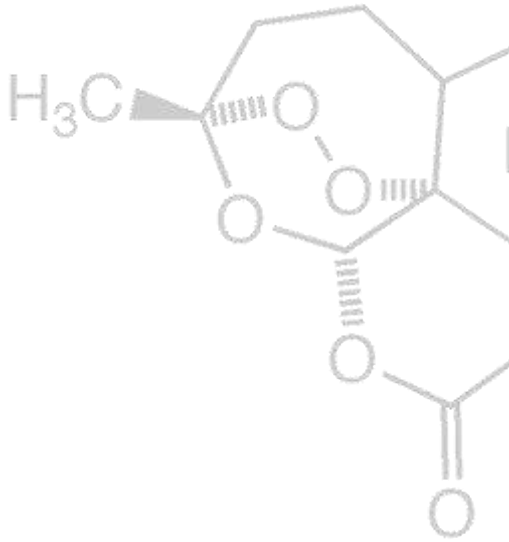


Artemisia BioMedical, Inc
Company Overview

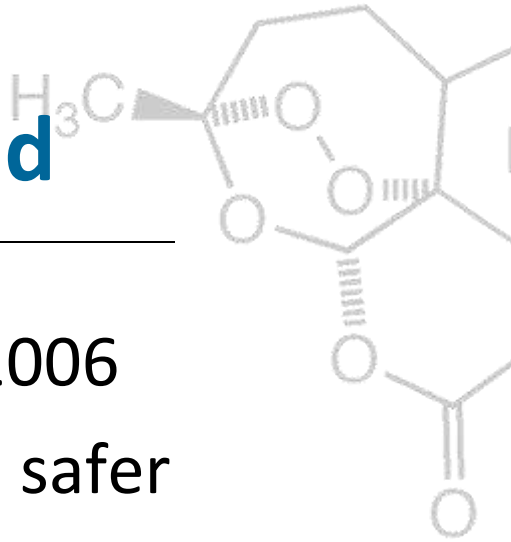
Better by Natural Design™

Michael Kuran
CEO

August 2011
Seattle, Washington

Artemisia BioMedical

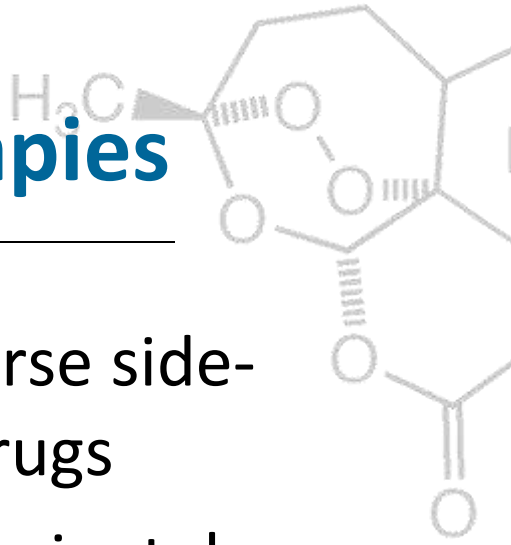
Artemisia BioMedical Background



- Emerging biotech company founded in 2006
- Advancing highly selective, effective and safer therapies for malaria and cancer
- Novel endoperoxide compounds based on redesign of old malaria drug artemisinin
- ~1,000x more potent than artemisinin, and 30,000x more selective to cancer cells than chemotherapy
- Exclusive Agreements with Johns Hopkins, University of Washington, and University of Alabama

Artemisia BioMedical

Need for Improved Cancer Therapies



- Major problem of chemotherapy is adverse side-effects that limit doses and efficacy of drugs
- General chemotherapy kills cells indiscriminately
- Targeted chemotherapy is often too specific, *e.g.*, women "cured" of breast cancer die from brain mets
- Unmet medical need for new cancer drugs that are:
  - Highly selective and toxic to cancer cells
  - Multi-targeted
  - More efficacious with fewer side-effects

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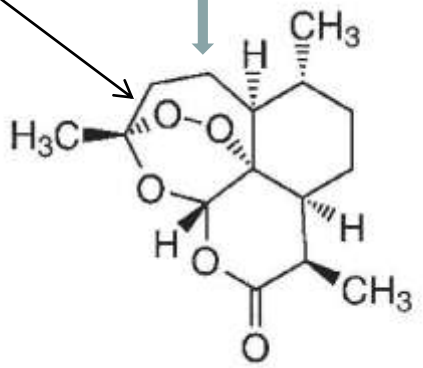
Artemisinin

- Isolated from sweet wormwood plant (*Artemisia annua*) in 1970's – used in traditional medicine for >2,000 years
- Internal "oxygen bridge" forms free radicals when exposed to free iron
- Only known natural product to contain a 1,2,4-trioxane ring
- Potent and safe antimalarial agent used for >30 years in millions of patients
- Selectively toxic to cells with high uncontrolled iron levels, e.g., malaria parasites and cancer cells

