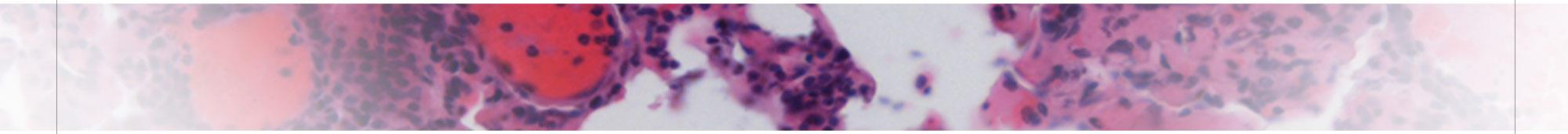
American Society *of* Hematology
Helping hematologists conquer blood diseases worldwide



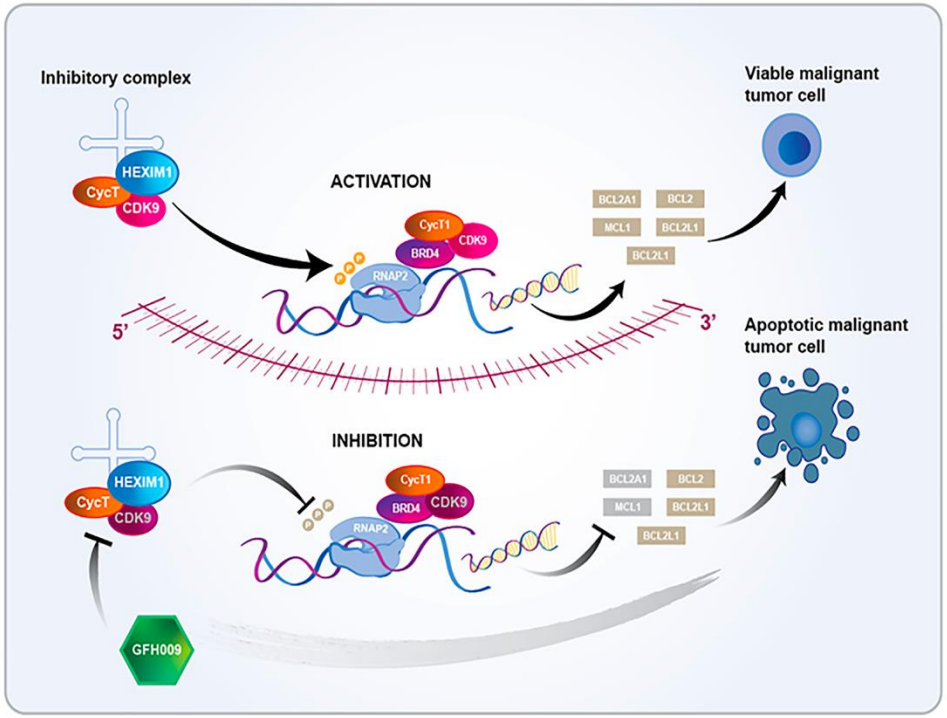
Phase 2a Study of SLS009, a Highly Selective CDK9 Inhibitor, In Combination with Azacitidine and Venetoclax for Relapsed/Refractory Acute Myeloid Leukemia After Prior Venetoclax Treatment

Joshua F. Zeidner, MD[a], *Omer Jamy, MD[b], Bradley W Christensen. MD[c] Sharif Khan, MD[d] , Dragan Cicic, MD[e], Tapan M. Kadia, MD[f]*

a. *University of North Carolina, Lineberger Comprehensive Cancer Center, Chapel Hill, NC*, b. *O'Neal Comprehensive Cancer Center at UAB – Hospital*, c. *Baylor Scott & White Research Institute*, d. *Bon Secours Hematology & Oncology – Oncology*, e. *Sellas Life Sciences Group*, f. *The University of Texas MD Anderson Cancer Center*

CDK9 as a Target & GFH009 Mechanism of Action

- Cyclin-dependent kinase 9 (CDK9) is a transcriptional regulator of multiple oncogenes, including short-lived ones like ***MCL-1*** and ***c-MYC***[1,2]
  - Upregulated in hematologic malignancies and play a role in proliferation and survival of cancerous cells[1,2]
- CDK9 inhibition can slow or stop cell cycle progression indirectly through a key mechanism[2,3]
  - Perturbation of the P-TEFb complex – which is required for initiation of RNA Polymerase II transcription
  - Downregulation of short-lived downstream proteins needed for cell differentiation and survival

