Veru Inc.
Nasdaq:VERU

Oncology Biopharmaceutical Company Focused on Prostate Cancer and Breast Cancer

Cantor Virtual Global Healthcare Conference
September 27-30, 2021

Forward looking statements

This communication contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements can be identified by the use of forward-looking words or phrases such as "anticipate," "believe," "could," "expect," "intend," "may," "opportunity," "plan," "predict," "project," "potential," "estimate," "should," "will," "would" or the negative of these terms or other words of similar meaning. These statements are subject to known and unknown risks, uncertainties and assumptions, and if any such risks or uncertainties materialize or if any of the assumptions prove incorrect, our actual results could differ materially from those expressed or implied by such statements. Factors that may cause actual results to differ materially from those contemplated by such forward-looking statements include, but are not limited to: risks related to the development of Veru Inc.'s (the "Company") product portfolio, including risks regarding the regulatory pathway to secure FDA or other regulatory approval of the Company's drug candidates, the anticipated timeframe for FDA submissions and approvals, costs for clinical studies and regulatory submissions, clinical study results, including potential benefits and absence of adverse events, and the depth of the Company's drug pipeline, the market potential for the Company's drug candidates; potential delays in the timing of and results from clinical trials and studies, including potential delays in the recruitment of patients and their ability to effectively participate in such trials and studies due to COVID 19, and the risk that such results will not support marketing approval and commercialization; potential delays in the timing of any submission to the FDA and regulatory approval of products under development and the risk that disruptions at the FDA caused by the COVID-19 pandemic may delay the review of submissions or approvals for new drugs; clinical results or early data from clinical trials may not be replicated or continue to occur in additional trials or may not otherwise support further development in the specified drug candidate or at all; our pursuit of a COVID-19 treatment candidate is at an early stage and we may be unable to develop a drug that successfully treats the virus in a timely manner, if at all; risks related to our commitment of financial resources and personnel to the development of a COVID-19 treatment which may cause delays in or otherwise negatively impact our other development programs, despite uncertainties about the longevity and extent of COVID-19 as a global health concern and the possibility that as vaccines become widely distributed the need for new COVID-19 treatment candidates may be reduced or eliminated; government entities may take actions that directly or indirectly have the effect of limiting opportunities for VERU-111 as a COVID-19 treatment, including favoring other treatment alternatives or imposing price controls on COVID-19 treatments; the risk in obtaining any regulatory approval and the products being commercially successful; risks relating to the ability of the Company to obtain sufficient financing on acceptable terms when needed to fund development and Company operations; product demand and market acceptance; competition in the Company's markets and therapeutic areas and the risk of new or existing competitors with greater resources and capabilities and new competitive product introductions; the risk in sales being affected by regulatory developments, including a reclassification of the products or repeal of the Patient Protection and Affordable Care Act; price erosion, both from competing products and increased government pricing pressures; manufacturing and quality control problems; compliance and regulatory matters including costs and delays resulting from the extensive governmental regulation, and effects of healthcare insurance and regulation, including reductions in reimbursement and coverage or reclassification of products; some of the Company's products are in development and the Company may fail to successfully commercialize such products; risks related to intellectual property, including the uncertainty of obtaining patents, the effectiveness of the patents or other intellectual property protections and ability to enforce them against third parties, the uncertainty regarding patent coverages, the possibility of infringing a third party's patents or other intellectual property rights, and licensing risks; government contracting risks, including the appropriations process and funding priorities, potential bureaucratic delays in awarding contracts, process errors, politics or other pressures, and the risk that government tenders and contracts may be subject to cancellation, delay, restructuring or substantial delayed payments; the risk that delays in orders or shipments under government tenders or the Company's U.S. prescription business could cause significant quarter-to-quarter variations in the Company's operating results and adversely affect its net revenues and gross profit; a governmental tender award indicates acceptance of the bidder's price rather than an order or guarantee of the purchase of any minimum number of units, and as a result government ministries or other public sector customers may order and purchase fewer units than the full maximum tender amount or award; penalties and/or debarment for failure to satisfy tender awards; the Company's reliance on its international partners and on the level of spending by country governments, global donors and other public health organizations in the global public sector; risks related to concentration of accounts receivable with our largest customers and the collection of those receivables; the economic and business environment and the impact of government pressures; risks involved in doing business on an international level, including currency risks, regulatory requirements, political risks, export restrictions and other trade barriers; the Company's production capacity, efficiency and supply constraints and interruptions, including potential disruption of production at the Company's and third party manufacturing facilities and/or of the Company's ability to timely supply product due to labor unrest or strikes, labor shortages, raw material shortages, physical damage to the Company's and third party facilities, COVID-19 (including the impact of COVID-19 on suppliers of key raw materials), product testing, transportation delays or regulatory actions; risks related to the costs and other effects of litigation, including product liability claims; the Company's ability to identify, successfully negotiate and complete suitable acquisitions or other strategic initiatives; the Company's ability to successfully integrate acquired businesses, technologies or products; and other risks detailed in the Company's press releases, shareholder communications and Securities and Exchange Commission filings, including Company's Annual Report on Form 10-K for the year ended September 30, 2020 and subsequent quarterly reports on Form 10-Q. This documents are available on the "SEC Filings" section of our website at www.verupharma.com/investors. All forward-looking statements are based on information available to us as of the date hereof, and Company does not assume any obligation and does not intend to update any forward-looking statements, except as required by law.

Oncology biopharmaceutical company
Focus on prostate cancer and breast cancer

Veru
Drug Pipeline

Prostate Cancer	Sabizabulin 32mg	VERU-100
Breast Cancer	Enobosarm	Sabizabulin 32mg
COVID-19	Sabizabulin 9mg	
BPH	TADFIN™ PDUFA – December 2021	

- Late-stage clinical pipeline focused on prostate cancer & breast cancer
- 6 pivotal and pivotal-enabling clinical studies planned to commence in calendar year 2021

UREV
Women's Health Division

FC2 Female Condom (internal condom)

FC2 FY 2020 Net Revenues:	$ 40.6 mm
FC2 FYTD 2021 Net Revenues:	$ 44.8 mm
Sexual Health Business FYTD 2021 Operating Income:	$ 32.8 mm
FC2 Q3 FY 2021 Net Revenues:	$ 17.7 mm

Veru Financials

Cash: $123.2 mm
Receivables: $8.3 mm

(as of June 30, 2021)

Veru FY 2020 Net Revenues:	$ 42.6 mm
Veru FYTD 2021 Net Revenues:	$ 45.6 mm
Veru FYTD 2021 Gross Profit:	$ 35.6 mm
Veru Q3 FY 2021 Net Revenues:	$ 17.7 mm
Veru Q3 FY 2021 Gross Profit:	$ 13.9 mm

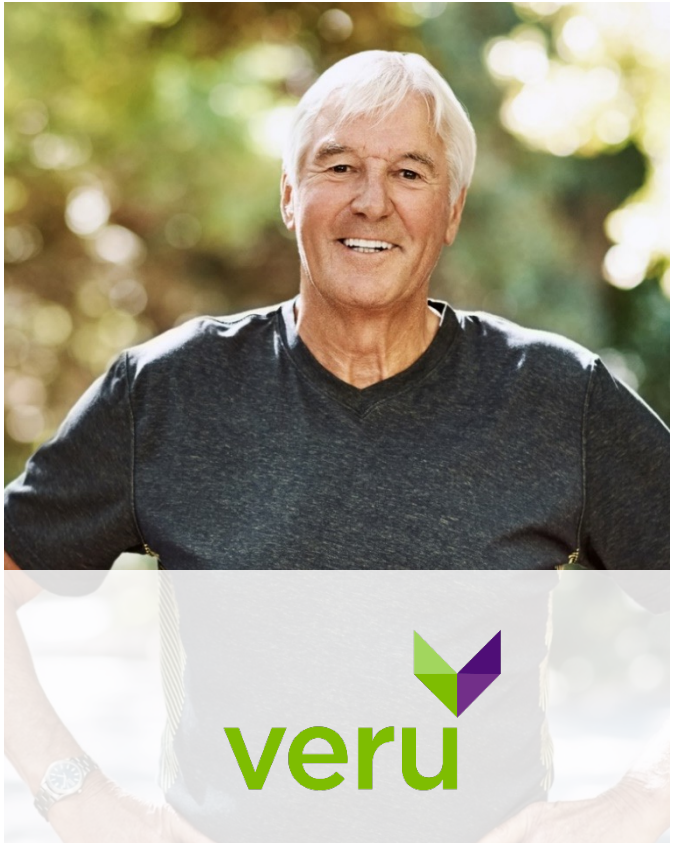
Drug candidate pipeline
Oncology biopharmaceutical company focused on prostate cancer and breast cancer

Program	Mechanism	Indication	Preclinical	Phase 1	Phase 2	Phase 3
Prostate Cancer						
Sabizabulin	Oral cytoskeleton disruptor and androgen receptor transport disruptor	Metastatic castration and AR targeting agent resistant prostate cancer				Phase 3 VERACITY: 245 Patients - Enrolling
VERU-100	Gonadotropin-releasing hormone antagonist 3-month subcutaneous depot injection	Hormone sensitive advanced prostate cancer			Phase 2: 35 Patients - Enrolling	
Breast Cancer						
Enobosarm	Selective androgen receptor targeted agonist	AR+ER+HER2- metastatic breast cancer (3rd line metastatic)				Phase 3 ARTEST: Planned Q3 2021 - 210 Patients
Enobosarm + abemaciclib combination	Selective androgen receptor targeted agonist + CDK4/6 inhibitor	AR+ER+HER2- metastatic breast cancer (2nd line metastatic)			Phase 2b: Planned Q4 2021 - 186 Patients	
Sabizabulin	Oral cytoskeleton disruptor	Metastatic triple negative breast cancer			Phase 2b: Planned Q3 2021 - 216 Patients	
Virology						
Sabizabulin	Oral cytoskeleton disruptor	Hospitalized COVID-19 patients at high risk for ARDS				Phase 3: 300 Patients - Enrolling

[1] Certain information herein represents objectives of the Company. Whether these objectives will be met as anticipated or at all depends on a variety of factors outside of the Company's control.

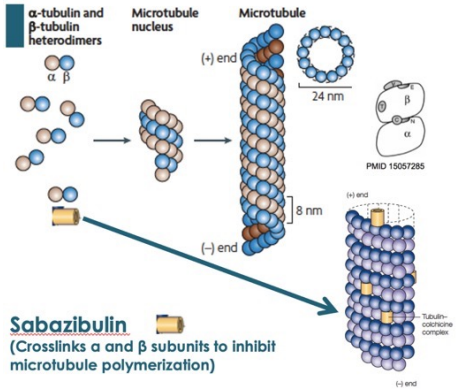
Prostate Cancer – Novel Medicines

Program	Mechanism	Indication	Preclinical	Phase 1	Phase 2	Phase 3
Sabizabulin	Oral cytoskeleton disruptor and androgen receptor transport disruptor	Metastatic castration and AR targeting agent resistant prostate cancer	Phase 3 VERACITY: 245 Patients			
VERU-100	GnRH antagonist 3-month subcutaneous depot injection	Hormone sensitive advanced prostate cancer	Phase 2: 35 Patients			



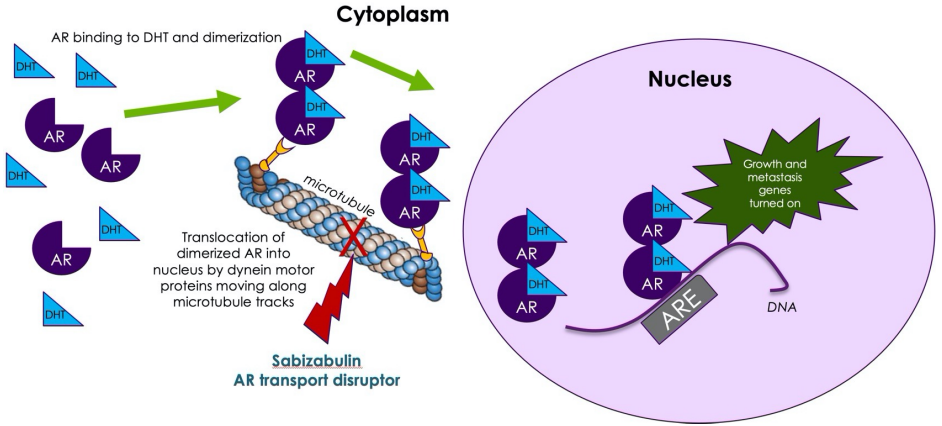
Sabizabulin is an oral agent that targets and disrupts the cytoskeleton

AR independent
Targets cytoskeleton to crosslink and inhibit microtubule assembly[1]



