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Reimagining Cancer Treatment

Corporate Presentation / August 2023

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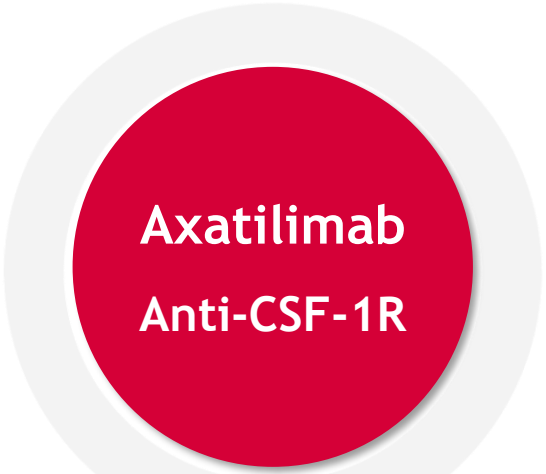
Revumenib and axatilimab on-track to file an NDA and BLA in 2023 with several opportunities for franchise expansion

Expand within acute leukemia and beyond to solid tumors

- Expect AUGMENT-101 pivotal data beginning in 3Q23
- Front-line and R/R combo trials ongoing with initial data by YE23
- Initial MSS CRC Phase 1 update by YE23



Expand into earlier lines of cGVHD and fibrotic disease

- Presentation of AGAVE-201 pivotal cGVHD data at medical meeting
- Initiate cGVHD combo trial with Jakafi® by YE23
- Initiate IPF Phase 2 trial by YE23

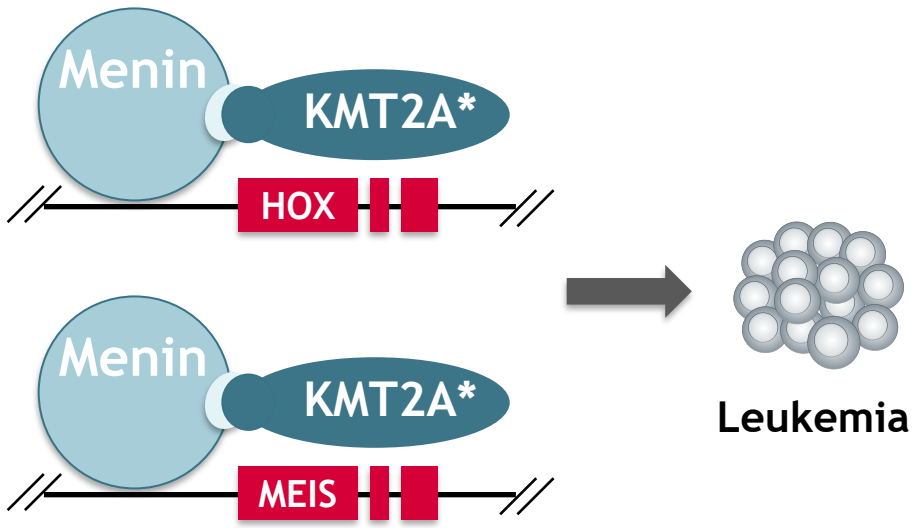
Expand pipeline through business development

- Targeting assets in late pre-clin to Phase 1
- Well-capitalized with $418M in cash and no debt

MSS CRC = Microsatellite Stable Colorectal Carcinoma, IPF = Idiopathic Pulmonary Fibrosis, cGVHD = chronic Graft-Versus-Host Disease, R/R = relapsed/refractory
Cash as of June 30, 2023; includes cash, cash equivalents and short- and long-term investments

Revumenib turns off leukemic transcriptional programs by binding to Menin and displacing KMT2A (MLL) complexes

KMT2Ar or mNPM1 acute leukemias



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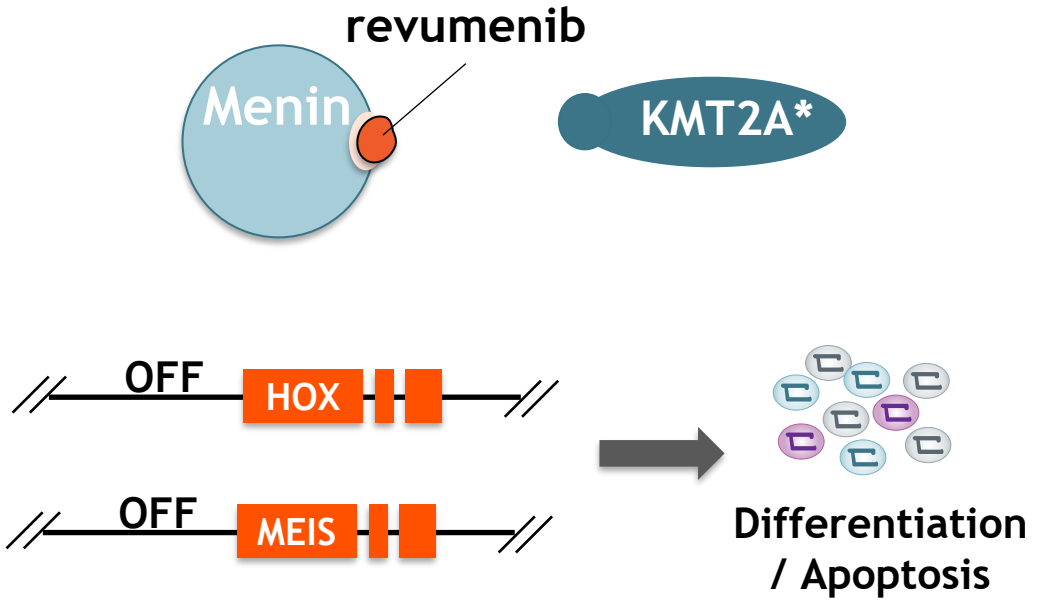
Menin inhibition with revumenib