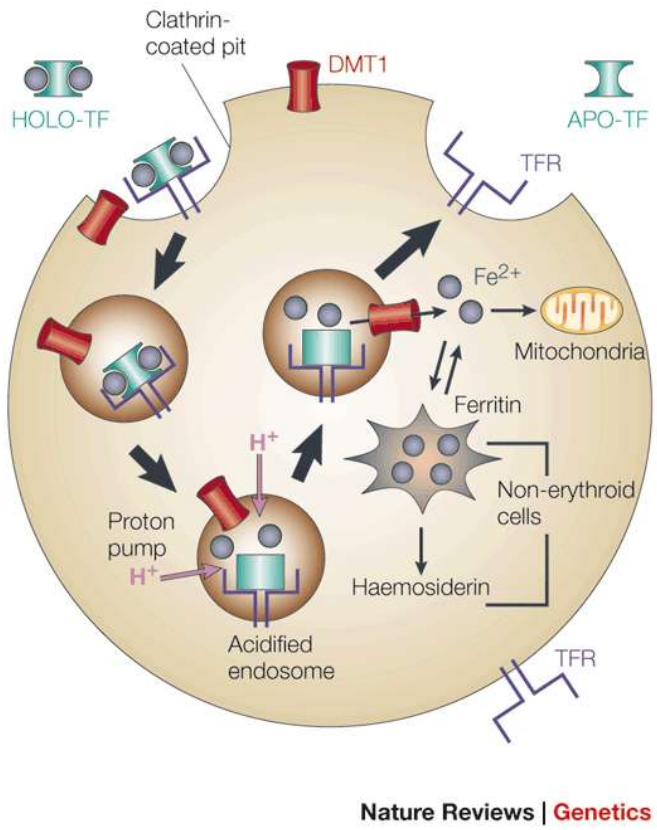
Artemisia annua L



Artemisinin

Artemisia BioMedical

Cellular Iron Acquisition



- Fe is necessary for cell division and growth through its role in DNA synthesis
- Fe acquired by cells from Transferrin (Tf) via transferrin receptor (TfR) uptake
- Binding relationship (stoichiometry) between Tf-TfR
- Inside endosome acidified to pH 5.5 (blood pH 7.4)
- Free iron is reduced from Fe (III) to Fe (II) before transport by DMT1 (iron transport protein)
- A Tf cycle take 4-5 minutes

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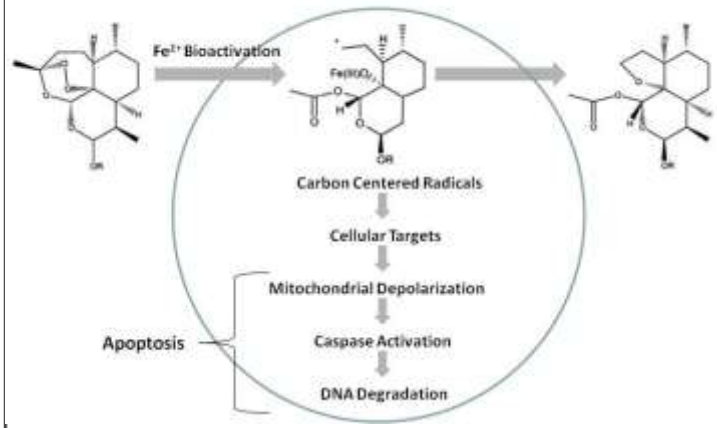
ART Regulated Cellular Processes/Pathways

Table 1. Summary of artemisinin-regulated cellular processes and pathways

Pathway regulated	Components regulated (expression and activity)	Refs
Apoptosis	Decreased *BCL2* and *BCL2L1* transcription	16
	Increased *BAX* and *BAD* transcription	16
	Increased cytoplasmic calcium	23
	Increased p38 MAPK phosphorylation	22
	Activation of caspase-3 and caspase-9	13, 14
	Increased genotoxic stress	32
	Decreased transcription of survivin	25
	Inhibition of glutathione *S*-transferase	11
Cell cycle	Decreased *CDK2*, *CDK4*, *CDK6*, cyclin D1, cyclin D3, cyclin E, cyclin A, *JAB1* and *E2F1* transcription	15, 18
	Inhibition of *CDK2* and *CDK4* promoter activity	18
	Increased p21, p27 and IFIT3	35
Growth factor receptor signalling	Decreased ERBB2, EGFR, p42/44 MAPK levels	34
	Decreased IFN-γ and IL-2 levels	36
	Increased expression of IFN-α response genes	35
	Increased AKT activity and IκB activity	35
	Decreased Ras-GTP and phosphorylated Raf	36
Steroid receptor and transcription factor expression and activity	Transcriptional ablation of *ERα* expression	17
	Protein degradation of AR	
	Increased ligand-dependent activities of CAR and PXR	59
	Decreased Sp1 expression and/or activity, loss of phosphorylated Sp1	18
	Decreased AP-1 transcription complex activity	
	Decreased NF-κB nuclear translocation and transcription factor activity	35
Angiogenesis/invasion	Decreased HIF-1α levels	33, 65
	Decreased *VEGFA* transcription	63
	Decreased KDR levels	66
	Decreased αvβ3 transcription	70
	Decreased MMP2, MMP9 and BMP1 levels	63



↑ Mercer AE *et al*. Evidence for the involvement of carbon-centered radicals in the induction of apoptotic cell death by artemisinin compounds. *J Biol Chem.* 2007

← Firestone GL, Sundar SN. Anticancer activities of artemisinin and its bioactive derivatives. *Expert Rev Mol Med*. 2009