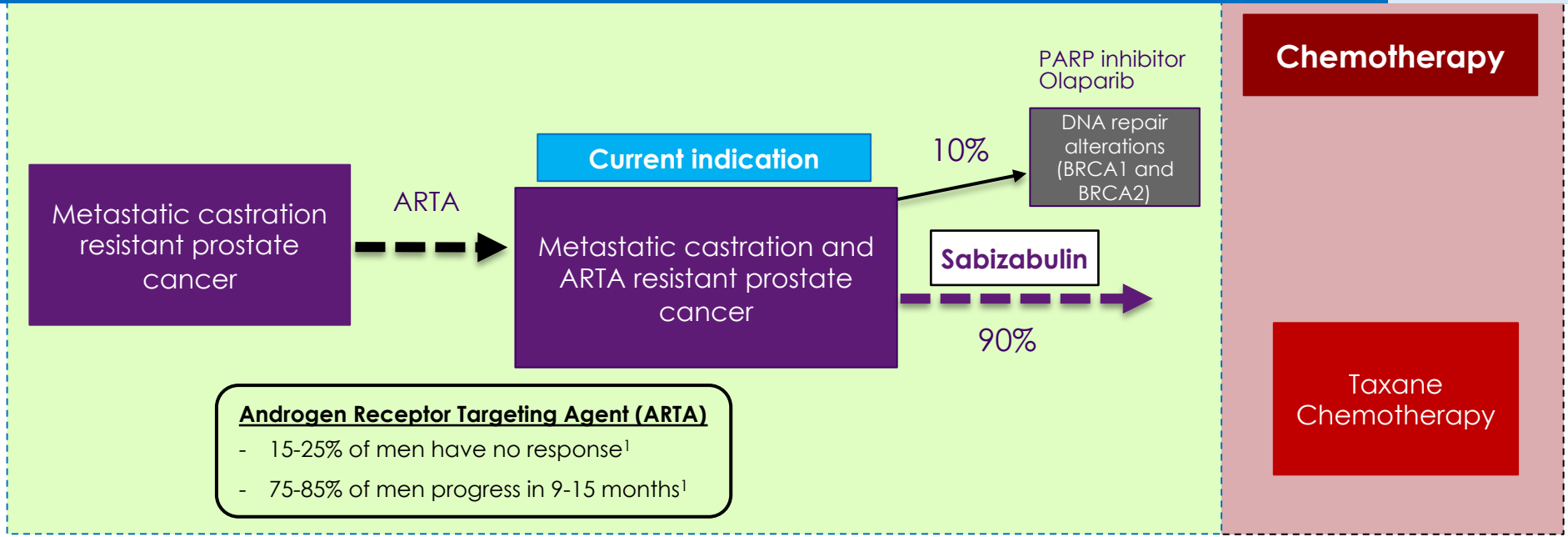
- Targets the "colchicine binding site" to crosslink α and β subunits to inhibit microtubule polymerization (low nM concentration)
- Not a substrate for multidrug resistance proteins (P-gp, MRPs, and BCRP)
- Favorable toxicity profile no neurotoxicity and no neutropenia or myelosuppression
- Demonstrated activity against taxane, vinca alkaloid, doxorubicin, enzalutamide, and abiraterone resistant prostate cancers
- Has broad activity against other tumor types as well: Triple negative breast cancer (taxane resistant)[7], Cervical cancer (taxane resistant)[8] , Lung cancer (taxane resistant)[9], Ovarian cancer (taxane resistant)[10], Uterine cancer[11], Pancreatic cancer[12], Melanoma[13], Human promyelocytic leukemia (vincristine resistant)[14]

AR directed
Disrupts androgen receptor transport



[1] Chen J et al. J Med Chem 55:7285-7289 2012 | [2] Li CM et al. Pharm Res 29:3053-3063 2012 | [3] Lu Y et al. J Med Chem 57:7355-7366 2014 | [4] 28 day rat and dog toxicity studies on file at Veru, Inc.| [5] Dumontet C et al. Nature Reviews Drug Discovery 9:790, 2010 | [6]Markowski M et al J Clin Onc 37:167, 2019 | [7] Deng S et al Mol Cancer Ther 19:348-63, 2020 | [8]Kashyap VK et al Cancer Lett 470:64-74, 2020 | [9]Foyez M et al Data on file Veru, Inc. 2020 | [10,11] Data on file Veru, Inc. 2020 | [12]Kashyap V et al J Experimental and Clinical Can Res 38:29, 2019 | [13] Chen J et al J Med Chem 55:7285-7289, 2012; Hwang DJ et al ACS Med Chem Lett 6:993-997, 2015| [14] Data on file Veru, Inc. 2014

Sabizabulin prostate cancer treatment paradigm:
Focus is on the prechemotherapy space which is a growing unmet need



Need for new safe and effective treatment alternatives with a distinct mechanism of action (non-AR dependent) and easy mode of administration remains an unmet need

[1]ES Antonarakis. *Clin Adv Hem Onc* 14:316-319 2016.

Sabizabulin clinical development
Phase 1b (expansion cohort) and Phase 2 clinical study design- ONGOING STUDY

Phase 1b- Dose escalation to evaluate safety of sabizabulin in men with metastatic castration resistant prostate cancer following at least one prior AR targeting agent therapy and up to one taxane

- 7 US sites – Johns Hopkins Kimmel Comprehensive Cancer Center (lead center)
- 39 patients enrolled
- Trial design -2 part dosing schedule using standard 3+3 dose escalation strategy
  - Part 1- 7-day dose schedule – At each dose level, orally administered daily on Day 1-7 every 21 days (i.e. 7 days on, 14 days off)
  - Part 2- Expanded dose schedule – If 7-day dosing tolerated/safe, patients increased frequency to Day 1-14 daily dosing every 21 days (i.e. 14 days on, 7 days off). If 14-day dosing tolerated/safe, then advance to dosing daily with continuously until disease progression/toxicity

Phase 2- Evaluate safety and efficacy of sabizabulin RP2D 63mg PO q d in metastatic castration resistant prostate cancer and following at least one prior AR targeting agent therapy, but prior to IV chemotherapy

- 13 U.S. clinical centers
- 44 men enrolled
- Completed enrollment in September 2020
- Trial design
  - Open label
  - Recommended Phase 2 dose is 63mg/day
  - PK study to evaluate Phase 2 dosage versus Phase 3 dosage formulation

Phase 1b and 2 clinical studies
Baseline demographics

Characteristic	Phase 1b N=39	Phase 2 N=41
Age, years		
Median (range)	74 (61-92)	73 (57-86)
Race/Ethnicity, n (%)		
Caucasian	28 (72%)	31 (76%)
African American	8 (21%)	4 (10%)
Hispanic	3 (8%)	5 (12%)
Other	0	1 (2%)
ECOG performance status, n (%)		
0	21 (54%)	30 (73%)
1	16 (41%)	10 (24%)
2	2 (5%)	1 (2%)
Metastatic disease location		
Bone only	21 (55%)	24 (59%)
Lymph node only	6 (16%)	8 (20%)
Bone and lymph node	8 (21%)	7 (17%)
Visceral only	1 (3%)	0
Bone and visceral	1 (3%)	1 (2%)
Lymph node and visceral	0	1 (2%)
Prior therapies		
Abiraterone	14 (36%)	7 (17%)
Enzalutamide	8 (20%)	13 (32%)
Abiraterone and enzalutamide or apalutamide or proxalutamide	17 (44%)	14 (34%)
Apalutamide or proxalutamide	0	5 (12%)
Abiraterone and enzalutamide and apalutamide or proxalutamide	0	2 (5%)
Taxane	9 (23%)	3 (7%)

Sabizabulin clinical development
Safety- Phase 1b (expansion cohort) and Phase 2 clinical study

Most prevalent adverse events regardless of grade (>10% frequency) in patients that received 63 mg dose
N=54

Adverse Event	All Grades regardless of relationship to study drug	Grade ≥3 regardless of relationship to study drug
Diarrhea	32 (59.3%)	4 (7.4%)
Fatigue	18 (33.3%)	3 (5.6%)
Nausea	17 (31.5%)	1 (1.9%)
Decreased appetite	17 (31.5%)	0
Constipation	9 (16.7%)	0
ALT increased	10 (18.5%)	3 (5.6%)
AST increased	9 (16.7%)	2 (3.7%)
Back pain	8 (14.8%)	1 (1.9%)
Vomiting	7 (13.0%)	1 (1.9%)
Abdominal pain	6 (11.1%)	0
Dysgeusia	6 (11.1%)	0

Diarrhea was mostly (88%) grade 1 and 2 and medically manageable as only 1 patient discontinued clinical study because of this adverse event; expect this adverse event to be less in Phase 3 because of better oral bioavailability of Phase 3 dosage form and reduced exposure of GI tract to non-absorbed sabizabulin

At the recommended Phase 2 dose (RP2D) of 63 mg oral daily dose of sabizabulin

- Sabizabulin was well tolerated with no reports of clinically relevant neutropenia or neurotoxicity
- Adverse events were mostly grade 1 and 2[1]
- Safety profile appears similar as what is reported for an androgen receptor targeting agent
- Daily chronic drug administration is feasible and safe

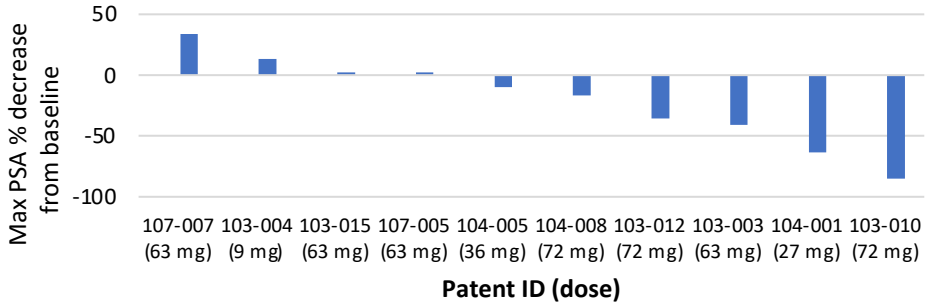
[1] Combined Phase 1b/2 efficacy data in men who received sabizabulin 63mg dose

Sabizabulin Phase 1b efficacy
PCWG3 criteria to evaluate efficacy after 12 weeks of treatment (4 cycles)

- **10 men reached at least four cycles of continuous dosing**
  - Disease (4 Bone;3 LN; and 3 LN+Bone)
  - Previous treatment- (5 Abi; 2 Enz; and 3 Abi+Enz)
- **PSA responses**
  - 6/10 had decrease in PSA
  - 4/10 had ≥ 30% decline in PSA
  - 2/10 had ≥ 50% decline in PSA
- **Best objective tumor responses**
  - 2 men had partial response (PR) (two additional objective responses occurred in subjects who did not reach 4 cycles)
  - 8 men had stable disease (SD)
- **Median radiographic progression free survival**
  - >12 months (range 6.0-28+ months)
- **2/10 men still on study as of August 2021**

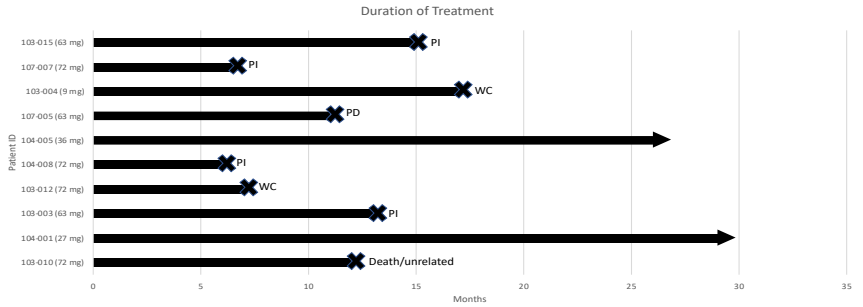
PSA waterfall plot

Ten men have reached ≥ 4 cycles of continuous dosing



Swimmers' plot

Ten men have reached ≥ 4 cycles of continuous dosing



Sabizabulin clinical development
Efficacy- Phase 1b (expansion cohort) and Phase 2 study

Sabizabulin had evidence of significant and durable objective tumor responses	
In ITT population, all patients with measurable disease at baseline (n=29)	ORR (5PR +1CR observed): 20.7%[1]
All evaluable patients that would qualify for Phase 3 (n=26)	ORR: 23.1%[1]
In all patients[1] that received ≥ 63 mg (n=55)	Median rPFS is estimated to be at least: 7.4 months (Actual median rPFS has not been reached in the Phase 2 as there are still 10 men on study[1])

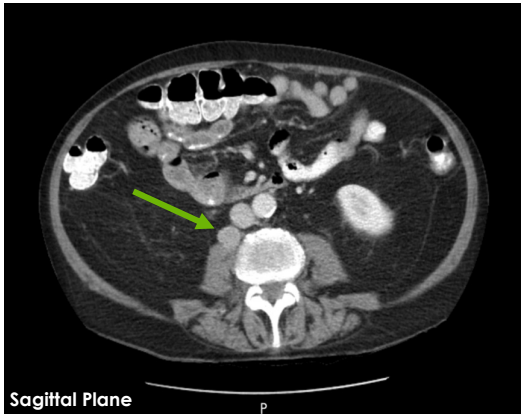
[1]Combined Phase 1b/2 efficacy data in men who received sabizabulin 63mg dose as of February 2021 and excluded superscan disease where follow up of lesions is not possible

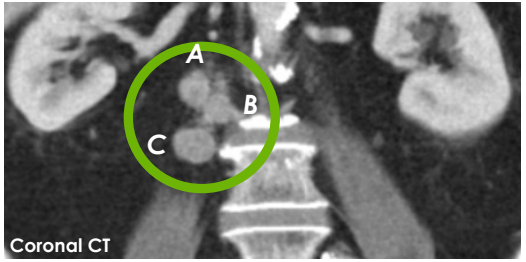
Sabizabulin clinical development
Phase 1b case study patient 104-001

Patient: 104-001

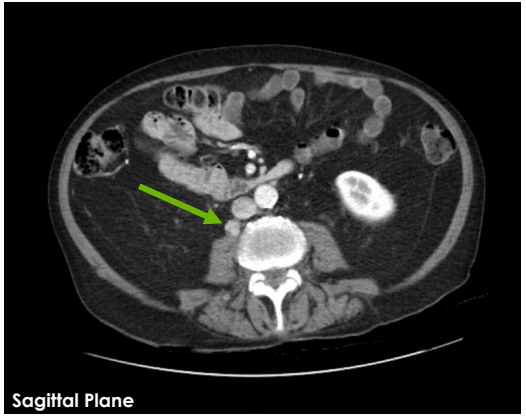
- mCRPC with lymph node only disease
- Prior treatment included:
  - Sipuleucel-T
  - Enzalutamide
  - Abiraterone
- Efficacy
  - Still on study >28 months
  - -63% PSA from 21day cycle initiation baseline
  - ORR= PR

