cytarabine (AnnAraC) for the Treatment of R/R/ AML to H2 2025
- Received Institutional Review Board Approval for MB-108 MIRACLE Phase 3 Pivotal Trial
- Announced Q3 Earnings, Updated MB-106 Preliminary Data and MIRACLE Site Recruitment
- Appoints Dr. Von Hoff, a Leading Expert in Pancreatic Cancer to MBRX's Scientific Review Board

# AnnAraC Performance in 2<sup>nd</sup> Line AML

CR	<b>50%</b>
CRc	<b>60%</b>
Durability	<b>8+ months</b>
OS	<b>~11 months</b>
MRD Neg	<b>78%</b>
BMT	<b>20%</b>

It is widely recognized that the majority of 2L AML patients are underserved by available approved therapies and that better options are needed for this unmet need. These performance numbers are significantly better than any therapy every approved for use in 2L AML. (See MB-106 data in following slides)



# Our Team



Walter V. Klemm  
 Founder, President, CEO and Chairman  
 soliton ZENO INC 50 Pfizer Green  
 Scuba



Donald Picker, PhD  
 Chief Scientific Officer  
 SYNERGY



Jonathan P. Foster  
 Executive VP & Chief Financial Officer  
 Deloitte



Dr. John Paul Waymack  
 Senior Chief Medical Officer  
 FDA kotiv



Sandra Silberman, MD, PhD  
 Chief Medical Officer – New Products  
 Roche



Robert Shepard, MD, FACP  
 Medical Advisor  
 FDA Tufts

7 FDA Approvals

2 Big Pharma Exits

14 Moleculin  
 Clinical Trials

\$.5 Million in Recent  
 Management Investment

200 Years of Drug  
 Development Experience



# Technology Portfolio

Program	Indication	Phase 1	Phase 2	Phase 3
<b>Annamycin</b> Next-Gen Anthracycline	R/R AML	Miracle: Adaptive Phase 3 Pivotal Initiating		
	STS Lung Mets	2 Trials Active; Alt. Dosing; P1B/2		
<b>WP1066</b> STAT3 Inhibitor	Adult GBM	NU IIT with Radiation Active; P2		
	Pediatric Brain Tumors	Emory IIT P2 Planning		
<b>WP1122</b> Anti-metabolite	GBM; Virology	IIT P2 Ready		



# MOLECULIN

DIAGNOSIS

## Current Market Cap Creates Opportunity

- Investors focused on targeted therapies, yet Venetoclax (a chemotherapy) created far more value over last 5 years
- For 50+ years anthracyclines have remained the bedrock treatment for many cancers
- Annamycin appears to be safer and more effective than currently prescribed anthracyclines
  - Enables increase in both dosage and number of cycles
  - Fills an unmet need for more than half of AML patients
  - Potential uses extend far beyond AML into other cancers

