





Developing Novel Solutions for Women's Health and Cancer Therapy

## **Investor Presentation**

August 2009

**NASDAQ: BNVI** 

This presentation contains forward-looking statements that are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties, and assumptions that could cause actual results to differ materially from those described. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial metrics, expected legal, arbitration, political, regulatory, or clinical results, and other such estimates and results. Forward-looking statements involve significant risks and uncertainties, including those discussed below and more fully described in the Securities and Exchange Commission (SEC) reports filed by Bionovo, including Bionovo's most recent annual report on Form 10-K and most recent periodic reports on Form 10-Q and Form 8-K. Please refer to Bionovo's most recent Forms 10-K, 10-Q, and 8-K for additional information on the uncertainties and risk factors related to our business. Unless otherwise noted, Bionovo is providing this information as of this date and expressly disclaims any duty to update information contained in this presentation.

No forward-looking statement can be guaranteed and actual results may differ materially from those we project. The Company's results may be affected by our ability to successfully develop, partner and market our products domestically and internationally, difficulties or delays in manufacturing our products, and regulatory developments (domestic or foreign) involving current and future products and manufacturing facilities. Discovery or identification of new product candidates cannot be guaranteed and movement from concept to product is uncertain; consequently, there can be no guarantee that any particular product candidate will be successful and become a commercial product. In addition, while we routinely obtain patents for our products and technology, the protection offered by our patents and patent applications may be challenged, invalidated, or circumvented by our competitors. Our business may be impacted by government investigations, litigation, and products liability claims.



#### Bionovo is developing innovative therapeutics from botanical extracts in Women's Health and Oncology

- Products are derived from botanicals which have the potential to offer increased safety and tolerability as compared to synthetic and biologic therapeutics
- Attractive late-stage lead product and robust pipeline
  - Menerba is entering Phase III clinical trials for menopausal hot flashes (\$10.0 billion market)
  - Bezielle is entering Phase II clinical trials for advanced breast cancer (\$4.6 billion market)
  - Seala is entering Phase I/II clinical trials for vaginal atrophy (\$4.0 billion market)
  - Two additional products in preclinical development
- Menerba is a first-in-class treatment for vasomotor symptoms associated with menopause
  - Novel mechanism of action with predictable tissue selectivity
  - Positive efficacy in Phase II placebo-controlled trial
  - Targeted Estrogen Receptor beta (ERβ) pathway mitigates risk of dangerous side effects associated with currently available non-selective SERMs and hormone therapies
- Broad patent estate, including an issued patent that protects assets to 2026 and beyond
- Scientific Advisory Board includes key opinion leaders in the Women's Health field
- Senior management team is comprised of four professionals with a combined 73 years of experience in management, industry, and research roles



Clinical and Preclinical Pipeline							
Product	Preclinical Development	Phase I	Phase II	Phase III	Markotod	Indication	Upcoming Milestones
Menerba	Development				Marketeu	Menopausal Hot Flashes	
Bezielle						Advanced Breast Cancer	<ul><li>Launch Phase II</li><li>Potential for interim data</li><li>Release Phase II data</li></ul>
Seala						Vaginal Atrophy	<ul><li>Launch Phase I/II</li><li>Release Phase I/II data</li></ul>
Bezielle	-					Pancreatic Cancer	<ul> <li>Results of grant application</li> </ul>
3N107	-					Advanced Breast Cancer	<ul> <li>File IND</li> </ul>
BN108	-					Advanced Breast Cancer	File IND



- Novel oral Selective Estrogen Receptor beta (ERβ) agonist targeting menopausal vasomotor symptoms (hot flashes) derived from botanical extracts
  - **80.0%** of menopausal women use some form of OTC botanical supplement to abate the symptoms of menopause<sup>(a)</sup>
- Does NOT activate the Estrogen Receptor alpha (ERα) pathway, known to be implicated in both breast and uterine cancer formation
  - Binds to both ER $\alpha$  and ER $\beta$ , but produces an atypical conformation in ER $\alpha$  which **does not** activate ER $\alpha$ -regulated proliferative genes *c*-*myc* and *cyclin D1* or stimulate *MCF*-7 breast cancer cell proliferation or tumor formation<sup>(b)</sup>
  - Unlike existing SERMs such as tamoxifen and raloxifene, that are mixed agonist/antagonist, Menerba is selective in transcriptional regulation to one of the two known estrogen receptor subtypes
  - Potential for increased safety and tolerability
  - Potential to be a first-line therapy for menopausal hot flashes
- FDA-approved products for hot flashes have seven black-box warnings: uterine cancer, breast cancer, stroke, cardiovascular disease, deep vein thrombosis, pulmonary embolism, and dementia
- Total addressable market opportunity of \$10.0 billion<sup>(c)</sup>

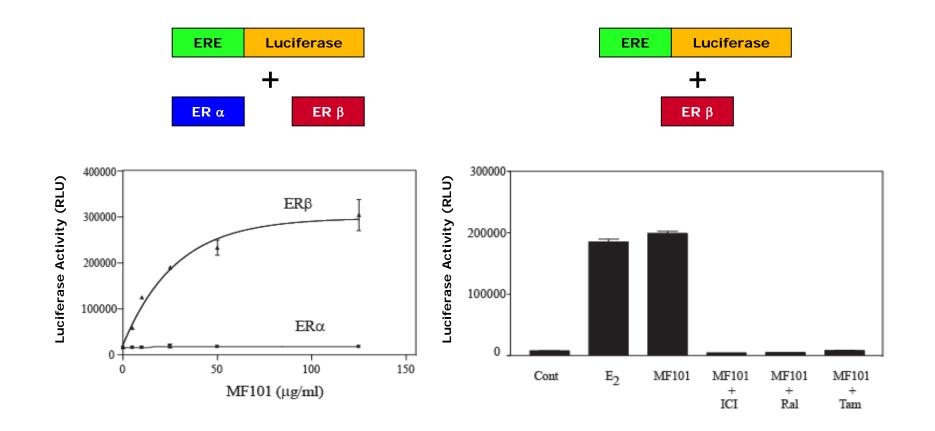
(b) Selective Activation of Estrogen Receptor  $\beta$  Transcriptional Pathways by an Herbal Extract. *Endocrinology*, November 9, 2006.