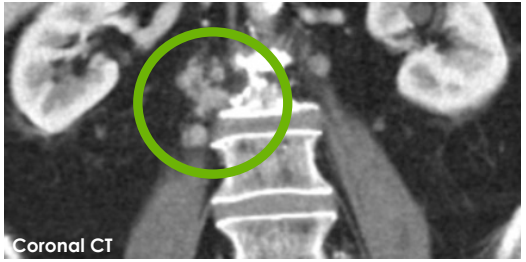
March 08, 2019: Screening CT scan
RP LN 1.7cm X 1.5cm
(measurable target lesion)





June 10, 2020: 15 months follow-up
RP LN 1.1cm X 1.0cm
(-33% decrease to nonpathologic node)



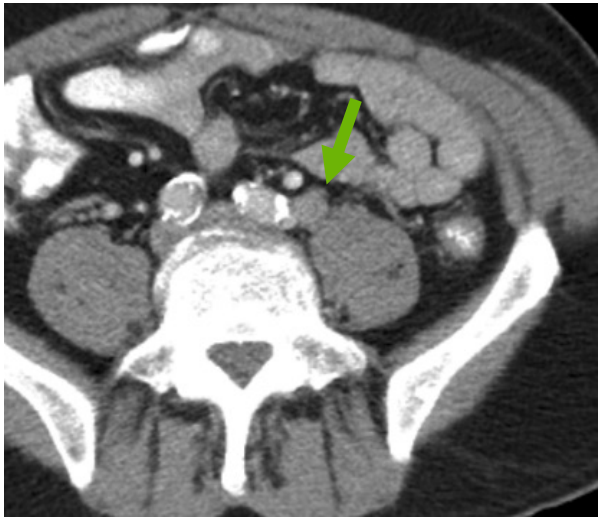


Sabizabulin clinical development
Phase 2 case study patient 104-017

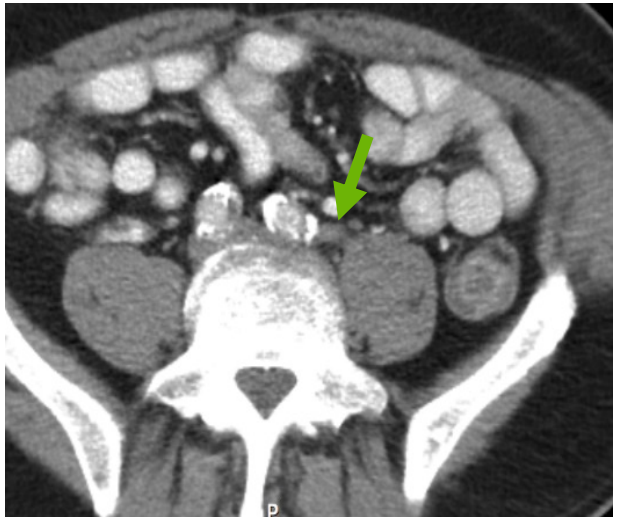
Patient: 104-017

- mCRPC with lymph node only disease
- Prior treatment included:
  - Apalutamide
- Efficacy
  - Still on study >12 months
  - -69% PSA from 21day cycle initiation baseline
  - ORR= CR

July 8, 2020: Screening CT scan
Left common femoral node 1.4 cm
(target lesion)



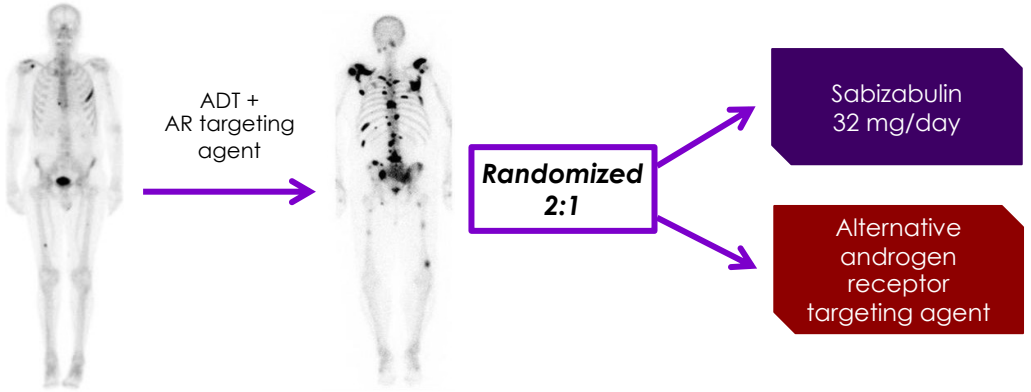
September 29, 2020: 3 months follow-up
Left common femoral node 0.7 cm
(-50% decrease to nonpathologic node)



Phase 3 VERACITY clinical trial (V3011102) (NCT#-04844749) Enrolling in approximately 45 clinical sites

VERACITY - Randomized, Active-Controlled, Open label Phase 3 Study of Sabizabulin 32mg for the Treatment of Metastatic Castration-Resistant Prostate Cancer in Patients Whose Prior Treatment Failed with at Least One Androgen Receptor Targeting Agent – Lead PI – Robert Dreicer, MD

- **Efficacy endpoints**
  - Primary endpoints
    - Radiographic progression free survival (rPFS)
  - Secondary endpoints
    - Objective response rate
    - Duration of objective response
    - OS (interim analysis)
    - Time to IV chemo
    - Pain progression
- **Assumptions**
  - Median rPFS- 7.4 months for sabizabulin vs 3.7 months for alternative AR targeting agent*
  - Sample size - 245 men
    - 2:1 randomization
    - 155 events expected
    - a = 0.05
    - 98% power
    - Drop out= 30%
    - 10 months recruitment time, 12 month follow up after last patient first dose



*Based on Olaparib study[1] and CARD study[2] an alternative androgen receptor targeting agent is expected to have a median rPFS of 3.6-3.7 months in this similar population

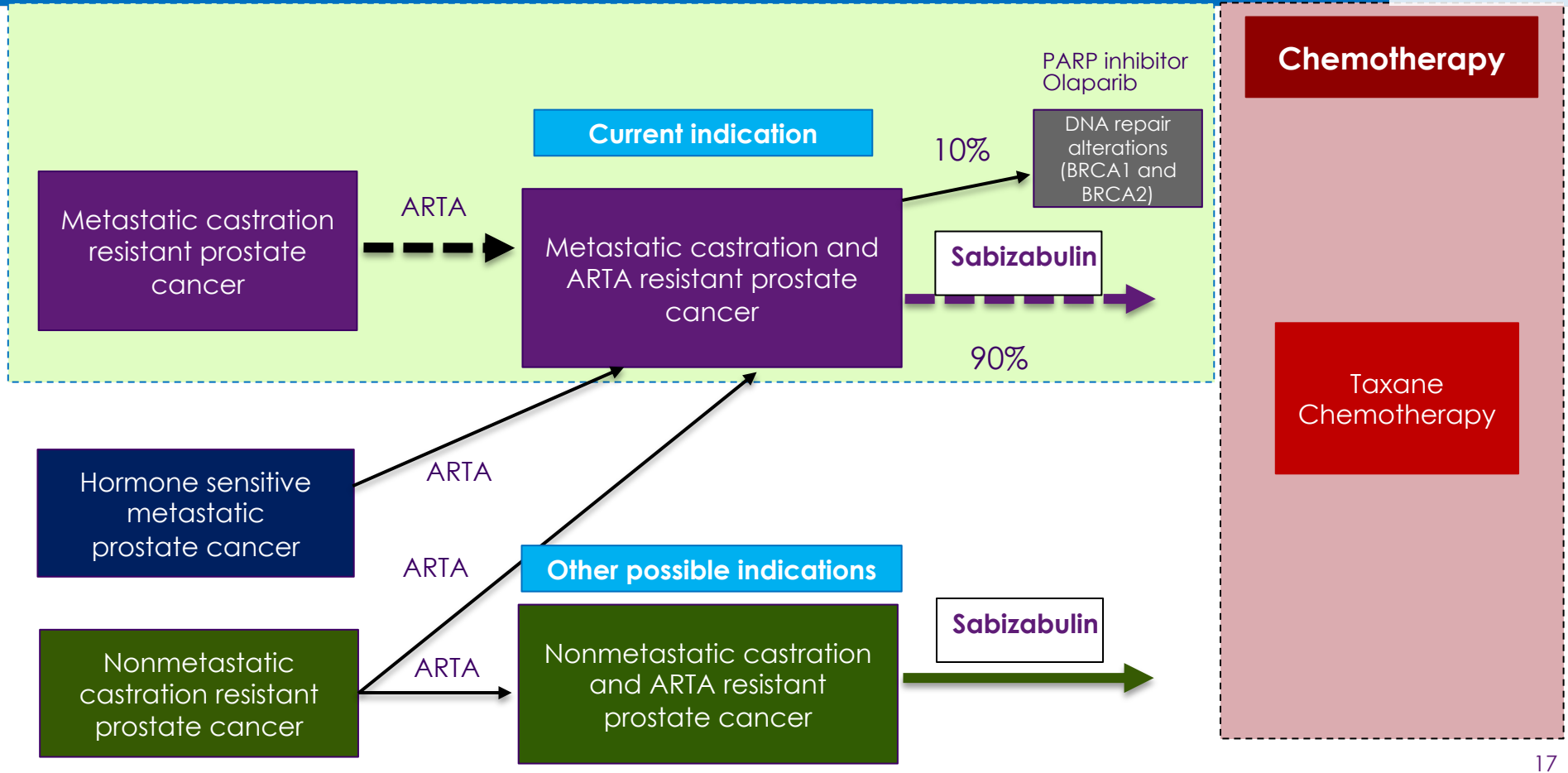
[1] de Bono J et al. NEJM April 28,2020 | [2] de Wit R et al. NEJM 381:2506-18 2019

Sabizabulin 1b/2 clinical development:
Conclusions

Sabizabulin was well tolerated with evidence of significant and durable objective tumor responses

- At the recommended Phase 2 dose (RP2D) of 63mg oral daily dose of sabizabulin
  - Well tolerated with no reports of significant neutropenia or neurotoxicity.
  - Daily chronic drug administration is feasible and safe
  - Safety profile appears similar to that reported in package inserts for an androgen receptor targeting agent
- Evidence of antitumor activity was observed including PSA reductions, objective and durable tumor responses (CR+PR)
- May be potentially prescribed by both Urologists and Medical Oncologists
- Phase 3 VERACITY clinical trial is currently underway to evaluate the efficacy and safety of sabizabulin versus an alternative AR targeting agent in men with mCRPC that have failed at least one AR targeting agent

Sabizabulin prostate cancer treatment paradigm:
Focus is on the prechemotherapy space- largest segment of advanced prostate cancer

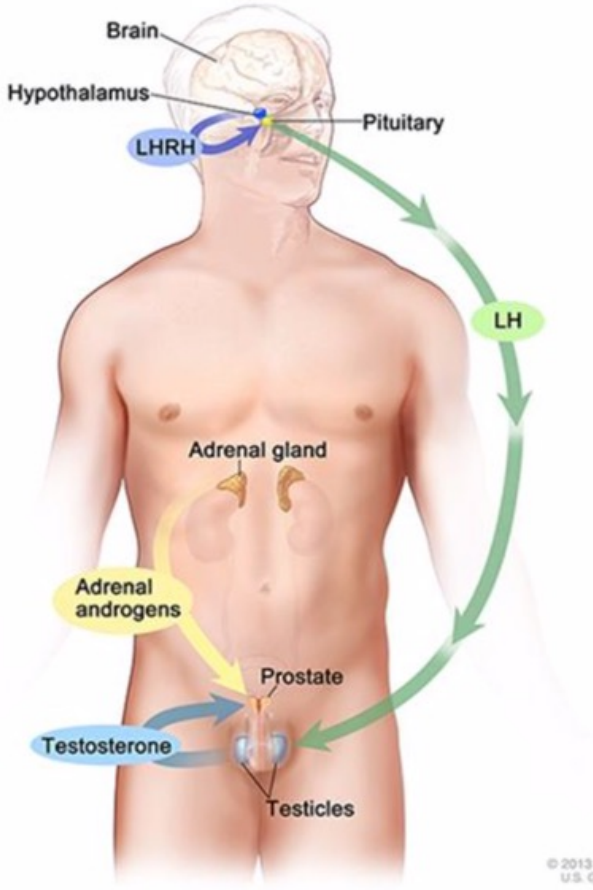


Quest for a better androgen deprivation therapy: VERU-100
Current commercial limitations

LHRH agonist

Long-acting products: LUPRON® Depot (IM) and ELIGARD® (SC) are leuprolide products

- Concerns over initial surge in T levels- "T surge"
- Escapes from castration T levels – periodic increases in T levels[1]
- Up to 17% of men do not achieve castration[1]
- Does not suppress FSH
- Black box warning for cardiovascular safety concerns



GnRH antagonist

FIRMAGON® (degarelix) (SC)

- Painful subcutaneous injections: large loading and maintenance doses
  - Loading 6mL (2 X 3 mL)
  - Maintenance 4 mL
- No long acting depot available
- Must be given every month

[1] Gomella LG et Rev Urol 2009 11:52-60.