### *Anthracyclines Used In:*

**Breast cancers = 32%**

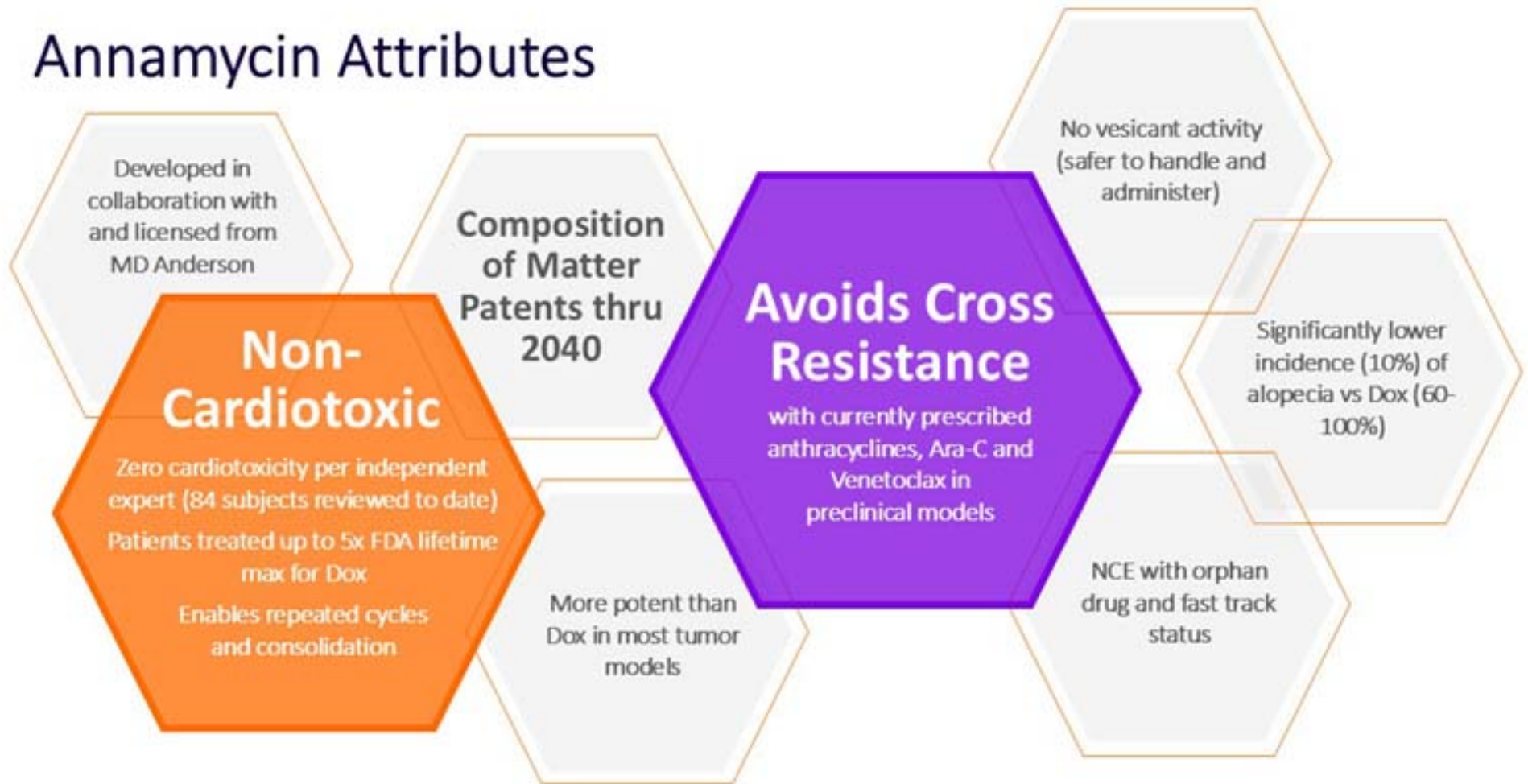
**AML patients = 50%**

**Lymphomas = 70%**

**Childhood cancers = 60%**



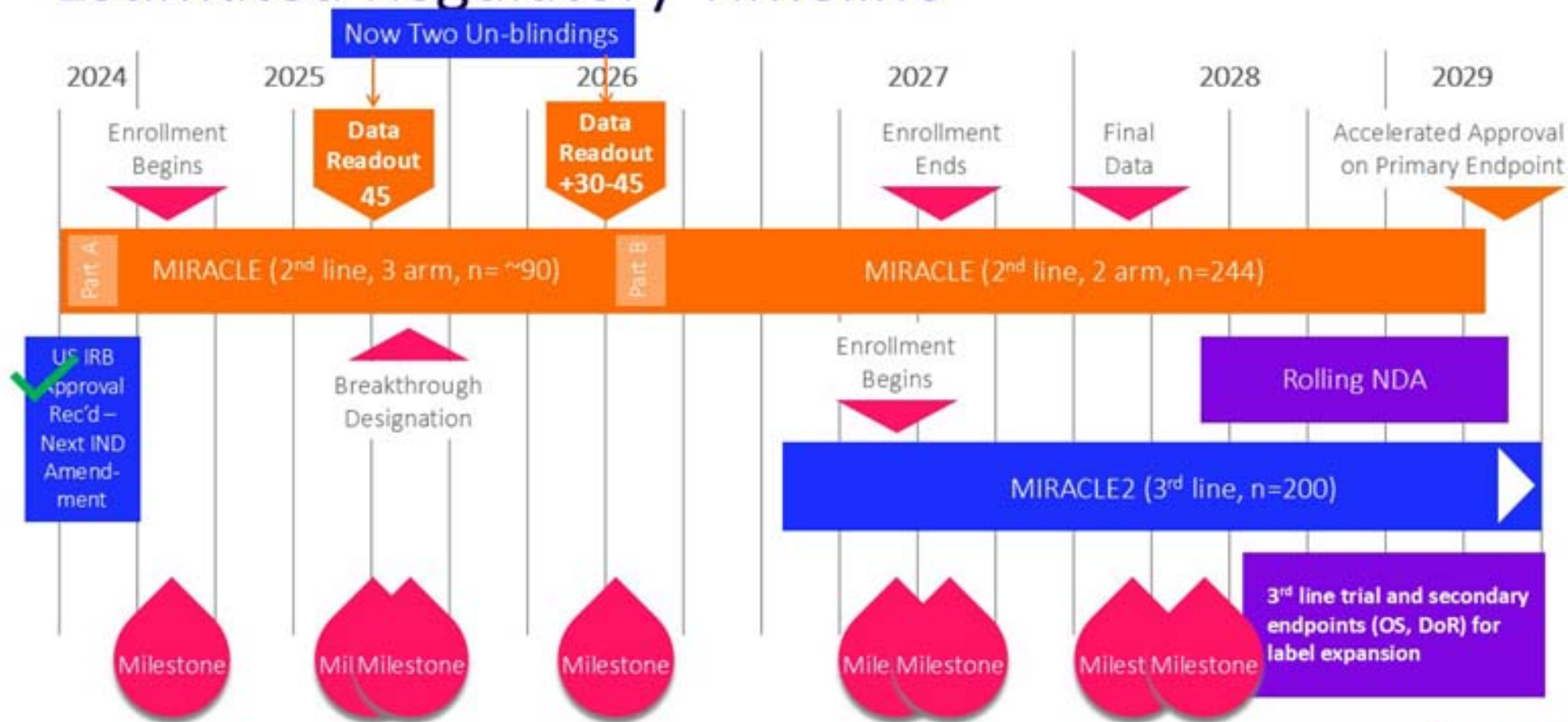
# Annamycin Attributes



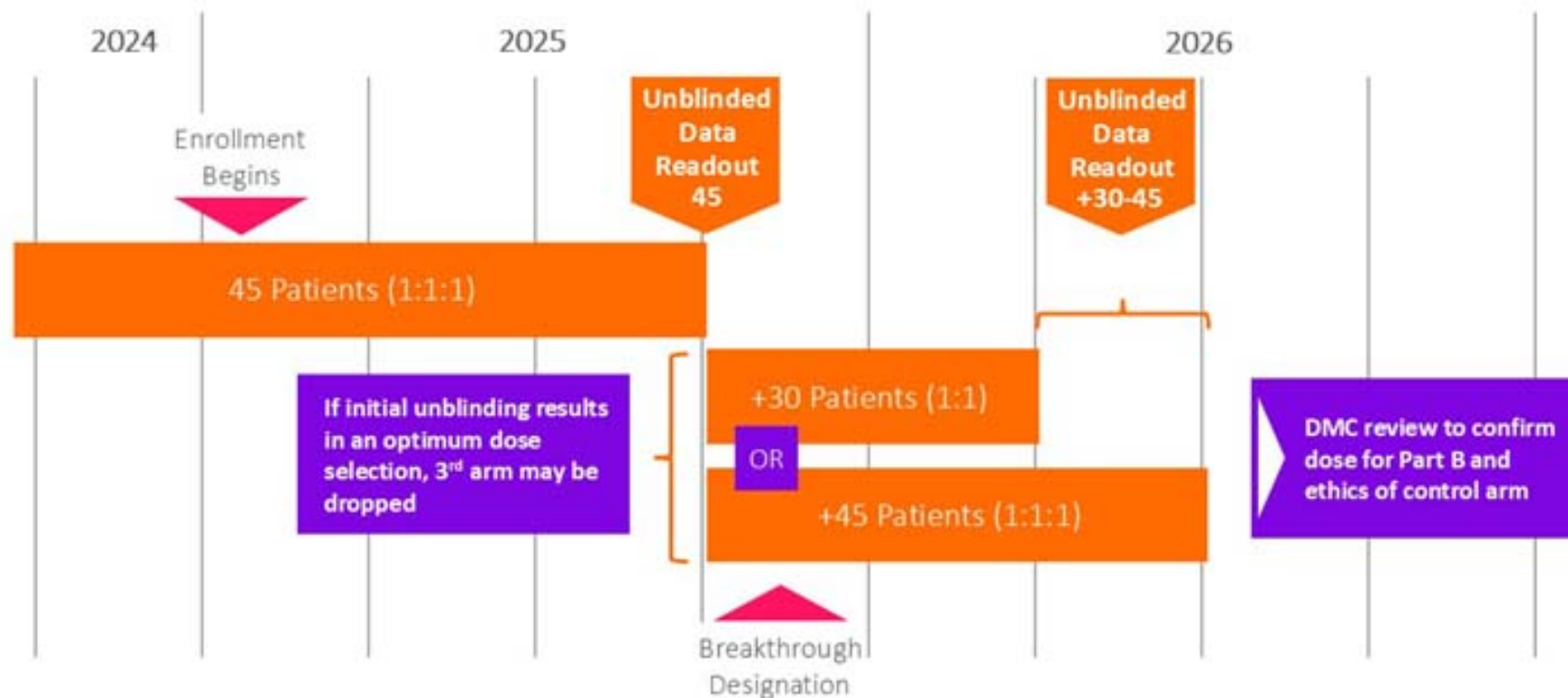
Notes: 1) Current Cardiology Review, Anthracycline Cardiotoxicity: Prevalence, Pathogenesis and Treatment, Maria Volkova and Raymond Russell III, Referenced from Cancer, 2009 Jun 1;97(11):2869-79. "Congestive heart failure in patients treated with doxorubicin: a retrospective analysis of three trials". Swain SM, Whaley FS, Ewer MS. PMID: 12767102; 2) Preliminary clinical studies from Moleculin; data subject to change; 3) Refer to Form 10K for FYE 2023 for discussion on latest subject with an increase in troponins and our Expert's opinion.



# Estimated Regulatory Timeline



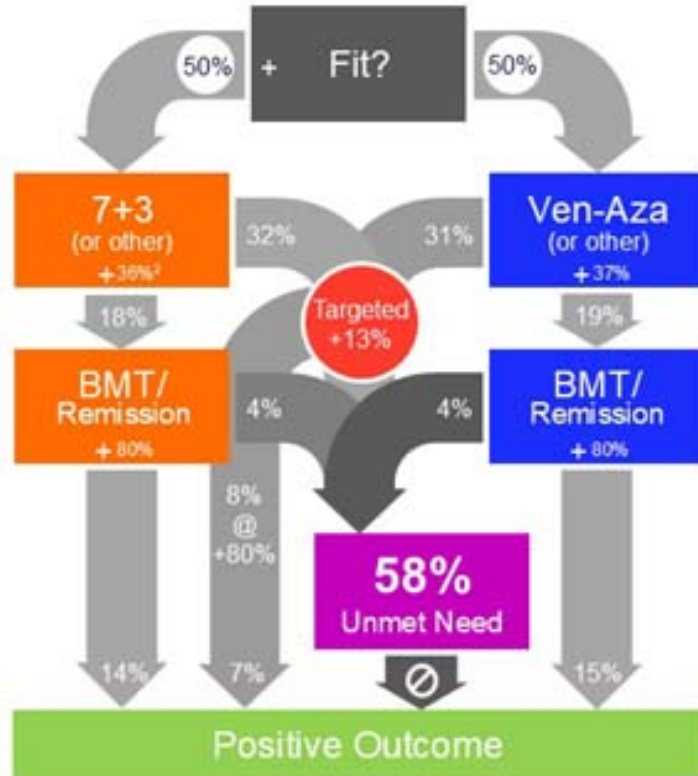
# Part A Acceleration



# Change to Protocol Explained

- Allows unblinding at 45 subjects for evaluation of primary endpoint, safety and tolerability
- If, at that point, it is apparent that one or the other of the two Annamycin doses (190 mg/m<sup>2</sup> or 230 mg/m<sup>2</sup>) is considered “optimum,” we will discontinue the non-optimum dosage arm and complete Part A with only 75 patients in total
- If not, we will continue Part A to 90 patients and determine “optimum” dose at that point
- It is possible that the Data Monitoring Committee could conclude at the end of Part A that the response rate of the control arm (HiDAC + placebo) as compared with the response rate of either of the Annamycin arms suggests that continuation of the control arm into Part B would be unethical

# Approved Therapies are Successful for Only ~40% of AML Patients<sup>1</sup>



	Daunorubicin (+ Ara-C)	Venetoclax (+ Azacitidine)	Targeted Therapy
Regimen	7+3	Ven-Aza	Gene-Targeted
Sub-population	Fit Patients (50%)	Unfit Elderly (50%)	55%-65% Eligible
Durable CR%	36% <sup>2</sup>	37%	~21%
All AML benefit <sup>3</sup>	14%	15%	7%
Critical characteristics	Cardiotox; de novo/acquired resistance	Still leaves significant unmet need	Limited to certain gene mutations



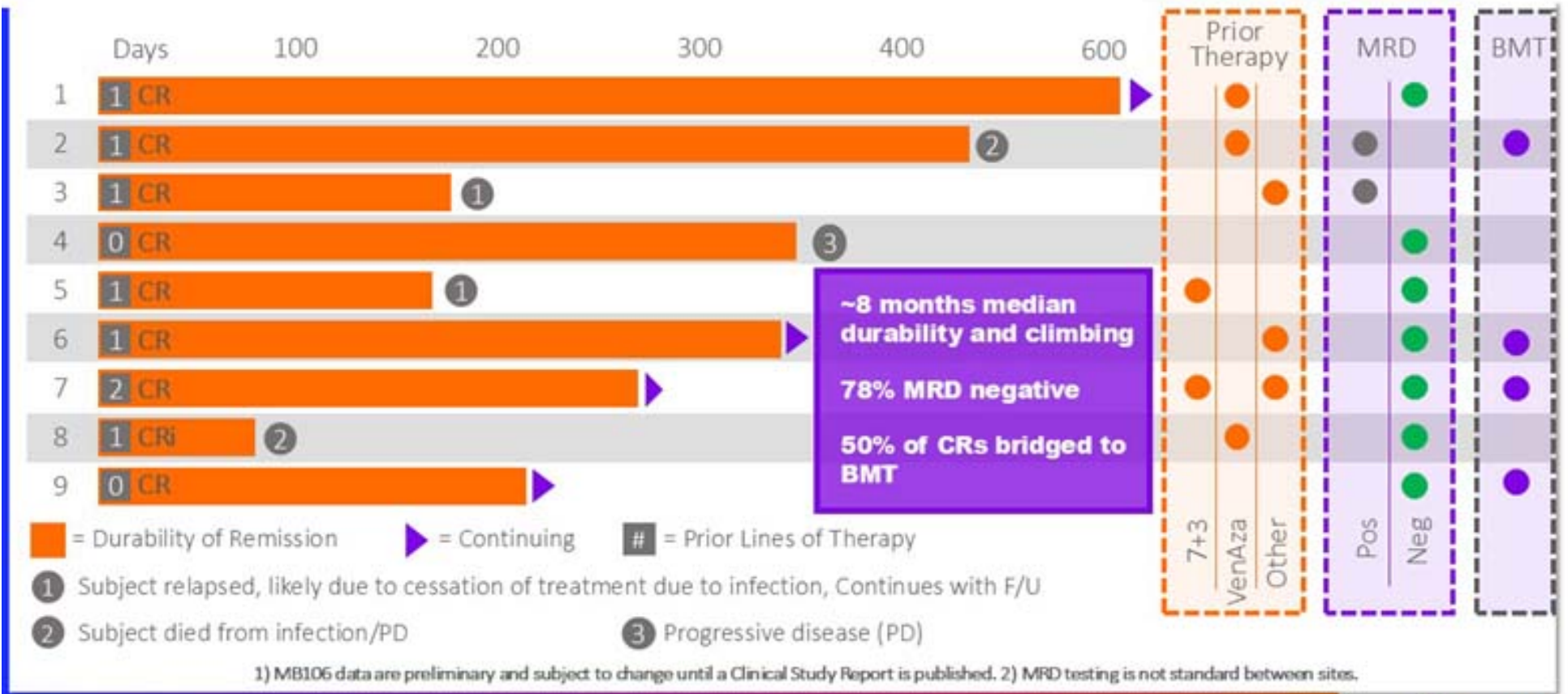
# MB-106 (Annamycin + Ara-C (AnnAraC); n=22)