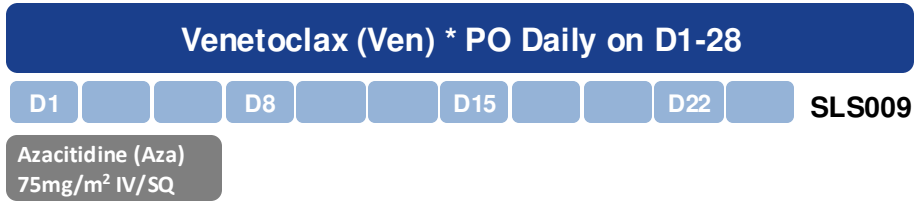


1. Zhou F, et al. *Oncotarget*. 2023;14(1):997-1008. 2. Zhou F, et al. AJPP. 2023;10(2):151. 3. Anshabo AT, et al. *Front Oncol*. 2021;11.

GFH009 + Aza/Ven Phase 2a Trial in Ven-R/R AML

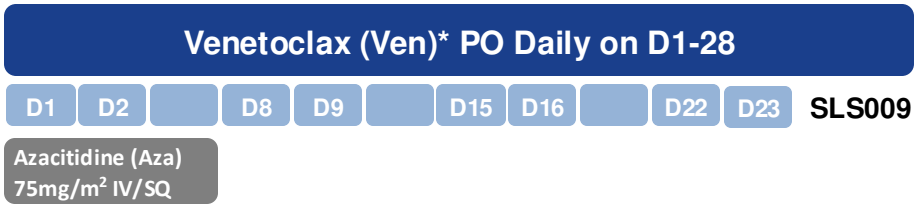
Study Design

Weekly Dosing



- *Ven 400 mg daily (dose reduced w/ azoles)
- DL1: SLS009 45 mg IV QW
- DL2: SLS009 60 mg IV QW

Bi-Weekly Dosing



- DL3: SLS009 30 mg IV BIW

Eligibility and Endpoints

Eligibility Criteria:

- ≥18 years w/ R/R AML after Ven-based regimen
- ECOG PS = 0-2
- N up to 30 pts

Primary Endpoints:

- Safety & tolerability of SLS009 + Aza/Ven
- Composite Complete Remission Rates

Secondary Endpoints:

- Overall Survival and Event-Free Survival
- PK of SLS009 w/ Aza/Ven

Patient Characteristics

- **30 patients treated overall**
  - DL1 (45 mg IVQW): n=10
  - DL2 (60 mg IVQW): n=9
  - DL3 (30 mg IVBIW): n=11