New potential product to addresses limitations of current ADT
Long-acting 3 month depot GnRH antagonist may provide better alternative

VERU-100 target product profile[1,2]

- Novel proprietary GnRH antagonist decapeptide delivery formulation
- 3 month slow release subQ depot with no loading dose
  - Better compliance
  - Injectable delivery formulation is consistent with current medical practice patient visit schedule and billing/reimbursement procedures (Medicare Part B)
- Better castration
  - Immediate testosterone suppression no initial testosterone surge
  - Suppression of testosterone to less than 20ng/dL
  - Fewer testosterone escapes (micro-increases in testosterone)
- No black box warning for cardiovascular adverse effects for this class of drugs

Phase 2 open label, dose finding VERU-100 GnRH antagonist long acting 3 month depot clinical trial actively enrolling approx. 35 men

[1]Developed in collaboration with Drug Delivery Experts, LLC (San Diego, California); [2]Veru Inc. VERU-100 Target Prescribing Information

Breast Cancer – Novel Medicines

Program	Mechanism	Indication	Preclinical	Phase 1	Phase 2	Phase 3
Enobosarm	Selective androgen receptor targeted agonist	AR+ER+HER2- metastatic breast cancer (3rd line metastatic)				Phase 3 ARTEST: Planned Q3 2021 – 210 Patients
Enobosarm + abemaciclib	Selective androgen receptor targeted agonist + CDK4/6 inhibitor	AR+ER+HER2- metastatic breast cancer (2nd line metastatic)			Phase 2: Planned Q3 2021 – 186 Patients	
Sabizabulin	Oral cytoskeleton disruptor	Metastatic triple negative breast cancer			Phase 2: Planned Q4 2021 – 216 Patients	

Endocrine therapies that target estrogen receptor pathways are effective against ER+ breast cancer

Current Endocrine Therapies

Selective estrogen receptor modulators (tamoxifen and toremifene)

ER antagonists and degraders (fulvestrant)

Aromatase inhibitors (AI)
- AROMASIN® (exemestane) - steroidal AI
- ARIMIDEX® (anastrozole) and FEMARA ®(letrozole) - nonsteroidal AI

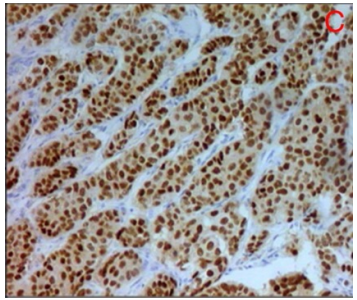
CDK 4/6 inhibitors in combination with nonsteroidal AI or fulvestrant

Resistance to endocrine and CDK4/6 inhibitor therapies eventually occurs which requires alternative treatment approaches including chemotherapy[1, 2]

[1]Alluri et al., Breast Cancer Res 16:494, 2014 | [2]Basile D et al. Cancer Treatment Reviews 61:15-22, 2017|

Androgen receptor is the most abundantly expressed sex hormone receptor in breast cancers with up to 95% of breast cancers[2-6]

- **What is the androgen receptor's function in breast tissue?**
- **Does activation of the androgen receptor stimulate or suppress breast cancer growth?**
  - In normal and cancerous breast tissue, androgens inhibit cellular proliferation [1-3]
  - AR positivity is an independent predictor of beneficial breast cancer outcome[2,3,5,6]
- **Historically, androgens have been used in breast cancer treatment with good efficacy, but their masculinizing effects, increase in hematocrit, and liver toxicity have prohibited their use as a viable treatment**
- **The development of novel strategies *to target and to activate* AR, tumor suppressor, as a treatment for AR+ER+ breast cancer that have become resistant to drugs that target the ER is warranted[3]**



Ductal infiltrating breast carcinoma 3+ AR nuclear positivity[7]

nature medicine ARTICLES
https://doi.org/10.1038/s41591-020-01168-7
Check for updates

The androgen receptor is a tumor suppressor in estrogen receptor–positive breast cancer

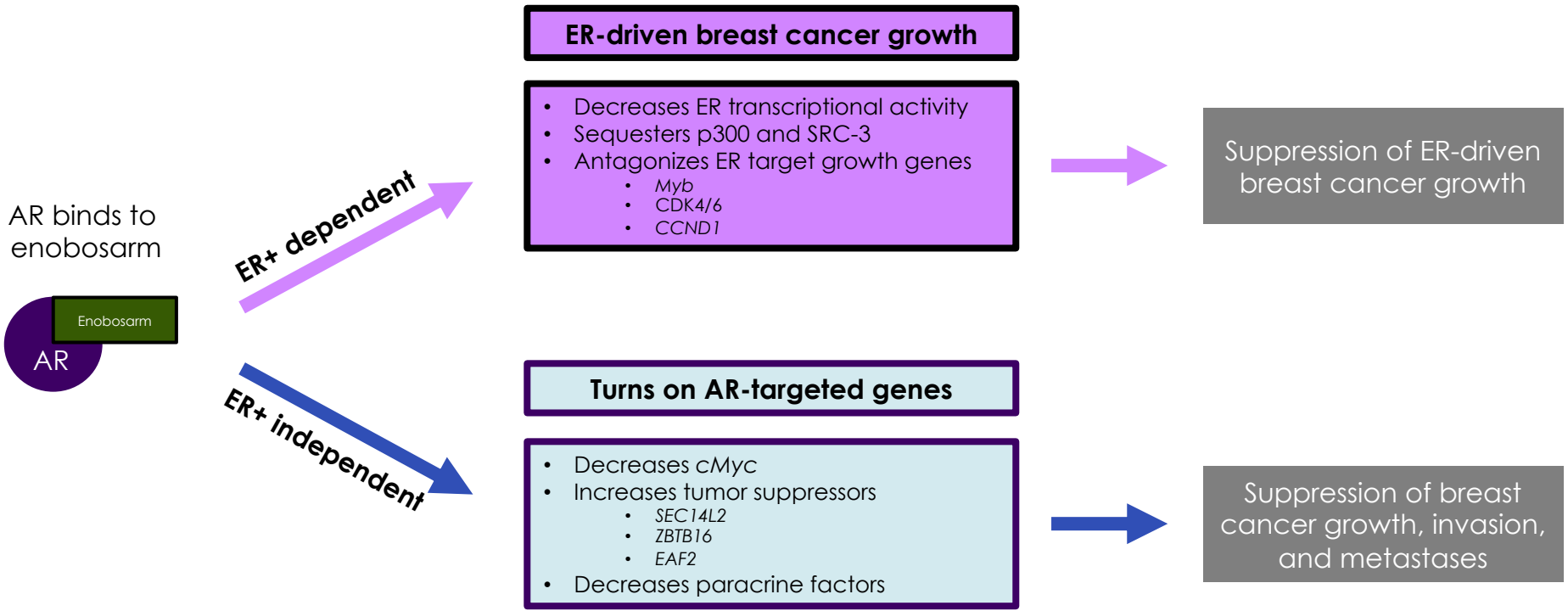
Theresa E. Hickey[1], Luke A. Selth[1,2,3], Kee Ming Chia[4], Geraldine Laven-Law[1], Heloisa H. Milioli[4], Daniel Roden[4], Shalini Jindal[1], Mun Hui[4], Jessica Finlay-Schultz[5], Esmaeil Ebrahimie[1], Stephen N. Birrell[1], Suzan Stelloo[6,11], Richard Iggo[1,7], Sarah Alexandrou[4], C. Elizabeth Caldon[4], Tarek M. Abdel-Fatah[8], Ian O. Ellis[8], Wilbert Zwart[6], Carlo Palmieri[9], Carol A. Sartorius[5], Alex Swarbrick[4], Elgene Lim[4], Jason S. Carroll[10] and Wayne D. Tilley[1,3]

The role of the androgen receptor (AR) in estrogen receptor (ER)-α-positive breast cancer is controversial, constraining implementation of AR-directed therapies. Using a diverse, clinically relevant panel of cell-line and patient-derived models, we demonstrate that AR activation, not suppression, exerts potent antitumor activity in multiple disease contexts, including resistance to standard-of-care ER and CDK4/6 inhibitors. Notably, AR agonists combined with standard-of-care agents enhanced therapeutic responses. Mechanistically, agonist activation of AR altered the genomic distribution of ER and essential co-activators (p300, SRC-3), resulting in repression of ER-regulated cell cycle genes and upregulation of AR target genes, including known tumor suppressors. A gene signature of AR activity positively predicted disease survival in multiple clinical ER-positive breast cancer cohorts. These findings provide unambiguous evidence that AR has a tumor suppressor role in ER-positive breast cancer and support AR agonism as the optimal AR-directed treatment strategy, revealing a rational therapeutic opportunity.

[1]Birrell et al, J Steroid Biochem Mol Biol 52:459-67, 1995 | [2]Peters et al, Cancer Res 69: 6131-40, 2009 | [3]Hickey et al, Nature Medicine 2021 | [4]Moinfar et al, Cancer 98:703–11, 2003 | [5]Hu et al, Clin Cancer Res 17:1867–74, 2011 | [6]Ricciardelli et al, Clin Cancer Res 24:2328-41, 2018 | [7]Bronte et al, Trans Oncol 11: 950–956, 2018 |

Mechanism of action of enobosarm in breast cancer[1,2]

Androgen receptor activation by enobosarm leads to breast cancer tumor suppression



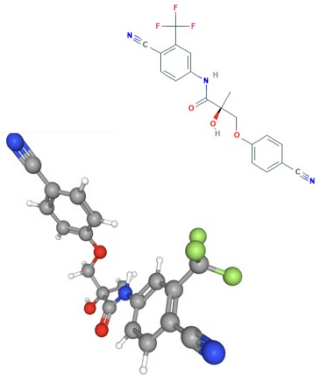
[1]Adapted from Hickey et al, Nature Medicine February 2021 | [2] Narayanan R et al. PLOS one 9:e103202, 2014

Enobosarm, first-in-class, novel oral selective AR targeting agonist for the treatment for AR+ER+ metastatic breast cancer

- **Enobosarm is a non-steroidal, selective androgen receptor agonist[1, 2]**
  - Once-a-day oral daily dosing
  - Selectivity to activate the androgen receptor with no cross-reactivity to other steroidal hormone receptors
  - Not a substrate for aromatase, thus cannot be aromatized to estrogen
  - Builds and heals bone- potential to treat antiestrogen-induced osteoporosis and prevent skeletal related events[3,4,5]
  - Anabolic on muscle to improve muscle mass and physical function[2,6]
  - Selective tissue activities translate to a favorable side-effect profile
    - Non-masculinizing (no unwanted hair growth or acne)
    - No liver toxicity
    - No changes in hematocrit
- **Enobosarm suppresses AR+ER+ breast cancer in cell and patient-derived xenograft models of endocrine sensitive and resistant disease[7]**

Enobosarm has been evaluated in 25 clinical trials comprising 2,091 subjects (348 subjects dosed at > 9mg) which includes:

- 6 Phase 2 studies in breast cancer (5) or breast disease (1)
- 12 Phase 1 studies for NDA label completed



Chemical structure of Enobosarm

[1] Narayanan R et al. Mol Cell Endocrinol 2017 | [2] Dalton JT et al. Curr Opin Support Palliat Care 7:345-351, 2013 | [3]Kamrakova M et al Calcif Tissue Int 106:147-157,2020 | [4]Hoffman DB et al. J Bone Metaab 37:243-255, 2019 | [5]KearbeyJD et al Pharm Res 26:2471-2477, 2009 | [6]Dobs AS et al. Lancet Oncol 14:335-45, 2013 | [7]Hickey et al., Nature Medicine

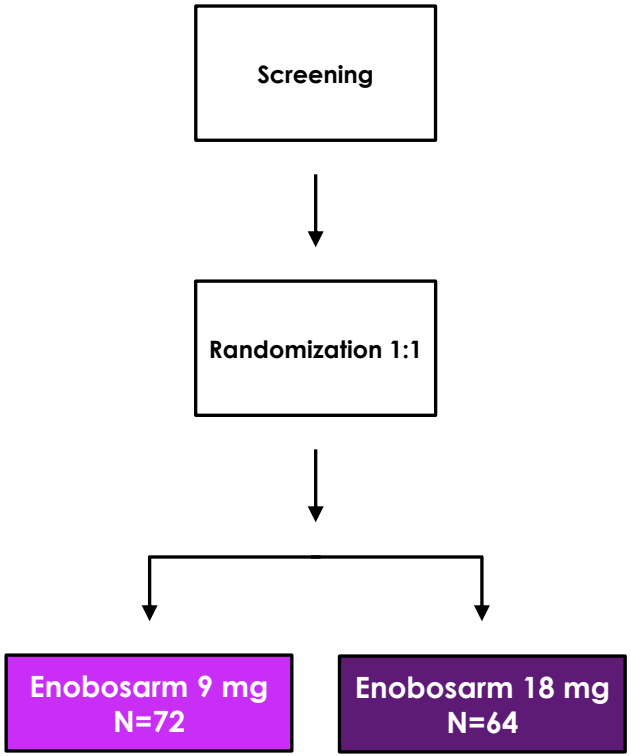
Phase 2 clinical trial (G200802) design
Targeting AR+ER+ metastatic breast cancer in a heavily pretreated population[1]

Trial design

- Open label, multicenter, multinational, randomized parallel design Phase 2 study to assess the efficacy and safety of enobosarm 9 mg or 18 mg oral daily dose in postmenopausal subjects with AR+ER+ metastatic breast cancer
- Efficacy primary endpoint- To assess the clinical benefit rate (CBR) (CR + PR + SD) in subjects with AR+ breast cancer treated at 6 months (by RECIST 1.1)

Patient population - 136 women enrolled

- ER+ metastatic or locally recurrent breast cancer not amenable to surgery
  - AR status was assessed centrally (>10%) and AR+ patients were included in the evaluable patients
  - Patients that were AR negative, not determined or uninformative were not in the evaluable population
- Previously responded to adjuvant endocrine Tx for ≥3 years, or most recent endocrine Tx for metastatic disease ≥ 6 months



[1]Palmieri C et al Phase 2 Clinical Trial results. San Antonio Breast Cancer Symposium Satellite Spotlight. December 2020