<sup>(</sup>c) Based on 2001 sales of Wyeth's Premarin family of products of 2.1 billion prescriptions. Assumes branded product cost of \$5 /day.





<sup>(</sup>a) Mahady G.B., Parrot J, Lee C, et al. Botanical dietary supplement use in peri- and postmenopausal women. Menopause, 2003, 10: 66-72.

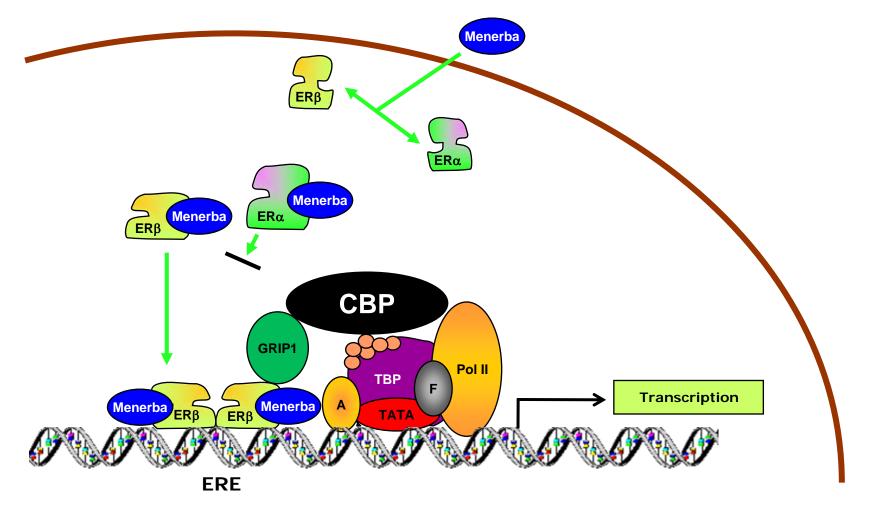


Source: Cvoro A, Endocrinology. November 9, 2006. (a) Menerba formerly known as MF101.





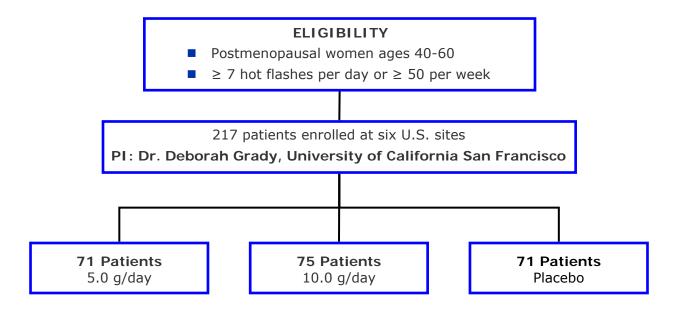
## Menerba<sup>(a)</sup> Selectively Recruits ERß & Coactivators to Target Genes

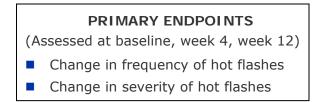


(a) Menerba formerly known as MF101.









Note: Dose defined by total amount, not active ingredient.



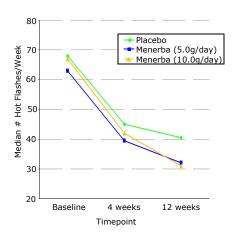


Menerba demonstrated statistically significant results in high dose group

Menerba exhibits a clear dose response curve, but has yet to reach maximum tolerated dose

Efficacy Resu						
Model	Placebo	5.0 g/day	p-value	10.0 g/day	p-value	
Number of All Hot Flashes at Baseline	68.0	63.0	NA	67.0	NA	
Number of All Hot Flashes at 12 Weeks	40.5	32.0	0.10	31.0	0.04	
Number of Moderate-to-Severe Hot Flashes at Baseline	55.0	45.0	NA	48.0	NA	
Number of Moderate-to-Severe Hot Flashes at 12 Weeks	23.5	19.0	_(b)	17.0	_(b)	
Severity Score at Baseline	138.0	114.0	NA	131.0	NA	
Severity Score at 12 Weeks	64.0	54.0	0.19	57.0	0.11	
Median Percent Change in Nighttime Awakening Hot Flashes at 12 Weeks	(44.0)%	(57.5)%	0.10	(66.7)%	0.05	

Reduction in Number of Hot Flashes Per Week<sup>(c)</sup>



<u>Safety</u>

- No difference in the number of uterine bleeding episodes between treatment and placebo
- No cases of endometrial hyperplasia
- "Transient loose stools" was most common side effect (12.0% vs. 3.0% for placebo)
  - Benefit from reduced constipation on Menerba (1.3% vs. 4.0%)
  - Benefit from lower BMI and lower blood pressure

#### Tolerability

- 91.0% of participants took > 75.0% of study medication at 12 weeks
  - Very low drop out rate (2.0%)

(a) P-values from rank-transformed analysis of variance (ANOVA) controlling for clinical site and strata.

- (b) Study not powered to identify statistical significance in the reduction of moderate-to-severe hot flashes.
- (c) Larger graph in Appendix (slide 29).





Comparable efficacy and lack of side effects positions Menerba to be a potential first-line therapy

Comparison of Menerba to Other Drugs for Hot Flashes						
	Hormone Therapy	Pristiq	Menerba			
Efficacy	70.0%	64.0%	≥61.8% <sup>(a)</sup>			
Side Effects	Uterine cancer, breast cancer, stroke, cardiovascular disease, deep vein thrombosis, pulmonary embolism, dementia	Asthenia, constipation, dry mouth, nausea, dizziness, insomnia, somnolence, myocardial infarctions, coronary artery occlusions requiring revascularization	Loose stools			
FDA Approved for Treatment of Hot Flashes	Yes	Νο	Not yet			
Cost per Month	\$30 /month	\$150 /month	\$150 /month			

(a) At 10.0 g/day dose which is the lowest efficacious dose in the planned Phase III trial.





