# Syndax

**Reimagining Cancer Treatment**

Corporate Presentation at the JP Morgan Healthcare Conference / January 8, 2024

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# Syndax: An oncology company with 2 near-commercial heme assets

- Two clinically **potential first-** and **best-in-class** hematology assets
  - **Revumenib**, novel menin inhibitor, targeting KMT2Ar and mNPM1 acute leukemia
  - **Axatilimab**, first CSF-1R mAb **targeting cGVHD**
- Revumenib NDA submitted for R/R KMT2Ar acute leukemia under RTOR
  - Potential to access ~$2B market opportunity in R/R KMT2Ar and mNPM1 acute leukemia; opportunity to access larger markets with expansion into frontline
- Axatilimab BLA submitted for refractory chronic GVHD with partner Incyte
  - ~$2B market opportunity for 3L+ cGVHD; opportunity to access larger markets with expansion into earlier lines and additional indications
  - Syndax exercised option to co-commercialize axatilimab in the U.S. with Incyte
- Strong IP supporting both assets with LOE to 2040
- Well capitalized with cash runway through 2026

**Significant Presence at ASH 2023**

**Safety and Efficacy of Axatilimab at 3 Different Doses in Patients with Chronic Graft-Versus-Host Disease (AGAVE-201)**

**Session:** Plenary Scientific

**Revumenib Monotherapy in Patients with Relapsed/Refractory KMT2Ar Acute Leukemia: Topline Efficacy and Safety Results from the Pivotal Augment-101 Phase 2 Study**

**Session:** Late-Breaking Abstracts



KMT2Ar, KMT2A rearrangement; mNPM1, mutated nucleophosmin; cGVHD, Chronic graft-versus-host disease; R/R, relapsed or refractory; LOE, Loss of exclusivity

# Revumenib - Menin Inhibitor

Potential approval in adult and pediatric R/R KMT2Ar acute leukemia in 2024 with opportunities for additional indications

# Despite recent advances in AML and ALL, treatment options are needed for patients with KMT2Ar and mNPM1 acute leukemias

## KMT2Ar Acute Leukemia

**10%**

of AML or ALL[1]

Most patients relapse after chemotherapy and HSCT

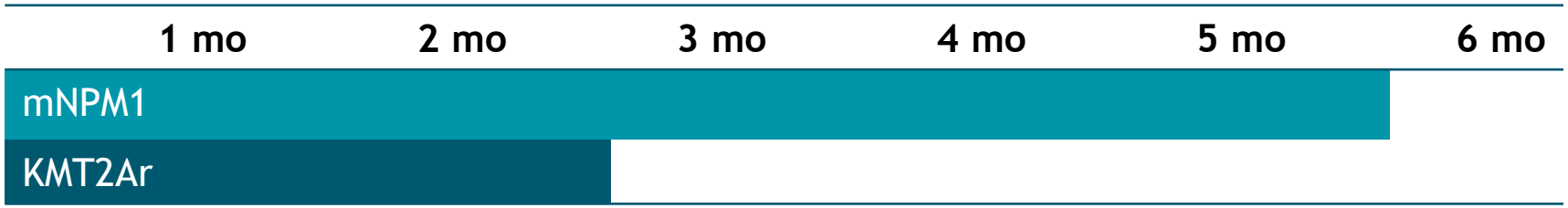
## NPM1 Mutant AML

**30%**

of AML[2]

Most frequent genetic alteration in AML

### Median overall survival in 3rd line AML[1,3]




Revumenib has demonstrated positive clinical results in both KMT2Ar and mNPM1 acute leukemia populations

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1) Issa, G. et al. (2021). Predictors of outcomes in adults with acute myeloid leukemia and KMT2A rearrangements. 2). Falini, B. et al, NPM1-mutated acute myeloid leukemia: from bench to bedside. Blood (2020) 136 (15) 3) Issa G. et al. Clinical outcomes associated with NPM1 mutations in patients with relapsed or refractory AML. Blood Adv. 2023 Mar 28;7(6) ; OS, Overall response; HSCT, Haematopoietic stem cell transplant