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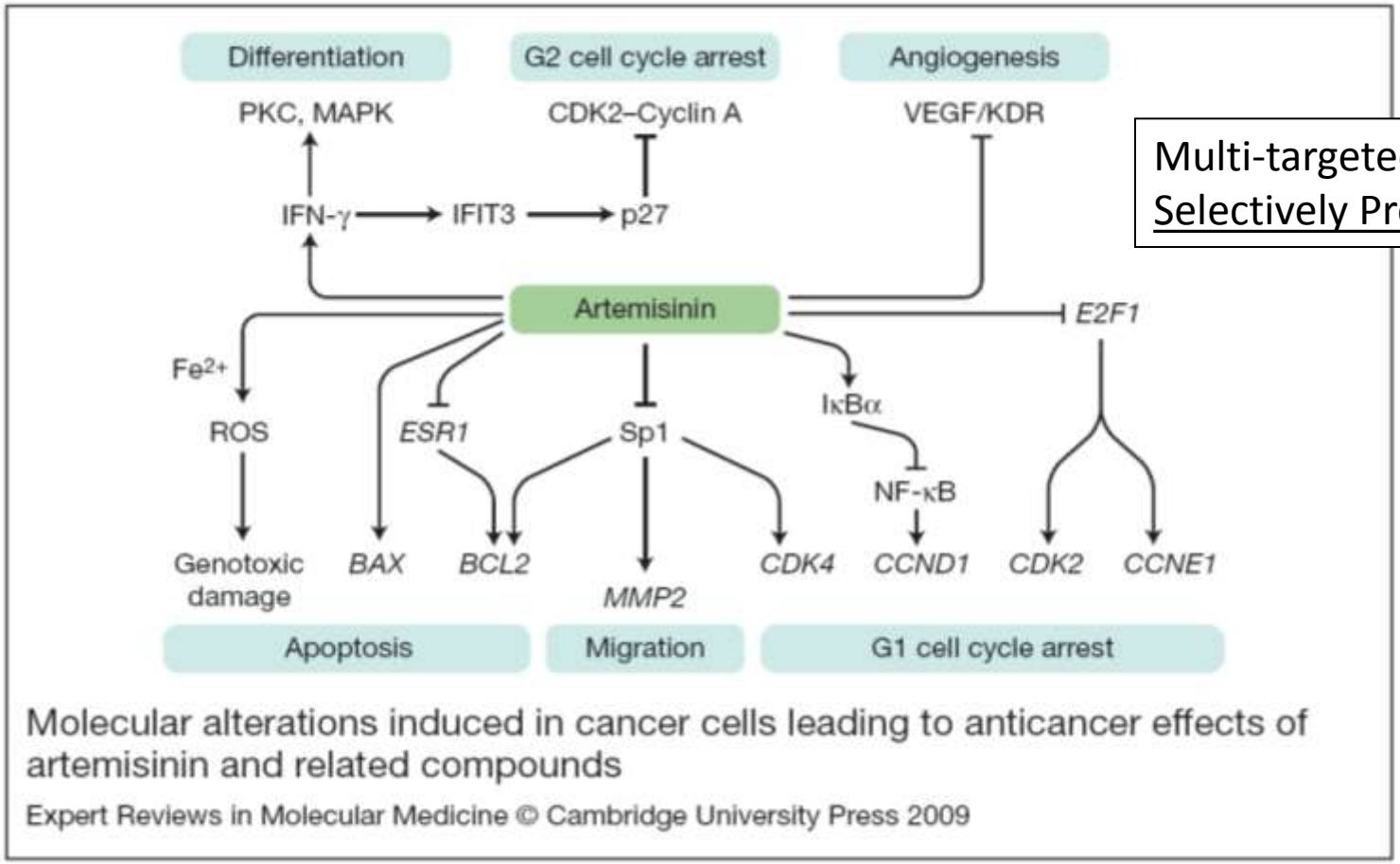
Artemisinin Multiple Anticancer Effects

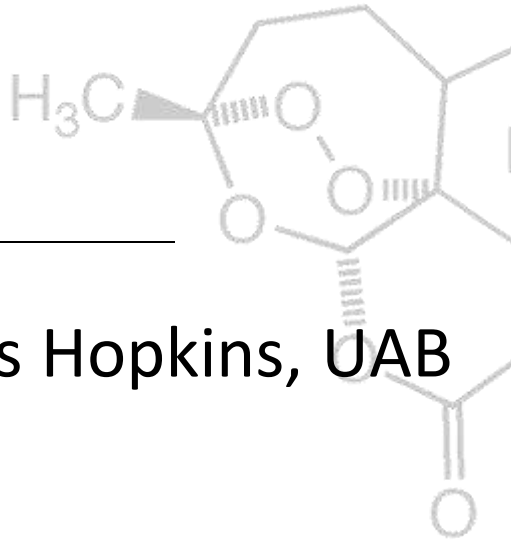


Multi-targeted,
Selectively Promiscuous™

Firestone GL, Sundar SN. Anticancer activities of artemisinin and its bioactive derivatives. *Expert Rev Mol Med*. 2009 Oct 30;11:e32.

Artemisia BioMedical

Technology Overview



- >30 years of collective R&D at UW, Johns Hopkins, UAB

  Novel Endoperoxides

  - Artemisinin Dimers (two ART molecules linked together)
  - Artemisinin-Peptides (ART + cell receptor-binding molecules)
  - Artemisinin-Iron Chelators (ART + iron-binding molecules)

  Novel Drug Delivery

  - Cell transferrin receptor-binding peptides
  - Unique binding site, independent of transferrin
  - May be suitable for hard-to-deliver agents, *e.g.*, RNAi

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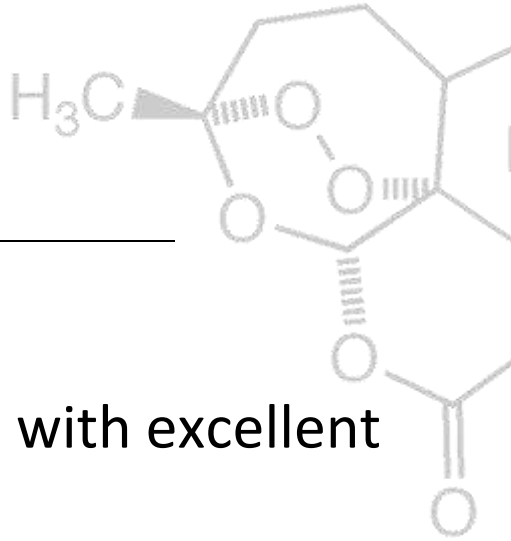
Technology Advantages