Competing products in development focused largely on repackaged hormone therapy and repurposed antidepressants

Selected Programs in the Clinic						
Drug	Sponsor	Phase	Туре			
Bazedoxifene/Conjugated Estrogen	Wyeth	III	SERM + estrogen			
Angeliq (2 mg drospirenone & 1 mg estradiol)	Bayer	III	HRT			
Desvenlafaxine succinate sustained release	Wyeth	III	SNRI			
Org 50081	Organon	III	Serotonin 2 Blocker			
Synthetic Conjugated estrogens	Duramed	III	HRT			
Estradiol transdermal delivery system	Bayer	III	HRT			
Cenestin 0.3 mg Tablets	Duramed	III	HRT			
Gabapentin	Depomed	III	α-2 δ receptor			
Esterified Estrogens (EE) & Methyltestosterone	Solvay	II	HRT			
GSK232802	GSK	II	SERM			
PD-0299685	Pfizer	II	α-2 δ receptor			
Mesafem capsules	Noven	II	Low-dose SSRI			

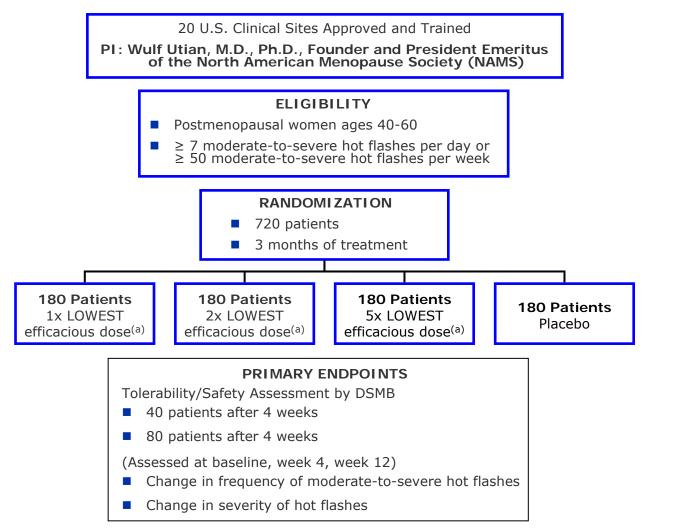




- Phase II study was conducted using 5.0 g/day and 10.0 g/day sachets added to water; compliance was very high
  - 98.0% completion rate;  $91.0\% \ge 75.0\%$  of the assigned dosing schedule
- Change in purification method enabled the reduction of physical dosage further optimization of CMC methods and controls
  - Addition of filtration step to optimize size of dose
  - Potential reduction in number of extracts
  - Could potentially reduce the incidence of loose stools
- No significant toxicities have been observed in any of the animal studies with doses ranging from 2,000 mg/kg/day in dogs to 16,000 mg/kg/day in rodents
- Concluded three CMC meetings with the FDA
  - Positive meetings with clear recommendations relating to analytical characterization to ensure drug consistency (very manageable)
  - Ex-FDA regulatory consultant confident in Company's strategy and performance to date







Note: Investigators meeting completed, contract negotiated, trial to start on regulatory approval. (a) Lowest efficacious dose as identified in Phase II clinical study.





"I'm delightfully surprised and impressed by the selectivity, safety and clinical effects of Menerba, Bionovo's drug candidate for menopausal hot flashes. To date, it is perhaps the most impressive SERM I've encountered."

Bert O'Malley, M.D. – 2008 National Medal for Science; Member of the National Academy of Science

"I'm very impressed by the scientific depth and innovative approach of Bionovo's drugs and drug discovery strategies. The utilization of natural compounds found in botanical sources, the targeted mechanisms of action seem to result in safer drugs with exciting clinical results.
 I believe the extensive pipeline of Bionovo will provide new therapies for women."
 Jan-Ake Gustafsson, M.D., Ph.D. — Discovered ERβ; Member of the National Academy of Science

"The rationale for Menerba is extremely compelling. It has no safety issues and many advantages"
 Daniel Shames, M.D. — former Director of the Division, Reproductive and Urologic Drug Products, FDA

"The combination of a trend to better efficacy with the higher dose of Menerba and a very strong safety profile of a drug that was extremely well tolerated by menopausal women is exciting news. These early positive clinical results are encouraging for discovering a safer therapy for hot flashes."

Deborah Grady, M.D. — Associate Dean, Clinical and Translational Science; Professor of Medicine and Director, Women's Health Clinical Research Center, University of California San Francisco

"Menerba provides a true paradigm shift in the treatment of menopausal hot flashes. The novel mechanism of action, the exciting preclinical and clinical safety, and the early efficacy are encouraging. I believe swift development is warranted so we can provide women with an alternative to hormone therapy,"

Wulf Utian, M.D., Ph.D., D.Sc. - Founder and President Emeritus, North American Menopause Society





- Novel oral cytotoxic agent undergoing Phase II clinical trials for advanced breast cancer
- Induces cell death by induction of reactive oxygen species (ROS) which causes DNA damage, PARP hyperactivation and inhibition of glycolysis
  - Glycolysis generates > 85.0% of the energy for cancer cells versus < 7.0% for normal cells
  - Selectively kills cancer cells without killing normal cells
- Powerful potential candidate as an adjuvant therapy for hormone independent breast cancer
- Excellent safety profile; early signs of clinical efficacy
- Botanically derived drugs in high demand by patient population
- Effective adjuvant therapy with no compromise in quality
- Total addressable market opportunity (ER +/-) of \$4.6 billion<sup>(a)</sup>







## Selectively Effective Against Cancer Cells

- Bezielle inhibits cancer cell lines derived from various malignancies
- Preclinical evidence suggests activity against breast, pancreatic, and lung cancers
- Bezielle does not inhibit normal breast cells (HuMEC)

	Lung		Pancreas		Prostate		Breast		
Cell Line	A549	LLC	Panc-1	Panc02	PC-3	LNCaP	MCF-7	MCNeuA	HuMEC
Effectiveness	+	++	+	++	+	+	++	++	-
IC <sub>50</sub> Values (ng/ml)	1424*	492	1054	594	1035	1516	818	619	NA

- < 50.0% Inhibition</p>
- + 51.0-75.0% Inhibition
- ++ > 75.0% Inhibition
- \* IC<sub>50</sub> Values (ng/mL)





## Enrolled 21 patients with Metastatic Breast Cancer

Patients had received an average 3.9 prior cancer treatments

Average expected patient survival post-trial was 327.5 days (Kaplan-Meier survival analysis)<sup>(a)</sup>

Efficacy Results					
Number	Percentage				
5.0	31.0%				
1.0	6.0				
5.0	31.3				
4.0	25.0%				
3.0	18.8				
	Number 5.0 1.0 5.0 4.0				

#### <u>Safety</u>

- No deaths, serious adverse events, or hematological adverse events
- All adverse events related to Bezielle were grade 1 and grade 2
  - No grade 3, or grade 4 adverse events
- Majority of related adverse events were gastrointestinal side effects that were expected
- Most common related adverse events were diarrhea, nausea, stomach bloating, and headaches

#### <u>Tolerability</u>

- Mean percentage of prescribed doses taken while on study was 85.0%
- Median percentage of prescribed doses taken while on study was 92.0%

(a) Expected patient survival pre-trial was 90-120 days.