Line of Therapy	All Lines (1 <sup>st</sup> – 7 <sup>th</sup> )	1 <sup>st</sup> Line	2 <sup>nd</sup> Line	2 <sup>nd</sup> & 3 <sup>rd</sup> Line Combined
Subjects Evaluable To Date	22	4	<b>10</b>	14
Subjects Evaluable Not Dosed Per Protocol	2	0	<b>1</b>	1
Median Age - Years (Range)	67.5 (19-78)	56.5 (19-69)	<b>71 (53 - 78)</b>	69.5 (53-78)
Complete Remission (CR)	8 (36%)	2 (50%)	<b>5 (50%)</b>	6 (43%)
Complete Remission Composite (CRc)	9 (41%)	2 (50%)	<b>6 (60%)</b>	7 (50%)
Partial Response (PR)	2	0	<b>1</b>	2
CRc Relapsed To Date	5	1	<b>4</b>	4
BMT To Date	4	1	<b>2</b>	3

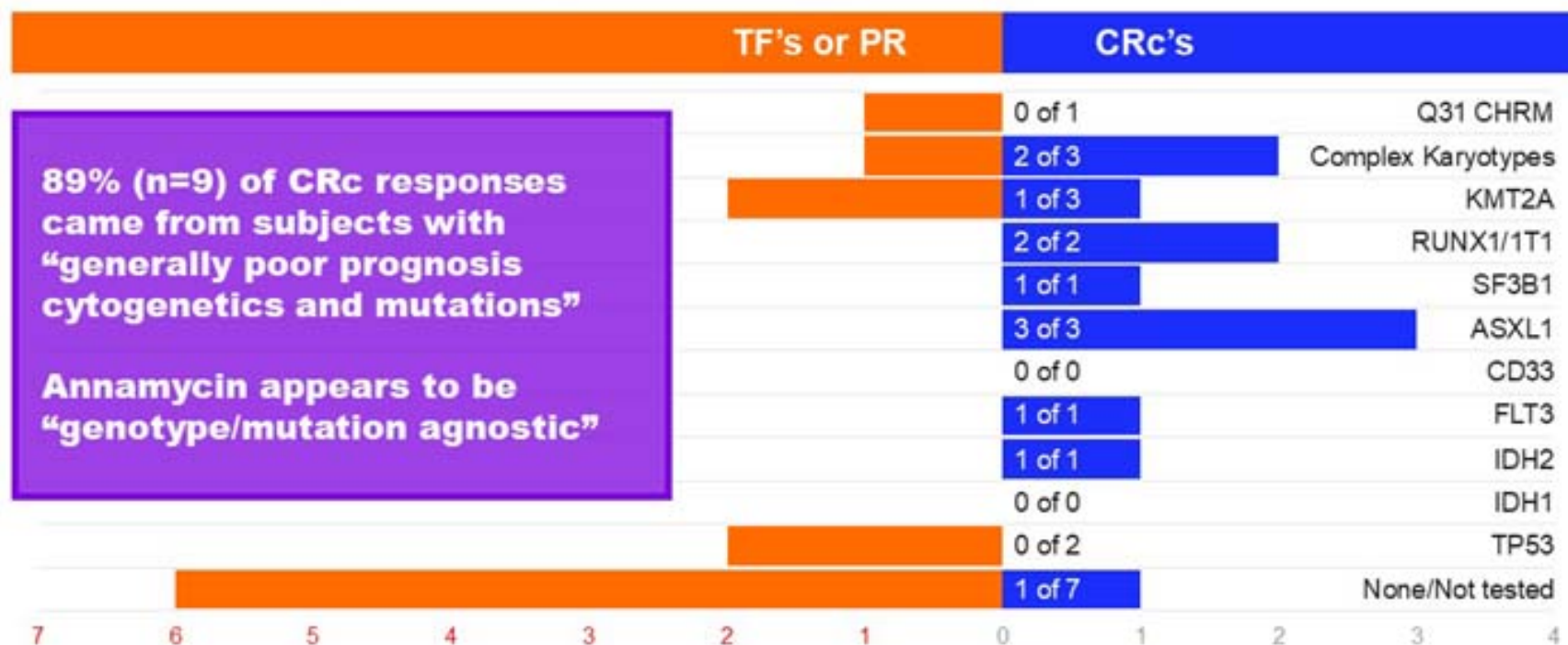
**Median CRc Durability = ~8 Months and Climbing**

Notes: 1) Data from MB-106 are for intent to treat subjects who had efficacy determined (n=22); 2) Data from MB-106 are preliminary and subject to change; and 3) Relapses include 1 death due to pneumonia (unrelated to drug).

# Durability, MRD, Prior Therapies



# MB-106 Response by Genotype and Mutation



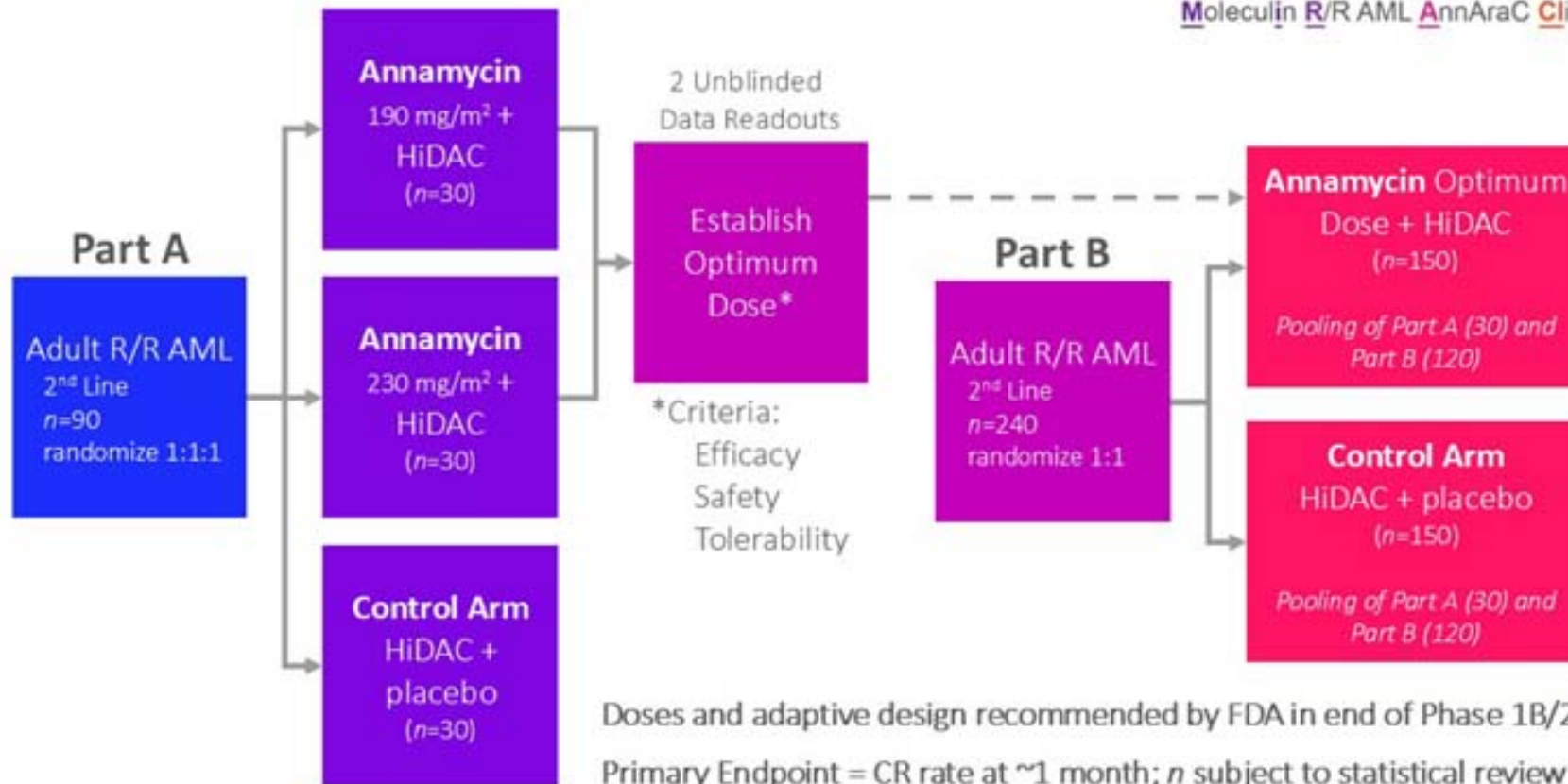
Note – n=20; Some subjects had multiple mutations or abnormalities, hence totals of treatment failures (TF), partial remissions (PR) or composite complete remissions (CRc) do not equal totals for each response category – TF's/PR's, or CRc's; Data are anecdotal only and not intended to indicate statistical significance. Not all mutations/subjects were tested.