Phase 2 clinical trial (G200802)
Patient baseline demographics

Demographics	9 mg cohort	18 mg cohort
Age (median), years (range)	60.5 (35-83)	62.5 (42-81)
Caucasian (%)	98.0	94.2
Initial presentation of Stage IV metastatic breast cancer	12%	26.9%
Median months since initial diagnosis (range)	110.0 (19-435)	86.0(15-323)
Median months since metastatic diagnosis (range)	34.3 (1-167)	27.4 (1-225)
Source of tissue AR primary/metastatic (%)	52/44	57.7/40.4
Median % of cells staining AR+ (range)	53.4 (11-96)	51.4 (14-98)
AR status confirmed centrally (%)	94.0	86.5
Bone only non-measurable (%)	38.0	32.7
Prior chemotherapy (%)	90.0	92.3
Median prior lines of endocrine therapy (range)	3.2 (1-7)	3.2 (1-7)

Phase 2 clinical trial (G200802)
Overall safety and efficacy summary

Enobosarm was well tolerated
majority of events were Grade 1 and 2

	9 mg N=75	18 mg N=61
Patients with any SAEs	8 (10.7%)	10 (16.4%)
Grade 3 Drug Related Adverse Events	5	9
Grade 4 Drug Related Adverse Events	1	1
Patients with Treatment-Emergent Adverse Events Leading to Death	0	0

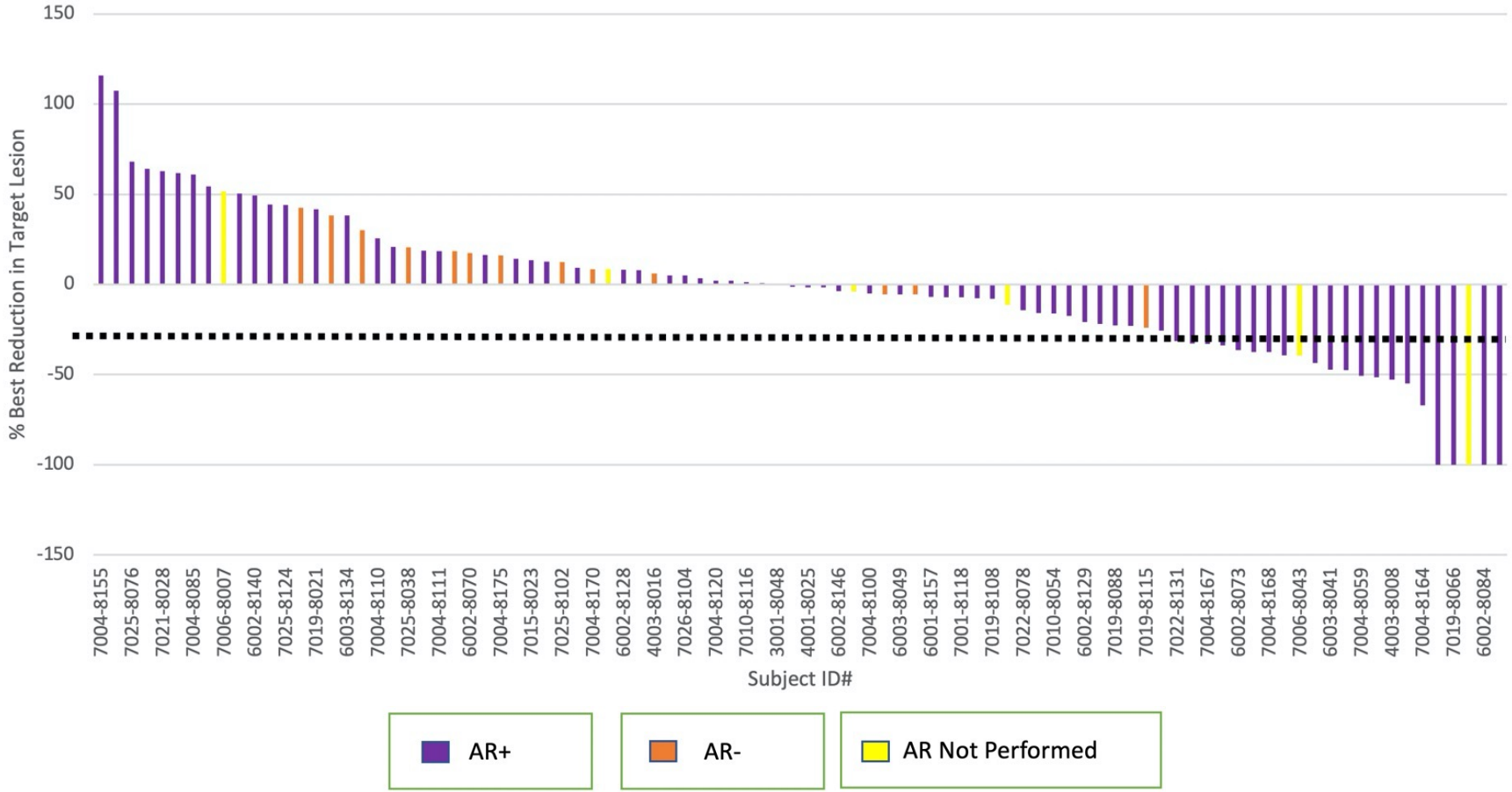
Grade 3 and 4 Drug Related Adverse Events	9 mg N=75	18 mg N=61
Increased alanine aminotransferase	1 (1.3%)	2 (3.3%)
Increased aspartate aminotransferase	2 (2.7 %)	
Hypercalcemia	2 (2.6%)	2 (3.3%)
Headache	1 (1.3%)	1 (1.6%))
Anemia	1 (1.3%)	
Dry mouth		1 (1.6%)
Decreased white blood cell count		1 (1.6%)
Decreased appetite		1 (1.6%)
Fatigue	1 (1.3%)	2 (3.3%)
Tumor flare		2 (3.3%)
Agitation		1 (1.6%)
Lymphadenopathy		1 (1.6%)
Acute kidney injury		1 (1.6%)

Efficacy overview
Evaluable population (AR+)

	9mg cohort	18mg cohort
Number of evaluable patients	50	52
Primary endpoint: CBR at 24 weeks	32% (95% CI: 19.5%;46.7%)	29% (95% CI: 17.1%;43.1%)

Phase 2 clinical trial (G200802)- AR is required for an objective tumor response

Best overall % target lesion reduction – Enobosarm 9 and 18 mg cohorts combined



Phase 2 clinical trial (G200802) - Post-hoc AR expression subset analysis
Efficacy outcomes correlate with degree of AR staining (9mg +18mg cohorts combined)

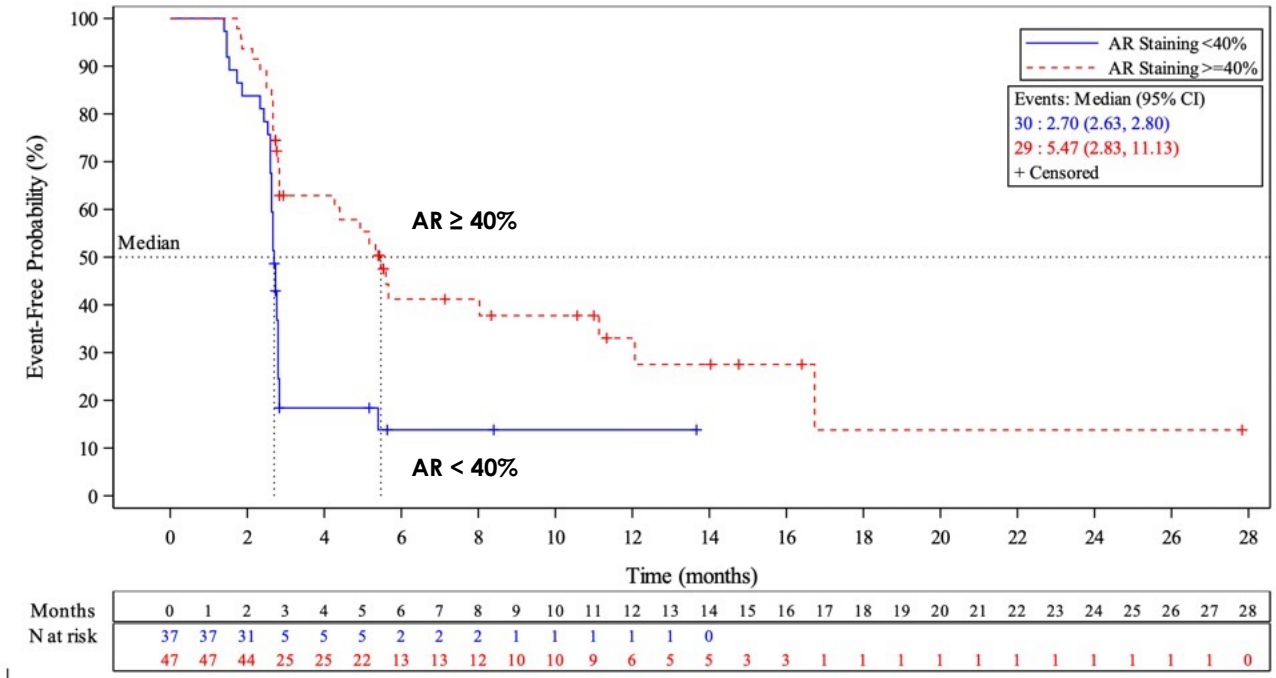
Post-hoc AR expression subset analysis:

- Subset of ITT with known AR status and have measurable disease (n=84)
- Combined both the 9mg and 18 mg cohorts to increase power of analysis

% AR staining	% of patients (n)	CBR at 24 wks*	Best ORR**	Median rPFS***
≥ 40%	56% (47)	52%	34%	5.47 months
< 40%	44% (37)	14%	2.7%	2.70 months

***p<0.0004; **p<0.0003; ***p<0.001**

Phase 2 clinical trial (G200802)
Radiographic progression free survival– Enobosarm 9 and 18 mg combined cohorts



p<0.001

Phase 2 clinical trial (G200802)- Post-hoc AR expression subset analysis
Duration of previous estrogen blocking agent response was similar regardless of AR status

- Analysis of ITT (FAS) group with known AR status and have measurable disease (n=84)
- Had received at least 2 prior therapies in a metastatic setting prior to randomization to Phase 2 study and duration of response information was available
- In estrogen blocking agent resistant breast cancer, the presence of AR was not sufficient to influence median duration of therapy with another estrogen blocking agent

	< 40% AR nuclei staining	≥ 40% AR nuclei staining
n=	15	22
Mean # of prior therapies	2.87 ± 1.06	2.72 ± 0.83
Median duration of therapy	**13 months**	**14 months**

Phase 2 clinical trial (G200802)- Conclusions
AR targeted therapy shows efficacy and safety in AR+ER+ metastatic breast cancer

- **Enobosarm AR targeted treatment demonstrated clinical benefit with objective tumor responses in women with heavily pretreated estrogen blocking agent resistant AR+ ER+ HER2- metastatic breast cancer**
- **The presence of AR and expression of AR ≥ 40% enriched for subjects most likely to respond to enobosarm treatment**
- **Quality of life measurements demonstrated overall improvement including mobility, anxiety/depression and pain**
- **Enobosarm appears safe and well tolerated without masculinizing effects, increase in hematocrit, or liver toxicity**
- **The 9 mg dose selected for Phase 3 clinical study**
  - 9 mg cohort had similar tumor responses with a slightly better toxicity profile than the 18 mg dose cohort
- **Enobosarm represents a new class of endocrine therapy that targets and activates the AR, tumor suppressor, in AR+ ER+ HER2- metastatic breast cancer**

Determination of AR status - companion diagnostic test (CDx)

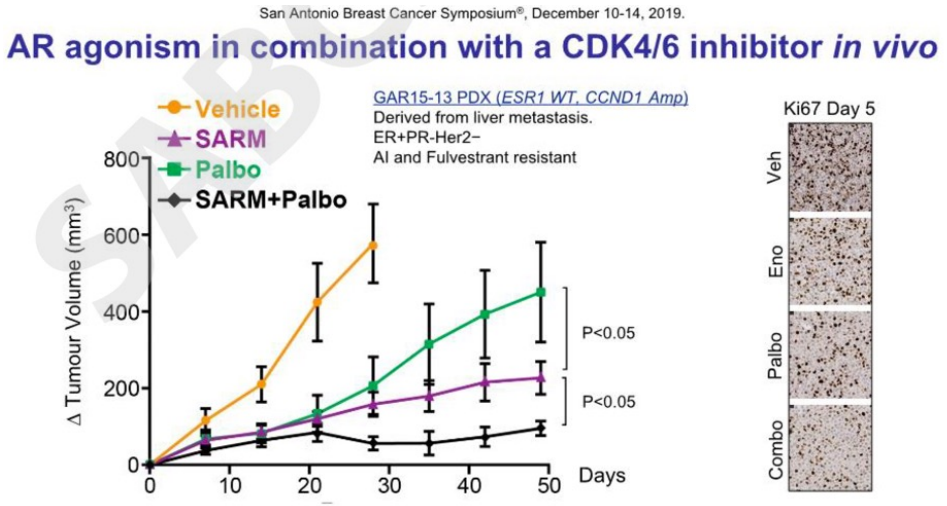
- AR staining was performed using a validated immunohistochemistry (IHC) protocol conducted by HistoGeneX as the central laboratory
- Slides were stained using an autostainer and then scanned and analyzed digitally with a pathology image analysis software which provided for quantitation of nuclear staining
- Collaboration with large global oncology diagnostic laboratory to validate companion diagnostic test

Enobosarm and CDK4/6 inhibitors in estrogen blocking agent resistant AR+ER+HER2- breast cancer

Preclinical models (Patient derived xenografts)[1,2]

- **Estrogen blocking agent resistant breast cancer**
  - CDK4/6 inhibitor inhibits growth of estrogen blocking agent resistant breast cancer[1,2]
  - Enobosarm monotherapy has greater inhibition of estrogen blocking agent resistant breast cancer than a CDK4/6 inhibitor[1,2]
  - Enobosarm + CDK4/6 inhibitor had greater inhibition of estrogen blocking agent resistant breast cancer than either alone[1,2]