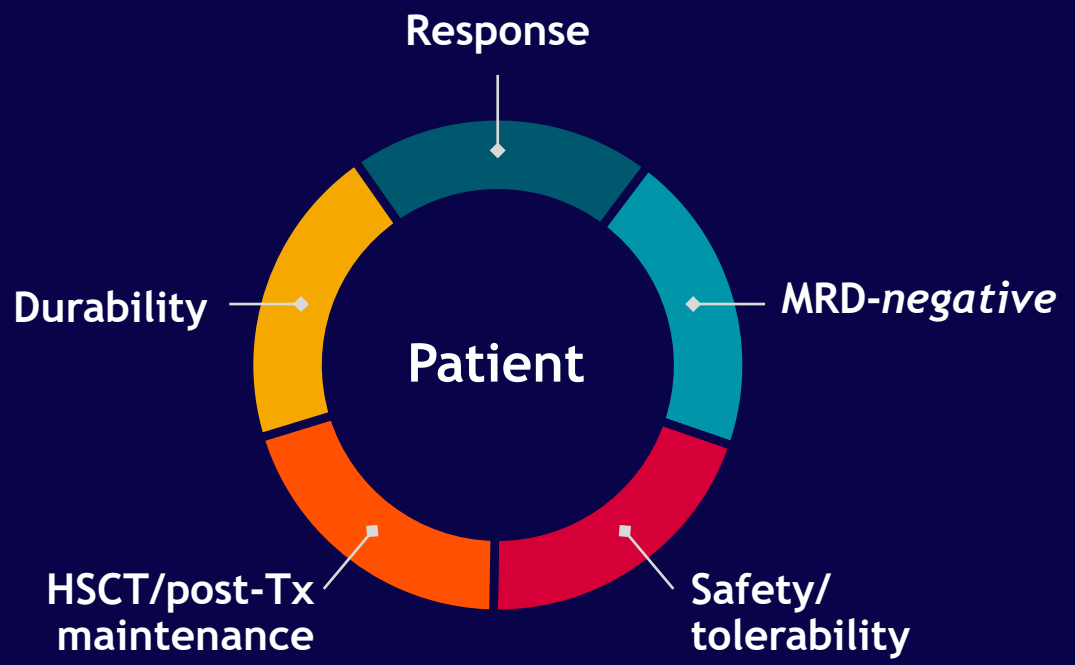
# Revumenib is a potential first- and best-in-class therapy for KMT2Ar and mNPM1 acute leukemia

**Revumenib monotherapy results to date:**

- Clinically meaningful efficacy in R/R KMT2Ar and mNPM1 acute leukemia
- Durable responses observed in post-transplant maintenance, even in heavily pretreated patients

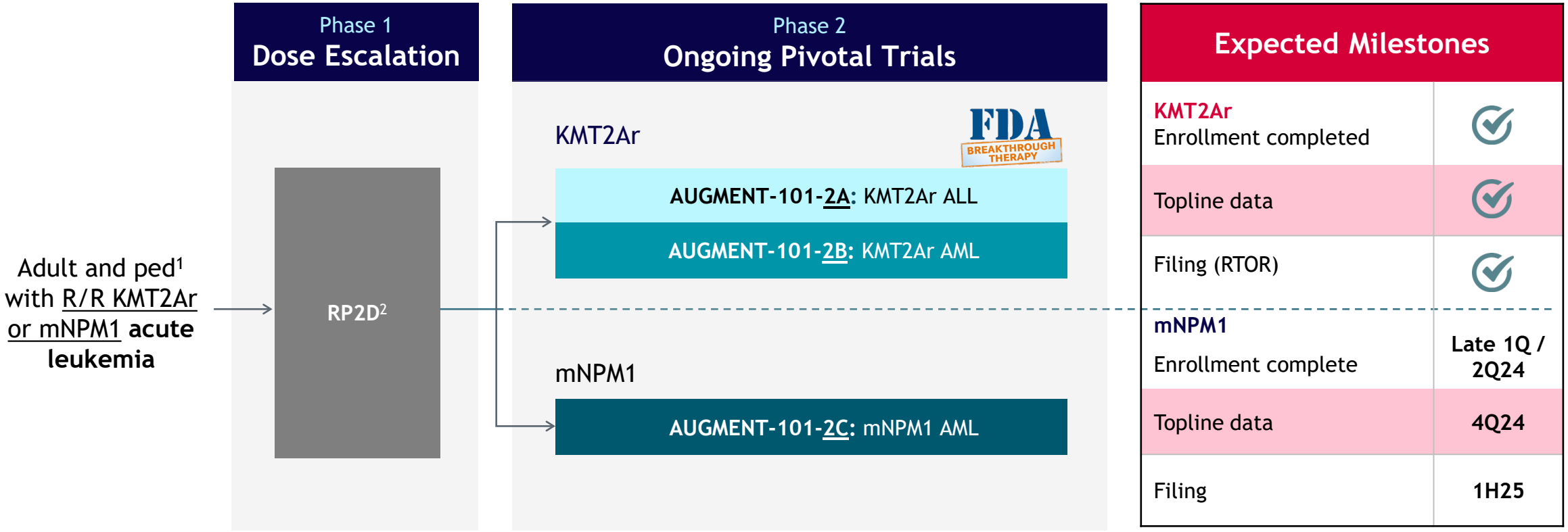
**Revumenib combination results to date:**

- Ven–HMA combos shows safe and highly effective profile for both frontline and R/R AML
- FLA chemo combo shows safe and effective profile in R/R AML patients, including those relapsed on FLA




Revumenib delivers on key metrics that address the needs of patients and drive physician utilization

# Pivotal AUGMENT-101 trial: Topline data supported NDA filing for KMT2Ar AML/ALL under RTOR in 4Q23; potential filing for mNPM1 in 1H25




Primary endpoint

**CR Rate** (CR + CRh)

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

# KMT2Ar pivotal data establishes compelling clinical activity across acute leukemia patients; drives durable, MRD$^{neg}$ responses

| | |
|---|---|
| 63% | Overall response rate in pooled analysis |
| 23% | CR/CRh rate in pooled analysis |
| 70% | MRD negative rate among CR/CRh responses |
| 8.0mos | Overall survival |
| 6.4mos | Median duration of CR/CRh at data cutoff |

Enables a high rate of deep, durable MRD$^{neg}$ responses in late line R/R patients

Responses observed across all major subgroups

Favorable safety and tolerability profile with low 6% treatment discontinuations due to TRAEs