<sup>(</sup>d) Partial response (remission) indicates a greater than 30.0% reduction in tumor size.





<sup>(</sup>b) Includes 16 of 21 patients evaluable according to RECIST criteria (greater than 28 days on trial).

<sup>(</sup>c) Minimal response indicates a less than 30.0% reduction in tumor size.

Enrolled 27 patients with Metastatic Breast Cancer

Patients had received an average 5.9 prior cancer treatments

Dose escalation reached 40 grams per day, 4x the dose evaluated in the Phase 1A study

Efficacy Results						
valuable Participants (N=16) <sup>(a)</sup>	Number	Percentage				
Objective Tumor Response						
Minimal Response <sup>(b)</sup>	3.0	18.8%				
Partial Response <sup>(c)</sup>	0.0	0.0				
Stable Disease	5.0	31.3				
Duration of Stable Disease						
Stable Disease for 90-180 Days	5.0	31.3%				
Stable Disease for > 180 Days	2.0	12.5				

#### Efficacy (cont.)

- 4 patients discontinued the study with stable disease
  - One had objective tumor regression during 449 days of Bezielle treatment and was stable for a total of 600 days
  - A second continues to be stable for 832 days without any new anticancer treatment
  - A third was stable for 591 days before evidence of progression

#### <u>Safety</u>

- No drug-related deaths, serious adverse events, or hematological adverse events
- 94% of adverse events related to Bezielle were grade 1 and grade 2
- Majority of related adverse events were gastrointestinal side effects that were expected
- Most common related adverse events were diarrhea, nausea, vomiting, fatigue, and headaches

#### **Tolerability**

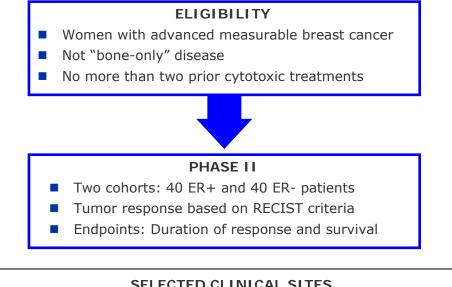
- Both median and mean treatment compliance was 90%
- (a) Includes 16 of 27 patients evaluable according to RECIST criteria (greater than 28 days on trial).
- (b) Minimal response indicates a less than 30.0% reduction in tumor size.

<sup>(</sup>c) Partial response (remission) indicates a greater than 30.0% reduction in tumor size.





PI: Banu Arun, M.D. — Breast Oncology, MD Anderson Cancer Research Center (Houston, TX); Alejandra Perez, M.D. – Memorial Cancer Institute (Hollywood, FL)



#### SELECTED CLINICAL SITES

- MD Anderson Cancer Center
- University of Chicago
- University of California San Francisco
- Ohio State University

- Montefiore Medical Center
- Duke University
- Columbia University
- Memorial Cancer Institute, Florida



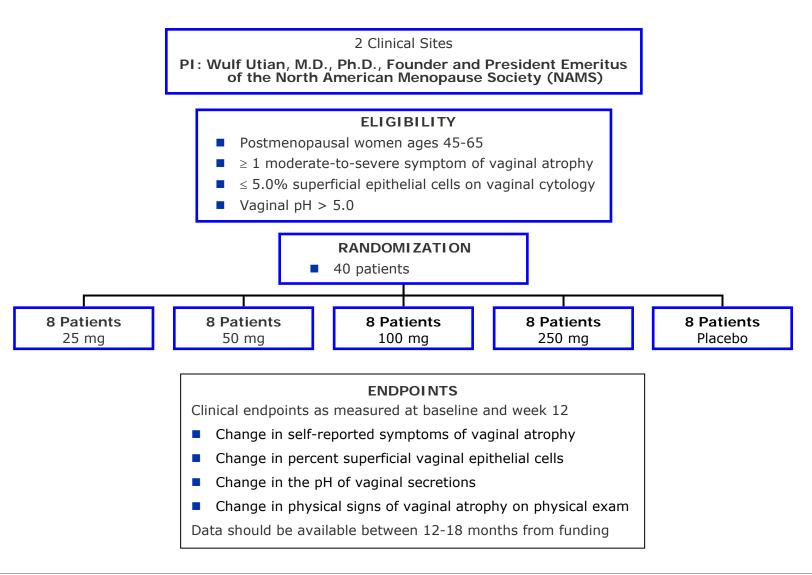


- Novel topical Estrogen Receptor beta (ERβ) modulator targeting vaginal atrophy
- Potential advantage over topical estrogens with regard to safety and efficacy
  - Approved products have seven black box warnings due to the risks of systemic absorption
  - Preclinical work indicates Seala may have superior efficacy in restoration of vaginal epithelium
- Vaginal atrophy is a significant unmet need
  - 75.0% of middle-aged women report that sex is moderately to extremely important
  - 55.0% of post menopausal women have vaginal dryness
  - 41.0% of post menopausal women experience painful intercourse
  - 40.0% of women taking oral hormone replacement have persistent vaginal dryness
- Mitigating AE risks associated with SERMs and HRT products could open up a \$4.0 billion market akin to the erectile dysfunction market<sup>(a)</sup>













- Filed 38 patent applications to protect Menerba
  - One patent has been issued by the U.S. Patent and Trademark Office and covers Menerba mixture
  - Other patent applications cover composition of matter, structure-function, and methods of treatment
- Filed six patent applications related to various aspects of Bezielle, including composition of matter, the combination of chemical components, and methods of therapeutic use
- Filed seven patent applications related to various aspects of Seala, including composition of matter and therapeutic use
- All patent applications have also been filed in key international jurisdictions



- Shares outstanding: 73.4 million
- Dilutive securities outstanding: 15.7 million
  - Warrants outstanding: 10.5 million (at \$2.58 on average)
  - Employee options outstanding: 5.2 million (at \$1.89 on average)
- Current stock price (7/17/09): \$0.43 /share
- Current market capitalization: \$31.5 million
- Net cash (as of 3/31/09): \$8.1 million
  - Cash burn approximately \$1 million per month
- Enterprise value: \$23.5 million

Source: FactSet and Company filings as of July 17, 2009.