- **Estrogen blocking agent and CDK4/6 inhibitor resistant breast cancer**
  - Enobosarm suppressed breast cancer cells that are resistant to both CDK 4/6 inhibitor and estrogen blocking agent[2]
  - Enobosarm and CDK4/6 inhibitor further suppressed breast cancer cells that are resistant to both CDK4/6 inhibitor and estrogen blocking agent – enobosarm restores CDK 4/6 sensitivity[2]



SARM= enobosarm and Palbo=Palbociclib, CDK4/6 inhibitor

[1] Lim E et al. 2019 SABCS presentation | [2] Hickey TE et al. Nature Medicine 2020

Phase 2 802 study
Evaluable patients (AR+) with palbociclib resistance in the metastatic setting

- **Objective tumor responses**
  - 30% overall
- **CBR at 24 weeks**
  - 50% overall
- **Mean duration on study (either PFS or censored)**
  - 7.3 months (9 mg and 18 mg groups)
  - 10.0 months (9 mg dose group)

Palbociclib resistant subjects with measurable disease

9 mg patient ID	Outcome
7004-8120	
7019-8066	Complete Response
7026-8083	
7019-8087	Complete Response
7019-8106	Stable Disease

18 mg patient ID	Outcome
6003-8133	
7001-8001	Partial Response
7001-8118	Stable Disease
7004-8100	
7022-8078	

AR% Staining	ORR	rPFS (mean) months
<40	0/3 (0%)	3.13
≥ 40	3/7 (43%)	9.04

NCCN 2020 guidelines: CDK 4/6 inhibitors are standard of care for treatment of ER+HER2- metastatic breast cancer

If disease progression on CDK4/6 inhibitor treatment, there are limited data to support additional line of treatment with another CDK 4/6 inhibitor containing regimen

First-Line Metastatic

- Nonsteroidal aromatase inhibitor + CKD4/6 inhibitor
- Fulvestrant + CDK 4/6 inhibitor

Second-Line Metastatic

- Fulvestrant + CDK 4/6; if CDK4/6 inhibitor was not previously used
- Enobosarm + Abemaciclib, CKD4/6 inhibitor

Third-Line Metastatic

- Enobosarm monotherapy

Phase 3 registration, open label, randomized ARTEST clinical trial (V3002401)(NCT#04869943)- 3rd line metastatic setting - anticipated start Q3 2021

ARTEST Indication

Treatment of AR+ER+HER2- metastatic breast cancer in subjects who have failed a nonsteroidal aromatase inhibitor, fulvestrant, and CDK4/6 inhibitor therapy (3rd line metastatic setting)

ARTEST Clinical Trial Design

Phase 3 open label, multicenter, multinational, randomized, active control pivotal study evaluating the efficacy and safety of enobosarm 9mg oral daily dose versus active control (exemestane ± everolimus or a SERM) in metastatic AR+ ER+ HER2- breast cancer

ARTEST Patient Population

- AR+ ER+ HER2-metastatic or recurrent locally advanced breast cancer, not amenable to curative treatment by surgery or radiotherapy, with objective evidence of disease progression
- Must have had received a nonsteroidal AI inhibitor, fulvestrant, and CDK 4/6 inhibitor for metastatic disease
  - Previously responded to hormone Tx for metastatic disease ≥ 6 months
  - No prior chemotherapy for the treatment of metastatic breast cancer
  - Centrally confirmed ≥ 40% AR nuclei staining from breast cancer sample

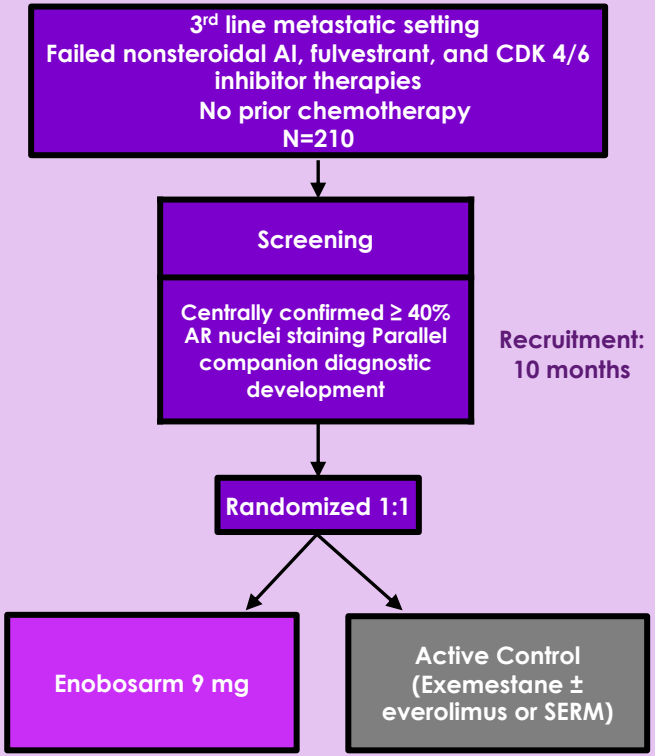
ARTEST Efficacy Endpoints

- Primary endpoint:
  - Median radiographic progression free survival (rPFS)
- Secondary endpoints:
  - Overall response rate (CR+PR)
  - Duration of response
  - Overall survival
  - Change in Short Physical Performance Battery (SPPB)
  - Change in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ)

ARTEST Sample Size Assumptions

- Total sample size: 210
- α = 0.05
- 99% power
- 20% drop out rate
- 169 events
- Active control group (exemestane± everolimus or a SERM): estimated median rPFS = 3 months[1-3]
- Enobosarm arm: estimated median rPFS=6 months

Phase 3 Pivotal AR+ER+HER2- Metastatic Breast Cancer



[1]Yeruva, S *et al. npj Breast Cancer* 4: 1, 2018|[2] Cook , M *et al. The Oncologist* 26:101,2021 |[3] Rozenblit M *et al. Breast Cancer Research* 23:14, 2021

Phase 2b (V2000701)- 2nd line metastatic setting

Open label, dose finding, efficacy and safety of CDK4/6 inhibitor (abemaciclib) + enobosarm combination versus active control estrogen blocking agent in AR+ER+HER2- metastatic breast cancer

Anticipated start date is calendar Q4 2021

Palbociclib resistance

Failed first line metastatic Tx

Failed Nonsteroidal AI + Palbo or Fulvestrant + Palbo

Centrally confirmed AR nuclei staining

Stage 1
N=up to 6

Open label safety study to determine the safety of enobosarm in combination with abemaciclib

Stage 2
2:1 rando
n = 180

Combination

Abemaciclib, CDK 4/6 inhibitor + Enobosarm

Active control

Alternative estrogen blocking agent

- **Primary endpoint:**
  - Median radiographic progression free survival (rPFS)
- **Secondary endpoints:**
  - Overall response rate (CR+PR)
  - Change in Short Physical Performance Battery (SPPB)
  - DEXA- body composition muscle and bone

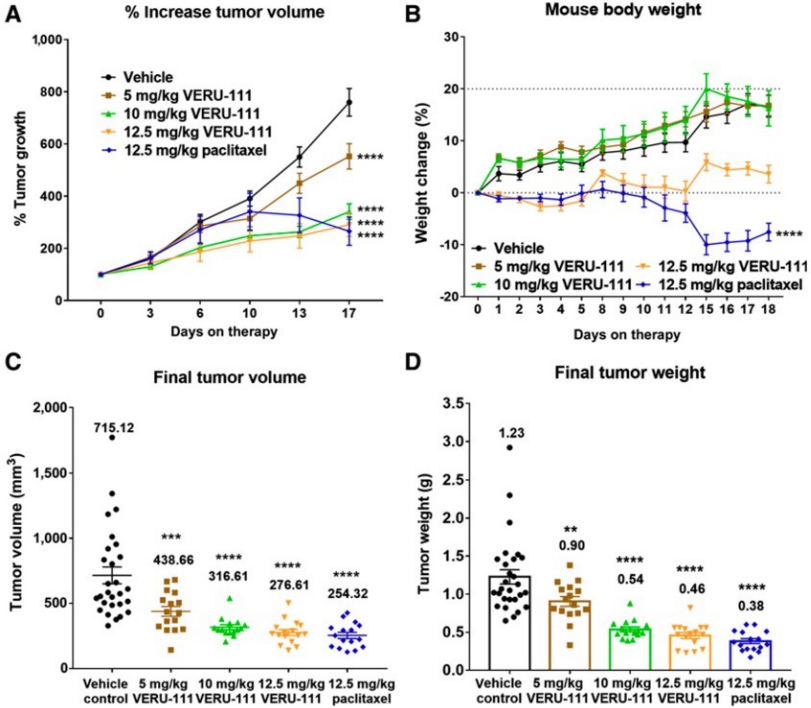
Alternative estrogen blocking agent= Fulvestrant ➢ nonsteroidal AI or nonsteroidal AI ➢ fulvestrant

Sabizabulin 32mg versus TRODELVY

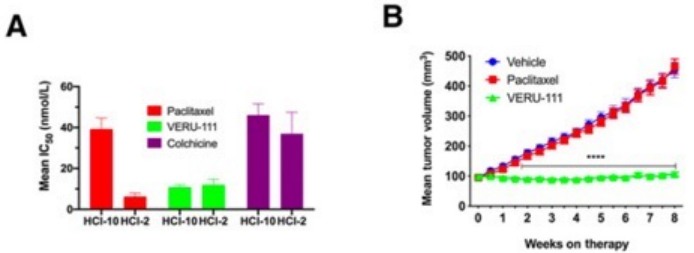
for the treatment of chemotherapy including taxane resistant metastatic triple negative breast cancer

Preclinical studies in taxane resistant triple negative breast cancer[1]

Taxane sensitive



Taxane resistant

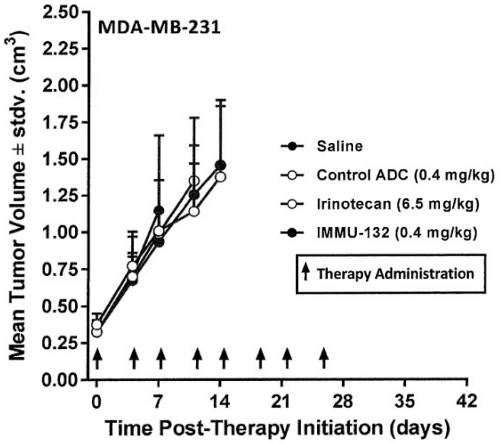


- HCI-10-Luc2 TNBC - taxane resistant
- HCI-2-Luc2 TNBC – taxane sensitive

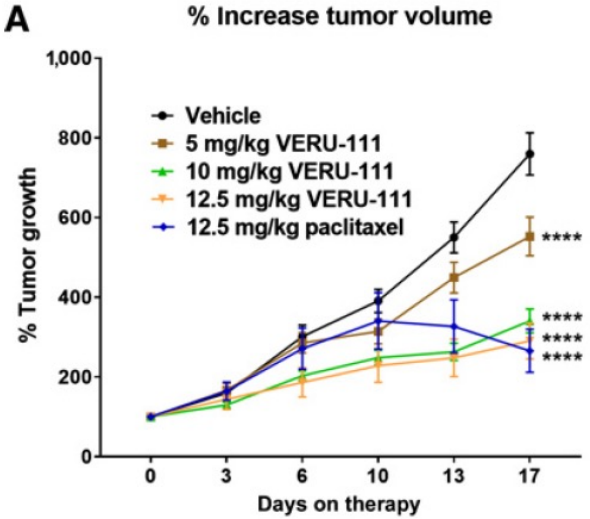
[1] Deng S et al. Mol Cancer Ther 19:348-63, 2020

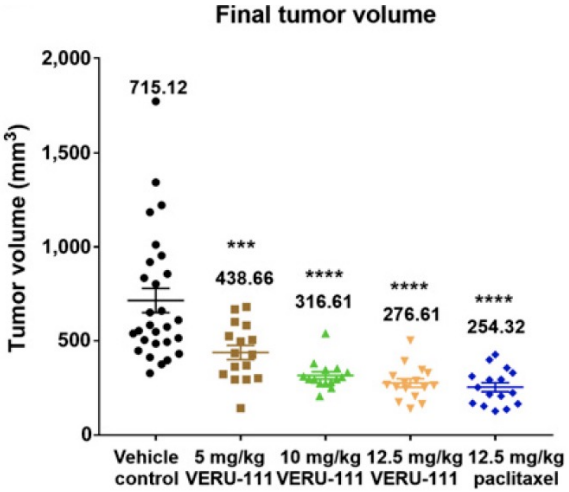
Comparison of IMMU-132 (TRODELVY) and Sabizabulin in MDA-MB-231 triple negative breast cancer animal model

TRODELVY (IMMU-132) has no activity in MDA-MB-231 TNBC Animal Model[1]



Oral sabizabulin has antitumor activity in MDA-MB-231 TNBC Animal Model[2]