# AML Clinical History

<b>Phase 1: MB-104</b> MONOTHERAPY 100-120 mg/m <sup>2</sup>	<b>Phase 1/2: MB-105</b> MONOTHERAPY 120-240 mg/m <sup>2</sup>	<b>Phase 1/2: MB-106</b> COMBINATION THERAPY Annamycin + Cytarabine
<ul style="list-style-type: none"> <li>N = 7</li> <li>17% CRi (at suboptimal dosing)</li> <li>Dosing limited by FDA Lifetime Anthracycline Dose (LTMAD)</li> <li>Trial location – US</li> </ul>	<ul style="list-style-type: none"> <li>N = 20</li> <li>Median lines of prior therapy = 4</li> <li>Median age of 240 mg/m<sup>2</sup> (RPD2) cohort = 65 years</li> <li>80% ORR in 240mg/m<sup>2</sup> Cohort (N=5)</li> <li>Trial location - Poland</li> </ul>	<ul style="list-style-type: none"> <li>N = 22 all lines (0-6), N = 10 (2<sup>nd</sup> line)</li> <li>All subjects (N=22) 41% CRc (ITT)</li> <li>2nd Line N=10, 60% CRc</li> <li>Prior therapies range 0-10</li> <li>Median age all subjects = 69</li> <li>Trial location – Poland &amp; Italy</li> </ul>
Key Findings		
<ul style="list-style-type: none"> <li>Well-tolerated in the study population</li> <li>Limited to low doses</li> <li>Morphologic leukemia free state was achieved in one subject in the 120 mg/m<sup>2</sup> cohort</li> </ul>	<ul style="list-style-type: none"> <li>Positive correlation between response rate and dose</li> </ul>	<ul style="list-style-type: none"> <li>"3+5" therapy</li> <li>Durability: ~8 months and increasing</li> <li>Early evidence of efficacy in patients with previous therapy failures</li> </ul>
Regulatory Significance		
<ul style="list-style-type: none"> <li>Demonstrated safe dosing within FDA-mandated limitations for anthracycline exposure</li> </ul>	<ul style="list-style-type: none"> <li>Demonstrated safe dosing beyond FDA (and EMA) limitations for cumulative anthracycline exposure and early efficacy as single agent</li> </ul>	<ul style="list-style-type: none"> <li>Addition of Cytarabine supported by compelling preclinical data showing improvement over Annamycin monotherapy</li> </ul>



# Adaptive Trial Design



# Project Optimus Guidance

FDA provided clear written guidance by recommending the comparison of 190 mg/m<sup>2</sup> vs. 230 mg/m<sup>2</sup>

Clinical experience to date shows no significant safety or efficacy difference between 190 and 230

Initial PK analysis shows no correlation between AUC or C<sub>max</sub> and change in dosage from 190 to 230

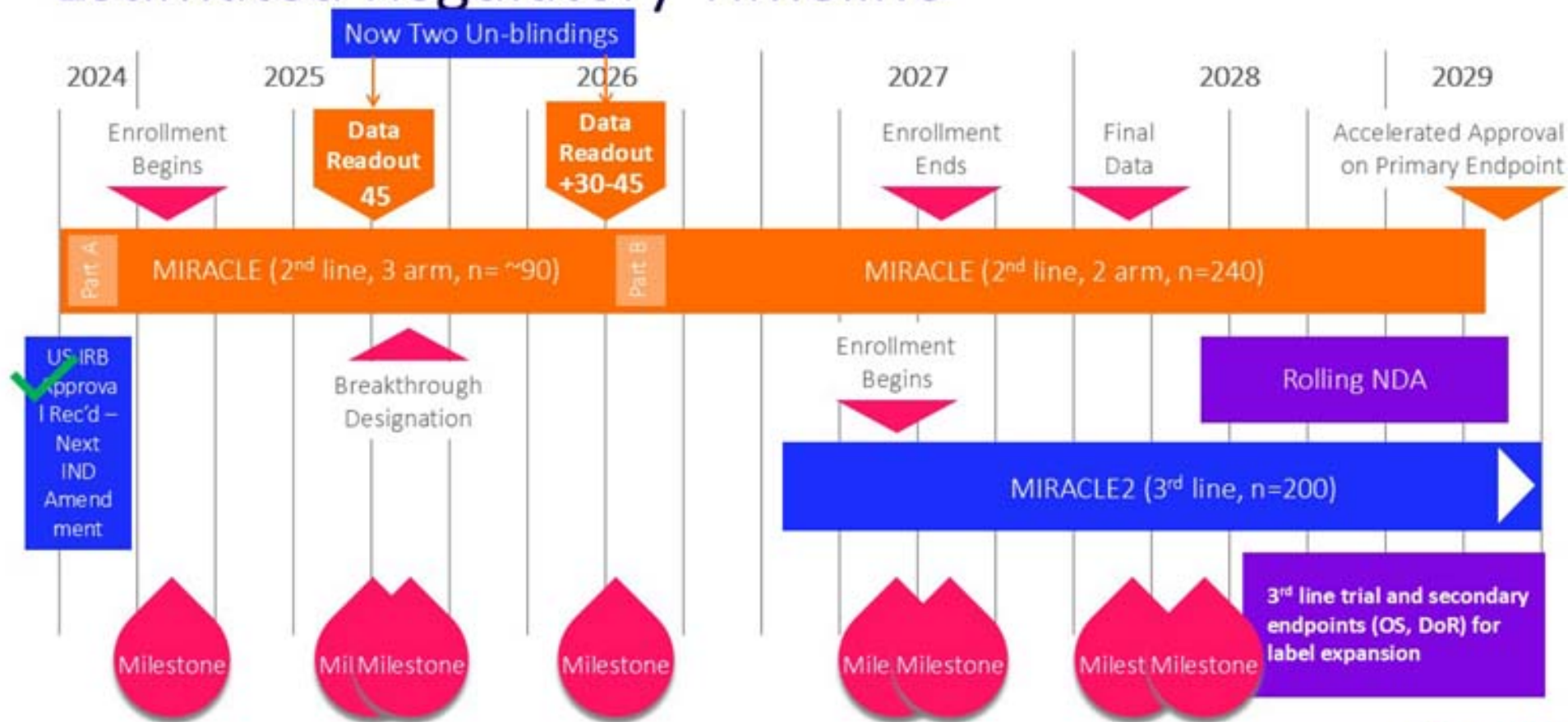
Corroborates clinical findings

Could reduce potential for future generic competition

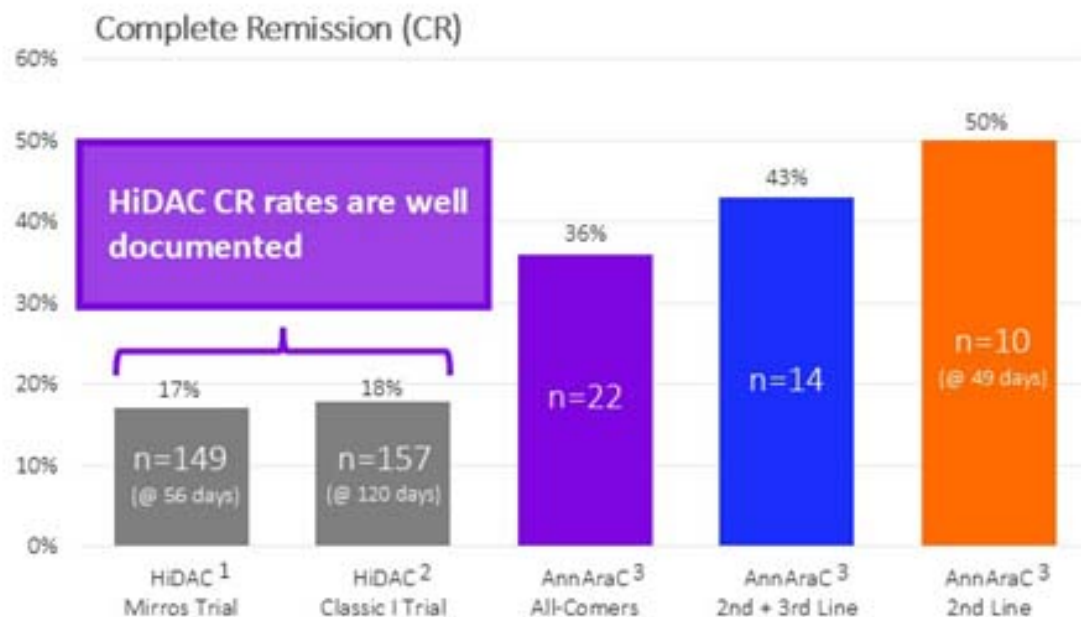
FDA is recommending the Sponsor make the choice between 190 and 230 based on totality of data (PK, PD, safety, efficacy)