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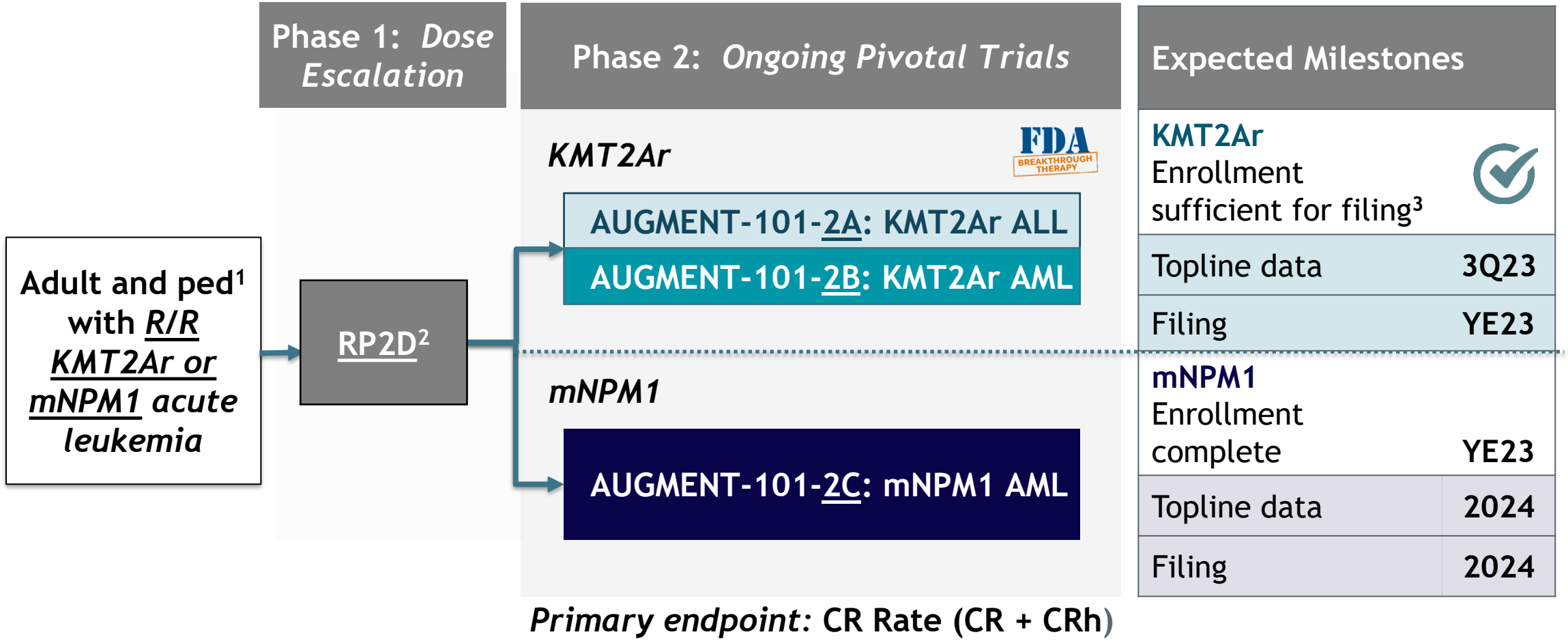
*KMT2A = KMT2A rearrangement or KMT2A wildtype; Adopted from: Uckelmann HJ, et al. Presented at ASH Annual Meeting, 2018

Pivotal AUGMENT-101 trial: Expecting KMT2Ar topline data in 3Q23, enrollment completion for mNPM1 by YE23



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Note: Patients taken to HSCT can restart treatment with revumenib post-transplant; Abbreviations: KMT2Ar = KMT2A rearrangement; mNPM1 = mutated nucleophosmin
[1]Allows patients ≥30 days of age [2]276mg q12h or 163mg q12h w/ strong CYP3A4 inhibitor [3]Completed enrollment of a sufficient number of KMT2Ar patients to support a registration filing

AUGMENT-101 patients heavily pretreated with a poor prognosis

Phase 1 portion of AUGMENT-101 presented at ASH 2022 and published in Nature

Baseline Characteristics	Safety Population N=68
Median age, years (range)	42.5 (0.8, 79)
Adult (n=60)	50.5
Pediatric (n=8)	2.5
Female, n (%)	42 (62)
Leukemia type, n (%)	
AML	56 (82)
ALL	11 (16)
MPAL	1 (2)
Median prior therapies (range)	4 (1,12)
Stem cell transplant, n (%)	31 (46)
Venetoclax, n (%)	41 (60)

Baseline Characteristics	Safety Population N=68
***KMT2Ar*, n (%)**	46 (68)
t(9;11)	10 (15)
t(11;19)	9 (13)
t(4;11)	6 (9)
t(6;11)	3 (4)
t(11;17)	2 (3)
Other	16 (24)
***mNPM1*, n (%)**	14 (21)
***KMT2A* and *NPM1* wild type, n (%)**	8 (12)
Co-occurring mutations*, n (%)	
FLT3	14 (25)
RAS	12 (29)
TP53	4 (10)

*In patients for whom co-occurring mutation data were available.
MPAL, mixed-phenotype acute leukemia. Data Cutoff of March 2022
Issa, G.C. et al. Nature **615**, 920-924 (2023).