- Old Drug
  - Re-designed, re-profiled, well-characterized with excellent therapeutic/safety profiles
  - Lower risk, higher probability of success
- Smart Drug
  - Higher selectivity and toxicity towards diseased cells than to rapidly dividing normal cells
  - Multiple cellular and molecular effects
  - Activated selectively inside target cells
- Solid IP portfolio

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Growth Inhibition and Selectivity

Compound	EC_{50} (µM)	Selectivity "Kill Ratio" (Normal : Cancer Cells)
Doxorubicin	0.1 N/A	1 : 2.5 4 ~ 6
Cisplatin	1.4	5.4
Paclitaxel	0.01 N/A	5.0 1 ~ 2
Thioguanine	2.0	10.0
Vincristine	0.15	6.7
Mitomycin C	3.5	2.9
Etoposide	10.0 N/A	1.0 2 ~ 15
Staurosporine	0.035	0.7
Dihydroartemisinin plus transferrin	2.59 1.64	88 36
$Artemisinin_1$-Peptide	1.06	>12,000
$Artemisinin_2$-Peptide	0.61	>16,000
Artemisinin Trioxane Dimers	0.009 ~ 0.0023	470 ~ 27,000*

* Depending on drug concentration, for every normal cell killed up to 27,000 cancer cells are killed.

Artemisia BioMedical

NCI In Vitro Screening Data Results (GI_{50})

LEUKEMIA	1	2	3	4	5
Tumor Cell Line	Dimer-Acid	Daunorubicin	Dimer-Sal	Dimer-Alcohol	Dimer-Hydrazine
CCRF-CEM	-8.30	-8.00	-8.00		-7.76
HL-60 (TB)	-8.30	-8.00	-8.00	-7.78	-7.68
K-562	-8.30	-8.00	-8.00	-7.91	-8.00
Molt-4	-8.18	-8.00	-8.00	-7.92	-7.97
RPMI-8226	-8.30	-8.00	-8.00	-8.00	-8.00
SR		-8.00	-8.00		-7.93
Average GI50	**-8.28**	**-8.00**	**-8.00**	**-7.90**	**-7.89**

CNS CANCER	1	2	3	4	5
Tumor Cell Line	Topotecan	Dimer-Sal	Dimer-O-NH2	Dimer-Hydrazine	Vincristine
SF-268	-7.70	-7.41	-7.06	-7.22	-6.80
SF-295	-7.20	-7.87	-7.38	-7.20	-6.90
SF-539	-7.70	-7.51	-7.09	-6.79	-6.90
SNB-19	-7.50	-6.40	-6.89	-6.08	-6.90
SNB-75	-7.20	-7.33	-6.43	-7.19	-6.40
U251	-7.50	-8.00	-7.36	-7.39	-6.90
Average GI50	**-7.47**	**-7.42**	**-7.04**	**-6.98**	**-6.80**

RENAL CANCER	1	2	3	4	5
Tumor Cell Line	Dimer-Sal	Dimer-Hydrazine	Topotecan	Doxorubicin	Dimer-O-NH2
786-0	-8.00	-6.53	-7.60	-7.20	-6.53
A498	-7.59	-6.01	-6.70	-7.20	-6.60
ACHN	-8.00	-7.20	-7.60	-7.30	-6.92
CAKI-1		-7.37	-7.80	-6.20	-6.69
RXF 393	-4.98	-7.03	-6.90	-7.50	
SN12C	-8.00	-7.46	-7.50	-7.30	-7.24
TK-10	-7.97	-7.29	-5.20	-6.00	-7.31
UO-31	-8.00	-7.63	-7.10	-6.70	-7.01
Average GI50	**-7.51**	**-7.07**	**-7.05**	**-6.93**	**-6.90**

COLON CANCER	1	2	3	4	5
Tumor Cell Line	Dimer-Acid	Dimer-Sal	Dimer-DHA	Dimer-Alcohol	Dimer-Hydrazine
COLO 205	-8.30	-8.00	-8.00	-8.00	-7.98
HCC-2998		-8.00		-7.50	-7.23
HCT-116	-8.30	-8.00	-8.00	-8.00	-8.00
HCT-15	-8.30	-8.00	-8.00	-8.00	-8.00
HT29	-8.30	-8.00	-8.00	-7.75	-7.84
KM12	-8.30	-8.00	-8.00	-8.00	-7.90
SW-620		-8.00	-7.50	-8.00	-7.75
Average GI50	**-8.30**	**-8.00**	**-7.92**	**-7.89**	**-7.81**

OVARIAN CANCER	1	2	3	4	5
Tumor Cell Line	Dimer-Sal	Docetaxel	Paclitaxel	Dimer-O-NH2	Dimer-Hydrazine
IGROV1	-7.66	-8.00	-7.50		-6.07
OVCAR-3	-8.00	-8.00	-8.40	-7.38	-7.35
OVCAR-4	-8.00	-4.70	-5.20	-7.15	-7.57
OVCAR-5	-8.00	-8.00	-7.20	-7.40	-7.38
OVCAR-8	-8.00	-8.00	-8.10	-7.29	-7.42
SK-OV-3	-5.60	-7.90	-7.70	-6.73	
Average GI50	**-7.54**	**-7.43**	**-7.35**	**-7.19**	**-7.16**