Moleculin utilizing Data Monitoring Committee to provide independent review

# Estimated Regulatory Timeline



# The Bar for Approval is Low

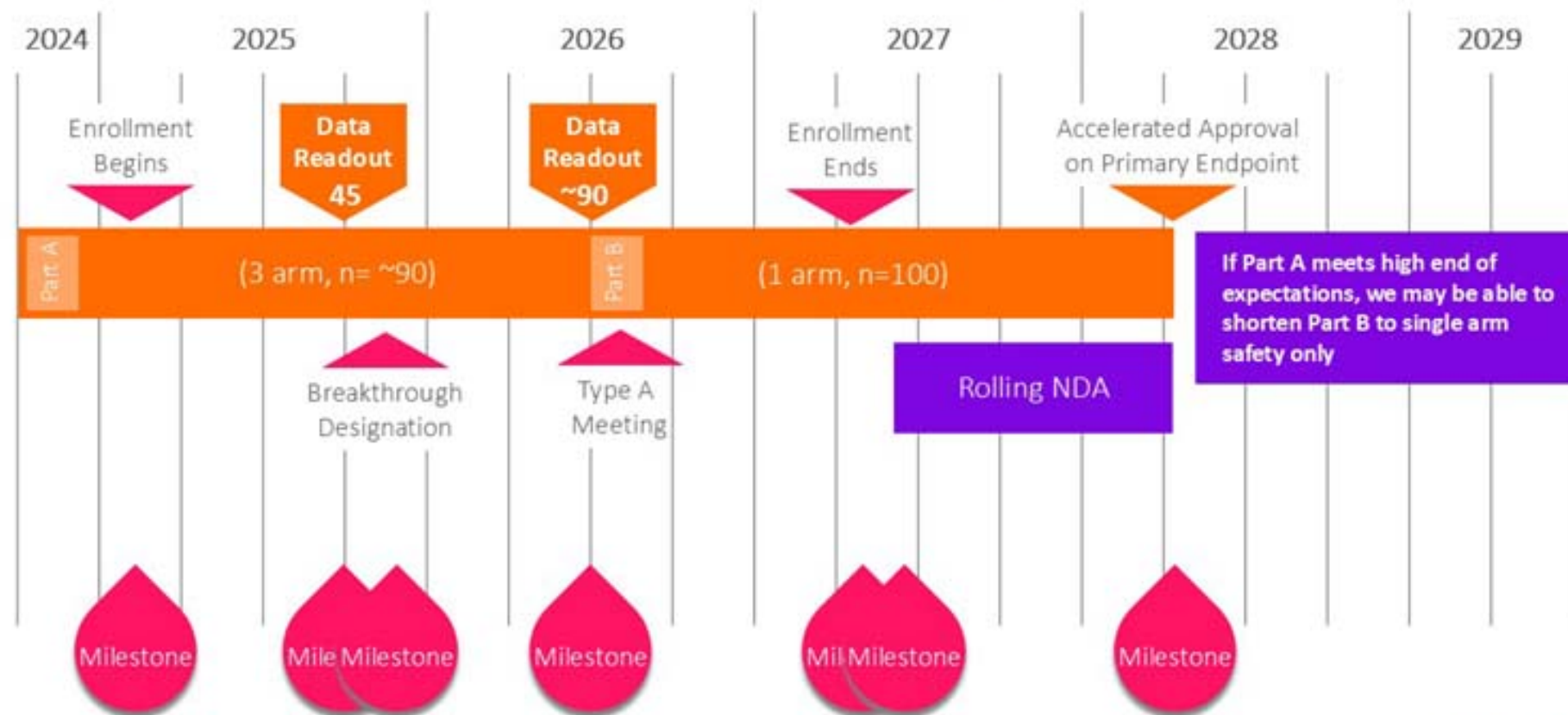


Annamycin NDA to be based on CR rate in 2<sup>nd</sup> line subjects at ~1 month

1 – Mirros Trial, 81% 2<sup>nd</sup> line patients; 17% CR, within 56 days, Konopleva et al, Blood Advances, 26 July 2022, Volume 6, Number 14; 2 – Classic I Trial, 18% CR rate within 120 days, Faderl et al, J Clin Oncol, July 2012, Volume 30, Number 20; 3 – MB-106 trial, 50% CR rate for 2<sup>nd</sup> line patients (n=10, within 49 days), 43% CR rate for 2<sup>nd</sup> + 3<sup>rd</sup> line patients (n=14), and 36% CR rate for all-comers (1<sup>st</sup> through 7<sup>th</sup> line, n=22)



# Potential Accelerated Regulatory Timeline



60 sites interested

17 more sites targeted

- Interested/visited
  - Interested
  - Additional Targeted
- Updated: 11/05/24

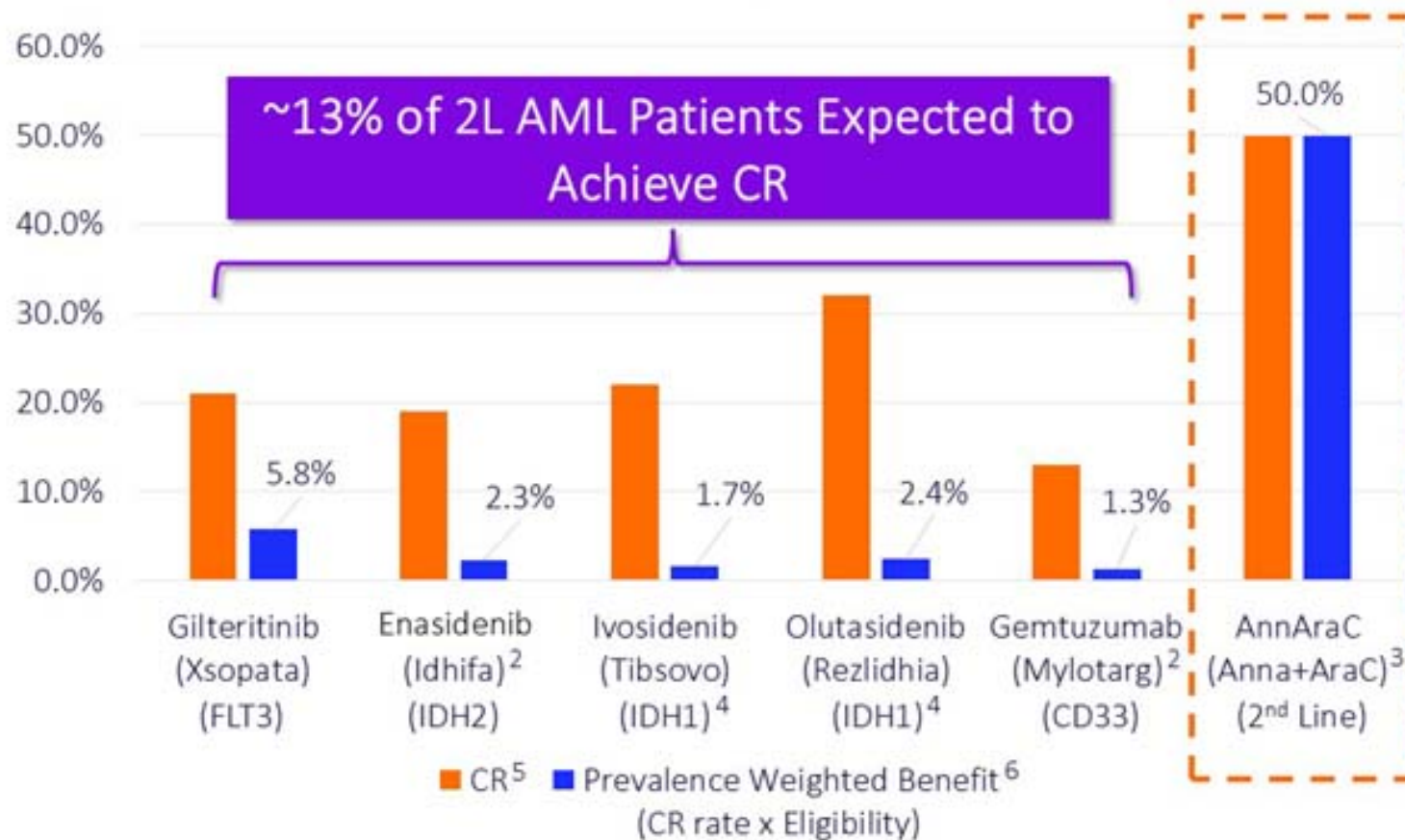


Ukraine  
Georgia



Site Selection is Moving Quickly

# AnnAraC Should Increase 2nd Line AML CRs 2-Fold or More



# Potential Asset Value



	Approved			Phase 2 Complete			
	1 <sup>st</sup> Line		2 <sup>nd</sup> Line				
	Jazz	AbbVie	Servier	Kura <sup>1</sup>	Syndax <sup>1</sup>	JNJ <sup>1</sup>	Moleculin
	Vyxeos	Ven-Aza	Idhifa/Tibsovo	Ziftomenib	Revumenib	617	Annamycin
N	153	286	199/174	20	57	17	10
CR	<b>38%</b>	<b>37%</b>	<b>19%/25%</b>	<b>35%</b>	<b>18%</b>	<b>24%</b>	<b>50%</b>
CRC	48%	64%	23%/33%	40%	25%	47%	60%
AML Population	50%	50%	15-23%	30% <sup>2</sup>	24% <sup>2</sup>	30% <sup>2</sup>	60%
Revenue <sup>3</sup>	\$128M	\$2B	~\$150M				
Valuation	<b>\$1.5B</b>	N/A	<b>\$2B</b>	<b>~\$1.5B</b>	<b>~\$1.9B</b>	N/A	<b>~\$.015B</b>
	<b>Exit<sup>4</sup></b> (Acquisition of Celator, 2016)		<b>Exit<sup>5</sup></b> (Acquisition of Agios, 2021)	<b>Market Cap<sup>6</sup></b>	<b>Market Cap<sup>6</sup></b>		<b>Market Cap<sup>6</sup></b>

1. All three are pursuing essentially the same patient population; best overall performance from either NPM1 mutation or KMT2A rearrangement cohorts; 2. Limited to 2<sup>nd</sup> Line due to low CRc performance; 3. Jazz and AbbVie revenue per SEC disclosure, Servier revenue per Management estimate based on Agios revenue disclosure for Tibsovo sales and Idhifa royalties; 4. Company press release - <https://investor.jazzpharma.com/news-releases/news-release-details/jazz-pharmaceuticals-and-celator-pharmaceuticals-announce>; 5. Company press release - [https://servier.com/wp-content/uploads/2022/11/servier-completes-acquisition-agios-oncology-business\\_PR.pdf](https://servier.com/wp-content/uploads/2022/11/servier-completes-acquisition-agios-oncology-business_PR.pdf); 6. As of April 11, 2024, calculation of Share Price multiplied by Shares Outstanding