No patients have discontinued due to treatment related adverse events

Phase 1 portion of AUGMENT-101

Any-grade treatment related AE (≥5%)	Safety Population N=68
Patients with ≥1 treatment-related AE, n (%)	53 (78)
ECG QTc prolonged	36 (53)
Nausea	18 (27)
Vomiting	11 (16)
Differentiation syndrome	11 (16)
Diarrhea	7 (10)
Dysgeusia	5 (7)
Decreased appetite	5 (7)

No treatment discontinuations for QTc prolongations, or associated arrhythmias

≥Grade 3 treatment related AE	Safety Population N=68
Patients with ≥Gr 3 treatment-related AE, n (%)	11 (16)
ECG QTc prolonged	9 (13)
Diarrhea	2 (3)
Anemia	2 (3)
Asthenia	1 (2)
Fatigue	1 (2)
Hypercalcemia	1 (2)
Hypokalemia	1 (2)
Neutropenia	1 (2)
Thrombocytopenia	1 (2)
Tumor lysis syndrome	1 (2)

10% of patients (5/52) had Gr 3 QTc prolongation at doses meeting criteria for RP2D

ECG, electrocardiogram; QTc, corrected QT interval. Data Cutoff of March 2022

AUGMENT-101 Phase 1 data supports best-in-class profile for revumenib

Phase 1 portion of AUGMENT-101

Best Response	Efficacy Population n = 60 (%)	
Overall Response Rate[1]	**32/60 (53%)**	
CR/CRh	18 (30%)	
MRD^{neg} Rate[2]	**18/32 (56%)**	
within CR/CRh MRD^{neg}	14/18 (78%)	
within CR/CRh/CRp MRD^{neg}	18/23 (78%)	
KMT2Ar Overall Response Rate[1]	**27/46 (59%)**	**Efficacy @ RP2D[3]**
CR/CRh	15/46 (33%)	10/37 (27%)
mNPM1 Overall Response Rate[1]	**5/14 (36%)**	
CR/CRh	3/14 (21%)	3/11 (27%)

- Median duration of CR/CRh response of **9.1 mos**
- Median time to CR/CRh response of **1.9 mos**
- Median overall survival of **7.0 mos**

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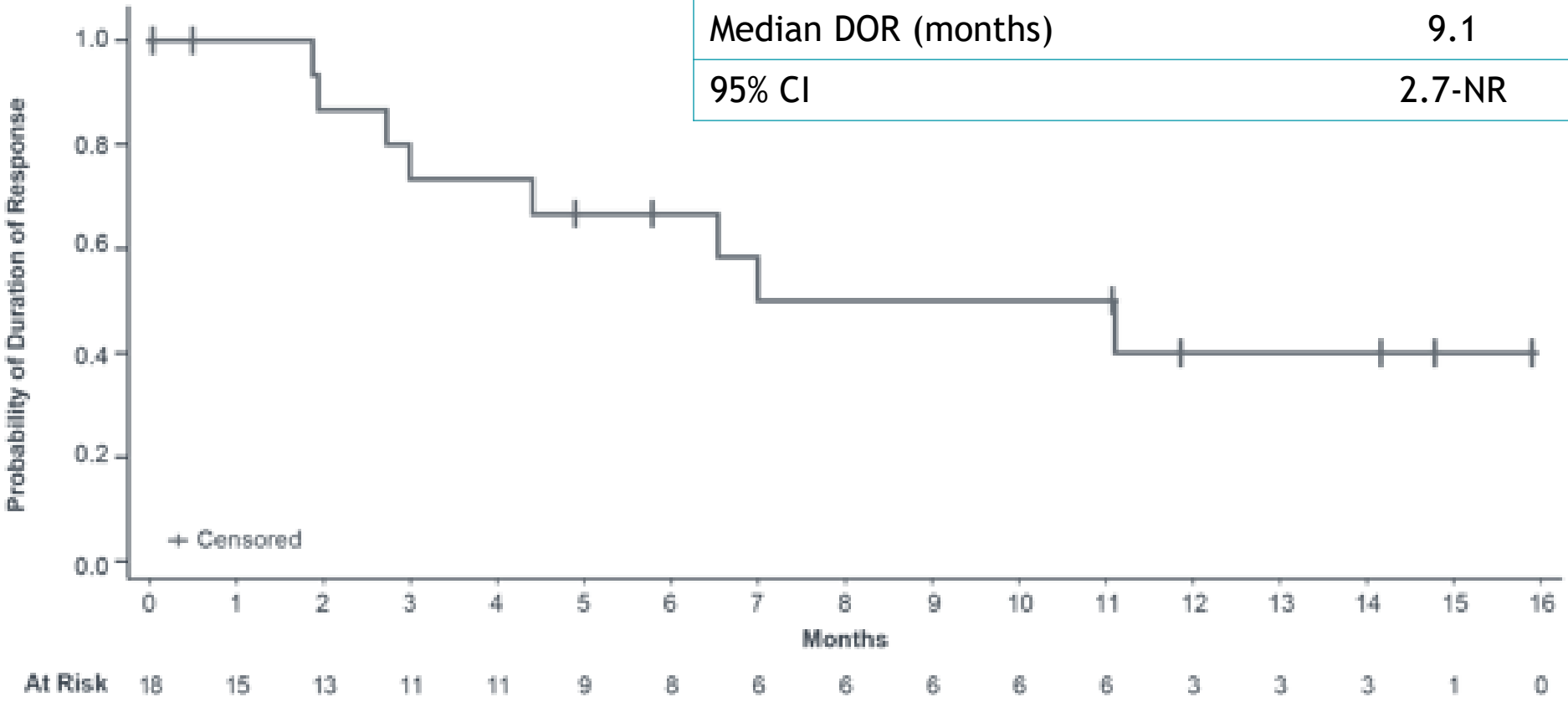
Data Cutoff of March 2022

