Sabizabulin

Presentation to the Pulmonary-Allergy Drugs Advisory Committee
EUA 000113

Veru Inc.

November 9, 2022

Introduction

Mitchell Steiner, MD
Chief Executive Officer and Chief Medical Officer
Veru Inc.

Agenda

Introduction	**Mitchell Steiner, MD** Chief Executive Officer and Chief Medical Officer Veru Inc.
Efficacy **Safety**	**K. Gary Barnette, PhD** Chief Scientific Officer Veru Inc.
Sensitivity Analysis	**Lee-Jen Wei, PhD** Professor of Biostatistics Harvard University, T.H. Chan School of Public Health
Benefit/Risk Assessment	**Christian Sandrock, MD, MPH** Division Vice Chief of Internal Medicine and Director of Critical Care University of California, Davis, School of Medicine
Concluding Remarks	**Mitchell Steiner, MD** Chief Executive Officer and Chief Medical Officer Veru Inc.

Hospitalized COVID-19 patients at high risk for ARDS remains a serious unmet medical need

- Over 1 million people have died from COVID-19 in the US
- Even with current standard of care treatments, COVID-19 infection is responsible for over 350 deaths each day in the US
- Risk of death and serious illness from COVID-19 infection remains high and unacceptable
- Another surge in new COVID-19 cases is expected this fall and winter in the US and has already begun in Europe
- We need effective and safe treatments to reduce deaths in hospitals, the greatest threat of the COVID-19 pandemic

Background

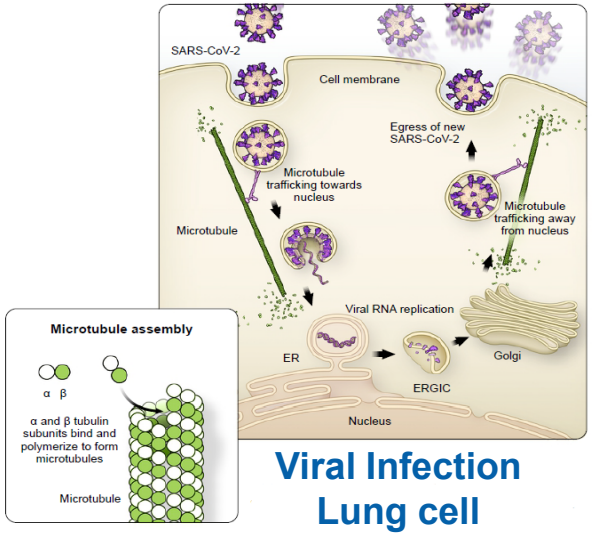
- Veru is a biopharmaceutical company focused on developing novel medicines for infectious disease and oncology
- Sabizabulin (VERU-111) is a novel oral microtubule depolymerization agent
  - When the COVID-19 pandemic started, sabizabulin was in Phase 3 clinical development for advanced prostate cancer
  - Mechanism of action suggests that sabizabulin could be both an antiviral and anti-inflammatory agent and novel treatment for COVID-19
- Initiated COVID-19 program, worked closely with the FDA, and received fast track designation based on our positive Phase 2 study in hospitalized critical COVID-19 patients
- In completed Phase 3 study, sabizabulin treatment demonstrated clear clinical benefit in hospitalized COVID-19 patients at high risk for ARDS and was published in the New England Journal of Medicine Evidence[1]

[1] Barnette KG, et al. Oral sabizabulin for high-risk hospitalized adults with COVID-19: Interim analysis. NEJM Evid. 2022;1(9).

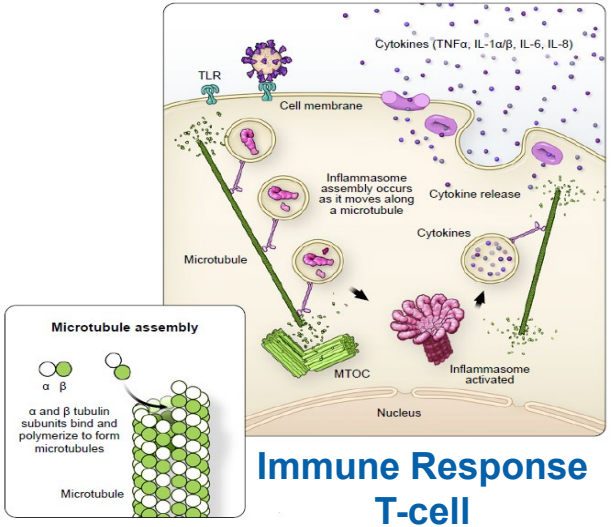
Sabizabulin has dual antiviral and anti-inflammatory activities to treat COVID-19 ARDS

Mechanism of action

- Sabizabulin targets and disrupts rapidly forming microtubules:
  - arresting **dividing cancer cells**
  - halting **virus transport**
  - suppressing **cytokine production and release**



Viral Infection Lung cell



Immune Response T-cell

References: 1. Baggin J, et al. *Nat Microbiol*. 2021;6:1219-1232; 2. V'kovski P, et al. *Nat Rev Microbiol*. 2021;19(3):155-170; 3. Bohn MK, et al. *Physiol* (Bethesda). 2020;35(5):288-301; 4. Zhang Q, et al. *Signal Transduct Target Ther*. 2021;6(1):233; 5. Boechat JL, et al. *Pulmonol*. 2021;27:423-437; 6. Hu B, et al. *J Med Virol*. 2021;93:250-256; 7. Montazersaheb S, et al. *Virol J*. 2022;19:92; 8. Wu D, et al. *Front Immunol*. 2022;13:826106. 9. Aminpour M, et al. *Life* (Basel). 2022;12(6):814.

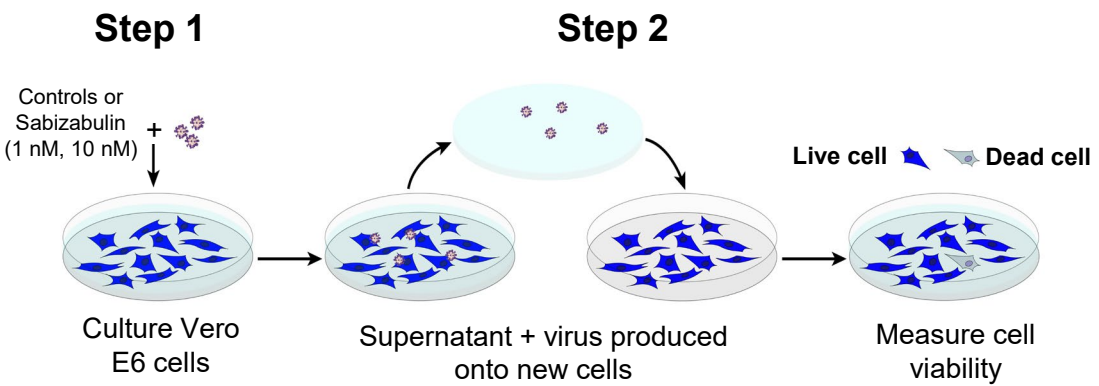
Preclinical studies confirm sabizabulin's dual mechanism of action against COVID-19

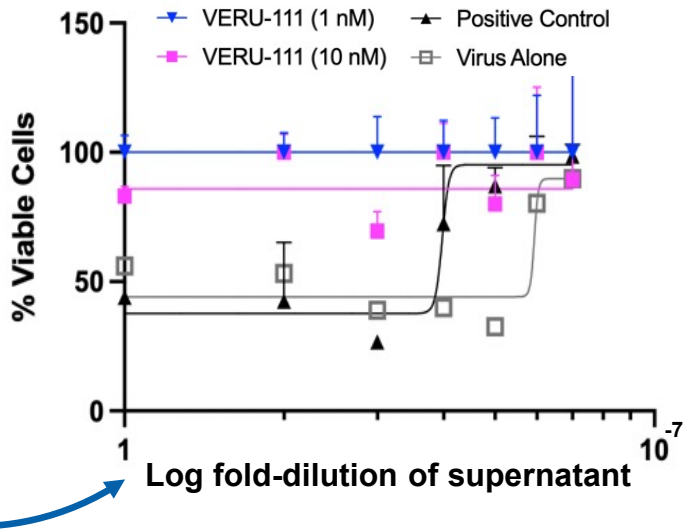
- Antiviral activity was observed in an infectious viral titer assay in SARS-CoV-2 infected cells *in vitro*
- Anti-inflammatory activity was demonstrated in septic shock mouse model *in vitro*

Sabizabulin suppressed production of SARS-CoV-2 infectious viruses *in vitro*

Targets rapidly forming microtubules used by virus

Infectious viral titer assay





$TCID_{50}$ infectious viral assay. Supernatants from untreated and drug treated virus infected Vero E6 cells and controls were diluted from 10^{-1} to 10^{-7} and incubated with fresh Vero E6 cells to determine cytopathic effect. Cell viability was measured by a luminescence assay (CellTiter-Glo) and $TCID_{50}$ was calculated.