(a) US\$ and shares in millions, except share price.

(c) Per latest available Company filings.



<sup>(</sup>b) Fully diluted shares outstanding as per the treasury stock method.

# Appendix



# Biographies



#### Isaac Cohen, O.M.D., L.Ac.

- Chairman & Chief Executive Officer
- Guest Scientist University of California, San Francisco Cancer Research Center and Center for Reproductive Endocrinology

#### Mary Tagliaferri, M.D., L.Ac.

- President & Chief Medical Officer
- Former Program Director University of California, San Francisco Breast Care Center

#### Thomas Chesterman, MBA

- Senior Vice President & Chief Financial Officer
- Former Senior Vice President & Chief Financial Officer, Aradigm Corporation and Bio-Rad Laboratories

#### Klaus Kohl, Ph.D.

- Senior Vice President & Chief Technical Officer
- Former Vice President, Program Management, CMC and Regulatory Affairs, Novo Nordisk Delivery Technologies

Note: Italics indicates positions formerly held or held outside of the Company.



#### David Naveh, Ph.D., MBA

Former Senior Vice President & Chief Technical Officer, Bayer Biological/Biotechnology Worldwide 2007

#### Michael Vanderhoof

President, Avintaquin Capital LLC (venture capital firm)

#### George Butler, Ph.D.

Former Global Chief Regulatory Officer, AstraZeneca and Novartis Pharmaceuticals

#### Louis Drapeau, CPA

- Current Chief Executive Officer and Chief Financial Officer, InSite Vision
- Former Chief Financial Officer, Nektar, Inc.
- Former Chief Executive Officer, BioMarin

#### John Baxter, M.D.

- Current Senior Member & Co-Director, Diabetes Center
- Member, National Academy of Sciences
- Former President, Endocrine Society
- Director, Genomics Core, The Methodist Hospital Research Institute
- Chief of Endocrinology, Department of Medicine, The Methodist Hospital (Houston, TX)
- Isaac Cohen, O.M.D., L.Ac.
- Mary Tagliaferri, M.D., L.Ac.



- Len F. Bjeldanes, Ph.D.
  - Department Chair & Professor of Nutritional Sciences and Toxicology University of California, Berkeley
- Michael J. Campbell, Ph.D.
  - Assistant Professor of Laboratory Medicine University of California, San Francisco
- Uwe Christians, M.D., Ph.D.
  - Professor of Pharmacological Sciences & Director of Research, Department of Anesthesiology University of Colorado Health Science Center
- Gary Firestone, Ph.D.
  - Professor of Cell and Developmental Biology University of California, Berkeley
- Deborah Grady, M.D., M.P.H.
  - Professor of Medicine & Director of the Center for Women's Health University of California, San Francisco
- I. Craig Henderson, M.D.
  - Former President, Keryx, Inc.; Former Chief Executive Officer, SEQUUS Pharmaceuticals; Professor of Medicine University of California, San Francisco
- Dale Leitman, M.D., Ph.D.
  - Associate Professor, Department of Nutritional Science and Toxicology University of California, Berkeley
- Willa Hsueh, M.D.
  - Professor of Medicine, University of Texas Methodist Hospitals; former Professor of Medicine University of California, Los Angeles
- Richard Gless, Ph.D.
  - Vice President & Chief of Chemistry, Arete Therapeutics (South San Francisco, CA)



#### John Baxter, M.D.

 Professor of Medicine, Chief of Endocrinology, Department of Medicine, The Methodist Hospital (Houston, TX); Member of the National Academy of Sciences

#### Moshe Rosenberg, D.Sc.

Professor of Physical Chemistry & Food Technology, Department of Food & Dairy Technology — University of California, Davis

#### Terry Speed, Ph.D.

- Professor, Department of Statistics University of California, Berkeley; Senior Principal Research Scientist & Head, Bioinformatics Division, Walter and Eliza Hall Institute of Medical Research (Melbourne, Australia)
- Zung Tran, Ph.D.
  - Professor of Biostatistics, Chair of the Department of Biostatistics University of Pennsylvania

#### Debu Tripathy, M.D.

Professor of Medicine & Director, Komen Alliance Breast Cancer Research Center — University of Texas Southwestern Medical Center

#### Ethan Weiss, M.D.

Assistant Professor of Medicine, Division of Cardiology — University of California, San Francisco

#### Jan Ake Gustafsson, M.D., Ph.D.

 Professor of Medicine, Division of Molecular Biology — University of Houston; Former-Professor of Medicine, Karolinska Institute (Sweden); Member of the National Academy of Sciences

#### Bert O'Malley, M.D.

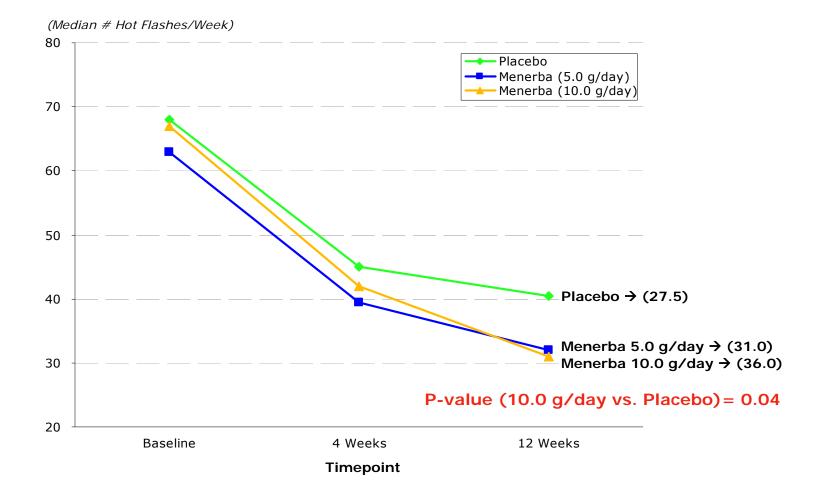
Professor of Medicine, Division of Molecular Biology — Baylor University (Houston, TX); Winner of the National Medal for Science (2008); Member of the National Academy of Sciences



## Preclinical Support for Menerba



## Menerba<sup>(a)</sup> Phase II — Reduction in Number of Hot Flashes / Week



Note: P-Values from rank-transformed analysis of variance (ANOVA) controlling for clinical site and strata. (a) Menerba formerly known as MF101.