[1] Overall Response Rate = CR + CRh + CRp + MLFS; [2] MRD status assessed locally by PCR or MCF; [3] RP2D defined as 113mg or 163 mg q12h for pts receiving concomitant strong CYP3A4 inhibitor therapy or 226mg or 276mg q12h for pts not receiving concomitant strong CYP3A4 inhibitor therapy

Median duration of CR/CRh response of 9.1 months

Phase 1 portion of AUGMENT-101

	Revumenib (n=18)
Median DOR (months)	9.1
95% CI	2.7-NR



DOR = duration of response; NR = not reached. Data Cutoff of March 2022

Durable remissions in transplant patients treated with revumenib

Phase 1 portion of AUGMENT-101

12 patients proceeded to HSCT[1]	
Patients who achieved MRD^{neg} status	11/12 (92%)
Remain in remission (1 receiving maintenance in CU[2])	9/12 (75%)
Remained in remission > 1 year	4/12 (33%)
Median follow-up	12.3 months

2 additional patients were treated under CU[2] with revumenib maintenance post HSCT or stem cell boost, and continue in remission for > 1 year

[1]As of data cutoff in March 2022. [2]CU = treated under compassionate use protocol

Significant unmet need remains in acute leukemia

No FDA-approved therapies specifically targeting KMT2Ar or mNPM1 acute leukemias

KMT2A Acute Leukemias

FDA BREAKTHROUGH THERAPY

Annual global incidence 5,000 - 7,000

~ 10% AML or ALL

- NCCN guidelines denote KMT2Ar predict poor prognosis
- Third-line treatment: Median OS of <3 months; 5% of patients achieve CR

mNPM1 Mutant AML

Annual global incidence ~20,000

~ 30% AML

- Most frequent genetic alterations in AML
- Typically associated with favorable prognosis, however beneficial impact decreases with age
- 5-year overall survival rate for adult mNPM1 AML is ~50%

Both KMT2A and mNPM1 acute leukemias are readily diagnosed

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Source: Issa, G. C., J. Zarka, K. Sasaki, W. Qiao, D. Pak, J. Ning, et al. (2021). Predictors of outcomes in adults with acute myeloid leukemia and KMT2A rearrangements. Blood Cancer J 11(9): 162. Dohner, H. et al. Blood, 2017; 129(4):424-447; Falini, B.et al. Blood 2011; 117(4):1109-1120. OS = overall response, CR = complete response

Revumenib could provide significant benefit in mNPM1 and KMT2Ar acute leukemias across the treatment paradigm

mNPM1 & KMT2Ar acute leukemia treatment paradigm

Revumenib Clinical Development Program (KMT2Ar and mNPM1 Acute Leukemia)

Pivotal

- **AUGMENT-101:** Rev Monotherapy *Ongoing*

Phase 1/2

- **BEAT AML:** Rev + Ven/Aza *Ongoing*
- **INTERCEPT:** Rev Monotherapy Tx *Ongoing*
- **AUGMENT-102:** Rev + Chemo *Ongoing*
- Rev + Intensive Chemo "7+3" → Maintenance *Starting YE 2023*
- **SAVE:** Rev + Ven + INQOVI® *Ongoing*

Revumenib expansion opportunities in acute leukemia have potential to add meaningful value