Data Cutoff July 24, 2023; TRAEs, Treatment related adverse events; DS, Differentiation syndrome

# Revumenib creates potential new opportunities for patients - enabling a meaningful shift in the treatment of R/R KMT2Ar acute leukemia

## Anticipated KMT2Ar treatment paradigm pending approval of revumenib

Relapsed or Refractory
(n = 57)

Revumenib

**63%** respond
(36/57)

HSCT

**39%** receive transplant^

Revumenib maintenance

**71%** received or eligible for post-transplant maintenance*
(10/14)

^ *8 of 14 patients went to transplant without achieving a CR or CRh*
* *7 patients received post-transplant maintenance, 3 remained eligible to choose post-transplant maintenance as of data cut*

Revumenib induces MRD- complete responses, supports high rates of stem cell transplant and long-term post-transplant maintenance

# mNPM1 AML: Phase 1 data suggest robust efficacy

## Pivotal trial enrollment ongoing

| Phase 1 Dose Escalation | |
|---|---|
| | n (%) |
| Total mNPM1 @ RP2D | 14 |
| CR/CRh | 5 (36%) |
| MRD- CR/CRh | 5 (100%) |
| ORR | 7 (50%) |

No treatment related discontinuations
No grade 4 or 5 QTc events
≤ grade 2 differentiation syndrome

- 3/7 responders proceeded to HSCT
- 1 patient restarted revumenib post HSCT*
- 3/5 of CR/CRh maintained response beyond 6 months, 2 for >22 months
- TRAEs in-line with overall AUGMENT-101 Phase 1/2 experience

* Data cutoff of July 24, 2023; 2023 amendment allowed patients to restart treatment with revumenib post-transplant following HSCT; mNPM1, mutated nucleophosmin; HSCT, Haematopoietic stem cell transplant; RP2D, Doses that met exposure equivalent of 226 mg q12h or 276mg q12h without strong CYP3A4 inhibitor or 113 mg q12h or 163 mg q12h with strong CYP3A4 inhibitor

# Beat AML: Ven/Aza + revumenib in newly diagnosed mNPM1 or KMT2Ar AML

| Summary of Enrolled Patients & Response Data | |
|---|---|
| | **N=13** |
| Total enrolled | KMT2Ar: 5<br>mNPM1: 8 |
| **Response and Transplant** | |
| **CRc** | **13 (100%)** |
| CR/CRh | 11* (85%) |
| CRi | 2 (15%) |
| **Transplant** | **2** |
| **Relapse** | **1** |
| **MRD Flow Status** | |
| $MRD^{neg}$ | 12 (92%) |
| Unk | 1 (8%) |

## Safety Summary

- No increased safety issues outside of known reported ven/aza toxicities
- 1 Hematologic DLT observed in DL1a: platelets exceeded 42 days to recover, no other DLTs across both dose levels (113 mg and 163 mg q12h)
- Cytopenias manageable with continuous dosing of venetoclax and full dose revumenib

Trials are expanding to validate RP2D; additional data expected in 2H24



Data Cutoff Dec 01, 2023; KMT2Ar, KMT2A rearrangement; mNPM1, mutated nucleophosmin; DLT, Dose limiting toxicity; RP2D, Recommended Phase 2 dose

# Save AML: Ven/HMA combo in relapsed mNPM1, NUP98 or KMT2Ar AML/MPAL

| Summary of Enrolled Patients & Response Data | | | |
|---|---|---|---|
| | | N (%) | Subtype |
| Total enrolled | | 9 | KMT2Ar: 5; mNPM1: 1<br>NUP98r: 2 |
| Median prior Tx | | 3 | 56% received prior VEN<br>67% received prior HSCT |
| **Best response** | | | **Subtype** |
| **ORR** | | **9 (100%)** | **KMT2Ar + NUP98r + mNPM1** |
| **CRc 78%** | **CR / CRh*** | **4 (44%)** | **3 KMT2Ar + 1 NUP98r** |
| | **CRp** | **3 (33%)** | **1 mNPM1 + 2 KMT2Ar** |
| | MLFS | 1 (11%) | 1 NUP98 |
| | PR | 1 (11%) | 1 NUP98r |
| MRD$^{neg}$ | | 6 (67%) | * 100% MRD$^{neg}$ CR/CRh |