BREAST CANCER	1	2	3	4	5
Tumor Cell Line	Dimer-Alcohol	Dimer-Sal	Dimer-Hydrazine	Paclitaxel	Dimer-O-NH2
MCF-7	-7.22	-8.00	-7.60	-8.20	-7.48
NCI/ADR-RES	-7.45	-6.70		-5.50	-6.60
MDA-MB-231/ATCC	-5.40	-7.31	-7.14	-7.00	-6.64
HS-578T	-4.82	-7.88	-7.23	-7.60	-7.23
MDA-MB-435	-7.50	-8.00		-8.50	-7.38
BT-549	-7.11		-7.73	-7.40	-7.46
T-47D	-8.00	-8.00	-8.00	-6.40	-7.45
MDA-MB-468		-8.00	-7.23		-7.14
Average GI50	**-7.92**	**-7.70**	**-7.49**	**-7.23**	**-7.17**

NSCLC	1	2	3	4	5
Tumor Cell Line	Dimer-Sal	Gemcitabine	Docetaxel	Dimer-Hydrazine	Dimer-O-NH2
A549/ATCC	-8.00	-8.00	-8.00	-7.40	-7.24
EKVX	-8.00	-4.00	-5.40	-7.48	-7.31
HOP-62	-7.71	-8.00	-8.00	-7.30	-6.49
HOP-92		-8.00	-5.00		
NCI-H226	-7.57	-7.00	-6.40	-7.32	-6.77
NCI-H23	-8.00	-8.00	-8.00	-7.56	-7.37
NCI-H322M	-5.78	-7.60	-8.00	-5.77	-6.22
NCI-H460	-8.00	-8.00	-8.00	-7.19	-7.34
NCI-H522	-8.00		-8.00	-7.52	-7.30
Average GI50	**-7.63**	**-7.33**	**-7.20**	**-7.19**	**-7.01**

MELANOMA	1	2	3	4	5
Tumor Cell Line	Dimer-Sal	Paclitaxel	Dimer-Hydrazine	Dimer-O-NH2	Dimer-Alcohol
LOX IMVI	-8.00	-9.40	-7.51	-7.38	-7.26
MALME-3M	-8.00	-5.60	-7.19	-7.27	-7.31
M14	-8.00	-8.10	-7.41	-7.20	-5.87
SK-MEL-2	-7.01	-9.00	-7.46		-7.33
SK-MEL-28	-5.43	-5.50	-5.43	-5.91	-4.95
SK-MEL-5	-8.00	-7.40	-7.37	-7.37	-7.90
UACC-257	-7.48	-6.90	-7.38	-7.37	-7.31
UACC-62	-8.00	-8.00	-7.44	-7.17	-6.85
Average GI50	**-7.49**	**-7.49**	**-7.15**	**-7.10**	**-6.85**

PROSTATE CANCER	1	2	3	4	5
Tumor Cell Line	Dimer-Acid	Docetaxel	Paclitaxel	Dimer-Sal	ART-Pyr-Sal
PC-3	-8.30	-8.00	-8.00	-8.00	-7.77
DU-145		-8.00	-7.50	-7.13	-6.55
Average GI50	**-8.30**	**-8.00**	**-7.75**	**-7.57**	**-7.16**

NCI DTP Service

9 Human Cancers

60 Cancer Cell Lines

5-Dose Assay

Company compounds superior to SOC drugs on all cell lines except CNS

SOC n=5 per cancer type

Dimer n = 5

Dimer Chelator n = 13

Dimer Peptide n=1

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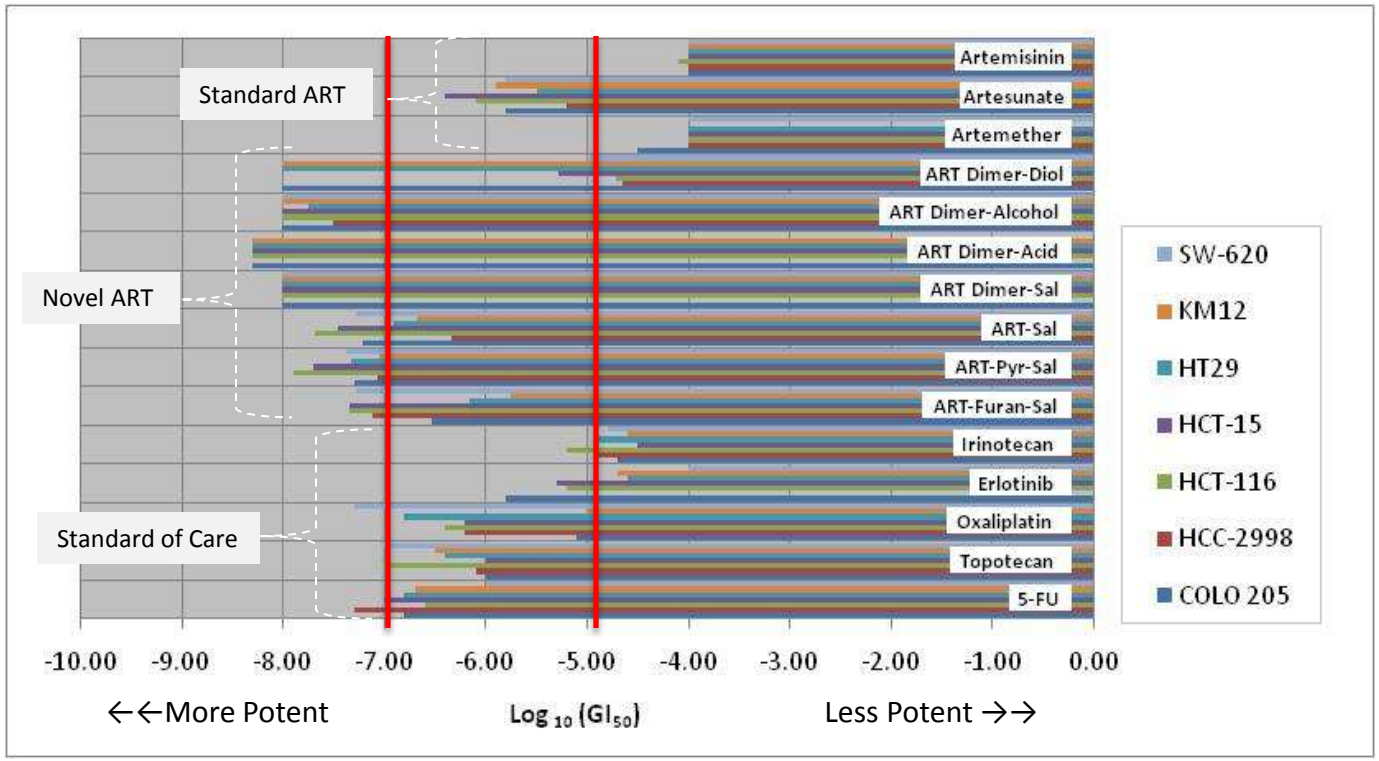
Colon Cancer Cell Growth Inhibition