## Menerba Phase II — Percent Reduction in Nighttime Awakenings

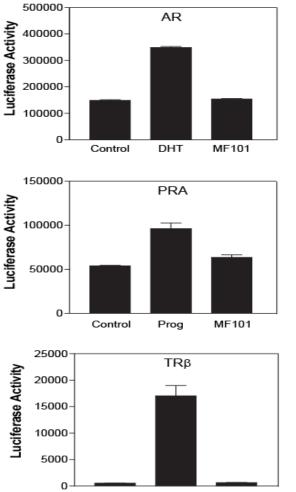


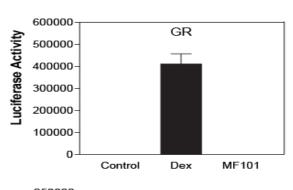
(Median % Reduction at 12 Weeks)

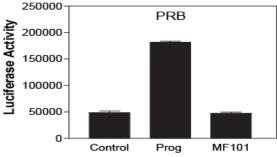
Note: P-values from rank-transformed analysis of variance (ANOVA) controlling for clinical site and strata.











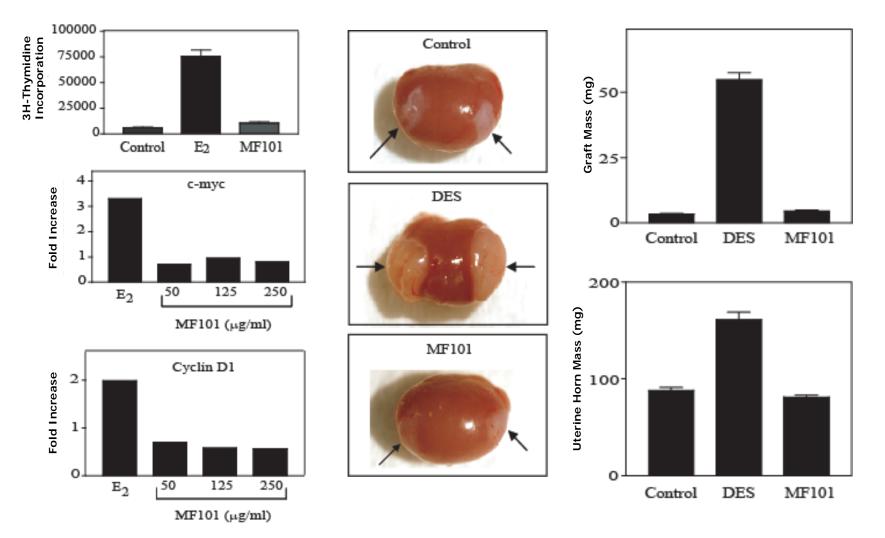
Control тз MF101

(a) Menerba formerly known as MF101.





## Menerba<sup>(a)</sup> Does NOT Stimulate Cell Proliferation

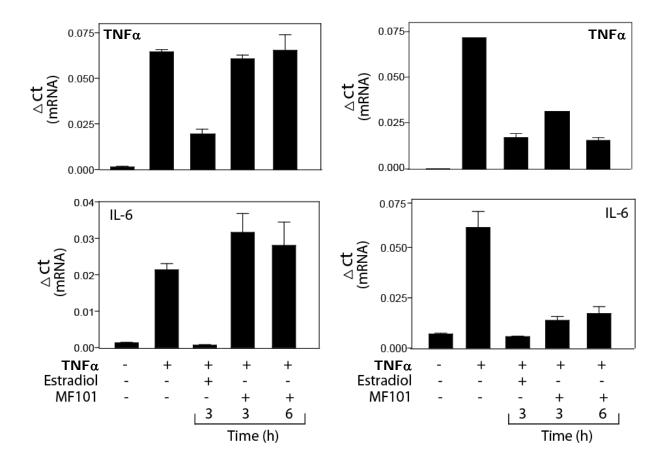


Source: Cvoro A, Endocrinology. November 9, 2006. (a) Menerba formerly known as MF101.





## Menerba<sup>(a)</sup> Selectively Represses TNF $\alpha$ and IL-6 Through ER $\beta$



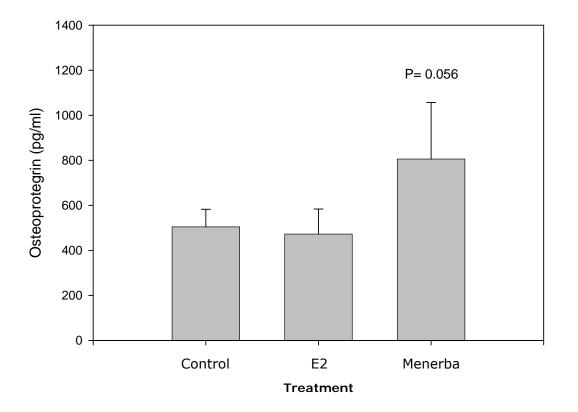
#### Menerba Regulation of Cytokines in Bone Cells

(a) Menerba formerly known as MF101.