Error bars: SEM

Sabizabulin has broad anti-inflammatory activity

Endotoxin septic shock mouse model *in vitro*

Sabizabulin (40nM) reduces cytokine production in mouse spleen cells stimulated with LPS

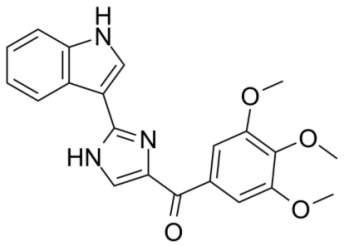
TNF-α	-31%	p=0.006
IL-1α	-123%	p=0.0005
IL-1β	-97%	p=0.0003
IL-6	-85%	p<0.00008
IL-8 homologue	-96%	p<0.0000007

University of Tennessee Health Science Center (laboratories of Professors Arnold Postlethwaite and Wei Li)

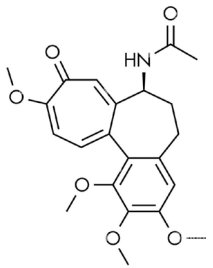
Sabizabulin is not colchicine

Sabizabulin versus colchicine

- Different chemical structure
- Targets microtubules differently
  - Sabizabulin has binding sites at β-tubulin and an additional one on α-tubulin to crosslink α- and β-tubulin subunits
- Different pharmacology and pharmacokinetics
- More potent inhibitor of tubulin polymerization
- Not a substrate for P-glycoprotein or CYP3A4

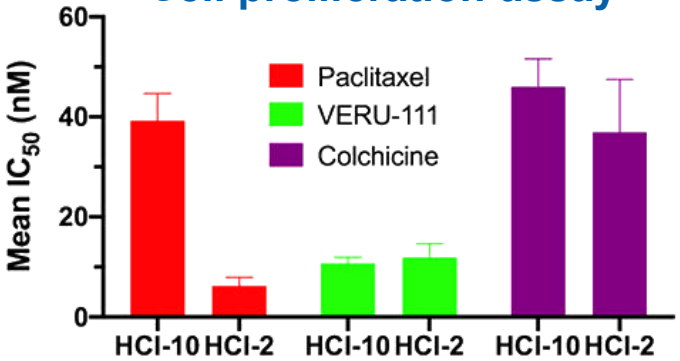


Sabizabulin



Colchicine

Cell proliferation assay



Human triple negative breast cancer cell lines

Chen J, et al. *J Med Chem* 55:7285-7289 2012; Li CM, et al. *Pharm Res* 29:3053-3063 2012; Lu Y, et al. *J Med Chem* 57:7355-7366 2014; Deng S, et al *Mol Cancer Ther* 19:348-63, 2020; Hwang DJ, et al *ACS Med Chem Lett* 6:993-997, 2015

Sabizabulin clinical development program

Phase 2 and Phase 3 COVID-19 studies were conducted during the pandemic period from June 2020-June 2022 while allowing standard of care treatments

ID# (status)	Phase	Type of study	Test article; regimen; route	Subject population	Number of subjects (ITT set)	Treatment duration
V0211901 (completed)	2	Efficacy and Safety	Sabizabulin 18 mg (powder in capsule) PO/NGT qd	Hospitalized COVID-19 patients who are at high risk for the development of ARDS and death	Placebo: 20 Sabizabulin: 19	Up to 21 days
V3011902 (completed)	3	Efficacy and Safety	Sabizabulin 9 mg (formulated capsule) PO/NGT qd	Hospitalized COVID-19 patients who are at high risk for the development of ARDS and death	Placebo: 70 Sabizabulin: 134	Up to 21 days
V1011101 (ongoing)	1b/2	Safety	Phase 1b Sabizabulin 4.5 mg to 81 mg (powder in capsule) PO qd Phase 2 Sabizabulin up to 63 mg (powder in capsule) PO qd	Advanced prostate cancer patients	80	Daily until DLT or cancer progression
V3011102 (ongoing)	3	Safety	Sabizabulin 32 mg (formulated capsule) PO qd	Advanced prostate cancer patients	245 planned, 59 reported	Daily until cancer progression

DLT = dose limiting toxicity; NGT = nasogastric tube; PO = oral; qd = daily.

Sabizabulin proposed EUA

Indication

- Treatment of hospitalized moderate to severe COVID-19 patients who are at high risk for acute respiratory distress syndrome (ARDS)

Dose and administration

- 9 mg oral capsule once daily for up to 21 days or discharge from hospital

Placebo mortality rate in Phase 3 sabizabulin study

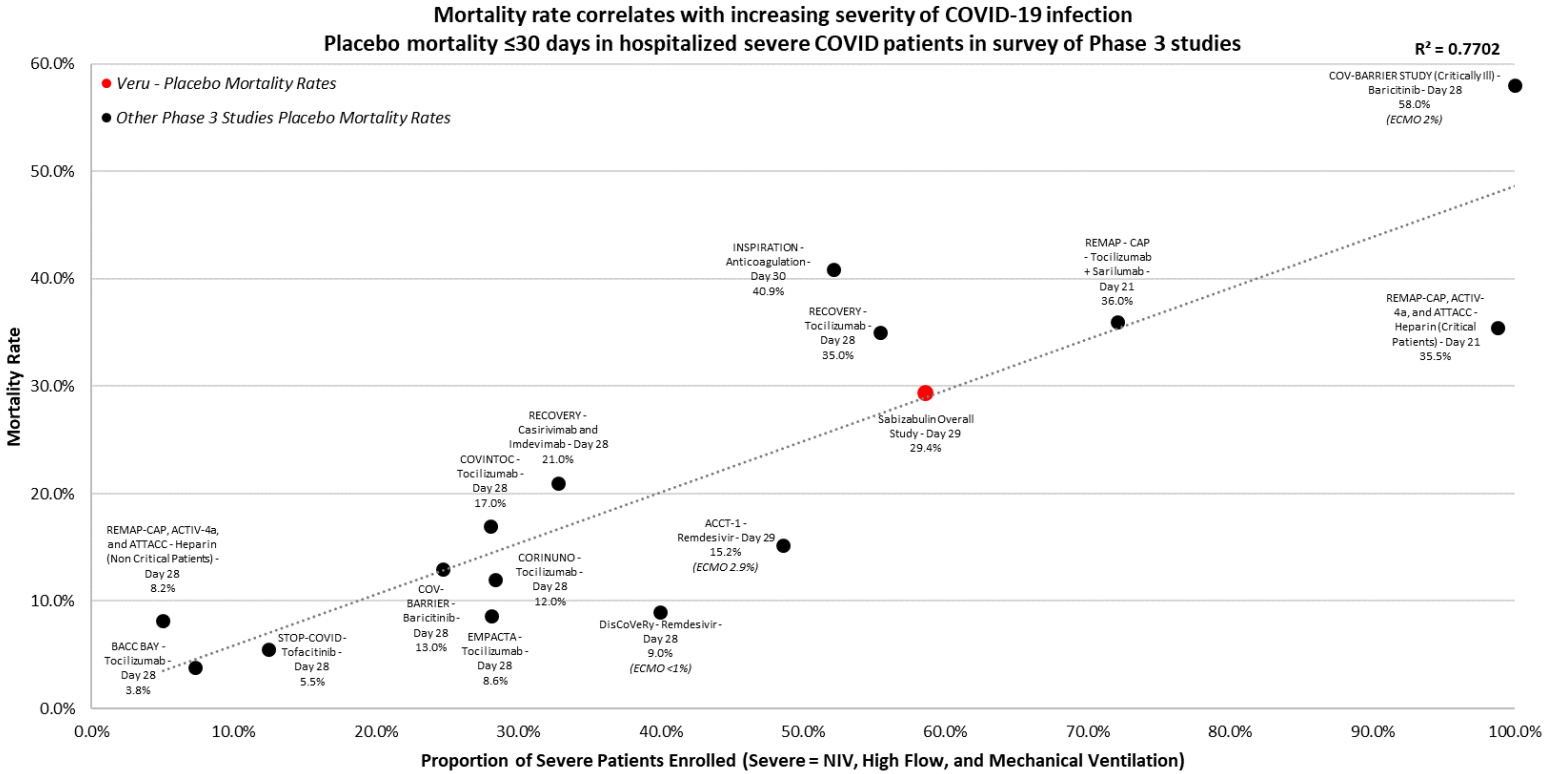
Sabizabulin treatment resulted in significant reduction of deaths across different placebo mortality rates

- Based on FDA consultations our studies:
  - **By design enrolled** very sick patients (June 2020 through April 2022)
  - **Selected mortality** as the most objective and important primary endpoint
- Sicker patients die at a higher rate
  - **Contemporaneous studies:** mortality rates for placebo + SOC in 15 contemporaneous COVID-19 clinical studies (EUA/NIH COVID-19 treatment guidelines) were analyzed and compared to the Phase 3 sabizabulin study
  - **Real world data:** in a recent study, CDC reported the mortality risk in hospitalized severe COVID-19 patients during the delta to omicron periods – July 2021 to June 2022 – from Premier Healthcare Database Special COVID-19, which captures 678 hospitals and 25% of annual hospital admissions

SOC, standard of care

Contemporaneous COVID-19 clinical studies

Placebo mortality rates (≤ 30 days) by proportion of severe COVID-19 patients enrolled



References and details on the studies can be found in the briefing book

CDC real world data of hospitalized patients from delta to omicron periods confirm that death rates were high in severe COVID-19 patients

- In a recent study, CDC reported the mortality risk in hospitalized COVID-19 patients during the delta to early omicron periods

Mortality rates of high risk COVID-19 patients based on variant

	Delta (July-Oct 2021)	Early omicron (Jan-Mar 2022)
ICU	46%	39%
WHO 5 – NIV	42.8%	37.2%
WHO 6 – MV	62.5%	56%

- **Phase 3 COVID-19 sabizabulin full study enrolled from June 2021 – April 2022 with overall placebo death rate of 29.4% at Day 29 and 39.7% at Day 60**
- In Phase 3 study, sabizabulin's treatment mortality benefit (effect size) was robust and clinically meaningful in every subgroup or sensitivity analysis of primary endpoint regardless of the placebo mortality rate
  - Hospitalized COVID-19 patients at high risk for ARDS and death then and now are the same people and will have the same benefit from sabizabulin treatment

Adjei S, et al. *MMWR Morb Mortal Wkly Rep*. 2022;71(37):1182-9.