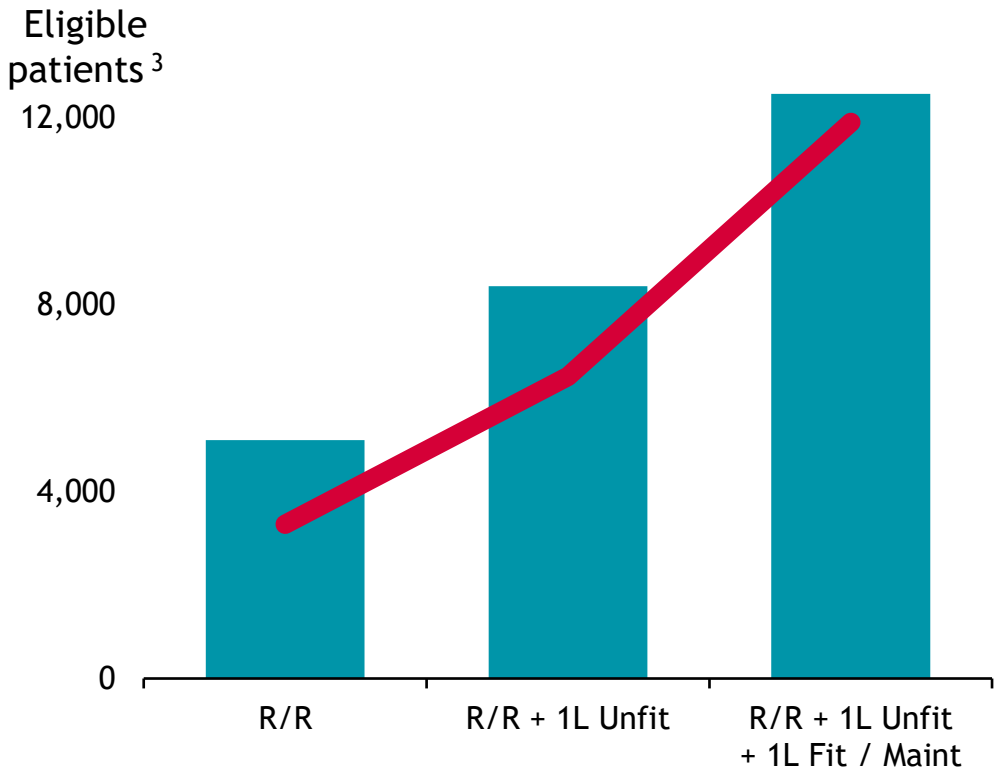
Potential first/best-in-class agent

- Clear activity in refractory, advanced mNPM1 and KMT2Ar acute leukemia
- High percentage of MRD negative responses

Profile supports potential use in front-line and maintenance

- Well-tolerated safety profile, no discontinuations due to treatment related AE
- Preclinical data supports combos with venetoclax[1], chemotherapy[2]

Est. US market opportunity for mNPM1 and KMT2Ar AML

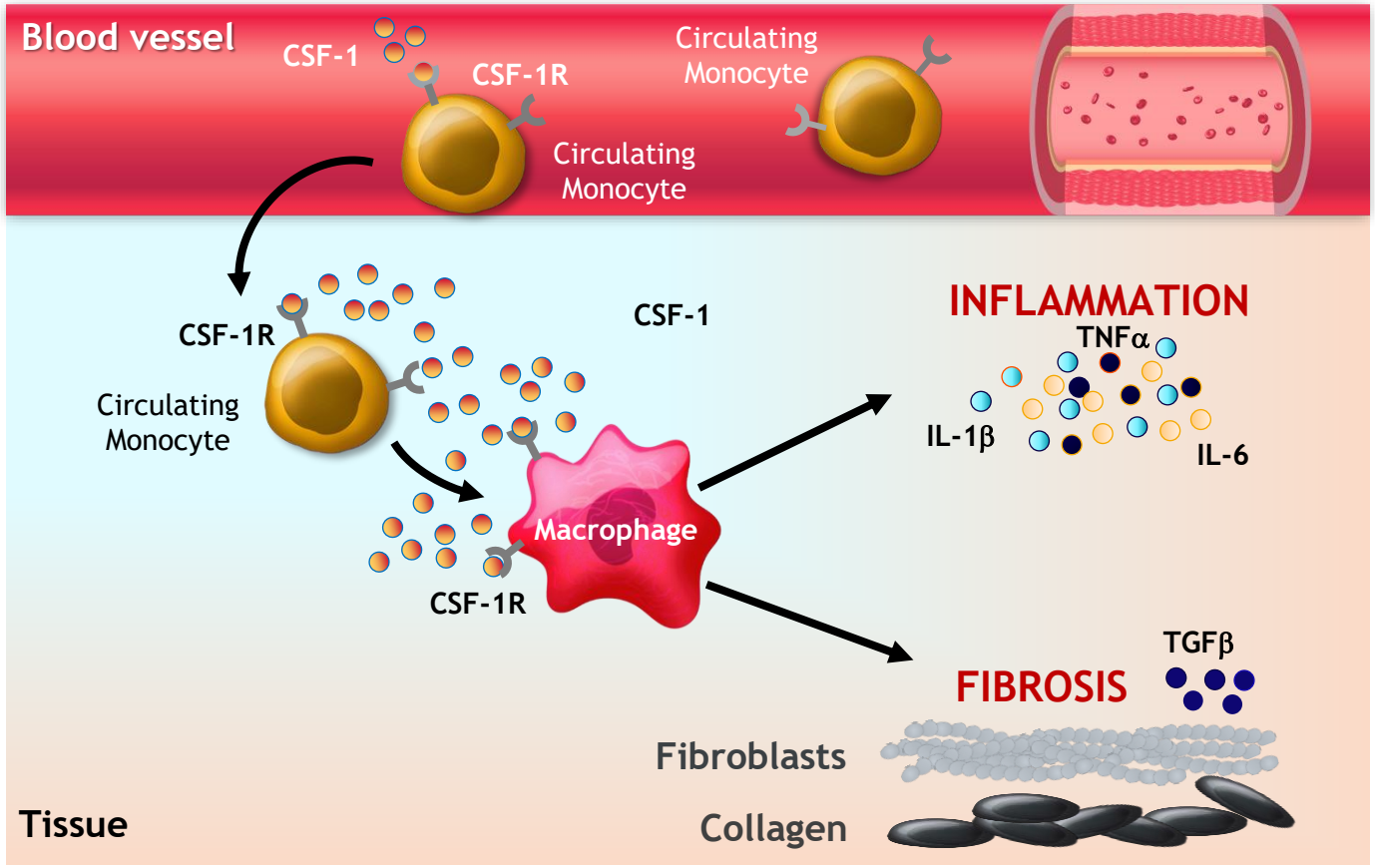


Expansion into solid tumors represents another significant opportunity for value

[1] Carter, B., et al., Blood 2021; [2] Data on file; [3] SEER + Roche IR presentation Sept 2020 AML incidence estimates

Axatilimab is the first cGVHD treatment to target the disease-modifying macrophage

CSF-1R mediates pro-inflammatory and pro-fibrotic monocyte/macrophage differentiation and activation[1]