## Safety Summary

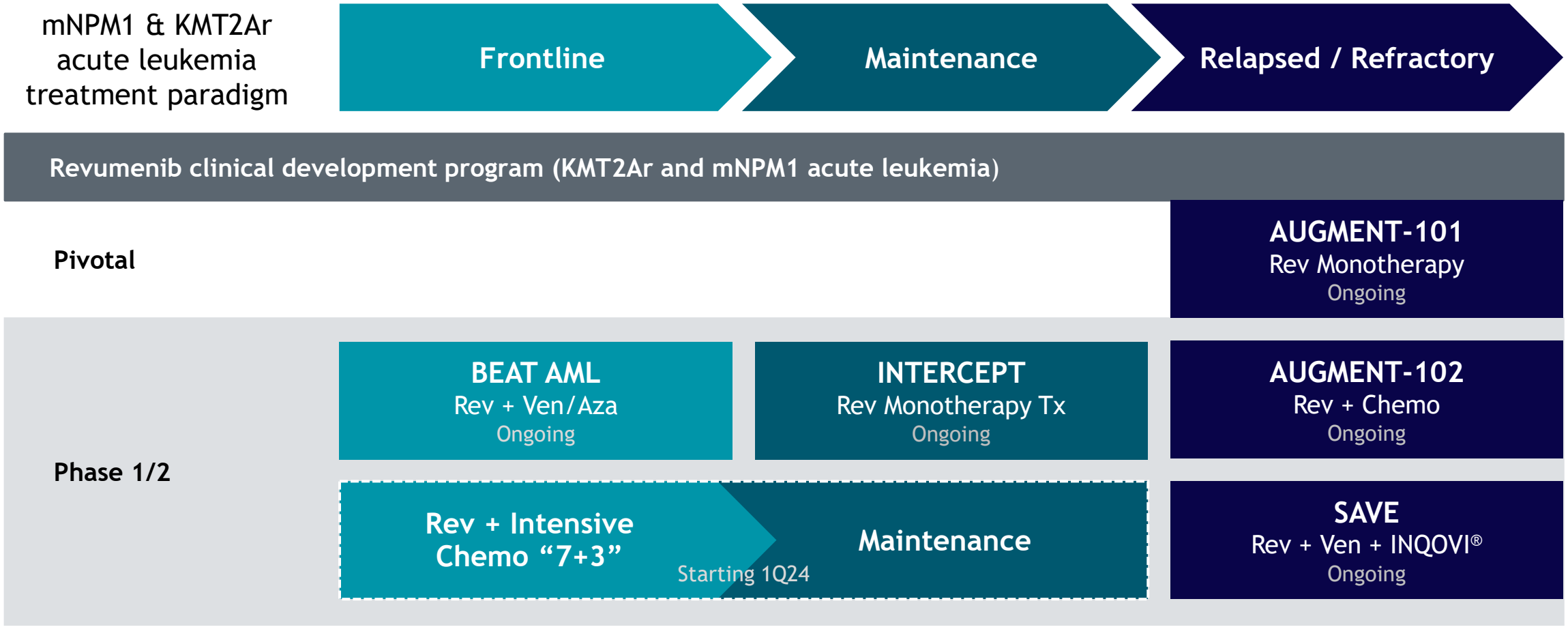
- No discontinuations for TRAEs, No ≥ Gr 3 QTc
- Myelosuppression comparable to venetoclax-HMA
- No new safety signals observed beyond those reported for venetoclax-HMA

Trials are expanding to validate RP2D; additional data expected in 2H24



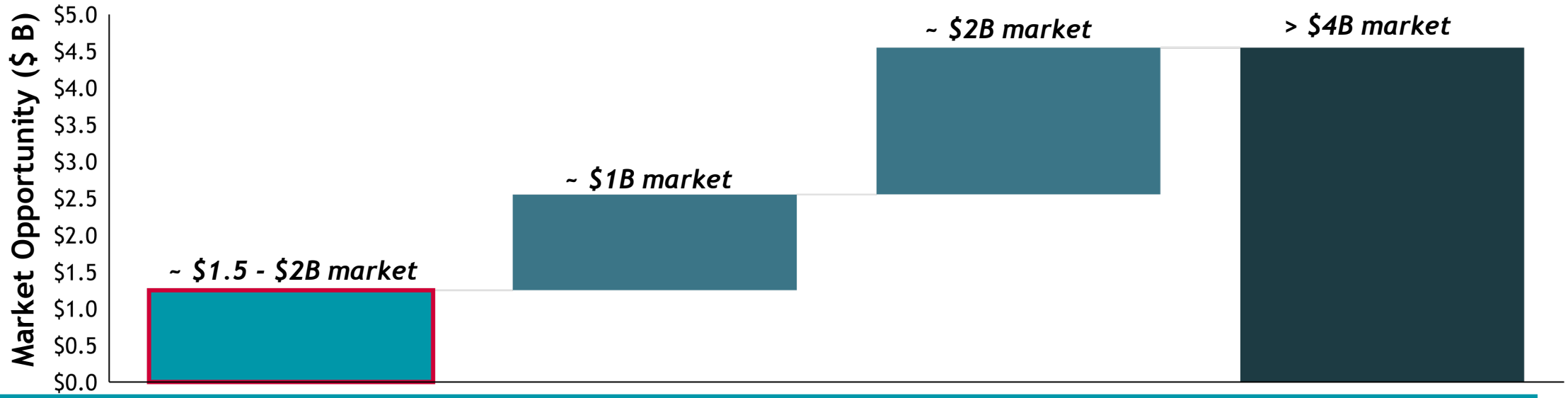
Data Cutoff Nov 01, 2023;' KMT2Ar, KMT2A rearrangement; mNPM1, mutated nucleophosmin, NUP98r, Nucleoporin 98; RP2D, Recommended Phase 2 dose

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



# Revumenib's profile supports use as backbone therapy across treatment continuum — providing access to >$4B US market opportunity