Safety database

Safety database supports an EUA

- Overall safety population database is 266 patients which consists of COVID-19 patients and prostate cancer patients
  - No remarkable safety findings in our safety population were observed
  - Well tolerated at doses 3.5x higher and up to 3 years duration in prostate cancer studies
- Sabizabulin has a short half life (5.5 hours) and short course of therapy (21 days or discharge from hospital)
- Any potential safety risk is minimized as the indicated population would be hospitalized and under direct care (constant safety monitoring)
- We are committed to working with the Agency to collect additional clinical information under the EUA to support the use of sabizabulin

Identifying the proposed population

The patient population we studied is what is in the Fact Sheet

- We propose that sabizabulin be indicated for the treatment of hospitalized adult patients with moderate to severe COVID-19 who are at high risk for acute respiratory distress syndrome
  - Matches the inclusion/exclusion criteria for the Phase 3 clinical trial
  - Sabizabulin treatment resulted in a robust statistically significant and clinically meaningful mortality benefit
- A serious unmet medical need still exists
  - Critical patients: WHO 4 with co-morbidities, WHO 5, and WHO 6 remain at high risk of death

Agenda

Introduction	**Mitchell Steiner, MD** Chief Executive Officer and Chief Medical Officer Veru Inc.
Efficacy **Safety**	**K. Gary Barnette, PhD** Chief Scientific Officer Veru Inc.
Sensitivity Analysis	**Lee-Jen Wei, PhD** Professor of Biostatistics Harvard University, T.H. Chan School of Public Health
Benefit/Risk Assessment	**Christian Sandrock, MD, MPH** Division Vice Chief of Internal Medicine and Director of Critical Care University of California, Davis, School of Medicine
Concluding Remarks	**Mitchell Steiner, MD** Chief Executive Officer and Chief Medical Officer Veru Inc.

Efficacy

K. Gary Barnette, PhD
Chief Scientific Officer
Veru Inc.

Phase 2, double blind, placebo-controlled study in hospitalized COVID-19 patients

Key efficacy endpoints

Efficacy Endpoints	Placebo	Sabizabulin	Relative Reduction
Deaths (ITT)	6/20 (30%)	1/19 (5.3%)	82%
Mean days in ICU +/- SD (EE)	9.6±12.4	2.6±5.8	73%
Mean days on Mechanical Ventilation +/- SD (EE)	5.1±11.2	1.2±6.1	78%

Safety–Any adverse event that occurred in ≥ 2 patients on study

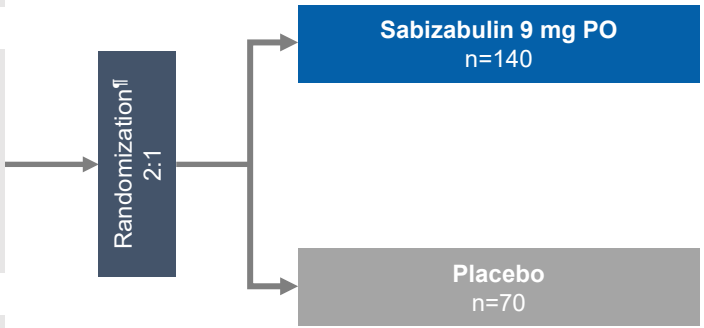
Preferred Term	Sabizabulin (n=19) N (%)/events	Placebo (n=20) N (%)/events
Any	10 (52.6%)/27	11 (55.0%)/41
Constipation	2 (10.5%)/2	2 (10.0%)/2
Septic shock	1 (5.3%)/1	2 (10.0%)/2
Alanine aminotransferase increased	1 (5.3%)/1	2 (10.0%)/2
Aspartate aminotransferase increased	2 (10.5%)/2	1 (5.0%)/1
Acute kidney injury	0	2 (10.0%)/2
Pneumomediastinum	0	2 (10.0%)/2
Pneumothorax	1 (5.3%)/1	3 (15.0%)/3
Respiratory failure	0	4 (20.0%)/4

Phase 3 study design

N≈210
Sample size calculation
- Placebo 30%
- Sabizabulin 15%
- α=0.05 (two-sided)
- Power >92%

Key Inclusion criteria:
- Age ≥18 years
- SARS-CoV-2 infection confirmed by PCR
- WHO 4 with ≥1 known comorbidity for being at high risk for ARDS; **OR** WHO 5 or 6 regardless of comorbidities
- Peripheral SpO_2 ≤94% on room air

Key exclusion criteria:
- Pregnant or breastfeeding
- Moderate to severe renal impairment
- Hepatic impairment
- Required ventilation plus additional organ support

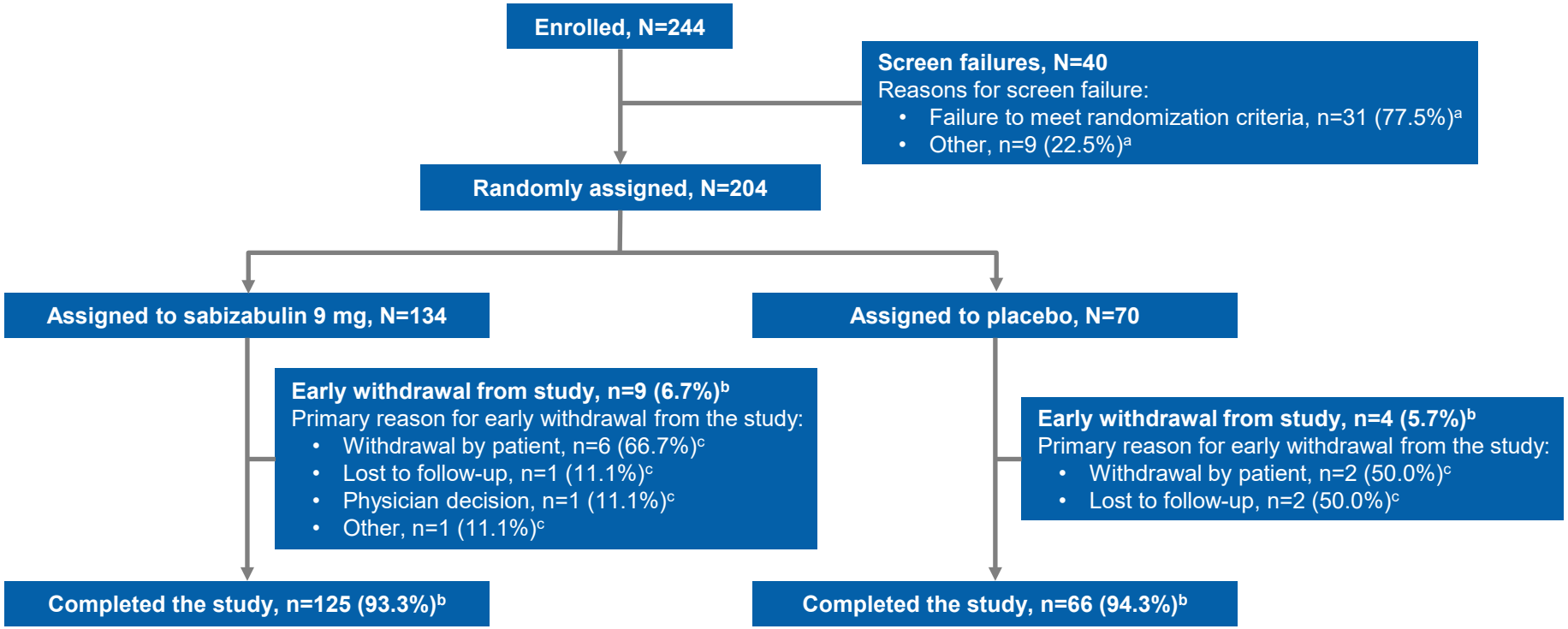


Treatment Period
Days 1-21 or until discharge

Follow-up Period
Days 22-60

WHO 4: Hospitalized, oxygen by mask or nasal prongs; WHO 5: Hospitalized, non-invasive ventilation (NIV) or high-flow oxygen; WHO 6: Hospitalized, intubation and mechanical ventilation.

Phase 3 study: patient disposition



[a]Percentages are based on the number of screen failures; [b]Percentages are based on the number of patients in the ITT Set; [c]Percentages are based on the number of early withdrawals from the study.

Phase 3 study: key demographics

Patient demographics (ITT)	Sabizabulin	Placebo
Number of patients	N=134	N=70
Mean age (±SD)	61.3 (14.14)	62.7 (13.90)
Gender		
Males (%)	67.2	62.9
Females (%)	32.8	37.1
Mean WHO Score at baseline (±SD)	4.6 (± 0.64)	4.7 (± 0.67)
Standard of care treatment use on study (prior or concomitant)		
Dexamethasone	84.3%	78.6%
Any corticosteroid	97.8%	95.7%
Remdesivir	29.9%	27.1%
IL-6 inhibitor (tocilizumab)	8.6%	10.0%
JAK inhibitor (baricitinib or tofacitinib)	6.7%	11.4%

Phase 3 study: study endpoints

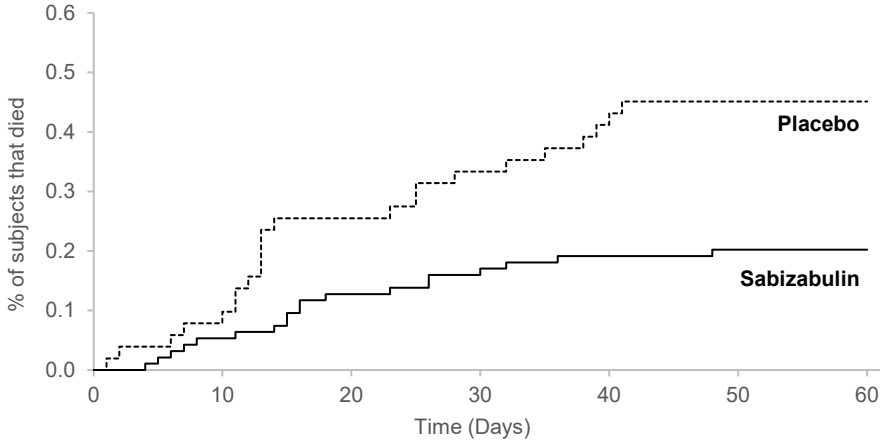
- Primary endpoint:
  - Proportion of patients who died on study (up to Day 60)

- Key secondary endpoints
  - Proportion of patients alive without respiratory failure at Days 15, 22, 29 and 60
  - Days in ICU
  - Days on mechanical ventilation
  - Days in hospital
  - Proportion of patients who died on study at Days 15, 22, and 29
  - Change from baseline in viral load (baseline to Day 9 and baseline to last-on-study)