- Axatilimab may offer a differentiated, practice-changing intervention in cGVHD
- Targeting monocyte-derived macrophages impacts both fibrotic and inflammatory processes and suggests potential to benefit patients alone or in combination with standard of care therapies already available for the management of this disease
- Benefits have been observed across all organ systems including lung, skin, and GI

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1. Figure Adapted from MacDonald KP et al. Blood. 2017;129(1):13-21; Chitu et al. Current Opinion in Immunology. 2006;18(1): 39-48

Axatilimab has the potential to be a differentiated treatment option for cGVHD

Positive pivotal data from the AGAVE-201 trial in cGVHD announced in July 2023

Unique MOA for cGVHD

- First agent to target disease causing macrophages to impact fibrosis & inflammation
- Potential synergy with SOC

High and durable ORR

- 74% ORR at 0.3 mg/kg
- 60% of patients treated at 0.3 mg/kg remained in response at 12 months

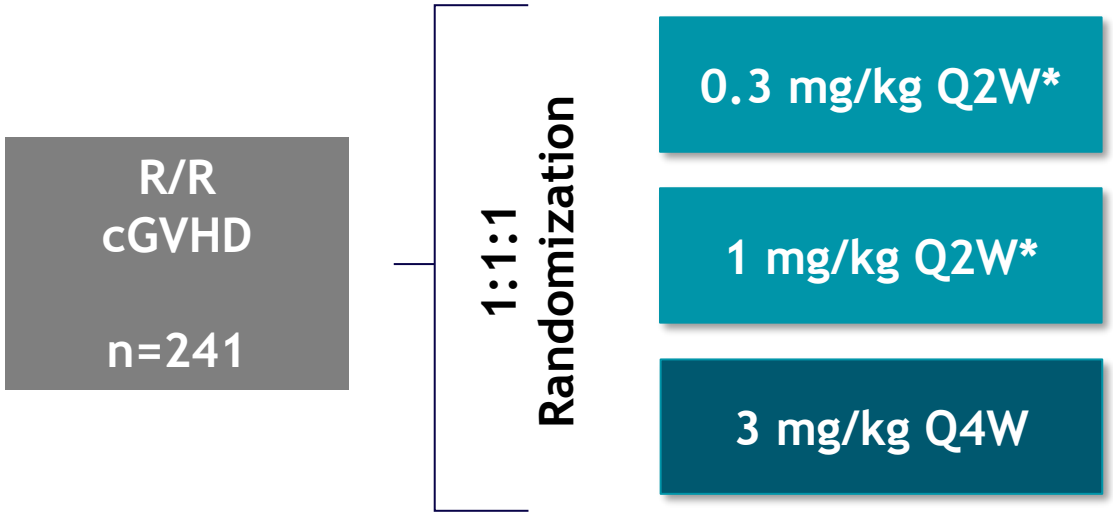
Well tolerated supporting broad use

- Low rate of SAEs and discontinuations at 0.3 mg/kg
- Antibody reduces potential for DDIs vs small molecule competitors

Enrolled population reflects real world

- Efficacy observed in patients following treatment with current SOC
- Option to switch to Q4W dose at 6mo

AGAVE-201, a global pivotal trial designed to identify an optimal dose of axatilimab in chronic GHVD patients



Inclusion criteria:

- 2 years and older[1]
- Recurrent or refractory active cGVHD after ≥ 2 lines of systemic Tx

Stratification factors:

- Prior treatment with ibrutinib, ruxolitinib or belumosudil
- Severity of cGVHD

Primary Endpoint: ORR[2] by Cycle 7 Day 1

- Statistical significance achieved if lower bound of the 95% CI of ORR exceeds 30%

Secondary Endpoints:

- Duration of response
- Modified Lee cGVHD Symptom Scale assessment
- Percent reduction in daily steroid dose
- Organ specific response rates