Growth inhibition of cancer cells by artemisinin compounds vs. gold standard chemotherapy. The lower the value (to left), the higher the anti-cancer activity. Source: US NCI Developmental Therapeutics Program.

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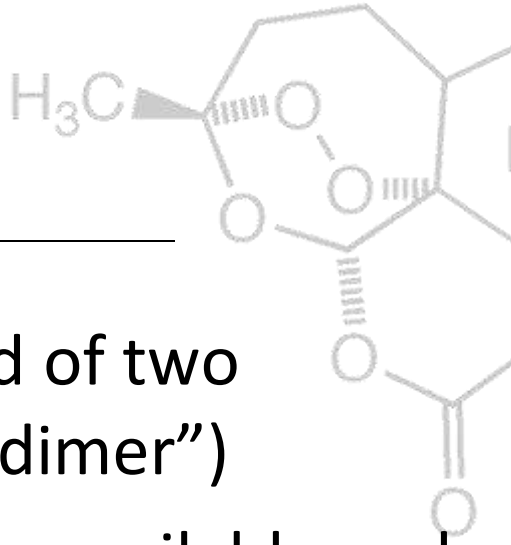
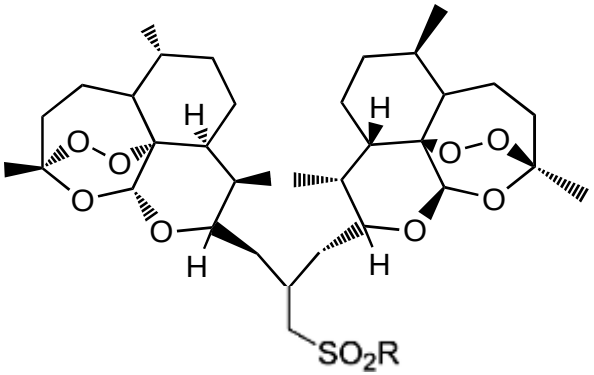
Trioxane Dimers



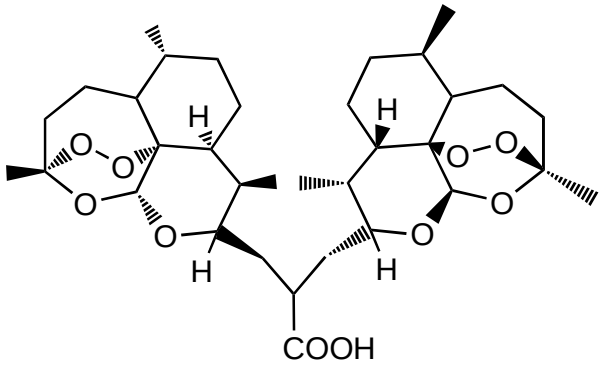
- Novel endoperoxide trioxanes comprised of two artemisinin molecules linked together ("dimer")
- Extremely stable, potent and safe – orally available and up to 1,000x more potent than standard artemisinin
- *In vivo* efficacy and safety data in malaria and cancer
- Malaria-infected mice cured with single low dose (po and ip); Monotherapy and ACT
- Global exclusive license from Johns Hopkins