## Significant growth potential with indications in earlier lines of treatment



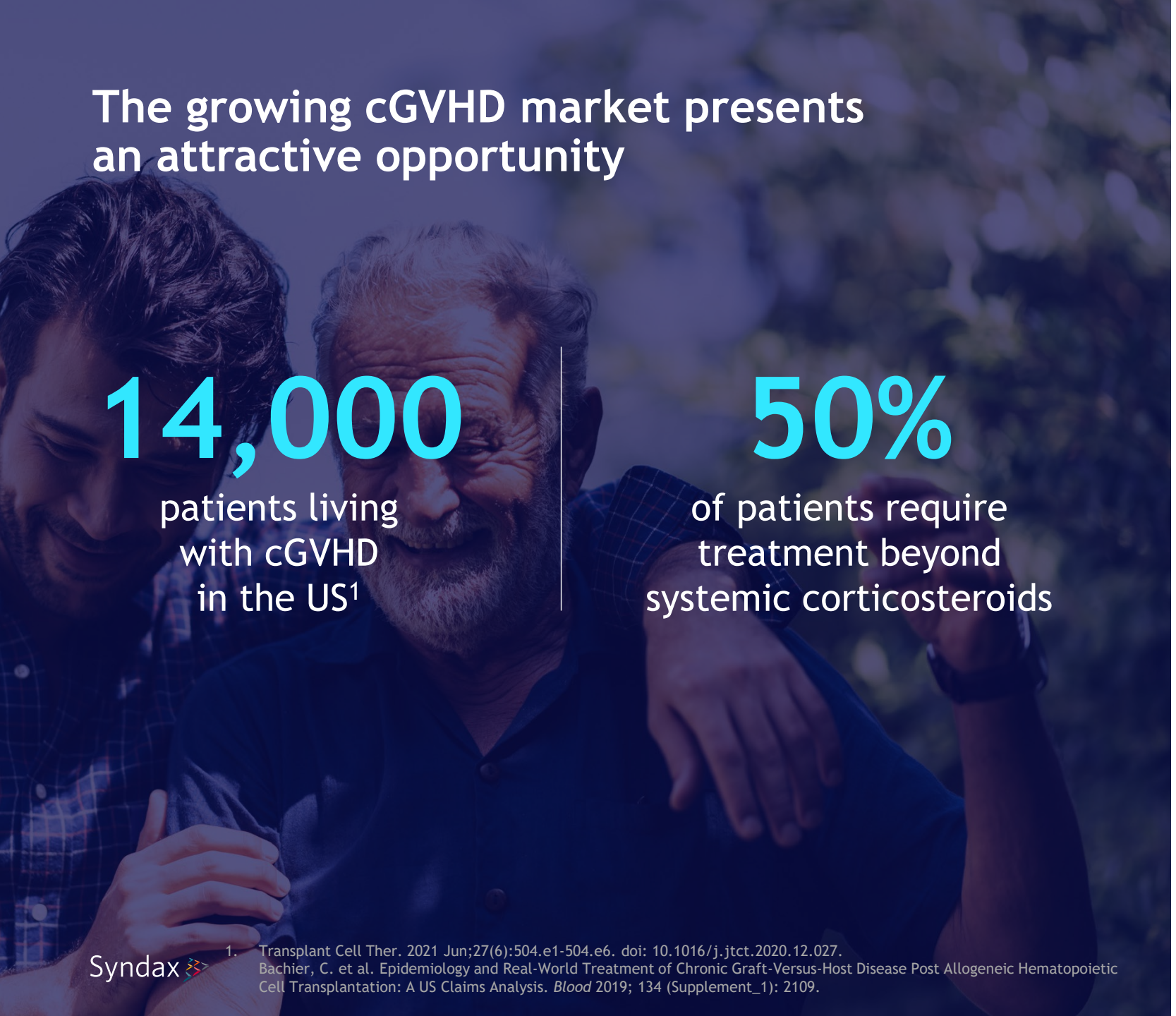

| | R/R KMT2Ar + NPM1 Acute Leukemia | 1L "Unfit" KMT2Ar + NPM1 Acute Leukemia | 1L "Fit" KMT2Ar + NPM1 Acute Leukemia | Total |
|---|---|---|---|---|
| Est. patient population | 5,000 - 6,500 | ~3,500 | ~5,500 | |

Source: Data on file; Redbook 2023

# Axatilimab – anti-CSF-1R

Potential approval in patients with refractory chronic graft-versus-host disease in 2024 with opportunities for additional indications

# The growing cGVHD market presents an attractive opportunity



**14,000**

patients living with cGVHD in the US[1]