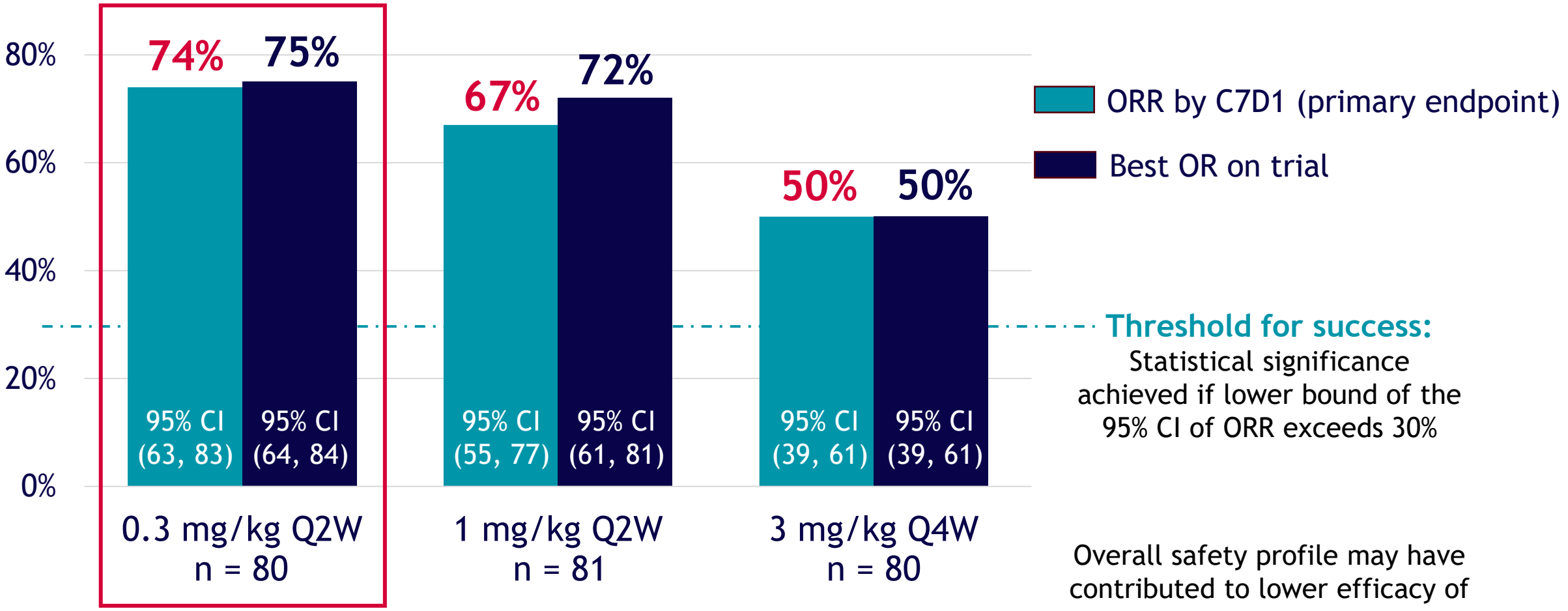
[1] Age inclusion criteria differs by country
[2] Overall response rate was assessed using the 2014 NIH Consensus Criteria for cGVHD
* Patients had the option to switch to cohort specific Q4W dose after 6 months on trial

AGAVE-201 enrolled refractory, late-line cGVHD patients, > 70% had prior treatment with ruxolitinib

Population (ITT)	Total N=241
Age median (min, max), years	53 (7, 81)
Male	63%
Race – white	83%
Median time since cGVHD diagnosis	48 months
≥ 4 organs involved	54%
% Patients with lung manifestations	45%
% patients with NIH severe cGVHD	80%
Median prior therapies	4
≥ 4 prior lines of treatment	65%
Prior ruxolitinib	74%
Prior ibrutinib	31%
Prior belumosudil	23%

Patient characteristics were well balanced across cohorts

All 3 cohorts in AGAVE-201 met the primary endpoint of ORR



ORR = Overall response rate
BOR = Best overall response rate

At 0.3 mg/kg every 2 weeks, responses were durable and accompanied by a reduction in symptom burden

60%

of responders maintained a response at 12 months[1]

55%

of patients showed a >7 pt decrease in mLSS

Responses were observed across patients with prior exposure to approved agents including ibrutinib, ruxolitinib, and/or belumosudil

1) Measured from first response to new systemic therapy or death, based on the Kaplan Meier estimate
2) mLSS = modified Lee chronic GVHD Symptom Scale score

Axatilimab was generally well tolerated

Parameter, n (%)	0.3 mg/kg Q2W
	N=79
≥ Grade 3 treatment-related AE	14 (17.7)
Discontinued treatment for AE	5 (6.3)

Most frequent adverse events of any grade	
Parameter, n (%)	**0.3 mg/kg Q2W**
	N=79
Aspartate aminotransferase increased	11 (13.9)
Blood creatine phosphokinase increased	9 (11.4)
Lipase increased	9 (11.4)
Blood lactate dehydrogenase increased	11 (13.9)
Alanine aminotransferase increased	10 (12.7)
Fatigue	18 (22.8)

Most common adverse events were consistent with on target effects of CSF-1 inhibition and prior trials of axatilimab

Higher frequency of adverse events were observed at doses above 0.3 mg/kg Q2W

Parameter, n (%)	0.3 mg/kg Q2W	1.0 mg/kg Q2W	3.0 mg/kg Q4W	Total
	N=79	N=81	N=79	N=239
≥ Grade 3 treatment-related AE	14 (17.7)	28 (34.6)	37 (46.8)	79 (33.1)
Discontinued treatment for AE	5 (6.3)	18 (22.2)	14 (17.7)	37 (15.5)

Any grade adverse events in >20% of patients				
Parameter, n (%)	**0.3 mg/kg Q2W**	**1.0 mg/kg Q2W**	**3.0 mg/kg Q4W**	**Total**
	N=79	N=81	N=79	N=239
Aspartate aminotransferase increased	11 (13.9)	31 (38.3)	43 (54.4)	85 (35.6)
Blood creatine phosphokinase increased	9 (11.4)	26 (32.1)	49 (62.0)	84 (35.1)
Lipase increased	9 (11.4)	21 (25.9)	39 (49.4)	69 (28.9)
Blood lactate dehydrogenase increased	11 (13.9)	22 (27.2)	32 (40.5)	65 (27.2)
Alanine aminotransferase increased	10 (12.7)	18 (22.2)	31 (39.2)	59 (24.7)
Fatigue	18 (22.8)	16 (19.8)	21 (26.6)	55 (23.0)

AGAVE-201 positive results observed in a heavily pretreated, late stage cGVHD population

Population (ITT)	ROCKSTAR N=132	AGAVE-201 N=241
Age median (min, max), years	56 (21, 77)	53 (7, 81)
Median time since cGVHD diagnosis	25.3 months	48 months
≥ 4 organs involved	52%	54%
% Patients with lung manifestations	36%	45%
% patients with NIH severe cGVHD	67%	80%
Median prior therapies	3	4
≥ 4 prior lines of treatment	49%	65%
Prior ruxolitinib	29%	74%
Prior ibrutinib	34%	31%
Prior belumosudil	N/A	23%