# The Full Annamycin Opportunity<sup>1</sup>

Potential for Significant Upside



# Financials

Nasdaq: MBRX



~\$9.4M Cash Balance<sup>2</sup>



~\$17.3M Market Cap<sup>3</sup>



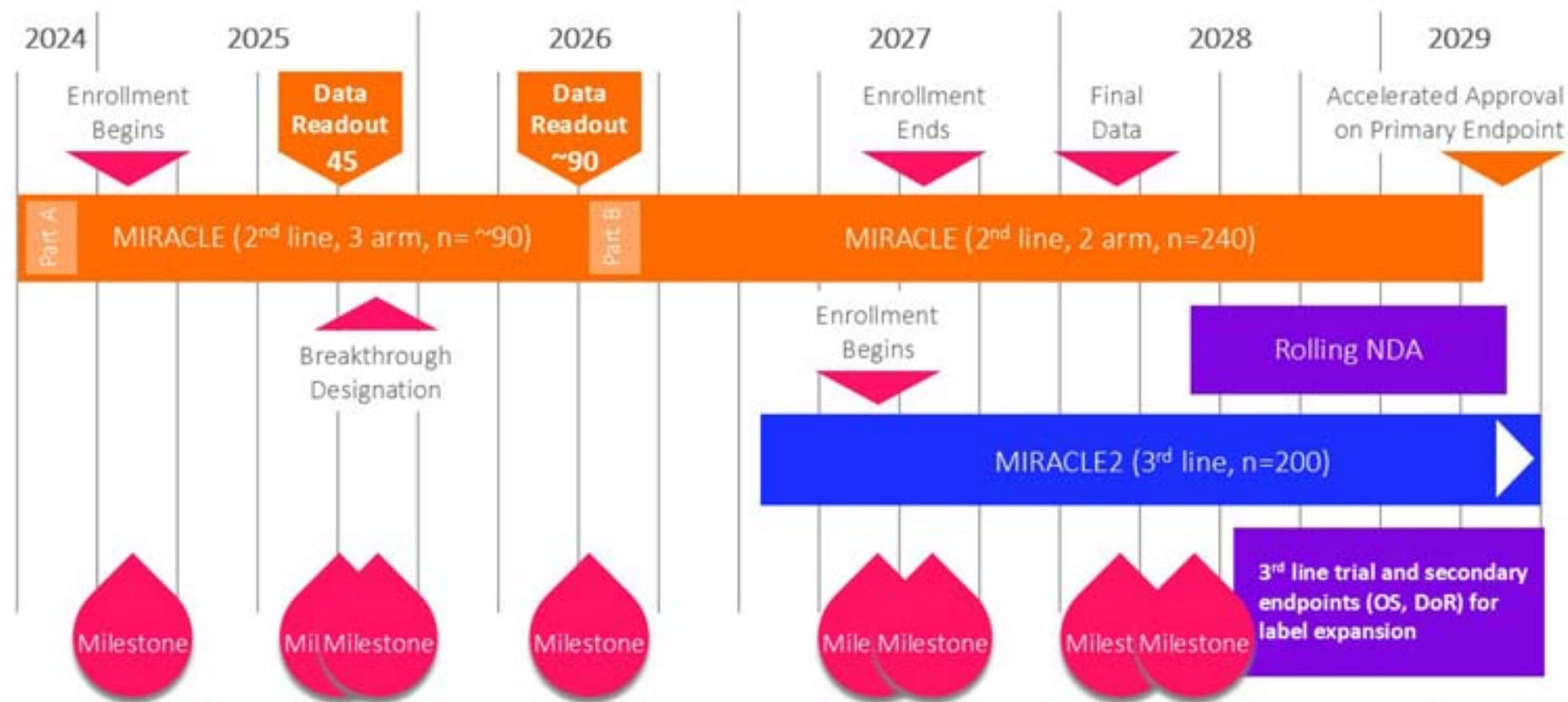
3.0M O/S and 6.1M Shares Fully Diluted  
Outstanding<sup>4</sup>



~32K – 65-day Avg. Daily Trading Vol.<sup>5</sup>

Notes: 1: Not Used; 2: Cash on hand as of September 30, 2024 ; 3: As of September 30,2024, and using fully diluted shares outstanding of 6.1M w/ price per share = \$2.84 per share; 4: Fully diluted common stock outstanding as of September 30, 2024; 5: Barrons.com Nov. 8, 2024 12.58PM

# Estimated Regulatory Timeline



# Upcoming Milestones



PROGRAM	MILESTONE	ESTIMATED TIME OF ACHIEVEMENT
<p style="text-align: center;">Annamycin AML</p>	Begin contracting with MIRACLE trial sites	2H 2024
	First subject treated in MIRACLE trial	1Q 2025
	Data Readout (n=45) (safety and overall efficacy review)	2H 2025
	Data Readout (n=~90) unblinded and Optimum Dose set for MIRACLE trial	2H 2026
	Begin enrollment of 3 <sup>rd</sup> line subjects in MIRACLE2	2027
	Enrollment ends for 2 <sup>nd</sup> line subjects	2027
	Primary efficacy data for 2 <sup>nd</sup> line subjects; Rolling NDA submission begins	2028
<p style="text-align: center;">Annamycin STS Lung Mets</p>	Final MB-107 Data Readout	2025
	Identify Next Phase of Development / Pivotal Program	2025



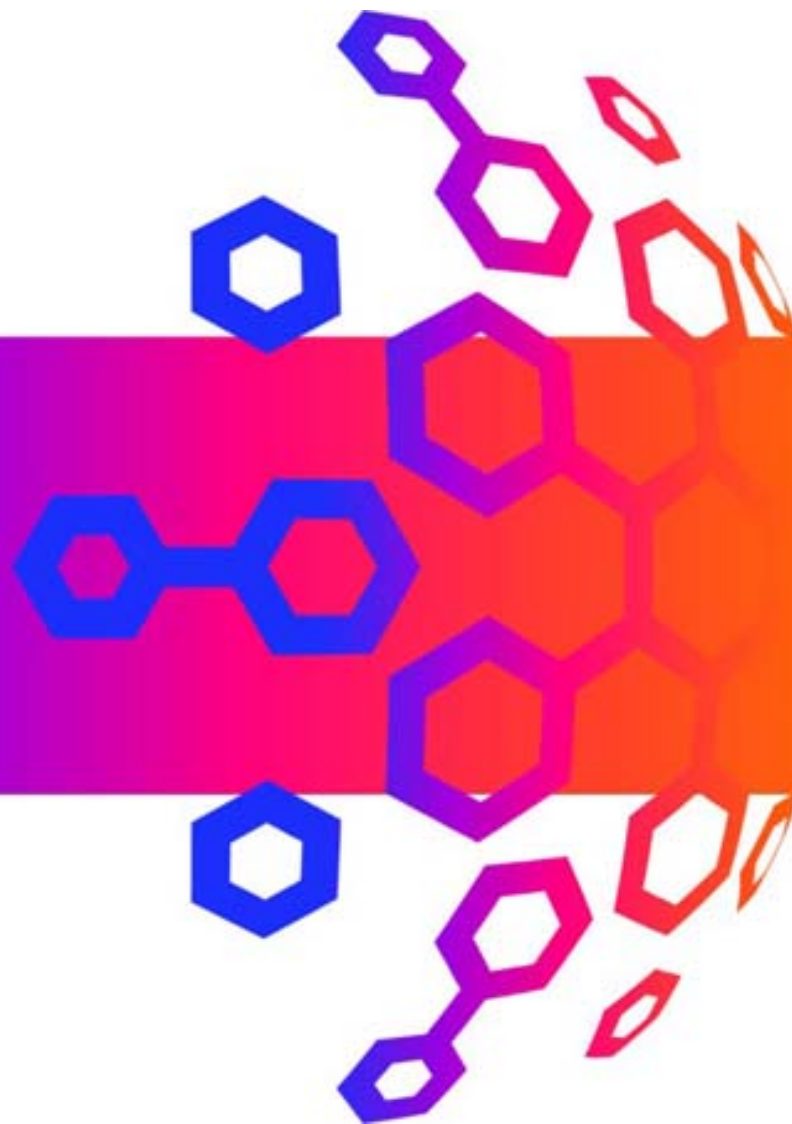
# miRACLE

Moleculin R/R AML AnnAraC Clinical Evaluation

Phase 3 pivotal clinical trial designed to seek accelerated new drug approval for Annamycin in the treatment of relapsed or refractory acute myeloid leukemia. Targeted to begin recruiting in the first quarter of 2025



# Appendix



# Soft Tissue Sarcoma Mets to the Lungs

MB-107 studied Annamycin monotherapy in Advanced STS subjects with lung metastases\*

All Comers (n=32)

Median prior tx = 3

**OS = ~11 months**

2<sup>nd</sup> Line (n=9)

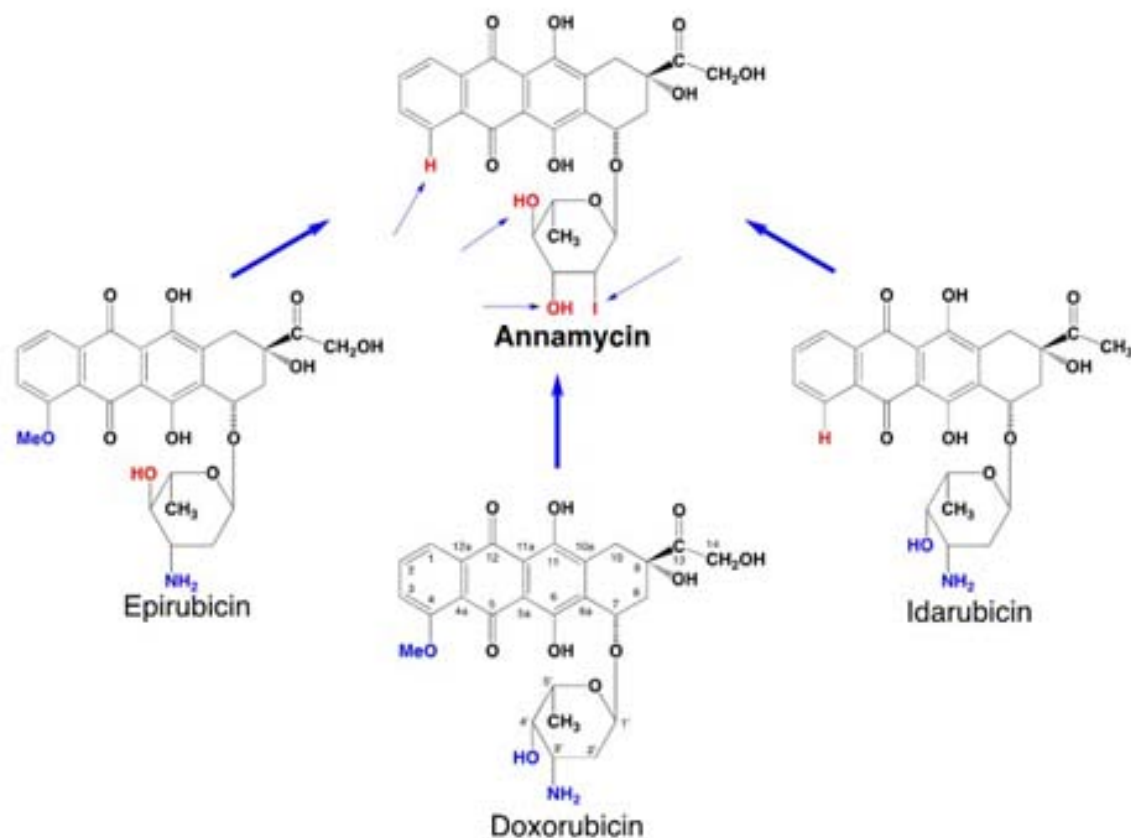
Median prior tx = 1

**OS = ~14 months**

*“We don’t expect to see these kinds of responses in STS patients with lung metastases who have stopped responding to 1<sup>st</sup> line therapy...let alone in 4<sup>th</sup> line!” STS KOL*