Artemisia BioMedical

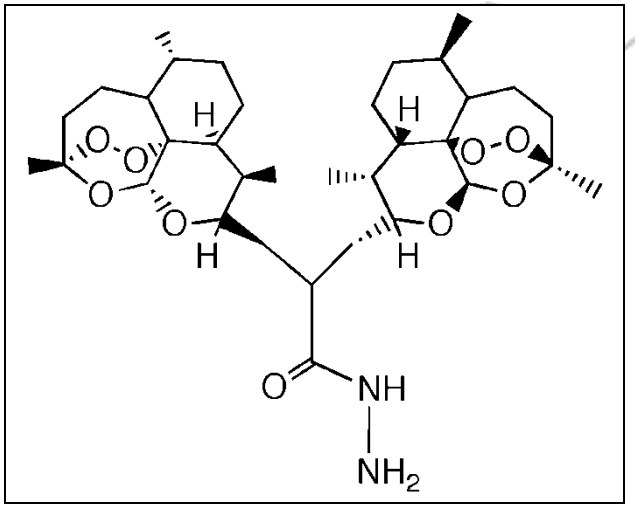
Representative Dimers



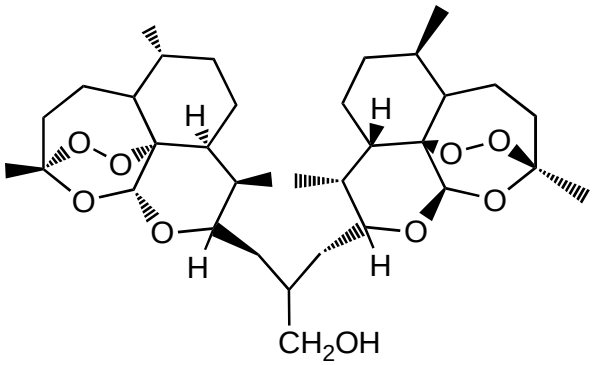
Dimer-sulfone



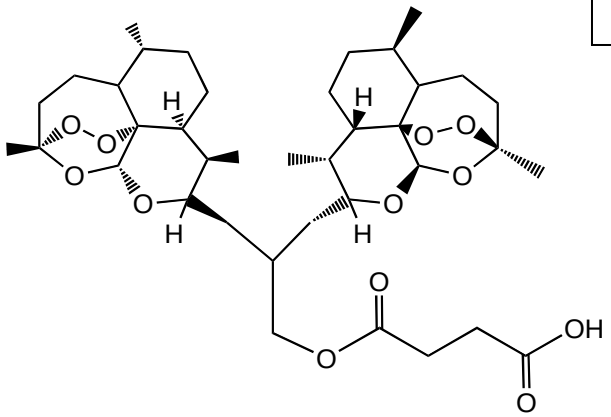
Dimer-acid



Dimer-hydrazine



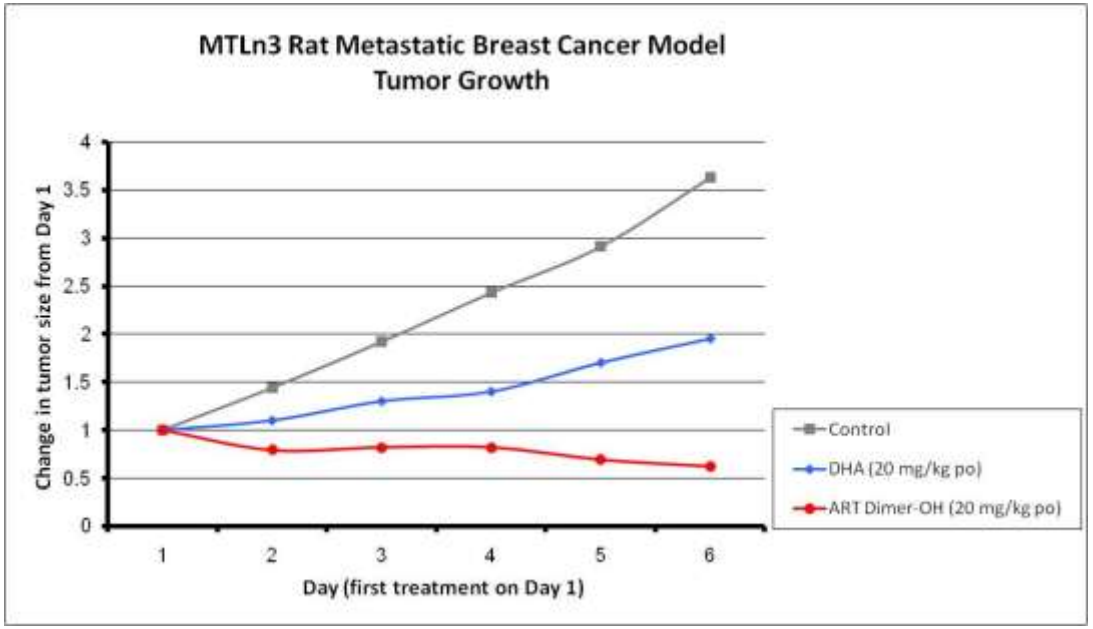
Dimer-alcohol →



Dimer-Alcohol Hemisuccinate Ester

Artemisia BioMedical

Dimer *In Vivo* Breast Cancer Study

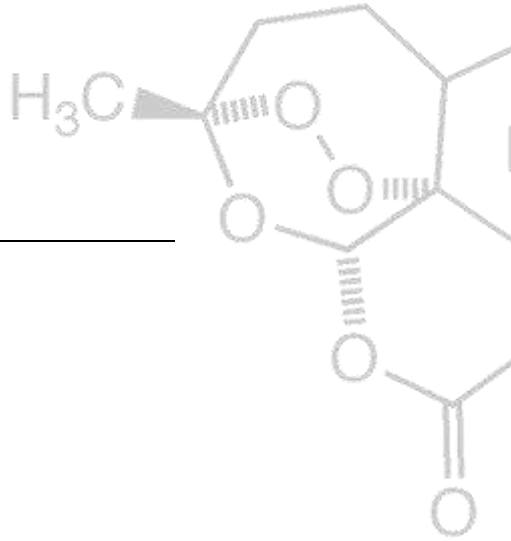


- Tumors induced by injecting 1 million rat MTLn3 breast cancer cells
- Tumors reach size of 5 mm to 10 mm in diameter
- Dimer-alcohol 20 mg/kg orally daily for 5 days
- Tumors did not grow in Dimer-alcohol treated rats