Phase 3 study: results (interim analysis)

Primary endpoint, mortality rate by Day 60, was met

After planned interim analysis of first 150 patients, Independent Data Monitoring Committee unanimously recommended early stopping of Phase 3 study for clear evidence of benefit



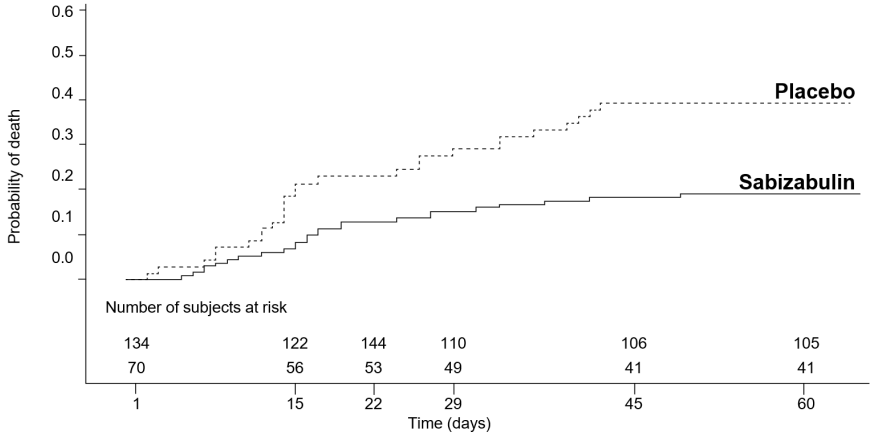
	Sabizabulin 9 mg	Placebo	Relative risk reduction	P-value (Fishers Exact)
Mortality Day 15	7/94 (7.4%)	13/51 (25.5%)	-71.0%	0.003
Mortality Day 29	15/94 (16.0%)	18/51 (35.2%)	-54.5%	0.008
Mortality Day 60	19/94 (20.2%)	23/51 (45.1%)	-55.2%	0.004*

Treatment comparison	Odds ratio	95% CI	p-value (logistic regression)
Sabizabulin 9mg vs. Placebo	3.21	(1.45, 7.12)	0.0042*

*Statistical analysis per SAP was logistic regression model with multiple imputation

Phase 3 study: results (ITT analysis)

Analysis of ITT set (n=204) is consistent with interim efficacy analysis



Sensitivity Analyses:

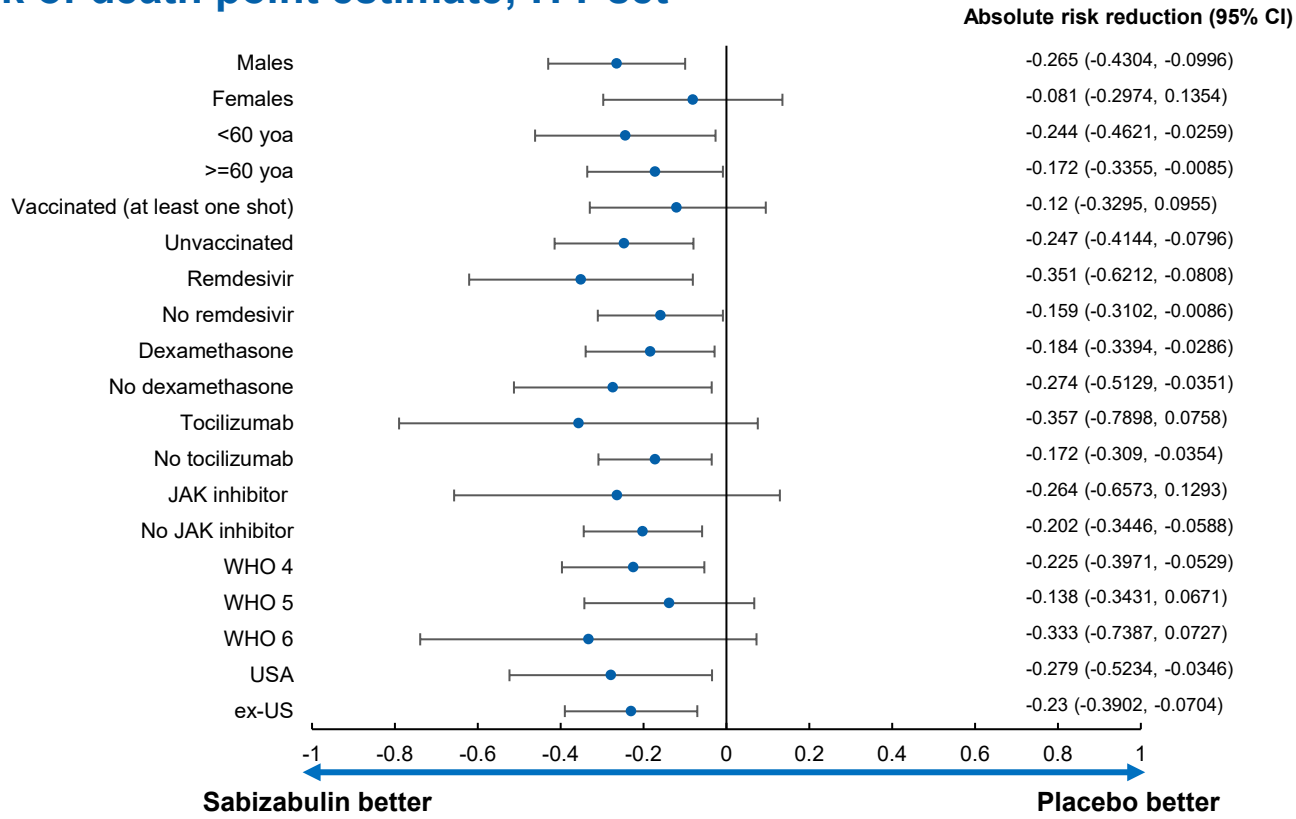
- **Kaplan-Meier Log-rank p=0.0019**
- **Kaplan-Meier Wilcoxon p=0.0023**
- **Cox Proportional hazard model p=0.0029**
- **Logistic Regression Proportion p=0.0046**

	Sabizabulin 9 mg	Placebo	Relative risk reduction	p-value (logistic regression)
Mortality Day 15	11/131 (8.4%)	15/69 (21.7%)	-61.4%	0.0291
Mortality Day 22	17/131 (12.9%)	16/69 (23.2%)	-44.0%	0.1621
Mortality Day 29	20/130 (15.4%)	20/68 (29.4%)	-47.6%	0.0459
Mortality Day 60	25/130 (19.2%)	27/68 (39.7%)	-51.6%	0.0046

Treatment comparison	Odds ratio	95% CI	p-value (logistic regression)
Sabizabulin 9 mg vs. Placebo	2.77	(1.37, 5.60)	0.0046

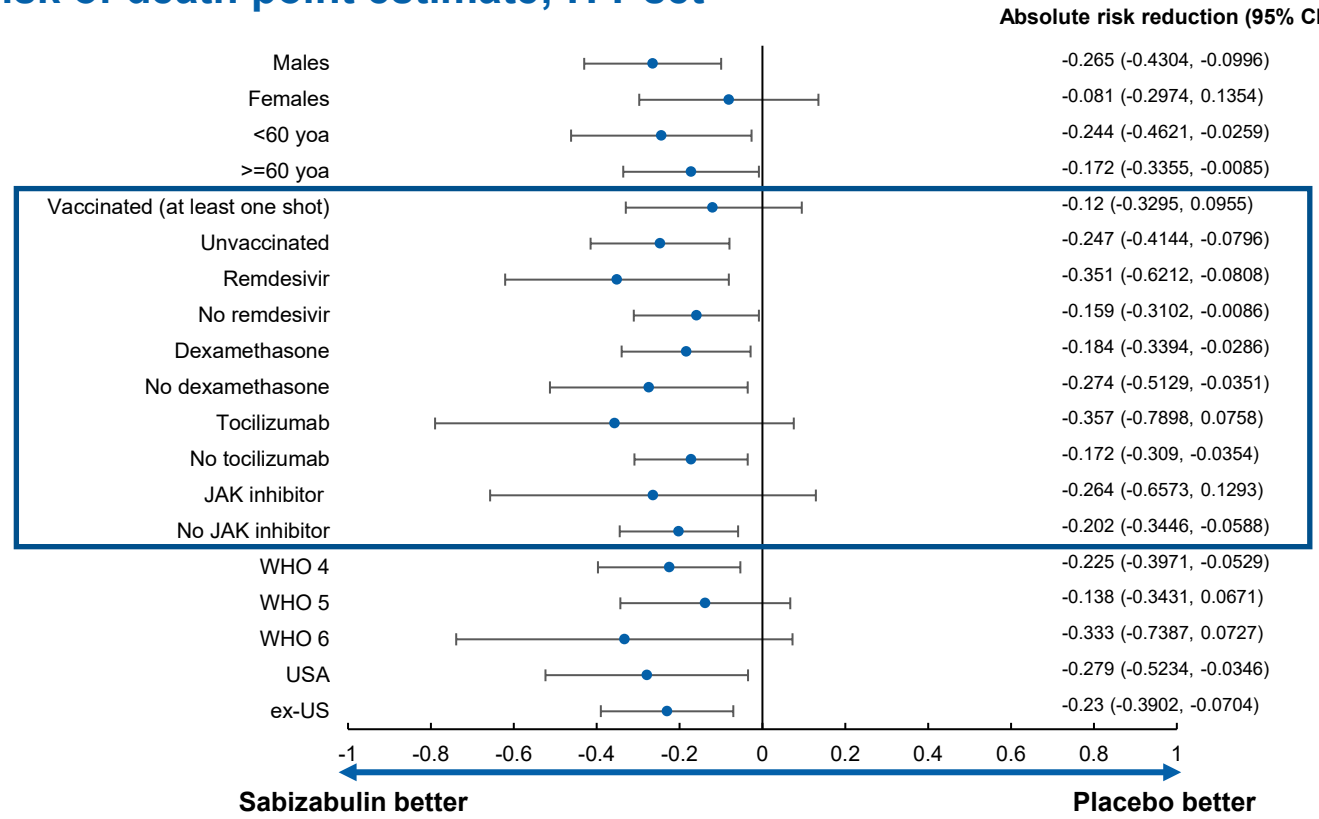
Phase 3 study: subgroup analyses of primary endpoint