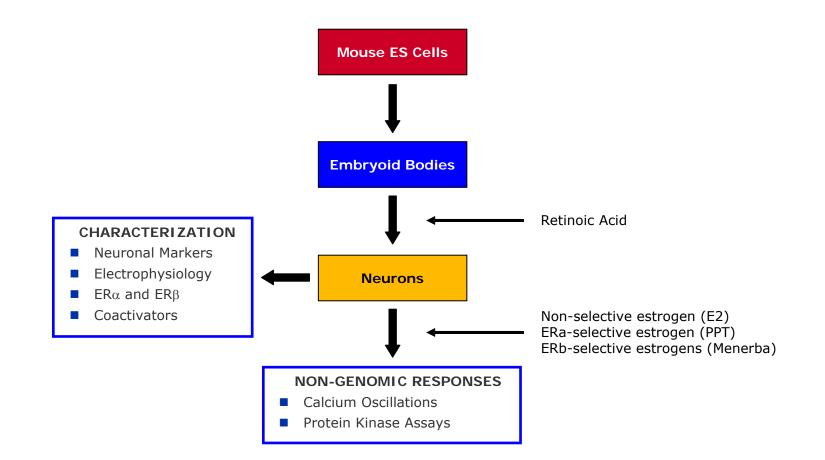










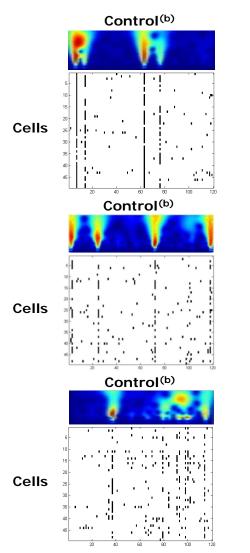




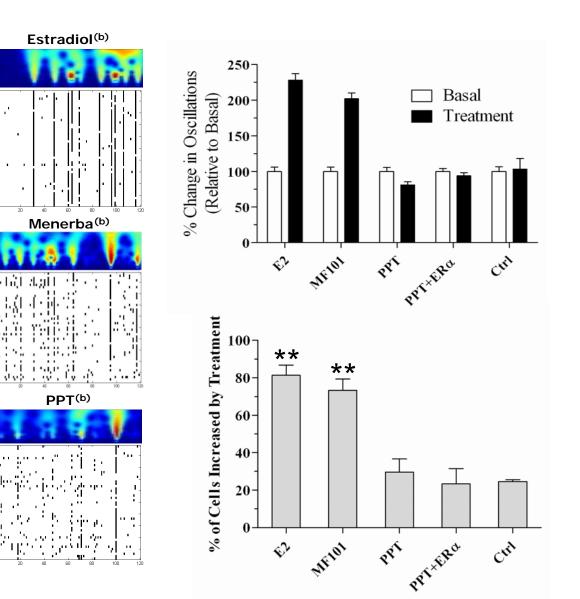


## Menerba<sup>(a)</sup> Stimulates Calcium Oscillations in MES-Derived Neurons

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Menerba formerly known as MF101. (a) (b) Time points measured at five second intervals.



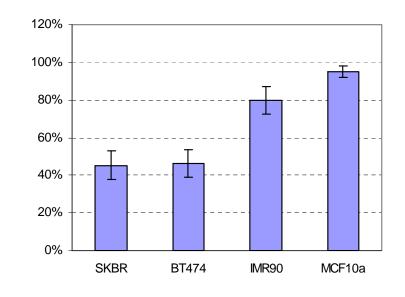
bioNovo



# Preclinical Support for Bezielle



## Bezielle induces cell death in breast cancer cell lines but not in normal mammary epithelium or fibroblasts



### Survival of Cells Treated with Bezielle for 24 Hours

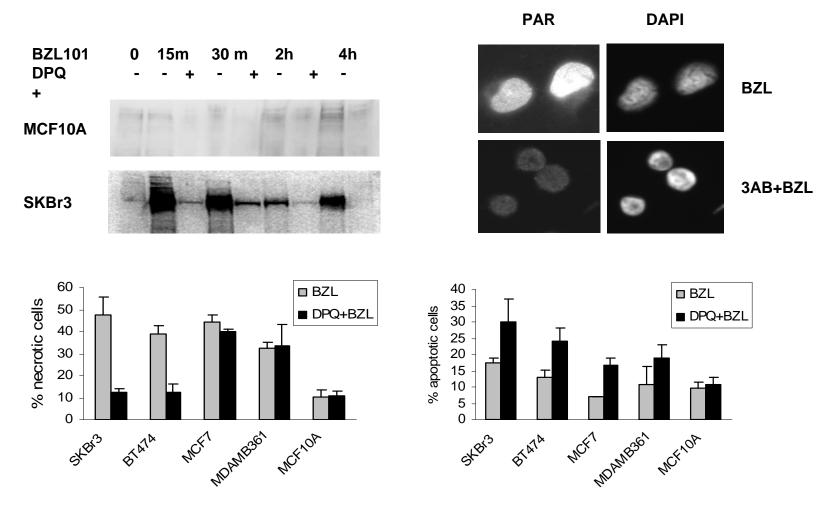
- Survival of cells treated with 500 ng/ml of Bezielle for 24 hours
- SKBr3 and BT474 breast carcinoma cells
- IMR90 normal fibroblasts
- MCF10A immortalized normal mammary epithelial cells

#### Source: Fong S, Cancer Biology & Therapy, April 2008.





# Bezielle<sup>(a)</sup> Induced Activation of PARP Leads to Necrotic Death

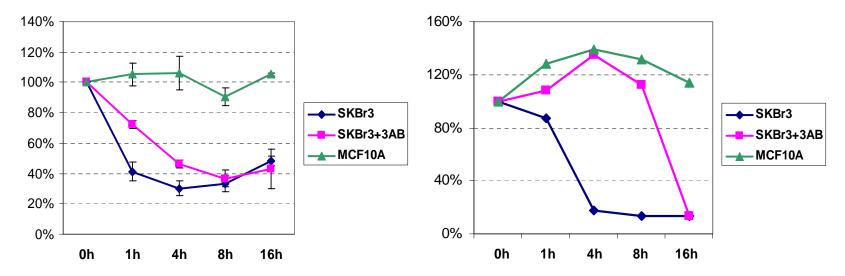


(a) Bezielle formerly known as BZL and BZL101.