**50%**

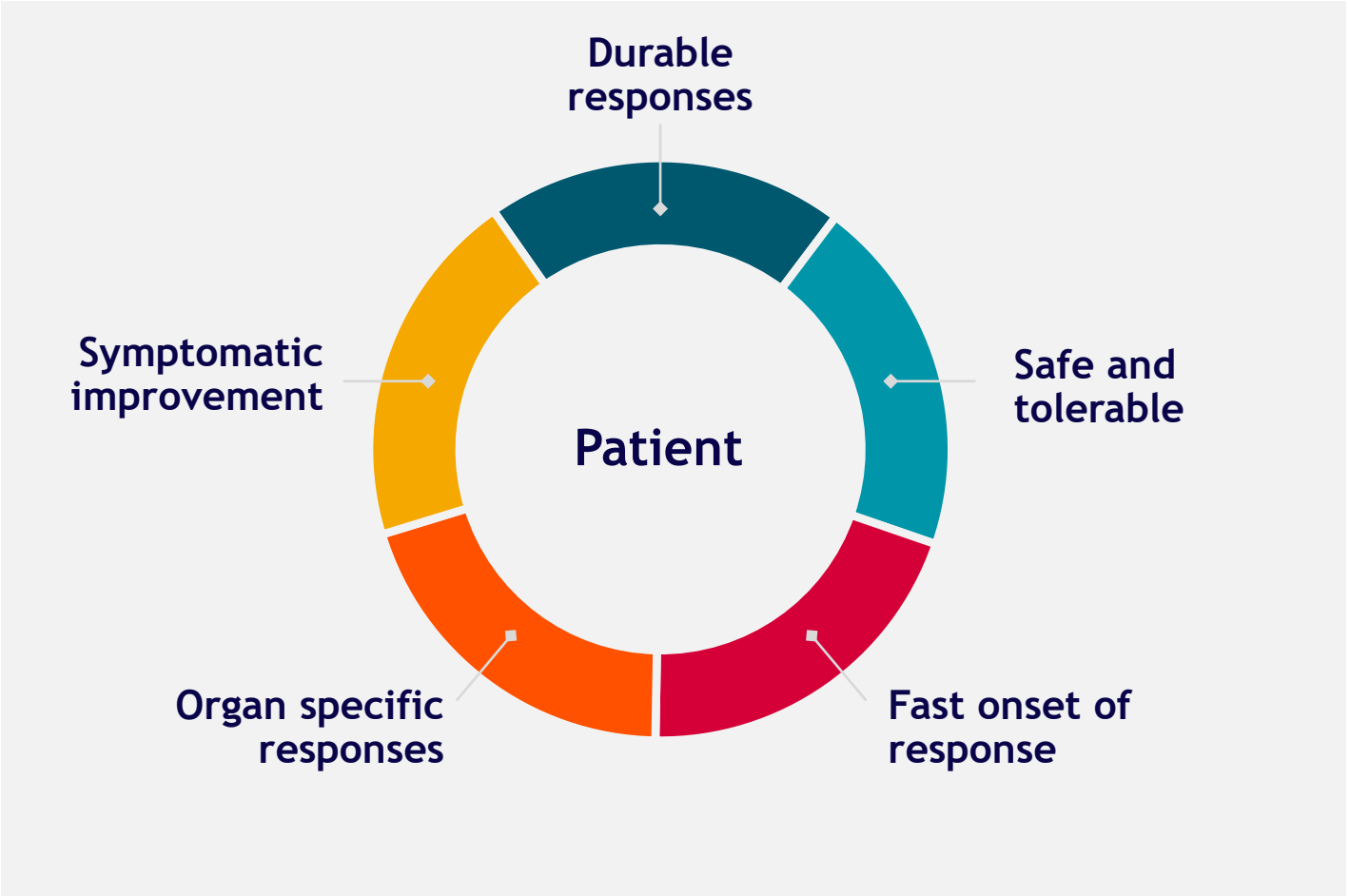
of patients require treatment beyond systemic corticosteroids

## The estimated global chronic GVHD market is expected to expand due to[1]:

- Rising prevalence of blood cancers boosted by an increase in the aging population
- Rise in stem cell transplants

1. Transplant Cell Ther. 2021 Jun;27(6):504.e1-504.e6. doi: 10.1016/j.jtct.2020.12.027. Bachier, C. et al. Epidemiology and Real-World Treatment of Chronic Graft-Versus-Host Disease Post Allogeneic Hematopoietic Cell Transplantation: A US Claims Analysis. *Blood* 2019; 134 (Supplement_1): 2109.

# Axatilimab is positioned to address what physicians and patients are seeking in a new cGVHD therapy



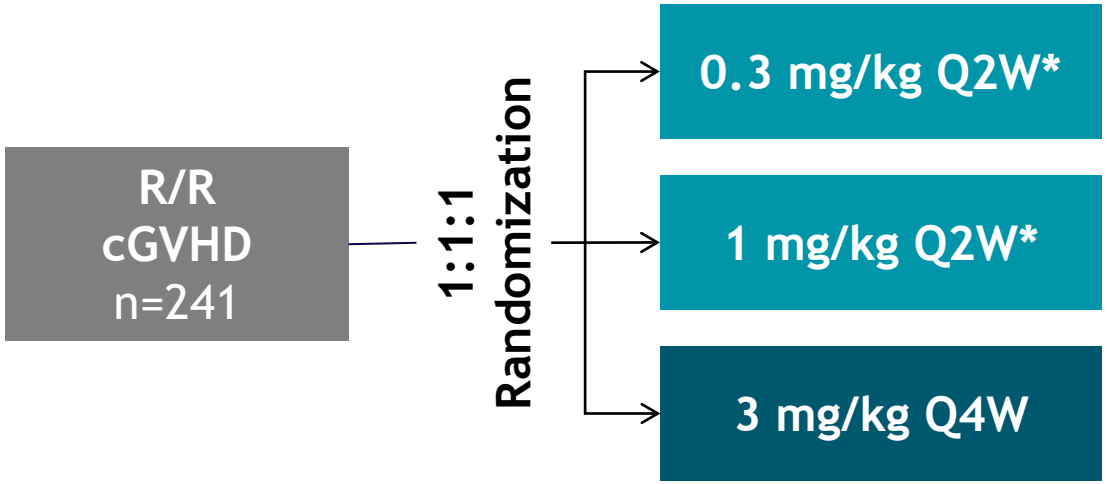

## Axatilimab Key Attributes

- Demonstrates compelling clinical profile
- Unique MOA in cGVHD
- Benefits in fibrotic and inflammatory components
- Consistent results across all key patient subsets with responses in all organ systems