Absolute risk of death point estimate; ITT set



Phase 3 study: subgroup analyses of primary endpoint

Absolute risk of death point estimate; ITT set



Phase 3 study: comorbidity subgroup analysis

Risk of mortality by Day 60 for subgroups based on comorbidities known to increase risk of ARDS

Subgroup	Sabizabulin	Placebo	Absolute difference	Relative difference
Hypertension	20/84 (23.8%)	17/45 (37.8%)	-14.0%	-37.0%
Pneumonia	16/76 (21.1%)	15/44 (34.1%)	-13.0%	-38.1%
Diabetes	12/45 (26.7%)	12/28 (42.9%)	-16.2%	-37.8%
Age ≥65 years	16/65 (24.6%)	16/40 (40.0%)	-15.4%	-38.5%
Severe respiratory issues*	4/36 (11.1%)	6/13 (46.2%)	-35.1%	-76.0%
Severe obesity (BMI ≥40)	3/23 (13.0%)	3/6 (50.0%)	-37.0%	-74.0%
Hypertension + 3 other comorbidities	9/40 (22.5%)	6/16 (37.5%)	-15.0%	-40.0%
Pneumonia + 3 other comorbidities	8/31 (25.8%)	5/15 (33.3%)	-7.5%	-22.5%
Age ≥65 years + 3 other comorbidities	5/28 (17.9%)	5/13 (38.5%)	-20.6%	-53.5%
≥4 comorbidities	10/43 (23.2%)	6/18 (33.3%)	-10.1%	-30.2%
≥3 comorbidities	16/73 (21.9%)	14/41 (34.1%)	-12.2%	-35.8%
≥2 comorbidities	25/106 (23.6%)	23/58 (39.7%)	-16.1%	-40.5%

*Severe respiratory issues = asthma, bronchiectasis, bronchitis chronic, COPD, interstitial lung disease, pulmonary fibrosis, and/or pulmonary sarcoidosis

Phase 3 study: backward logistic regression analysis

Assessment of the effect and combination of effects of various factors on primary endpoint (Day 60 mortality)

• Region • Sex • Age ≥65 years • Severe obesity (BMI ≥40 kg/m^2) • WHO scale score at randomization • Treatment • Remdesivir use at baseline • Dexamethasone use at baseline • Asthma • Selected respiratory issues (asthma, bronchiectasis, bronchitis chronic, chronic obstructive pulmonary disease, interstitial lung disease, pulmonary fibrosis, pulmonary sarcoidosis) • History of heart failure • Diabetes • ≥3 of selected respiratory issues/history of heart failure/diabetes/BMI ≥40/age ≥65

Treatment	Odds	95% CI	p-value
Sabizabulin 9 mg	6.40	(2.70, 15.20)	<0.0001
Placebo	2.18	(0.89, 5.36)	0.0883

Treatment comparison	Odds ratio	95% CI	p-value
Sabizabulin 9 mg vs. Placebo	2.93	(1.38, 6.22)	0.0050

Phase 3 study: variant subgroup analysis

Risk of mortality by Day 60 for subgroups based on SARS-CoV-2 variant

Subgroup	Sabizabulin 9mg	Placebo	Absolute difference	Relative difference
Delta variant (randomized prior to 12/15/2021)	13/48 (27.1%)	12/26 (46.2%)	-19.1%	-41.3%
Omicron variant (randomized on or after 12/15/2021)	12/82 (14.6%)	15/42 (35.7%)	-21.1%	-59.1%
Omicron variant (randomized on or after 1/15/2022)	7/61 (11.5%)	9/32 (28.1%)	-16.6%	-59.1%

Phase 3 study: effect of NG tube dosing

Potential unblinding due to NG tube dosing is not observed

Kaplan-Meier analysis of mortality or dosing via NG tube (ITT started treatment orally)

Probability of treatment failure	Sabizabulin 9 mg	Placebo	Absolute difference	Relative difference
Day 60	22.4% (15.8, 31.1)	39.6% (28.6, 53.1)	-17.2%	-43.4%

Treatment comparison	Log-Rank p-value	Wilcoxon p-value
Sabizabulin 9 mg vs. Placebo	0.0179	0.0228

Phase 3 study: key secondary endpoints

Sabizabulin shows a significant benefit in secondary endpoints

Proportion of patients alive and free of respiratory failure (Responder = WHO 0-4)

	Sabizabulin 9 mg	Placebo	Relative difference	p-value (logistic regression)
Responders Day 29	96/130 (73.8%)	38/68 (55.9%)	+32.0%	0.0186
Responders Day 60	104/130 (80.0%)	41/68 (60.3%)	+32.7%	0.0066

Treatment comparison	Odds ratio	95% CI	p-value (logistic regression)
Sabizabulin 9 mg vs. Placebo at Day 29	2.39	(1.16, 4.92)	0.0186

Imputation model included treatment, region, sex, remdesivir use, dexamethasone use, WHO strata at baseline, subjects' discharge status, and early treatment discontinuation status.

Phase 3 study: key secondary endpoints (cont'd)

Days in the ICU		**n**	**Mean**	**SD**	**Median**
	Sabizabulin	134	16.0	23.50	2.0
	Placebo	70	26.3	28.11	9.0
		LS mean	**SE**	**95% CI**	**p-value**
	Treatment comparison	-9.9	3.44	(-16.7, -3.1)	0.0045
Days on mechanical ventilation		**n**	**Mean**	**SD**	**Median**
	Sabizabulin	134	13.7	23.57	0.0
	Placebo	70	24.6	29.00	0.0
		LS mean	**SE**	**95% CI**	**p-value**
	Treatment comparison	-10.4	3.56	(-17.5, -3.4)	0.0038
Days in the hospital		**n**	**Mean**	**SD**	**Median**
	Sabizabulin	134	24.0	21.78	13.0
	Placebo	70	31.0	24.61	16.5
		LS mean	**SE**	**95% CI**	**p-value**
	Treatment comparison	-6.3	3.13	(-12.4, -0.1)	0.0463

Viral load (9 days or last on-study)		**Mean absolute change**	**SD**	**Mean % change from baseline**
	Sabizabulin 9 mg	-1,383,566	30,516,153	-42.9%
	Placebo	+9,761,507	83,144,880	+412.1%
		LS mean	**95% CI**	**p-value**
	Treatment comparison	+9,760,000	(-27,200,000, +7,700,000)	0.2712

Efficacy conclusions

- Sabizabulin demonstrated 20.5% absolute risk reduction of 60-day mortality in ITT set (primary endpoint; 51.6% relative risk reduction)
  - All sensitivity analyses and all subgroup analyses confirm the overwhelming benefit of sabizabulin in reduction of death
- The secondary efficacy endpoints consistently demonstrate the statistically significant and clinically meaningful efficacy of sabizabulin
- Number needed to treat (NNT) = 5 (for every 5 patients treated, 1 life saved)

Agenda

Introduction	**Mitchell Steiner, MD** Chief Executive Officer and Chief Medical Officer Veru Inc.
Efficacy Safety	**K. Gary Barnette, PhD** Chief Scientific Officer Veru Inc.
Sensitivity Analysis	**Lee-Jen Wei, PhD** Professor of Biostatistics Harvard University, T.H. Chan School of Public Health
Benefit/Risk Assessment	**Christian Sandrock, MD, MPH** Division Vice Chief of Internal Medicine and Director of Critical Care University of California, Davis, School of Medicine
Concluding Remarks	**Mitchell Steiner, MD** Chief Executive Officer and Chief Medical Officer Veru Inc.

Safety population

- Overall safety population is 266 patients (as of 28 April 2022)
  - 149 patients with moderate to severe COVID-19 infection who are at high risk for ARDS (9 mg administered daily for up to 21 days)
  - 117 patients (patients still being enrolled in a phase 3 study) with advanced prostate cancer (32 mg daily dose for up to 3 years)

- Phase 3 study safety set is 199 patients (n=130 sabizabulin; n=69 placebo)

Adverse events (phase 3 safety set)

Any adverse event that occurred in ≥5% of patients in either treatment group

	Sabizabulin (n=130) N (%)/Events	Placebo (n=69) N (%)/Events
Any	82 (**63.1%**)/369	54 (**78.3%**)/294
Pneumonia	8 (6.2%)/12	9 (13.0%)/12
Pneumonia bacterial	2 (1.5%)/2	5 (7.2%)/5
Septic shock	2 (1.5%)/2	5 (7.2%)/5
Acute kidney injury	11 (8.5%)/11	8 (11.6%)/8
Acute respiratory failure	7 (5.4%)/7	3 (4.3%)/3
Hypoxia	3 (2.3%)/4	4 (5.8%)/4
Pneumothorax	1 (0.8%)/1	7 (10.1%)/7
Respiratory failure	13 (10.0%)/14	14 (20.3%)/14
Hypotension	5 (3.8%)/9	8 (11.6%)/8
Anemia	7 (5.4%)/7	3 (4.3%)/3
Atrial fibrillation	6 (4.6%)/6	5 (7.2%)/5
Bradycardia	6 (4.6%)/7	5 (7.2%)/5
Constipation	9 (6.9%)/9	6 (8.7%)/10
Hyperkalemia	6 (4.6%)/6	6 (8.7%)/7
Hypernatremia	6 (4.6%)/6	4 (5.8%)/4
Hypokalemia	6 (4.6%)/7	5 (7.2%)/7
Hypophosphatemia	2 (1.5%)/3	4 (5.8%)/5
Anxiety	4 (3.1%)/5	4 (5.8%)/4
Delirium	5 (3.8%)/5	4 (5.8%)/4
Urinary tract infection	8 (6.2%)/8	1 (1.4%)/1