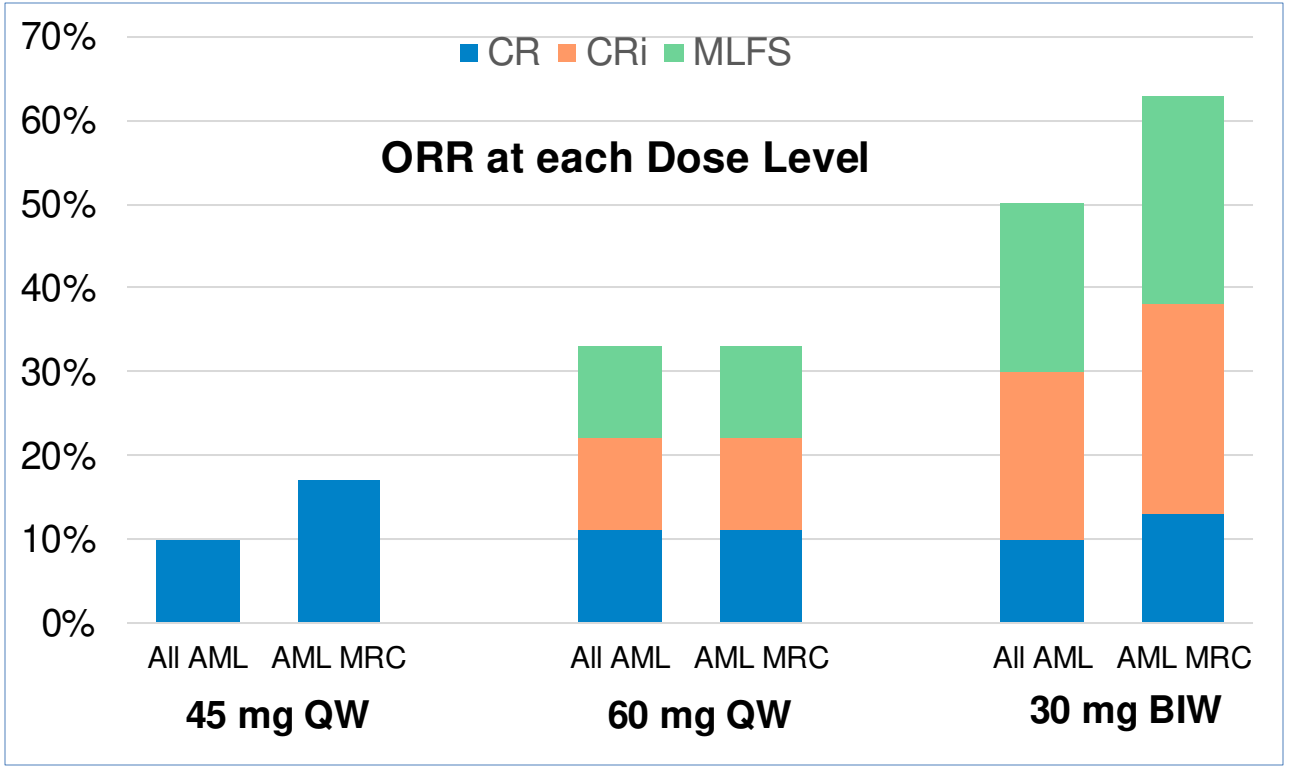
Characteristic	N=30
Age: Median (Range), Years	71 (41-84)
>70 years	20 (67%)
Female	13 (43%)
# of prior lines of therapy: Median (Range)	2 (1-4)
2022 ELN Risk Favorable-Risk Intermediate-Risk Adverse-Risk	 0 1 (3%) 29 (97%)
AML-MR	23 (77%)
Most frequent mutations *RUNX1* *ASXL1* *TP53* *TET2*	 11 (37%) 9 (30%) 9 (30%) 6 (20%)

Safety and Tolerability

- **Across all 3 dose levels, no dose limiting toxicities (DLTs) were observed**
  - No treatment-related mortality and no serious adverse reactions were observed

Toxicity	45 mg QW (N=10)		60 mg QW (N=9)		30 mg BIW (N=11)		All patients (N=30)	
	Any grade(%)	≥G3 (%)	Any grade(%)	≥G3 (%)	Any grade(%)	≥G3 (%)	Any grade(%)	≥G3 (%)
Nausea	3 (30%)	**0 (0%)**	2 (22%)	**0 (0%)**	2 (18%)	**0 (0%)**	7 (23%)	**0 (0%)**
Diarrhea	2 (20%)	**0 (0%)**	0 (0%)	**0 (0%)**	2 (18%)	**0 (0%)**	4 (13%)	**0 (0%)**
Pyrexia	1 (10%)	**0 (0%)**	1 (10%)	**0 (0%)**	0 (0%)	**0 (0%)**	2 (7%)	**0 (0%)**
Hyperphosph.	2 (20%)	**0 (0%)**	0 (0%)	**0 (0%)**	0 (0%)	**0 (0%)**	2 (7%)	**0 (0%)**
Leukopenias	3 (30%)	**3 (30%)**	1 (11%)	**1 (11%)**	0 (0%)	**0 (0%)**	4 (13%)	**4 (13%)**

Efficacy



- Among 29 evaluable patients-> 16 (55%) had >50% reduction in BM blasts compared to baseline
- 9 (31%) pts achieved ORR (CR+CRi+MLFS)
  - 5 (17%) achieved CR/Cri
  - 8/9 responses occurred w/in 1st cycle
- All 9 responders had AML-MR
  - 9/15 (39%) pts w/ AML-MR achieved ORR
- 5/9 (56%) pts w/ ASXL1 mut achieved ORR

Conclusions

- Addition of SLS009 to Aza/Ven safe and feasible without DLT's observed at any dose level in R/R AML patients after prior Venetoclax
- RP2D of SLS009 30 mg IV BIW + Aza/Ven in R/R AML
- Clinical activity observed with SLS009 + Aza/Ven
  - Primary endpoint (ORR > 20%) met
  - AML-MR enriched in responders
  - Highest clinical activity seen in *ASXL1* mutations
- Further development of SLS009 focused on AML-MRC patients after prior Venetoclax with and without *ASXL1* mutations.

Acknowledgements

We thank all of the patients and families who participated in this study