MOA, Mechanism of action

# Pivotal AGAVE-201 trial: 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

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[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

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

**74%** ORR by cycle 7 day 1 (95% CI [63, 83])

**60%** Of responders maintained a response at 1 year

**55%** Of patients had a ≥7 point decrease in mLSS

Met the primary endpoint in patients with R/R cGVHD

Durable responses with a reduction in symptom burden

Well tolerated, and the most common adverse events were consistent with on-target effects and prior trials

Complete responses were observed across all organ system, and across patients with prior exposure to approved agents including ibrutinib, ruxolitinib, and/or belumosudil

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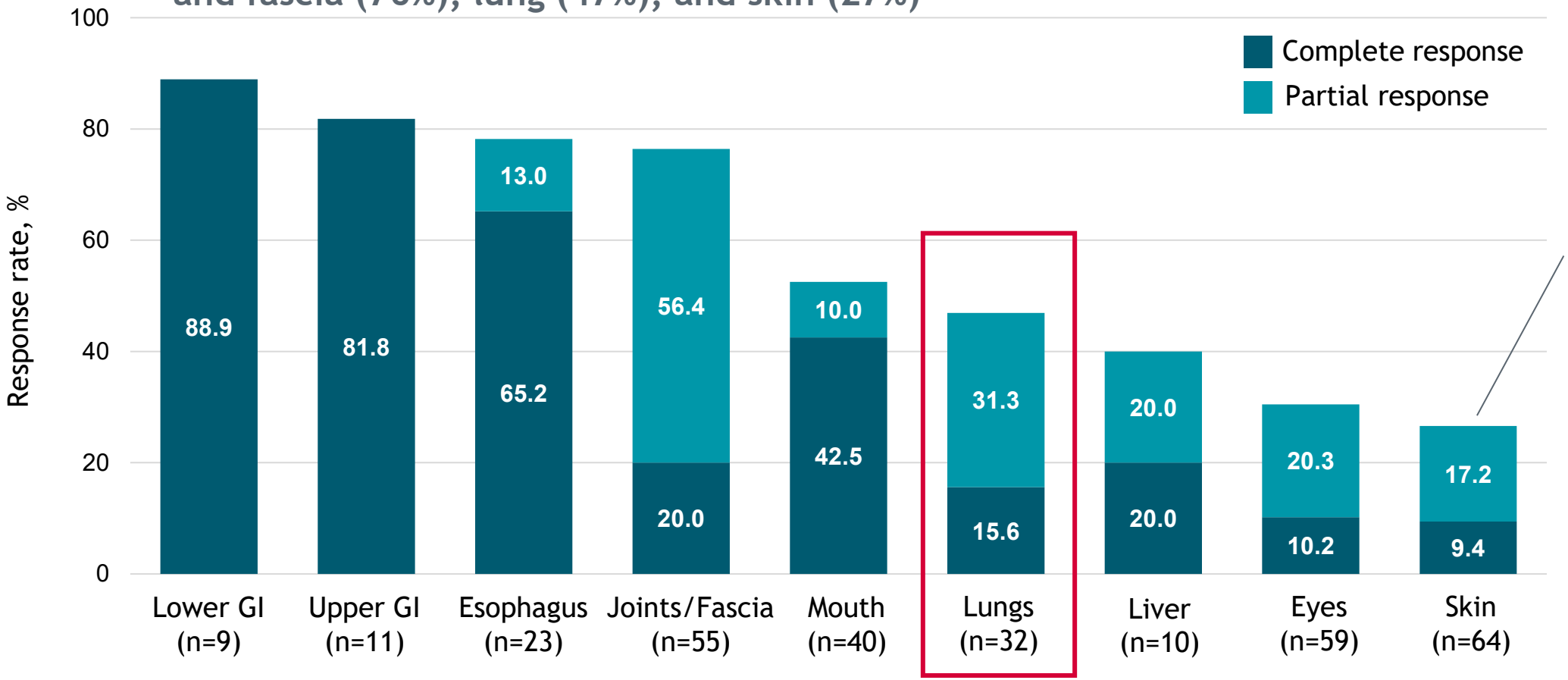
Data source: AGAVE-201 topline data at the 0.3 mg/kg dose

[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

# Organ responses in 0.3 mg/kg Q2W

## Responses notable in fibrosis-dominated organs, including esophagus (78%), joints and fascia (76%), lung (47%), and skin (27%)