Safety - AEs

The proportion of patients that experience any AE was 24% higher in the placebo group compared to the sabizabulin treated group

TEAE leading to treatment discontinuation (phase 3 safety set)

	Sabizabulin (n=130) N (%)/events	**Placebo (n=69)** N (%)/events
Any	6 (**4.6%**)/7	3 (**4.3%**)/3
Dysphagia	1 (0.8%)/1	0
COVID-19	1 (0.8%)/1	0
Endocarditis staphylococcal	1 (0.8%)/1	0
Alanine aminotransferase increased	1 (0.8%)/1	0
Hepatic enzyme increased	0	1 (1.4%)/1
Liver function test abnormal	0	1 (1.4%)/1
Liver function test increased	1 (0.8%)/1	0
Acute kidney injury	1 (0.8%)/1	0
Dyspnea	0	1 (1.4%)/1
Respiratory failure	1 (0.8%)/1	0

Serious adverse events (phase 3 safety set)

Any serious adverse event that occurred in ≥2% of patients in either treatment group

	Sabizabulin (n=130) N (%)/Events	**Placebo (n=69)** N (%)/Events
Any	38 (**29.2%**)/84	32 (**46.4%**)/85
Cardiac arrest	0	3 (4.3%)/4
Multiple organ dysfunction syndrome	0	2 (2.9%)/2
COVID-19	4 (3.1%)/4	3 (4.3%)/3
Pneumonia	4 (3.1%)/6	4 (5.8%)/5
Pneumonia bacterial	0	2 (2.9%)/2
Sepsis	4 (3.1%)/5	2 (2.9%)/2
Septic shock	2 (1.5%)/2	5 (7.2%)/5
Acute kidney injury	6 (4.6%)/6	6 (8.7%)/6
Acute respiratory failure	5 (3.8%)/5	3 (4.3%)/3
Hypoxia	2 (1.5%)/3	3 (4.3%)/3
Pneumothorax	1 (0.8%)/1	6 (8.7%)/6
Pulmonary embolism	3 (2.3%)/3	3 (4.3%)/3
Respiratory failure	13 (10.0%)/14	14 (20.3%)/14

Safety - SAEs

The proportion of patients that experienced any SAE was 59% higher in the placebo group compared to sabizabulin treated group

Fatal adverse events (phase 3 safety set)

	Sabizabulin (n=130) N (%)	Placebo (n=69) N (%)
Number of deaths	23 (**17.7%**)	25 (**36.2%**)
Bradycardia	0	1 (1.4%)
Cardiac arrest	0	1 (1.4%)
Cardio-respiratory arrest	1 (0.8%)	1 (1.4%)
Cardiovascular insufficiency	0	1 (1.4%)
Death not otherwise specified	1 (0.8%)	0
Multiple organ dysfunction syndrome	0	2 (2.9%)
Burkholderia cepacia complex infection	1 (0.8%)	0
COVID-19	3 (2.3%)	2 (2.9%)
Device related infection	1 (0.8%)	0
Pneumonia	1 (0.8%)	3 (4.3%)

	Sabizabulin (n=130) N (%)	Placebo (n=69) N (%)
Sepsis	1 (0.8%)	0
Septic shock	1 (0.8%)	2 (2.9%)
Severe acute respiratory syndrome	2 (1.5%)	0
Cerebrovascular accident	0	1 (1.4%)
Coma	1 (0.8%)	0
Renal failure	1 (0.8%)	0
Acute respiratory failure	2 (1.5%)	3 (4.3%)
Hypoxia	1 (0.8%)	2 (2.9%)
Pulmonary embolism	0	1 (1.4%)
Respiratory failure	5 (3.8%)	4 (5.8%)
Hypovolemic shock	0	1 (1.4%)
Shock	1 (0.8%)	0

Safety conclusions

- Sabizabulin was well-tolerated in COVID-19 studies
  - Most common TEAE were respiratory failure, acute kidney injury, pneumonia
    - All 3 were experienced in a higher proportion of subjects in the placebo group
  - Most common serious TEAE were respiratory failure, acute kidney injury, and acute respiratory failure
    - All 3 were experienced in a higher proportion of subjects in the placebo group
- Safety observations confirm the efficacy findings of sabizabulin in treating COVID-19
- Safety findings from the prostate cancer program at a dose of 3.5-fold higher show sabizabulin is well tolerated

Additional safety data to be generated

- Planned phase 3 double-blind, placebo-controlled efficacy and safety studies
  - Study V3011903 – hospitalized adult patients with less severe COVID-19 (WHO 3 patients and WHO 4 patients without a comorbidity)
  - Study V3011904 – hospitalized adult patients with influenza
  - Study V3011915 – hospitalized adult patients with virus-related ARDS

Benefit-risk: sponsor perspective

- The benefit-risk assessment is overwhelmingly positive with reductions in death observed in the overall population and in all subgroup analyses

- Sabizabulin is intended for use in hospitalized patients at high risk or “non-negligible risk of death” and are under constant surveillance, thereby mitigating risk

- Additional safety data will be obtained
  - under the EUA for this indication: spontaneous reporting, pregnancy registry
  - through additional planned clinical studies with sabizabulin for other indications (e.g., less severe hospitalized COVID, influenza, and virus-related ARDS)

Agenda

Introduction	**Mitchell Steiner, MD** Chief Executive Officer and Chief Medical Officer Veru Inc.
Efficacy **Safety**	**K. Gary Barnette, PhD** Chief Scientific Officer Veru Inc.
Sensitivity Analysis	**Lee-Jen Wei, PhD** Professor of Biostatistics Harvard University, T.H. Chan School of Public Health
Benefit/Risk Assessment	**Christian Sandrock, MD, MPH** Division Vice Chief of Internal Medicine and Director of Critical Care University of California, Davis, School of Medicine
Concluding Remarks	**Mitchell Steiner, MD** Chief Executive Officer and Chief Medical Officer Veru Inc.

Sensitivity Analysis

Lee-Jen Wei, PhD
Professor of Biostatistics
Harvard University, T.H. Chan School of Public Health

Disclosures

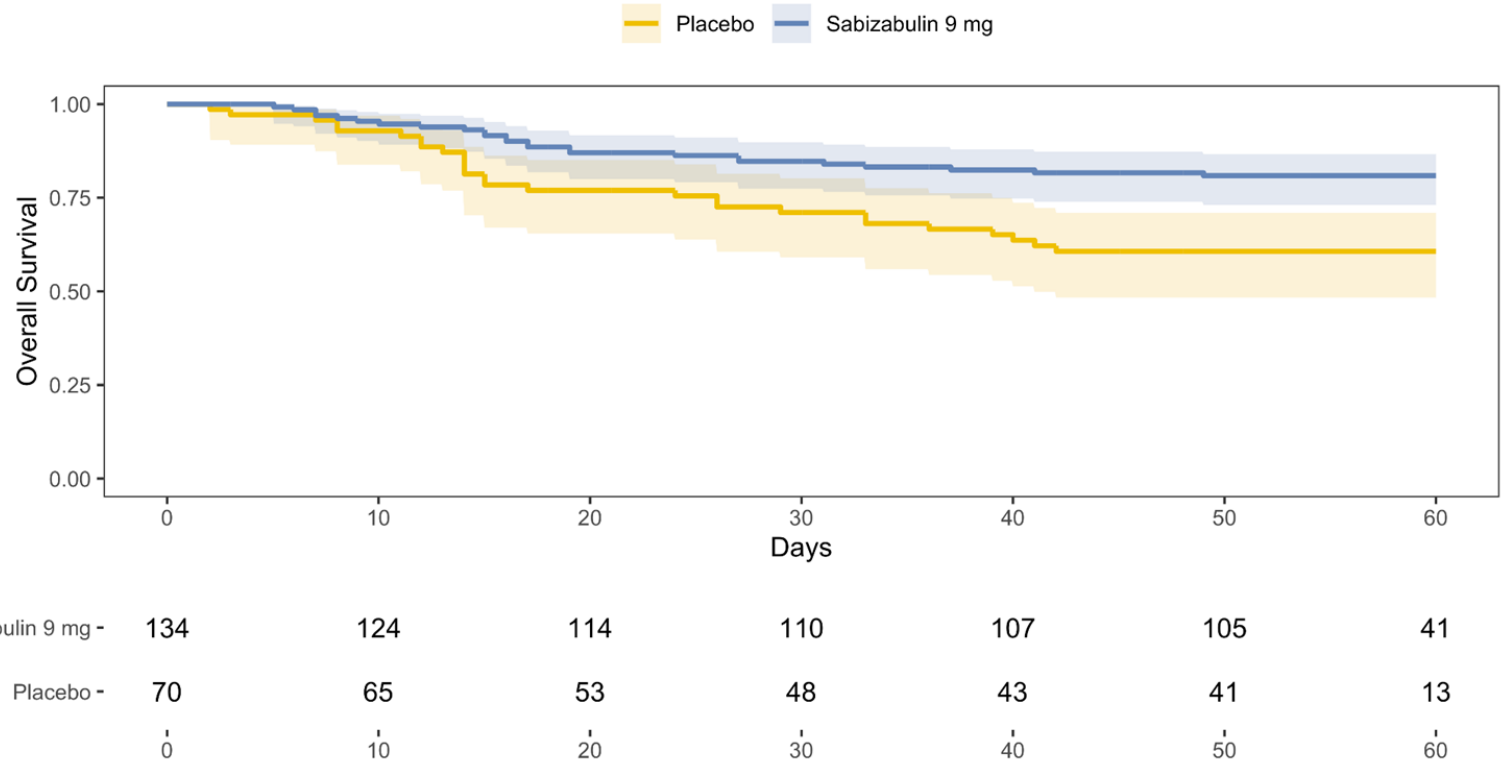
- Consultant for: Novartis, Pfizer, Johnson and Johnson, Ionis Pharmaceutical, Merck & Co., Biogen, Veru