# Bezielle Leads to Depletion of NADH and Energy in Cancer Cells



**ATP Content in Bezielle Treated Cells** 

### NADH Content in Bezielle Treated Cells

Bezielle also induces:

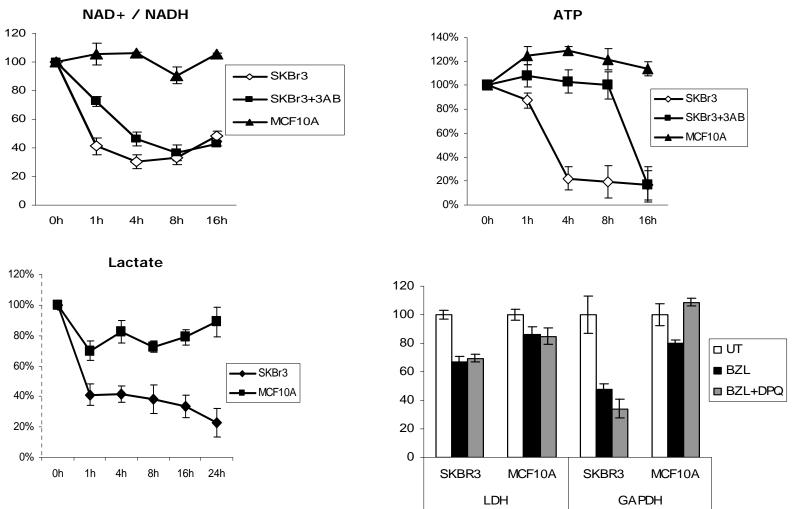
- Decrease in levels of lactate
- Decrease in activity of LDH and GAPDH

#### Source: Fong S, Cancer Biology & Therapy, April 2008.





## Bezielle<sup>(a)</sup> Inhibits Glycolysis Selectively in Cancer Cells



Source: Fong S, Cancer Biology & Therapy, April 2008. (a) Bezielle formerly known as BZL and BZL101.



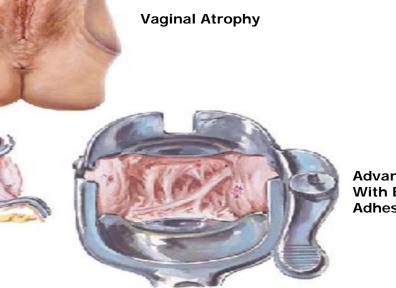


# Preclinical Support for Seala

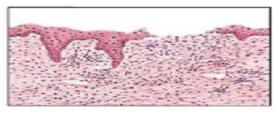


# Postmenopausal Vaginal Atrophy

- Atrophic Vaginitis Early Stage Symptoms:
  - Pallor
  - Loss of rugae
  - Denuded areas
  - Petechial hemorrhages
  - Funnel-like narrowing
  - Thin discharge







Histology of Vagina After Menopause

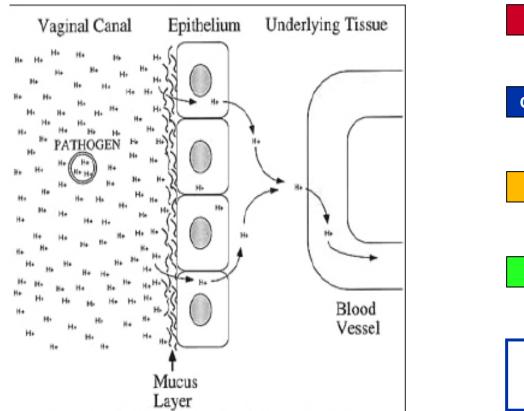


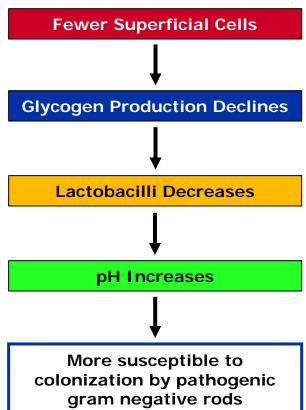
Smear From Postmenopausal Vagina - Atrophic Epithelial Cells





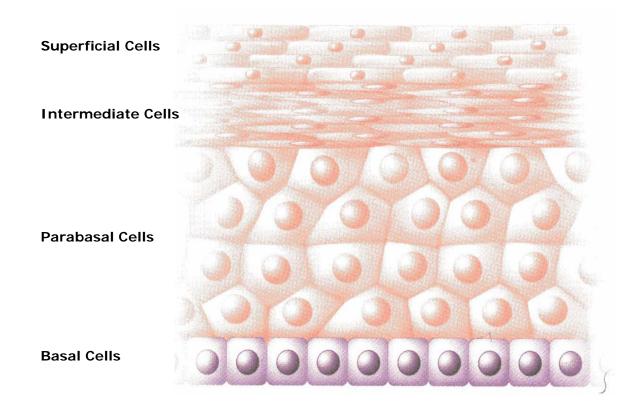












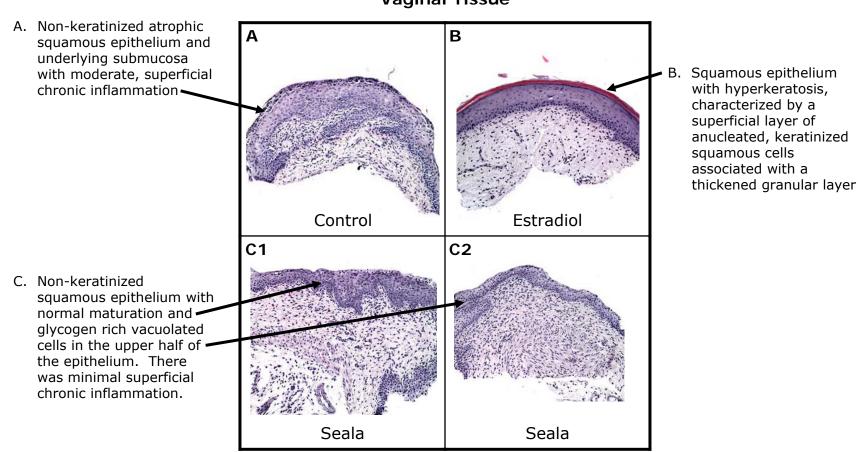
## The Vaginal Epithelium

- Premenopausal Women 30-50% Superficial Cells on Vaginal Smear
- Postmenopausal Women with Vaginal Atrophy < 5% Superficial Cells on Vaginal Smear</p>





# In Vivo Seala Restores Vaginal Epithelium



Vaginal Tissue





## In Vivo Seala is Safe on the Uterus, Unlike Estrogen