AGAVE-201 Differentiation

Significantly longer time since diagnosis

More severe cGVHD

More reflective of real-world treatment

Significant unmet need remains across all lines of therapy

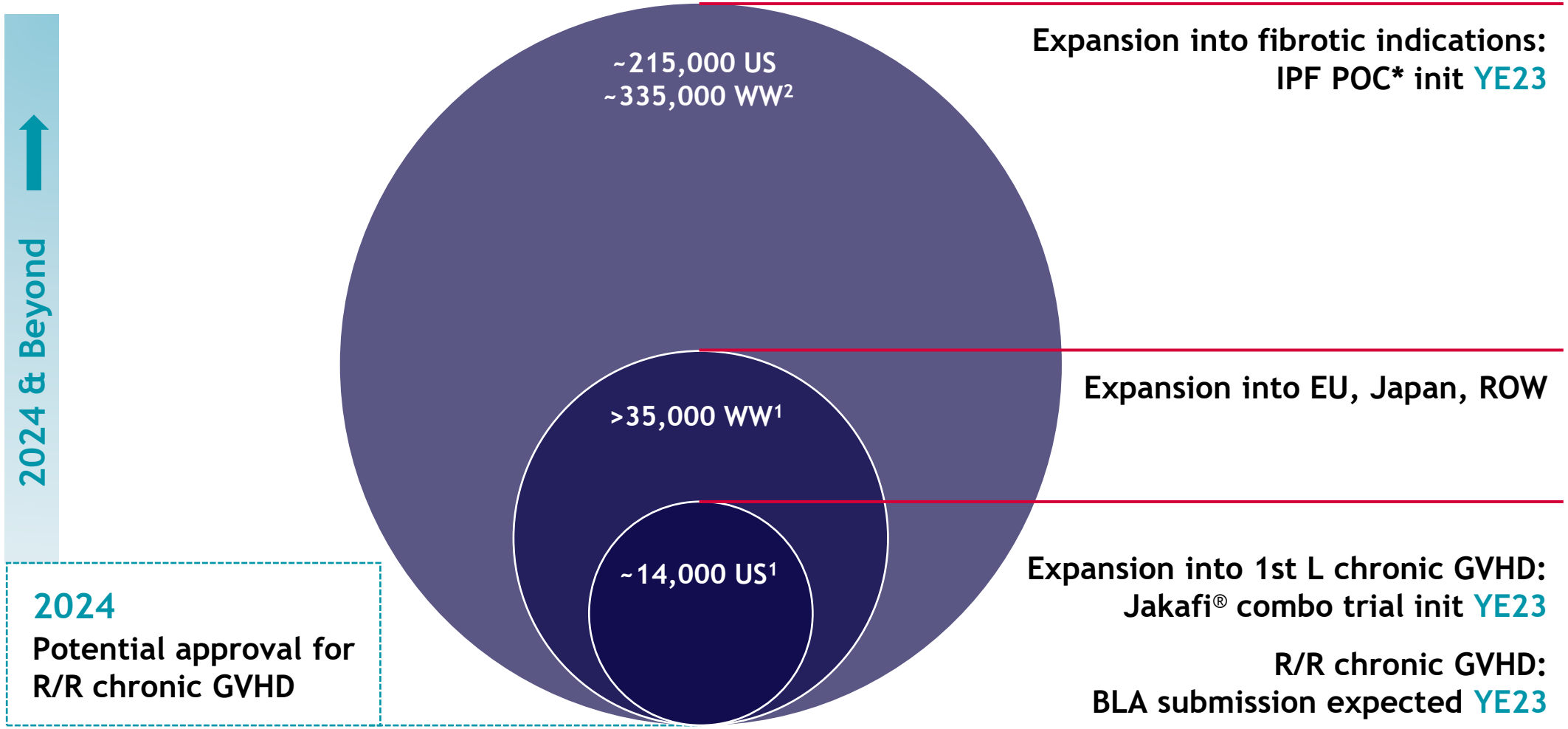
If approved, axatilimab will provide a differentiated mechanism from currently approved agents for patients with refractory cGVHD despite at least 2 prior therapies

Current Standard of Care[1]

1st Line	Corticosteroids
2nd Line	JAKAFI® IMBRUVICA®
3rd Line	REZUROCK®

1. U.S. Regulatory approvals in cGVHD: Imbruvica® - August 2017, Rezurock® - July 2021, Jakafi® - September 2021

Axatilimab has the potential to expand into additional high value indications and new geographies



1 SmartImmunology Insights cGVHD report March 2020; 2 SmartImmunology Insights IPF report March 2020. * IPF trial will be conducted and funded by Syndax

Financial highlights and financial guidance

Ticker	SNDX (NASDAQ)
Cash and equivalents✦ (at 30 June 2023)	$418.3 million
Shares outstanding* (at 30 June 2023)	69.7 million

2023 Operating Expense Guidance		
	3Q 2023	FY23 (no change)
Research and development	$39 – $43 million	$160 – $175 million
Total operating expenses^	$57 – $62 million	$225 – $240 million

* *Includes pre-funded warrants to purchase 1.1 million common shares (rounded)*
^ *Includes an estimated $30 million in non-cash stock compensation expense for the full year 2023*
✦ *Includes short- and long-term investments*


Determined to realize a future in which people with cancer live longer and better than ever before.