Introduction

- Independently conducted analyses
- Robustness for primary endpoint analysis (60-day mortality)
- Robustness for secondary endpoint analysis

Survival analysis (ITT, n = 204), no imputation

Supports robustness of primary endpoint finding



Comparisons of 60-day survival rates

Treatment	60d Survival
Sabizabulin	80.9%
Placebo	60.7%

Group contrast (Sabizabulin v. Placebo)	Estimate	95% CI lower	95% CI upper	p-value
Difference	0.202	0.070	0.334	0.0028
Odds ratio	0.365	0.192	0.695	0.0022

Model-free, imputation-free analysis for Risk difference (60d rates) with covariate adjustments

- Covariates:
  - Baseline WHO category (categorical) • baseline treatment with dexamethasone (binary) • baseline treatment with remdesivir (binary) • region (categorical) • age (continuous) • sex (binary) • receipt of any vaccine (binary) • receipt of a US approved vaccine (binary)
- Model-free covariate adjusted analysis via augmentation method

Ignoring 6 patients without survival outcomes

Estimator	Difference (95% CI)	p-value
Unadjusted	20.5% (6.9% to 34.0%)	0.00305
Adjusted	20.0% (8.0% to 32.1%)	0.00113

Assuming 4 patients died for Sabizabulin and 2 patients survived for control

Estimator	Difference (95% CI)	p-value
Unadjusted	16.9% (3.5% to 30.4%)	0.0136
Adjusted	16.8% (4.7% to 28.9%)	0.0064

Treatment effect for survival via Cox model

Covariates	Hazard ratio (Sabizabulin v. Placebo)	95% CI lower	95% CI upper	p-value
None	0.432	0.251	0.745	0.0025
Covariate adjusted	0.380	0.195	0.742	0.0046

Robust secondary endpoint analysis

Mean hospital-free survival time for 60d followup

Treatment	Hospital-free
Sabizabulin	36.1
Placebo	28.0

Group contrast (Sabizabulin v. Placebo)	Estimate	95% CI lower	95% CI upper	p-value
Difference	8.11	1.45	14.80	0.017

Mean ICU-free survival times

Treatment	ICU-free
Sabizabulin	44.2
Placebo	34.2

Group contrast (Sabizabulin v. Placebo)	Estimate	95% CI lower	95% CI upper	p-value
Difference	10.0	2.88	17.20	0.0060

Mean mechanical ventilation-free survival times

Treatment	Mechanical ventilation-free
Sabizabulin	46.8
Placebo	37.5

Group contrast (Sabizabulin v. Placebo)	Estimate	95% CI lower	95% CI upper	p-value
Difference	9.29	2.33	16.30	0.0089

Sensitivity analysis conclusions

- Robust treatment effect for every subgroup, sensitivity analyses, and secondary endpoints
- Augmentation method and Cox model for primary endpoint
- Event-free analyses for secondary endpoints

Agenda

Introduction	**Mitchell Steiner, MD** Chief Executive Officer and Chief Medical Officer Veru Inc.
Efficacy **Safety**	**K. Gary Barnette, PhD** Chief Scientific Officer Veru Inc.
Sensitivity Analysis	**Lee-Jen Wei, PhD** Professor of Biostatistics Harvard University, T.H. Chan School of Public Health
Benefit/Risk Assessment	**Christian Sandrock, MD, MPH** Division Vice Chief of Internal Medicine and Director of Critical Care University of California, Davis, School of Medicine
Concluding Remarks	**Mitchell Steiner, MD** Chief Executive Officer and Chief Medical Officer Veru Inc.

Benefit/Risk Assessment

Christian Sandrock, MD, MPH
Division Vice Chief of Internal Medicine; Director of Critical Care
University of California, Davis, School of Medicine

Disclosures

- Grant funding: NIH, CMS, CDC
- Clinical trials (principal or sub-investigator): Pluristem, Gilead, Shionogi, Paratek, Pfizer, Johnson and Johnson
- Advisory: Shionogi, Paratek, Pfizer, Johnson and Johnson, Abbvie
- Speaker: Shionogi, Paratek, Abbvie, Pfizer

A significant unmet medical need continues to exist for safe and effective therapeutics for COVID-19

- Risk of death and serious illness from COVID-19 infection remains high
  - Death rate for moderate to severe COVID-19 is estimated to be 21% – 67%
  - In the US, average daily death of 426 in the month of September 2022[1]
  - Globally, more than 1 million people died from COVID-19 in January – August of 2022[1]
- Up to 33% of hospitalized COVID-19 patients have Acute Respiratory Distress Syndrome (ARDS)[2,4]
  - 75% – 92% COVID-19 patients admitted to ICU have ARDS[2,3]
  - Mortality rate of COVID-19 associated ARDS is 30 – 50%[4,5,6]
    - Once progressed to ARDS, mortality is thought to be agnostic of cause[5,6]
    - Among deaths from COVID-19, the incidence of ARDS is 90%[4]
    - Additional safe and effective options are required to manage the evolving nature of the pandemic

1. Daily cases and deaths by date reported to WHO, accessed 10/19/2022; 2. Chand, et al. *J Intensive Care Med*. 2020:35;963-970. doi:10.1177/0885066620946692; 3. Patel, et al. *SN Compr Clin Med*. 2020:2;1740-1749. doi:10.1007/s42399-020-00476-w; 4. Tzotzos, et al. *Crit Care*. 2020:24;516. doi:10.1186/s13054-020-03240-7; 5. Dmytriw, et al. *Expert Rev Respir Med*. 2021;15(10):1347-1354. doi:10.1080/17476348.2021.1920927; 6. Sjoding, et al. *Ann Am Thorac Soc*. 2021;18(11):1876-1885. doi:10.1513/AnnalsATS.202008-1076OC

Crude mortality rate of COVID-19 by variant

Risk factors to COVID-19 mortality remain identical

- Data reported by CDC (Adjei, et al.) in Morbidity and Mortality Weekly Report
- Lower in-hospital deaths from Delta to Omicron periods
- However, highest risk patients (e.g., with high oxygen requirements) still have very significant mortality
- Identical risk factors can be found in patients who die from COVID-19, regardless of virus variant
  - Combined with above, highlights a still-unmet medical need in patients with risk factors

Crude mortality risk (cMR) of COVID-19 by virus variant

Risk factors	Delta (Jul-Oct 2021)	Early Omicron (Jan-Mar 2022)	Later Omicron (Apr-Jun 2022)
All hospitalized patients with primary COVID	15.1%	13.1%	4.9%
ICU patients	46%	39%	21%
Severe cases (WHO 5+6; NIV + MV)	51.5%	45.3%	23.0%

Presence of risk factors among hospitalized primary COVID-19 patients who died in hospital

Risk factors	Delta (Jul-Oct 2021)	Early Omicron (Jan-Mar 2022)	Later Omicron (Apr-Jun 2022)
3 or more co-morbidities	61.7%	70.8%	73.4%
Older than 65 years	53.7%	73.5%	81.9%
Admitted to ICU	76.1%	64%	57%
NIV	61.8%	51.2%	35%
MV	71.9%	57.6%	43.6%

Adjei S, et al. *MMWR Morb Mortal Wkly Rep*. 2022;71(37):1182-9.

COVID pandemic projections

- It is difficult to predict the future of the Pandemic, due to many factors including strain(s), vaccine/booster rates, behavior and testing practices
- Must be prepared for Best- and Worst-Case Scenarios

	Best-Case Scenario: No new variant	**Worst-Case Scenario:** High Immune Escape Variant X
Assumptions of model	• Reformulated boosters available Sep-2022 • Protection from natural immunity & vaccine effectiveness • **Risk of severe disease conditional on infection remains unchanged**	• Reformulated boosters available Sep-2022 • 40% immune escape against infection (natural immunity + vaccine) • **20% increased risk of hospitalization and death with variant X,** relative to Omicron, conditional on infection and immune status
Model prediction of mortality	• Model predicts 1,600 new deaths (95% CI 56 – 4,700) in the week ending in Dec 31, 2022	• Model predicts 4,700 new deaths (95% CI 72 – 23,000) in the week ending in Dec 31, 2022

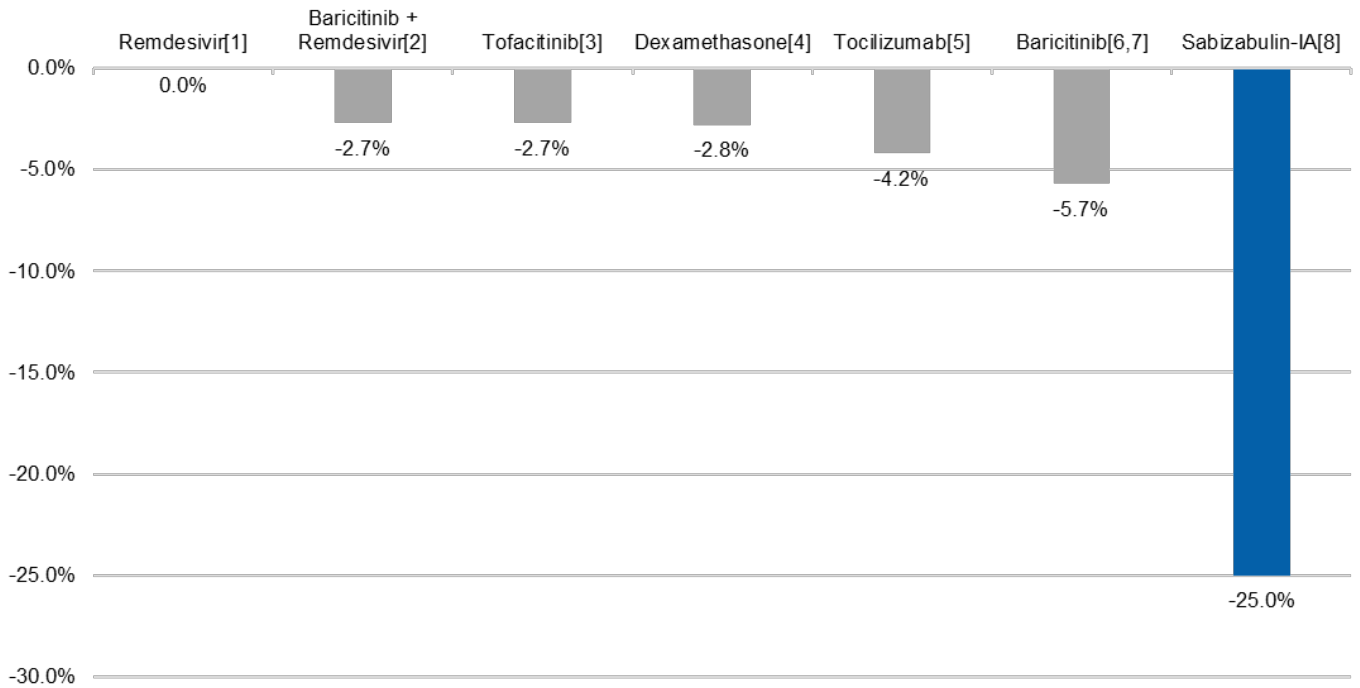
Source: COVID-19 Scenario Modeling Hub Coordination Team. “Projected Incident Cases by Epidemiological Week and by Scenario for Round 15 - US.” COVID-19 scenario modeling hub.