44% had reduction in BSA involved by sclerosis

66% had improvement in skin and joint tightening severity

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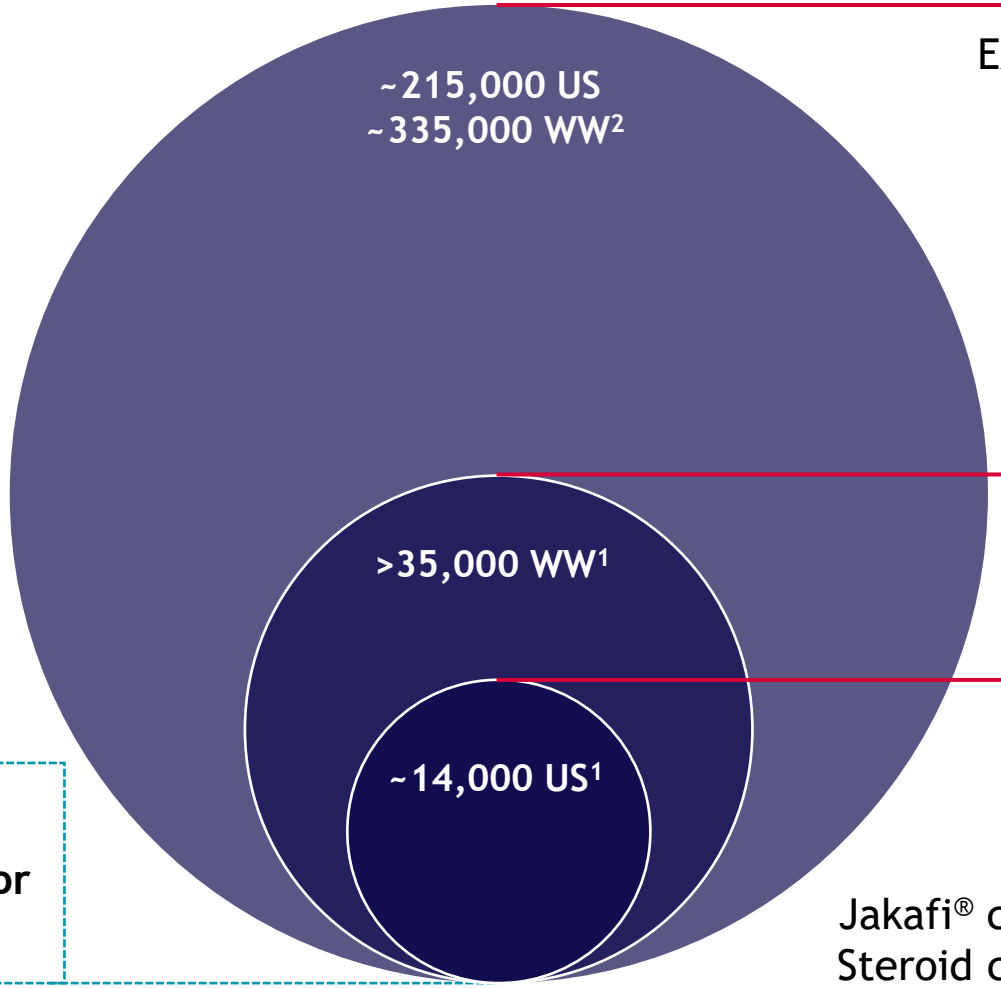
BSA; body surface area; GI, gastrointestinal; Q2W, every 2 weeks.

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

2024 & Beyond




Expansion into fibrotic indications:
IPF POC* initiated in 4Q23

Expansion into EU, Japan, ROW

R/R chronic GVHD:
BLA submitted YE23

Expansion into 1st L chronic GVHD:
Jakafi® combo trial expected to init mid-24
Steroid combo trial expected to init mid-24

**2024**
**Potential approval for R/R chronic GVHD**

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

# Financial highlights

| Ticker | SNDX (NASDAQ) |
|---|---|
| Cash and equivalents✦ (30 Sept 2023) | $379.3 million |
| Approximate net proceeds from follow-on offering and ATM in 4Q23# | $258.0 million |
| Shares outstanding* # (19 Dec 2023) | 84.8 million |

| 2023 Operating Expense Guidance | |
|---|---|
| | FY23 |
| Research and development | $160 - $165 million |
| Total operating expenses^ | $225 - $230 million |

✦ *Includes short- and long-term investments*
* *Includes pre-funded warrants to purchase 285,714 common shares (rounded)*
# *Includes approximate net proceeds a*fter deducting underwriting discounts and commissions and estimated offering expenses payable by us for December follow-on offering and *$42.1 million from the sale of shares pursuant to the Company's ATM program subsequent to 30 Sept 2023*
^ *Includes an estimated $32 million in non-cash stock compensation expense for the full year 2023*

# Expected upcoming clinical milestones

## REVUMENIB
*Menin-KMT2A disruption*

- Potential approval in adult and pediatric R/R KMT2Ar acute leukemia in 2024
- Initiate combination trial with intensive chemo (7+3) in 1Q24
- Phase 1 metastatic CRC data from dose escalation phase in 1H24
- Complete pivotal mNPM1 enrollment in late 1Q24/early 2Q24; topline data in 4Q24
- Expansion cohort data for several Phase 1 combination trials in 2H24
- Initiate pivotal combination trial with ven/aza by year-end 2024

## AXATILIMAB
*Anti-CSF-1R*

- Potential approval in adult and pediatric patients ≥ 6 years with cGVHD after failure of at least two prior lines of systemic therapy in 2024
- Initiate combination trial with Jakafi® in mid-24
- Initiate combination trial with steroids in mid-24