\* Preliminary results, subject to final clinical study report which is expected to be issued in late 2024 or early 2025

# Annamycin: A Next-Generation Anthracycline



## Unique new structure:

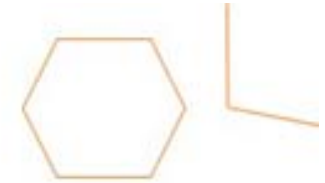
- Incorporates key structural elements of 3 different clinically used anthracyclines, plus
- The 3'-deamination and introduction of iodine at C-2

## Result:

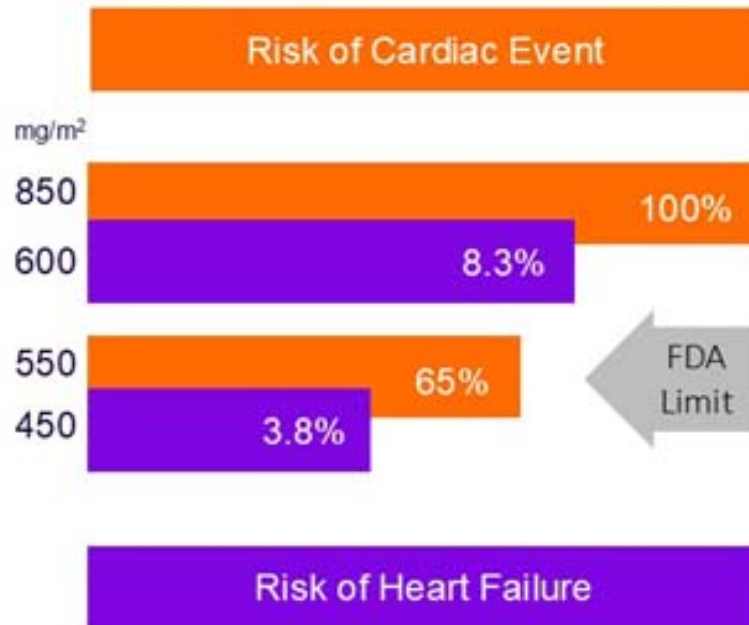
- Elimination of cardiotoxicity
- Overcomes MDR1 resistance mechanisms
- Increased potency
- Rapid cellular uptake
- Improved tissue and organ distribution
- Active against leukemias resistant to:
  - a) clinically use anthracyclines
  - b) Ara-C
  - c) Venetoclax



# Annamycin Has Demonstrated Substantially Greater Cardiac Safety Compared to Approved Anthracyclines



## Current Anthracyclines

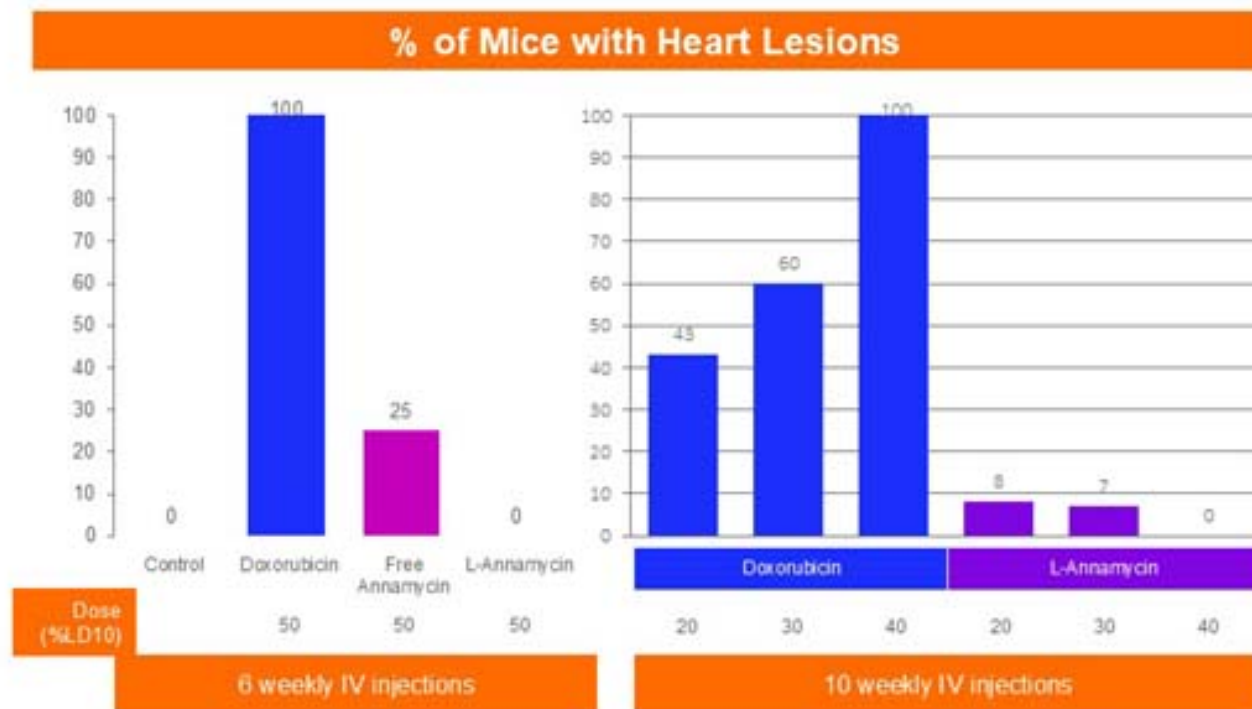


## Annamycin

### Zero Cardiotoxicity

- Wider therapeutic window
- Avoids multidrug resistance
- Better tissue/organ targeting

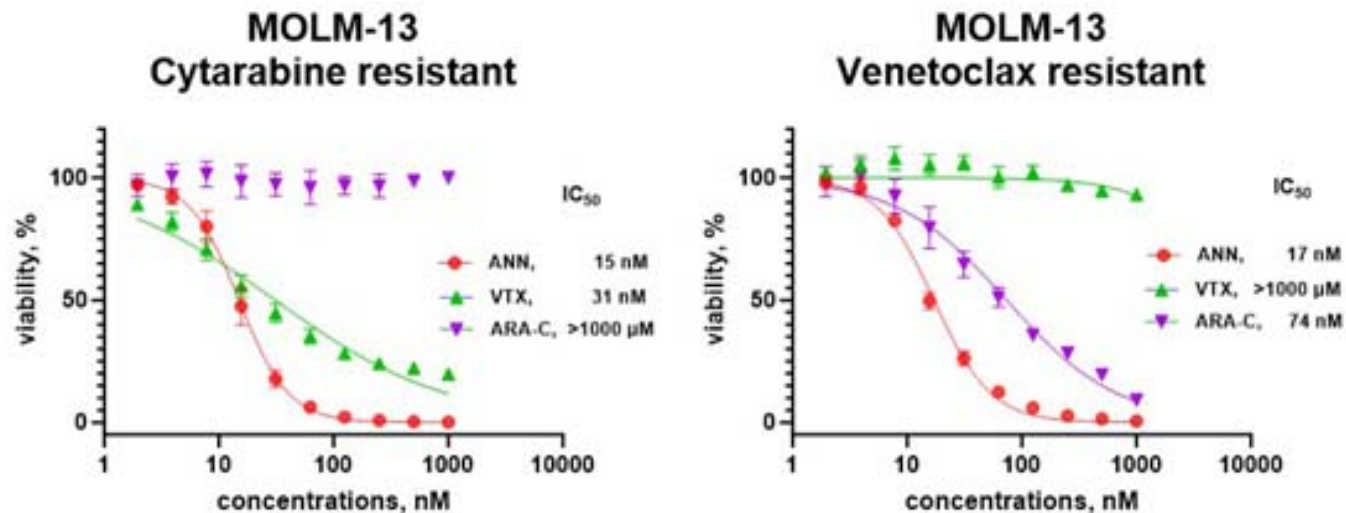
# FDA Recommended Model Shows Annamycin's Lack of Cardiotoxicity



The gold standard preclinical Bertozzoli model for measuring cardiotoxicity shows Annamycin is effectively non-cardiotoxic when compared with doxorubicin.

Free Annamycin (API only) is substantially less cardiotoxic than doxorubicin and L-Annamycin (as formulated) is essentially non-cardiotoxic.