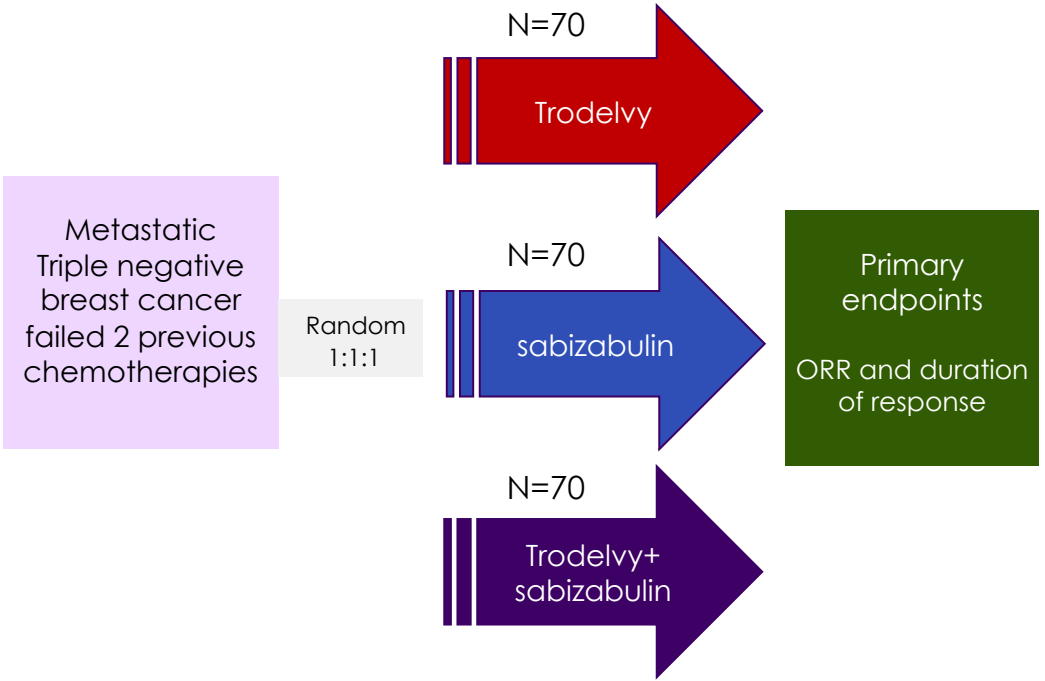
[1]US patent US2018/0271992 A1 | [2] Deng et al, Mol Can Therapeutics, 29:348-363, 2020

Phase 2b clinical study (V2011801): anticipated start calendar Q3 2021
Sabizabulin for metastatic triple negative breast cancer that has failed 2 chemotherapies-

Trial study design

- Patients previously treated with a least 2 systemic chemotherapies for metastatic triple negative breast cancer
- Safety run-in of Sabizabulin + TRODELVY IV (sacituzumab govitecan-hziy)
- Randomized 3 arm open label study
  - Oral Sabizabulin 32 mg
  - Sabizabulin 32 mg + TRODELVY IV*
  - TRODELVY IV- active control
- Expected to initiate Q3 2021 - 216 subjects
- Primary endpoint
  - ORR
  - Duration of response
- Other endpoints
  - Median rPFS
  - Safety

*Plinabulin model



Sabazibulin 9 mg

For the treatment of hospitalized COVID-19 patients at high risk for acute respiratory distress syndrome

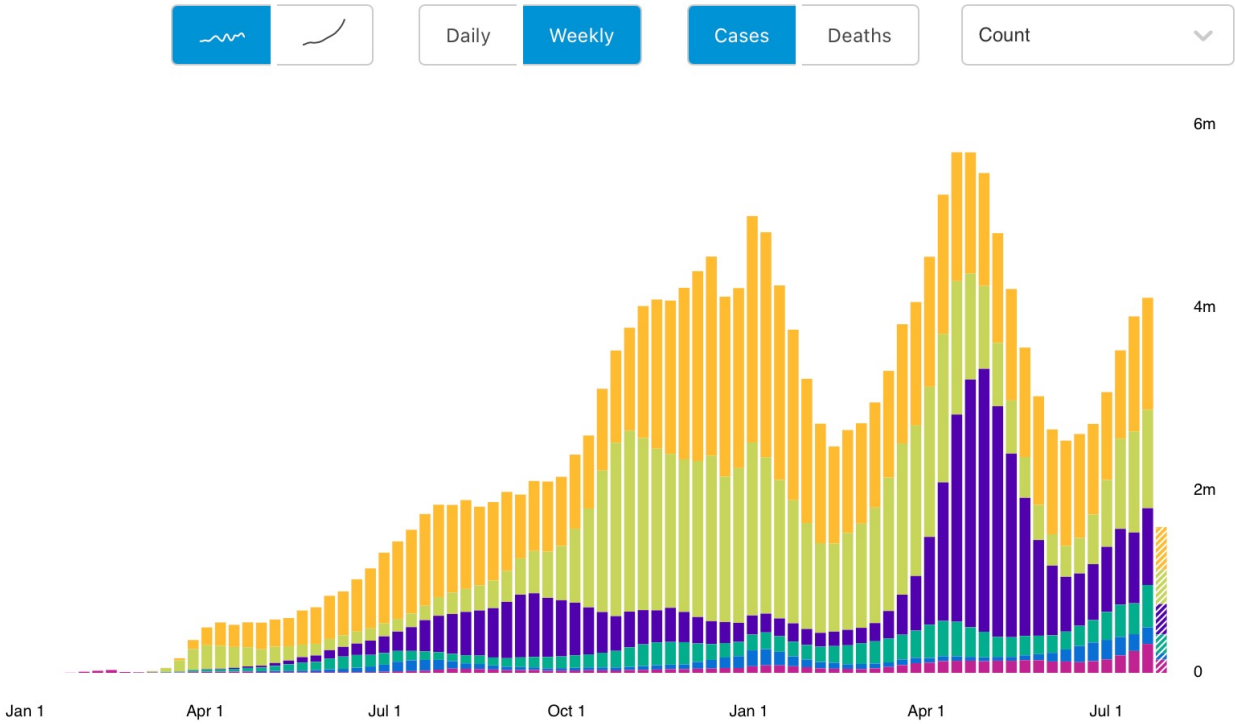
Coronavirus is not going away!

Situation by WHO Region

Americas	77,688,636 confirmed
Europe	60,566,865 confirmed
South-East Asia	38,711,821 confirmed
Eastern Mediterranean	12,804,451 confirmed
Africa	5,023,726 confirmed
Western Pacific	4,669,948 confirmed

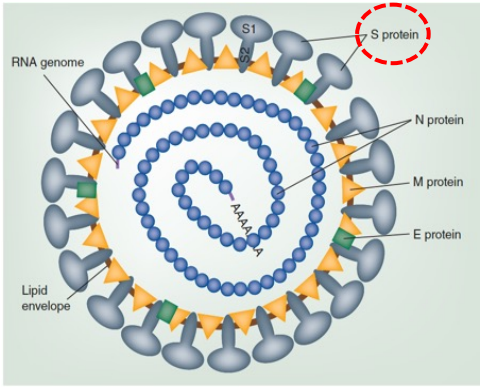
Source: World Health Organization

Data may be incomplete for the current day or week.



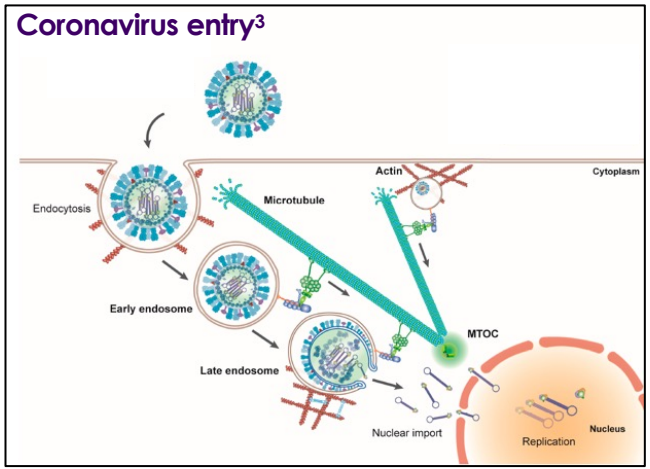
Coronavirus's spike(S) protein is the key structure that interacts with microtubules in the cytoskeleton during intracellular trafficking[4]

SARS-CoV-2 structure[4]

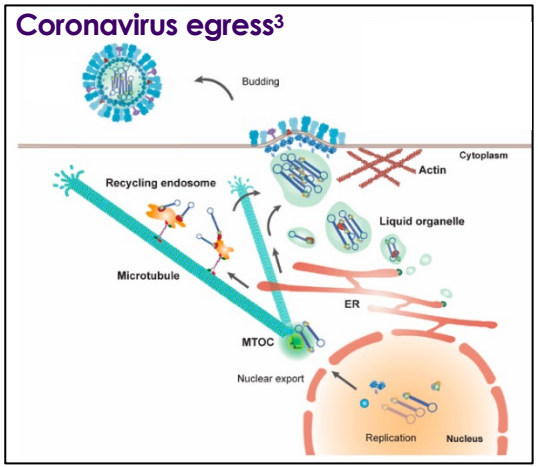


- **Virus's most critical task is to hijack the host's internal transportation system, the microtubules in the cytoskeleton[1-3]**
- **Sabizabulin disrupts the microtubule trafficking system**
  - Antiviral
  - Anti-inflammatory

Coronavirus entry[3]



Coronavirus egress[3]



[1] Ren et al Scientific Reports 5:11451,2015; [2] Rudiger et al Virology 497:185-197, 2016 | [3]Taken and adapted from Simpson et al. Viruses 12:117, 2020 | [4]Taken from Alsaadi et al Future Virology 14:275, 2019

Sabizabulin: Phase 2 clinical trial design for COVID-19

Double-Blind, Placebo-Controlled, Phase 2 Study of Sabizabulin for the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in Patients at High Risk for Acute Respiratory Distress Syndrome (ARDS)[1]

Trial design

- Approximately 40 subjects were randomized 1:1 (20 18mg sabazibulin and 20 Placebo groups)
- Hospitalized subjects with COVID-19 infection symptoms for less than 8 days and who are at high risk for ARDS were enrolled
- Subjects received study drug for up to 21 days
- The primary efficacy endpoint of the study was the proportion of patients that are alive and without respiratory failure at Day 29
- Most important secondary endpoints were all-cause mortality (death), days in ICU, and days on mechanical ventilation
- Enrollment completed December 2020

Patient demographics

		Sabizabulin	Placebo
Number of patients		19	20
Mean age (±SD)		59.3 (11.4)	57.8 (13.3)
Gender	Males (%)	10 (53%)	17 (85%)
	Females (%)	9 (47%)	3 (15%)
Mean WHO Score at baseline (±SD)		4.47 (0.61)	4.7 (0.57)
Standard of care treatment use on study	Remdesivir (%)	9 (47%)	15 (75%)
	Dexamethasone (%)	13 (68%)	15 (75%)
	No dexamethasone or remdesivir (%)	4 (21%)	2 (10%)

[1] Veru Inc, *Clinical Trial Protocol*, VERU-111 SARS-CoV-2 (May 2020)

Phase 2 clinical trial of sabizabulin 18 mg

Endpoints

Primary Endpoint	Placebo	Sabizabulin	Relative Reduction	p-value
Treatment failures, i.e. death or respiratory failure at Day 29 (MITT)	6/20 (30%)	1/18 (5.6%)	81%	p=0.05

Secondary Endpoints	Placebo	Sabizabulin	Relative Reduction	p-value
Deaths (ITT)	6/20 (30%)	1/19 (5.3%)	82%	p=0.04
Treatment failures, i.e. death or respiratory failure at Day 29 in >60 years of age	4/8 (50%)	1/11 (9%)	82%	p=0.05
Treatment failures, i.e. death or respiratory failure at Day 15 in patients with a WHO Score of Disease Severity ≥5 at baseline	7/13 (54%)	1/9 (11%)	80%	p=0.04
Mean days in ICU +/- SE	9.55±11.54 (n=20)	3.00±7.16 (n=18)	69%	p=0.04

Endpoints – patients that received standard of care (remdesivir and/or dexamethasone)	Placebo	Sabizabulin	Relative Reduction	p-value
Days in ICU	8.83±13.07 (n=18)	1.43±3.96 (n=14)	84%	p=0.02
Days on mechanical ventilation	6.00±10.57 (n=18)	0 (n=14)	100%	p=0.04

Safety outcomes for Sabizabulin 18mg from Phase 2 clinical trial

Safety

- There were no treatment related adverse events observed on the study
- There were no treatment related serious adverse events observed on the study
- There is no imbalance against sabizabulin in adverse events observed in the study

Any adverse event that occurred in ≥ 2 patients on study

Preferred Term	Sabizabulin 18 mg (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

Double-Blind, Placebo-Controlled, Phase 3 Study of Sabizabulin for the Treatment of in Hospitalized COVID-19 Patients at High Risk for Acute Respiratory Distress Syndrome (V3011902)(NCT#04842747) – enrolling

- Trial size is N=300 with a 2:1 randomization
- Dosing: daily dosing up to 21-days or until discharge from hospital
- Treatment arms: Sabizabulin 9 mg Formulated Capsule vs. Placebo
  - All patients will be allowed standard of care on the study (Remdesivir/dexamethasone/convalescent plasma)
- Key inclusion criteria: high risk for ARDS, hospitalized, WHO Ordinal Scale for Disease Progression ≥4
- Primary endpoint: proportion of patients who die prior to Day 60 (mortality)
- Key secondary endpoints: Respiratory failure, days in ICU, days on mechanical ventilation, days in the hospital, and viral load
- Multinational clinical sites in United States, Brazil, Mexico, Argentina, and Colombia with aim to complete recruitment by year end

Statistical assumptions

- In the Phase 2, the sabizabulin treated group showed a 5.3 % mortality rate in patients with WHO disease severity score ≥4 at baseline compared to a 30% mortality rate in the Placebo group in the same patient population
- With significance level a=0.05, and a 2:1 ratio of enrollment into the sabizabulin and Placebo arms respectively, the sample size is adequate to achieve >99% power

TADFIN™ for BPH

TADFIN™ capsule (tadalafil 5mg + finasteride 5mg combo) for treatment of BPH with improvement of erectile dysfunction[3]

Co-administration of CIALIS (tadalafil 5 mg) and PROSCAR (finasteride 5 mg) is currently approved for the initial treatment of symptoms of BPH for up to 26 weeks[1]

- Drug-drug interaction and co-administration studies are completed for combination indication[2]

Each component is approved for:

- CIALIS (tadalafil 5 mg) daily- symptoms of ***BPH and erectile dysfunction***
- PROSCAR (finasteride 5 mg)- symptoms and signs of prostate enlargement to decrease prostate size, reduces risk of acute urinary retention and need for surgery and prevents growth
- PROPECIA (finasteride 1mg) daily- symptoms of ***male pattern hair loss***

The solution: proprietary TADFIN™ tablet formulation:
Increases convenience and compliance

BPH TREATMENT THAT PREVENTS BPH PROGRESSION & ALSO IMPROVES ERECTILE DYSFUNCTION
PDUFA date 12/2021

[1] Cialis (tadalafil) FDA Package Insert | [2]Casabé A et al. J Urol 191:727-733 2014 | [3]Glina S et al. Sexual Function in Men :Study of Tadalafil Coadministered with Finasteride J Sex Med 2015;12:129-1238

TADFIN™, only BPH treatment that prevents progression of BPH and improves sexual function[1,2]

ED symptom score[2]
Men with baseline ED

ED symptom score[2]
Men without baseline ED

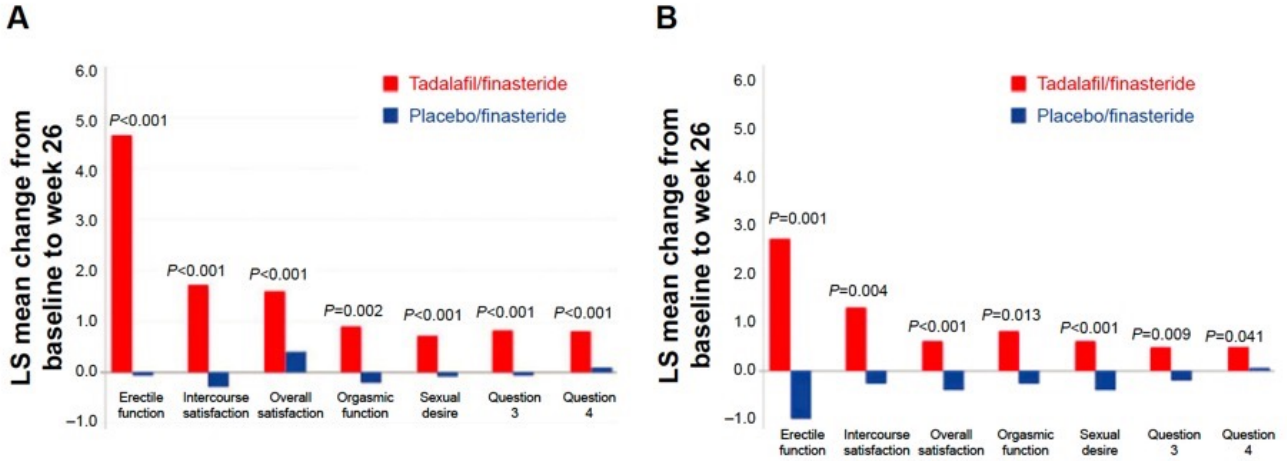


Figure 2 Comparison of treatment results with regard to IIEF scores reported by Glina et al.[27]
Notes: (**A**) IIEF domains in men with baseline erectile dysfunction. (**B**) IIEF domains in men without baseline erectile dysfunction. (**A** and **B**) Question 3 related to vaginal penetrative ability. Question 4 related to erection maintenance. Figure reproduced with permission from John Wiley and Sons, from Glina S, Roehrborn CG, Esen A, et al. Sexual function in men with lower urinary tract symptoms and prostatic enlargement secondary to benign prostatic hyperplasia: results of a 6-month, randomized, double-blind, placebo-controlled study of tadalafil coadministered with finasteride. *Journal of Sexual Medicine*. 2015;12(1):129–138. Copyright © 2014 International Society for Sexual Medicine.
Abbreviations: IIEF, International Index of Erectile Function; LS, least squares.

- International, randomized, double-blind study in approximately 700 men
- 350 men treated with placebo + 5mg finasteride each day
- 345 men treated with 5mg tadalafil + 5mg finasteride each day

[1]Casabe A et al. J of Urol 2014; 191:717-733 | [2]Glina S et al. Sexual Function in Men…Study of Tadalafil Coadministered with Finasteride J Sex Med 2015;12:129-1238

TADFIN™, only BPH treatment that prevents progression of BPH and improves sexual function[1,2,4]

Market potential

- BPH market is up to 25% of male population and estimated 1.1 billion males worldwide in 2018[1]
- Target men who have BPH as a cause for symptoms
  - Other men who may benefit according to Eikelany O et al.[4]
    - Suboptimal response to 5a reductase inhibitor (PROSCAR® or AVODART®) alone with prostate enlargement
    - Suboptimal response to an alpha blocker (tamsulosin) alone or in combination with 5a reductase inhibitor (JAYLN®)
    - Optimal response to 5a reductase inhibitor, but also has erectile dysfunction

Market Potential
US and global markets expected to be >$200 million through telemedicine channels[3]

[1] Cialis (tadalafil) FDA Package Insert | [2]Casabé A et al. J Urol 191:727-733 2014 | [3]IQVIA Data (2018) Assumption: $120 per prescription | [4] Eikelany O et al. Therapeutics and Clinical Risk Management 11:507-513, 2015

UREV
Women's Health Division

FC2® Female Condom (internal condom) business revenues are growing

UREV
Women's Health

FC2 Female Condom (internal condom) is the only FDA approved female use product to prevent pregnancy and transmission of sexually transmitted infections

Rapidly growing US prescription business for high margin revenues

Prescription business is growing via existing and anticipated new contracts with additional telemedicine and telepharmacy partners

Sold in U.S. and 149 other countries

Manufacturing plant with annual capacity of 100 million units

Public sector customers include UNFPA, USAID, Brazil, and South Africa

FC2 business profitable from FY 2006-present[1]

Medical Device

Telemedicine Companies

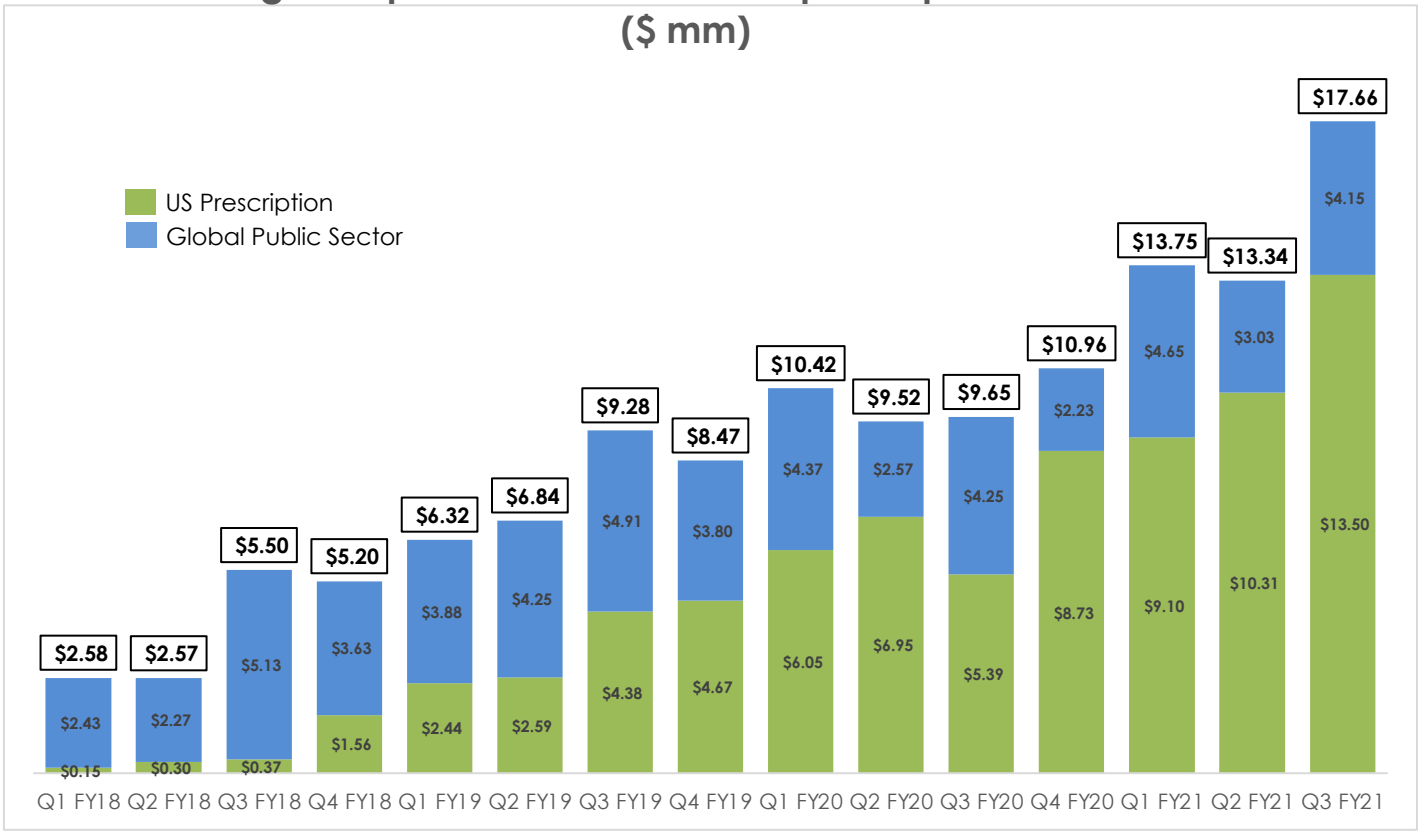
FC2 by prescription

[1]For fiscal year 2006 through fiscal year 2016, profitability is based on Veru's net income attributable to common stockholders. Beginning fiscal year 2017, the first fiscal year which includes the financial results of Aspen Park Pharmaceuticals, Inc., profitability is based on operating income from our commercial segment.

FC2 revenues

UREV
Women's Health

FC2 global public sector & FC2 US prescription revenues ($ mm)



FC2 Revenues

FY 2018: $ 15.9 mm
FY 2019: $ 30.9 mm
FY 2020: $ 40.6 mm
FYTD 2021: $ 44.8 mm

FC2 US Prescription 12-Pack Units Sold

FY 2018: 24,000
FY 2019: 159,000
FY 2020: 342,000
FYTD 2021: 413,000

Financial highlights

Veru – Fiscal year Results of operations	
FYTD 2021 Net Revenues (3 quarters)	$ 45.6 mm
FY 2020 Net Revenues	$ 42.6 mm
FY 2019 Net Revenues	$ 31.8 mm
FY 2018 Net Revenues	$ 15.9 mm
FY 2017 Net Revenues	$ 13.7 mm

Veru – Fiscal Year To Date Results of operations	
FYTD 2021 Net Revenues (3 quarters)	$ 45.6 mm
FYTD 2021 Gross Profit	$ 35.6 mm
FYTD 2021 Operating Income	$ 14.8 mm
FYTD 2021 Adjusted Operating Loss[1]	$ 3.6 mm

Veru – Quarter 3 Results of operations	
Q3 FY 2021 Net Revenues	$ 17.7 mm
Q3 FY 2021 Gross Profit	$ 13.9 mm
Q3 FY 2021 Operating Loss	$ 2.9 mm

UREV – Women's Health Results of operations	
FC2 FY 2020 Net Revenues	$ 40.6 mm
Q3 FY 2021 Net Revenues	$ 17.7 mm

Veru – Balance Sheet as of June 30, 2021	
Cash	$ 123.2 mm
Receivables	$ 8.3 mm
PREBOOST Payment Due	$ 5.0 mm[3]
US/UK NOL carryforward	$ 42.0/$61.3 mm
Common Shares Outstanding[2]	~ 79.9 mm

Record revenue FYTD from sexual health business $45.6 million

Veru closes public offering of $115 million in February 2021[4,5]

PREBOOST sale for $20 million[3]

[1] Represents a non-GAAP financial measure calculated by subtracting $18.4 mm gain on PREBOOST sale from Operating Income, a GAAP measure
[2] An aggregate of 10.8 million stock options and stock appreciation rights are outstanding and are, or could potentially be, dilutive in excess of the 79.9 million common shares above
[3] PREBOOST sale was $15 million in cash and $2.5 million in receivables at 12 months and $2.5 million in receivables at 18 months
[4] Cash received from the public offering, net of underwriting discounts and commissions, was $108.1 million
[5] Veru issued 7,419,354 shares of common stock in the public offering

Milestones

Program	Mechanism	Indication	2021	2022	2023	2024
Prostate Cancer						
Sabizabulin	Oral cytoskeleton disruptor and androgen receptor transport disruptor	Metastatic castration and AR targeting agent resistant prostate cancer	Phase 3 Initiation	Phase 3 Full enrollment	NDA	Launch
VERU-100	Gonadotropin-releasing hormone antagonist 3-month subcutaneous depot injection	Hormone sensitive advanced prostate cancer	Phase 2 Initiation	Phase 2 Full enrollment; Phase 3 Initiation	Phase 3 Full Enrollment	NDA; Launch
Breast Cancer						
Enobosarm	Selective androgen receptor targeted agonist	AR+ER+HER2- metastatic breast cancer (3rd line metastatic)	Phase 3 Initiation	Phase 3 Full enrollment	NDA	Launch
Enobosarm + abemaciclib combination	Selective androgen receptor targeted agonist + CDK4/6 inhibitor	AR+ER+HER2- metastatic breast cancer (2nd line metastatic)	Phase 2 Initiation	Phase 2 Full enrollment		
Sabizabulin	Oral cytoskeleton disruptor	Metastatic triple negative breast cancer	Phase 2 Initiation	Phase 2 Full enrollment		
Virology						
Sabizabulin	Oral cytoskeleton disruptor	Hospitalized COVID-19 patients at high risk for ARDS	Phase 3 Initiation	Phase 3 Full enrollment	EUA/NDA	