Treatment landscape and limitations

- Existing therapies (both in terms of type and number) unlikely sufficient to address current and expected needs
  - For hospitalized, moderate to severe COVID-19 patients at high risk for ARDS, currently recommended treatment options (remdesivir, baricitinib, tocilizumab, and dexamethasone) offer modest mortality benefits (0% – 5.7% ARR)
  - Antibody treatments (e.g., bamlanvimab/estesevimab, bebtelovimab) are strain-specific and therefore of limited use as new variants emerge
- COVID-19 surges are expected to continue to create strains on hospital capacity
  - Result in deaths in all critical care patient populations, including COVID-19
- Given the above, there is an unmet need for additional treatment modalities for moderate to severe hospitalized COVID-19 patients

Mortality benefit of COVID-19 treatments in hospitalized patients at high risk of progression to ARDS

Absolute risk reduction; available data in current published literature



1. Beigel, et al. *N Engl J Med*. 2020;383(19):1813-26. doi:10.1056/NEJMoa2007764; 2. Kalil, et al. *N Engl J Med*. 2021;384(9):795-807. doi:10.1056/NEJMoa2031994; 3. Guimarães, et al. *N Engl J Med*. 2021;385(5):406-15. doi:10.1056/NEJMoa2101643; 4. RECOVERY Collaborative Group. *Lancet*. 2021;397(10285):1637-1645. doi:10.1016/S0140-6736(21)00676-0; 5. RECOVERY Collaborative Group. *N Engl J Med*. 2021;384(8):693-704. doi:10.1056/NEJMoa2021436; 6. Marconi, et al. *Lancet Respir Med*. 2021;9(12):1407-18. doi:10.1016/S2213-2600(21)00331-3; 7. Ely, et al. *Lancet Respir Med*. 2022;10(4):327-36. doi:10.1016/S2213-2600(22)00006-6; 8. Barnette, et al. *NEJM Evid*. 2022;1(9). doi:10.1056/EVIDoa2200145

Sabizabulin COVID-19 program results

Robustness and generalizability of mortality benefit

- 50% reduction (relative; 20% absolute reduction) in death vs. standard care in Phase 3 study
  - Effect size clinically meaningful in every subgroup or sensitivity analysis, regardless of baseline mortality rate
  - Analysis of any small imbalances did not reduce the clear clinical benefit of sabizabulin
  - Meaningful improvement in secondary endpoints (days in hospital, ICU, on mechanical ventilation)
- Sponsor analysis shows placebo mortality in Phase 3 study (29.4%) in line with contemporaneous studies
- CDC data show mortality in high-risk patients with COVID-19 remains stubbornly high, even in the later Omicron period
  - Among hospitalized deaths, high risk COVID-19 patients continue to be the major contributor

Adjei S, et al. *MMWR Morb Mortal Wkly Rep*. 2022;71(37):1182-9.

Benefit/Risk Assessment of sabizabulin in context of proposed EUA

Benefits

- Sabizabulin is a 1st-in-class, new chemical entity
- 50% reduction in mortality vs standard care
  - Fewer days on mechanical ventilation and in the ICU
- Effective regardless of
  - virus variant or vaccination status
  - comorbidities
- Well tolerated
  - Moderate to severe COVID-19 (hospitalized)
  - Cancer (3x dose vs COVID-19 patients, up to 3 years)
- Short-term intervention (21 days or until discharge)
- Effective in decreasing viral replication and inflammation

Potential Risks

- Lower rates of AE/SAEs associated with sabizabulin vs. placebo in Phase 2 and 3 studies in those with COVID-19
  - Can be attributed to adverse experiences associated with COVID-19 progression
- The safety risk associated with providing sabizabulin under an EUA is minimized as the indicated population would be hospitalized and under direct care and constant safety monitoring.

Benefit/risk conclusion: sabizabulin meets the criteria for EUA

- COVID-19 remains serious/life-threatening – responsible for >6 million deaths globally
  - New variants and/or surge in cases will result in increased hospitalizations, deaths and costs
- Sabizabulin therapy vs. placebo resulted in a 20.5% absolute reduction (51.6% relative reduction) in 60-day mortality over a broad range of background mortality (25% – 45%)
  - These substantial mortality reduction data for hospitalized patients with moderate to severe COVID-19 at a high risk for ARDS are far greater than for other recommended drug options
  - Remdesivir, baricitinib, tocilizumab, tofacitinib and dexamethasone offer only modest absolute mortality reductions of (0% – 5.7%)
- The totality of evidence for sabizabulin shows clear efficacy with a strongly favorable benefit:risk profile supporting its use under an EUA as likely effective and safe
- Sabizabulin addresses a significant unmet medical need for safe and effective oral therapy to treat hospitalized patients with moderate to severe COVID-19

Agenda

Introduction	**Mitchell Steiner, MD** Chief Executive Officer and Chief Medical Officer Veru Inc.
Efficacy **Safety**	**K. Gary Barnette, PhD** Chief Scientific Officer Veru Inc.
Sensitivity Analysis	**Lee-Jen Wei, PhD** Professor of Biostatistics Harvard University, T.H. Chan School of Public Health
Benefit/Risk Assessment	**Christian Sandrock, MD, MPH** Division Vice Chief of Internal Medicine and Director of Critical Care University of California, Davis, School of Medicine
Concluding Remarks	**Mitchell Steiner, MD** Chief Executive Officer and Chief Medical Officer Veru Inc.

Concluding Remarks

Mitchell Steiner, MD
Chief Executive Officer and Chief Medical Officer
Veru Inc.

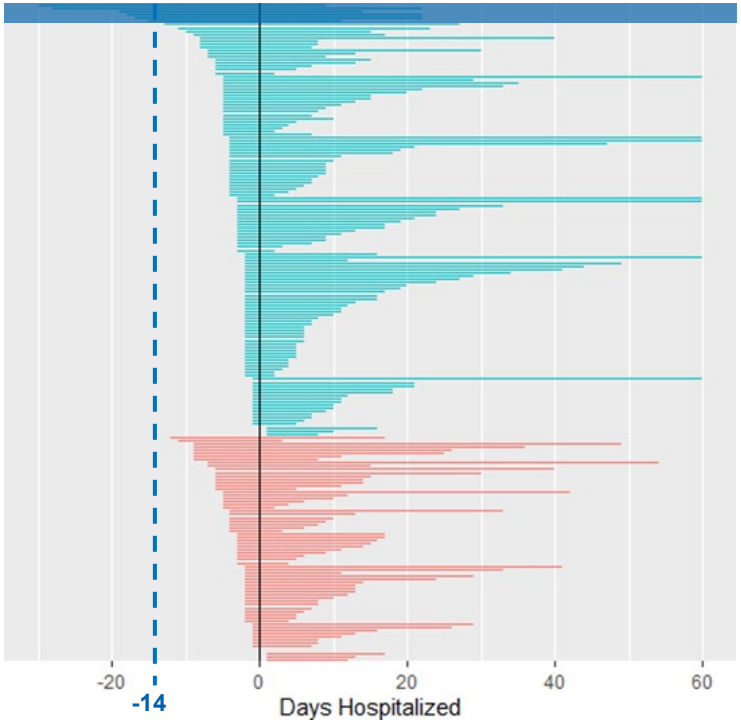
Backup Slides

Veru Inc.

Table 12: Study V3011902: Subjects by WHO Status on Day 1 of the Study

		Sabizabulin	Placebo	Absolute Change (percentage points)	Relative Change (%)	p-value
WHO 4		58	29			
	Deaths (%)	3 (5.2%)	8 (27.6%)	-22.4	-81.2%	0.0090
WHO 5		60	31			
	Deaths (%)	20 (33.3%)	15 (48.4%)	-15.1	-31.2%	0.3206
WHO 6		12	8			
	Deaths (%)	2 (16.7%)	4 (50.0%)	-33.3	-66.7%	0.2100

EFF108-2
Phase 3 study: results (ITT analysis excluding ≥14 days hospitalization)



	Sabizabulin 9 mg	Placebo	Relative risk reduction	p-value (logistic regression)
Mortality Day 15	10/125 (8.0%)	15/69 (21.7%)	-63.1%	0.0240
Mortality Day 22	16/125 (12.8%)	16/69 (23.2%)	-44.8%	0.1528
Mortality Day 29	19/124 (15.3%)	20/68 (29.4%)	-48.0%	0.0422
Mortality Day 60	24/130 (19.4%)	27/68 (39.7%)	-51.1%	0.0046

Treatment comparison	Odds ratio	95% CI	p-value (logistic regression)
Sabizabulin 9 mg vs. Placebo	2.71	(1.14, 6.46)	0.0046