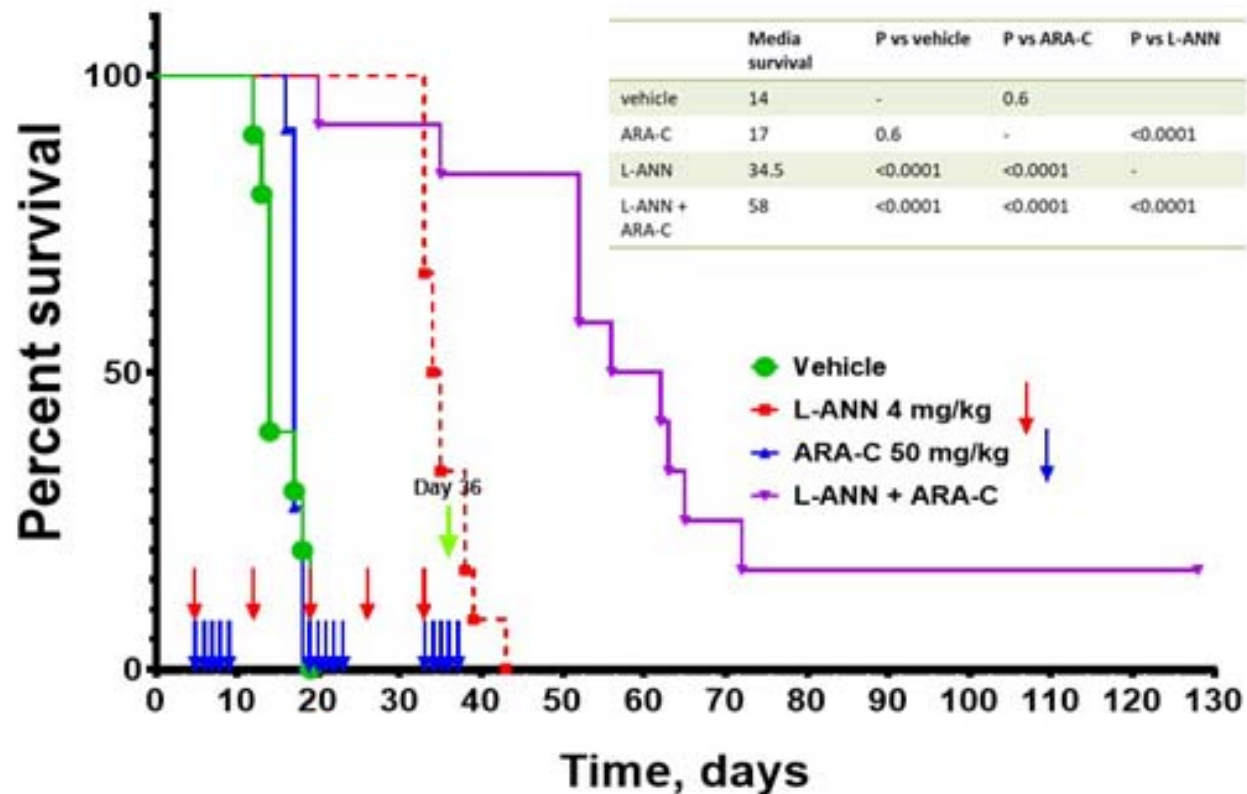
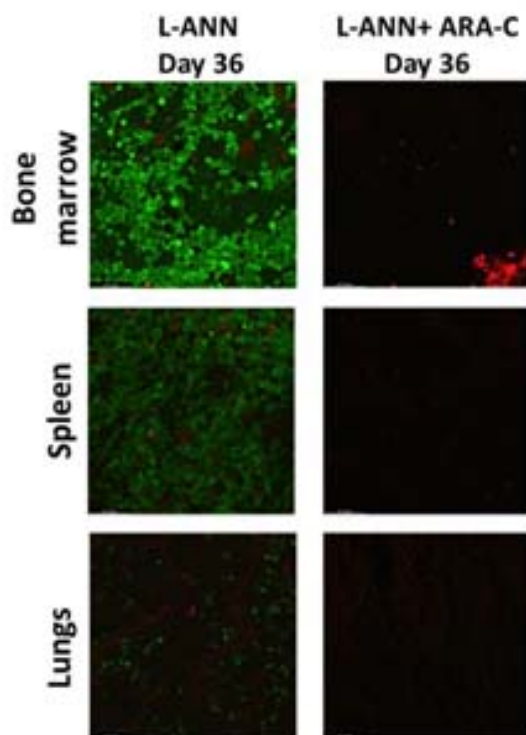
# Annamycin Shown Effective Against both Cytarabine and Venetoclax Resistant Cell Lines



The Cytarabine and Venetoclax resistant phenotypes of MOLM-13 cell line were count and plated in two 96-wells plate,  $8 \times 10^3$  cells in 190  $\mu$ l of complete RPMI media each well. Starting from 1  $\mu$ M, ten serial dilutions at 1:2 factor were added (10  $\mu$ l) to the cells. After 72h under treatment, viability was evaluated with resazurin and data were analyzed using GraphPad to calculate the IC<sub>50</sub> for each compound.

## Annamycin Synergizes with ARA-C in Increasing Survival in p53-null, FLT3 mutated AML Model (AML-mTurquoise2)

### Analysis of Minimal Residual Disease (MRD)





# Performance of AML Therapies in 2<sup>nd</sup> Line

CLAVELA: International Randomized Phase III Study of Elacytarabine Versus Investigator Choice in Patients with Relapsed/Refractory Acute Myeloid Leukemia

381

R/R AML  
subjects

Elacytarabine

(compared with)

7 different NCCN  
recommended therapies

Therapies compared:

- high-dose cytarabine (HiDAC)
- MEC
- FLAG/FLAG-Ida
- low-dose cytarabine
- hypomethylating agents
- hydroxyurea
- supportive care

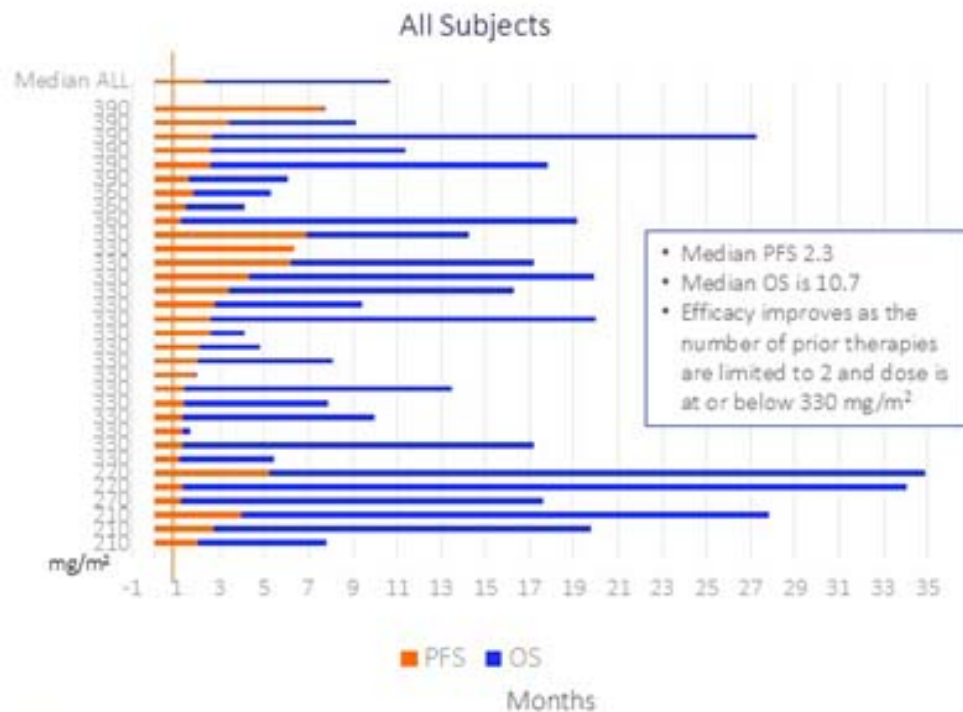
## Results:

There were no significant differences in OS (3.5 v 3.3 months), response rate (CR = 15% v 12%) between the elacytarabine and control arms, respectively. There was no significant difference in OS among any of the investigator's choice regimens.

*Gail J. Roboz, Todd Rosenblat, Martha Arellano, Marco Gobbi, Jessica K. Altman, Pau Montesinos, Casey O'Connell, Scott R. Solomon, Arnaud Pigneux, Norbert Vey, Robert Hills, Tove Flem-Jacobsen, Athos Ganeito-Barradori, Olivind Fass, Sylvia Vetthuisand, and Francis J. Giles*

# Annamycin Demonstrates Efficacy in STS Lung Metastases (MB-107) - As Reported in Feb 2024

Demonstrated Stable Disease After Two Treatment Cycles



Demonstrated Improvement with Dose  $\leq 330$  mg/m<sup>2</sup> and Fewer Prior Therapies

Preliminary MB-107 Summary as of Sep 23, 2024

Progression Free Survival Months (mos)	All Subjects	Phase 1B All Subjects	Phase 2 All Subjects (330&360 mg/m <sup>2</sup> )	All Subjects Treated at 330mg/m <sup>2</sup>	All Subjects with 2 or Fewer Prior Therapies ( $\leq 2PT$ )	All Subjects $\leq 330$ mg/m <sup>2</sup> & $\leq 2PT$
1 mos or >	100%	100%	100%	100%	100%	100%
2 mos or >	59%	67%	53%	61%	75%	67%
3 mos or >	28%	27%	29%	30%	42%	44%
4 mos or >	19%	13%	24%	22%	25%	22%
5 mos or >	16%	13%	18%	17%	17%	22%
6 mos or >	13%	7%	18%	13%	17%	11%
n =	32	15	17	23	12	9
Median PFS mos	2.3	2.0	2.6	2.0	2.7	2.8
Median Prior Therapies (Range)	3 (1-11)	4 (1-8)	3 (1-11)	3 (1-11)	2 (1-2)	2 (1-2)
Median O/S mos	10.7	13.5	10.2	9.4	12.8	14.3

# Science Advisors



Waldemar Priebe, PhD  
MD Anderson Cancer Center  
Founding Scientist & SAB Chair



Dr. Daniel Von Hoff  
Mayo Clinic

## Hematology Oncology



Dr. Martin Tallman  
Northwestern University



Dr. Jorge Cortes  
Augusta University



Dr. Michael Andreef  
MD Anderson Cancer Center



Dr. Giovanni Martinelli  
Bologna University

# Global Network



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Supports continuing preclinical research on our technology at MDACC close to \$1M per year



Active contractors in US, EU and Asia for drug production and distribution as well as for clinical trial management



Past & current externally funded trials – MD Anderson Cancer Center; Emory University, Aflac Cancer & Blood Disorders Center, Children's Healthcare of Atlanta; Northwestern University (NIH & BrainUp); Madame Curie Institute (Poland), and others in discussion