Effect of ART dimer-alcohol and dihydroartemisinin (DHA) on tumor growth of MTLn3 breast cancer in rats (Unpublished)

Artemisia BioMedical

Dimer-Succinate Study -1-



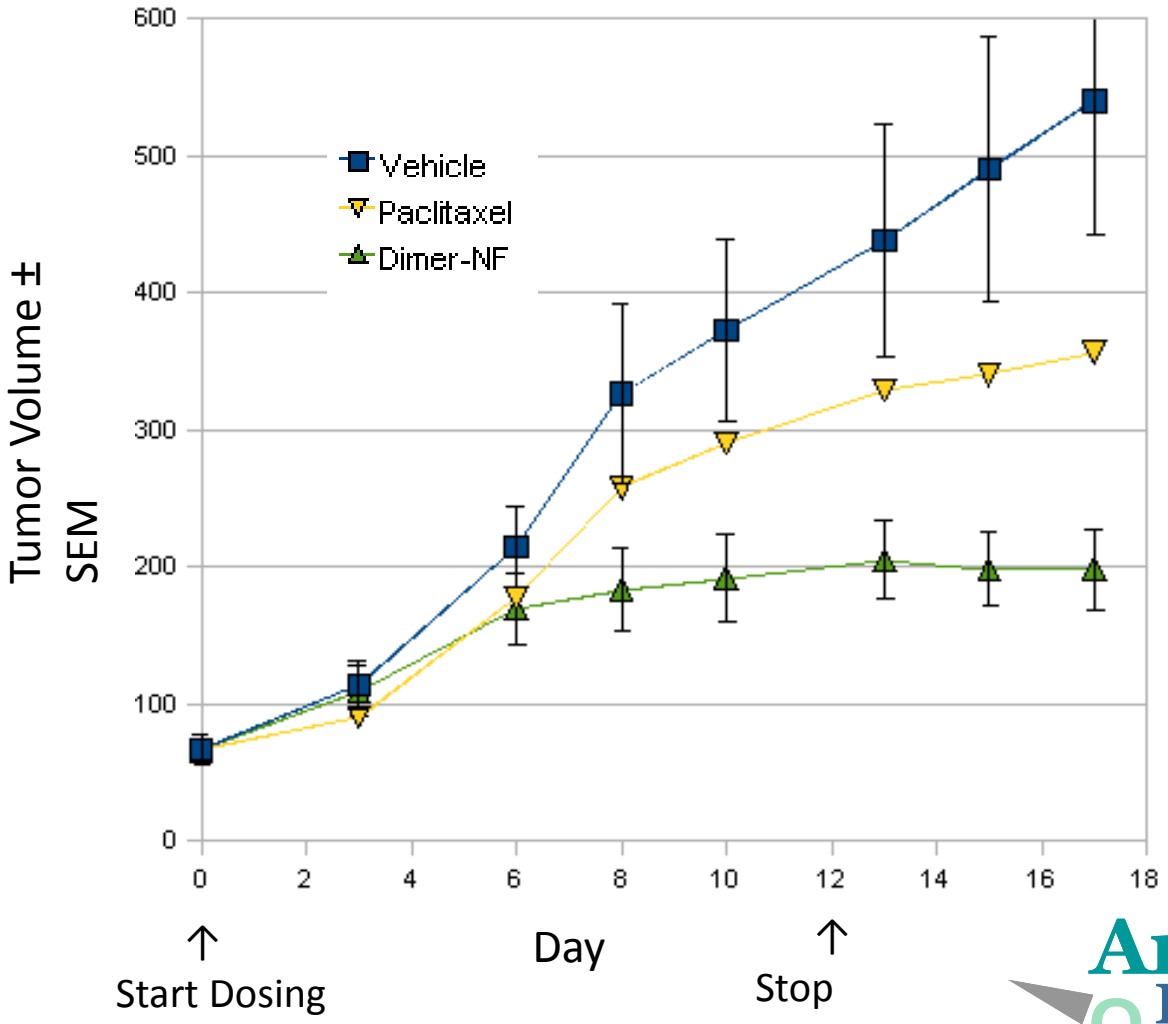
MDA-MB-231 (human breast cancer)
Xenograft Model

Group No.	No. Mice	Test Material	Dose (mg/kg)	ROA	Regimen
1	10	Vehicle	N/A	SC	BID
2	10	Paclitaxel	15	IV	q4x4
3	10	test compound	13	SC	BID
4	10	test compound	13	SC	BID
		Paclitaxel	15	IV	q4x4

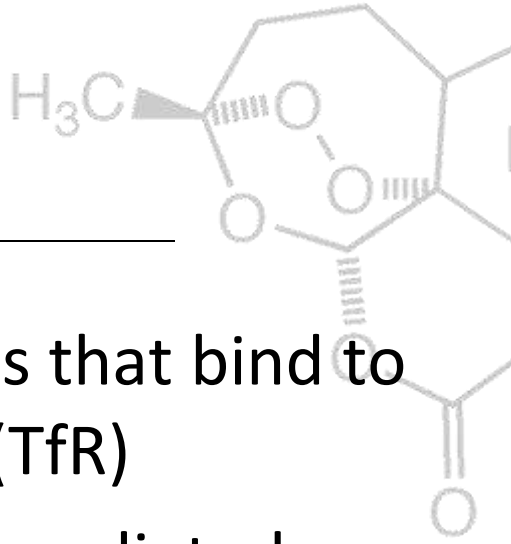
(Unpublished)

Artemisia BioMedical

Dimer-Succinate Study -2-



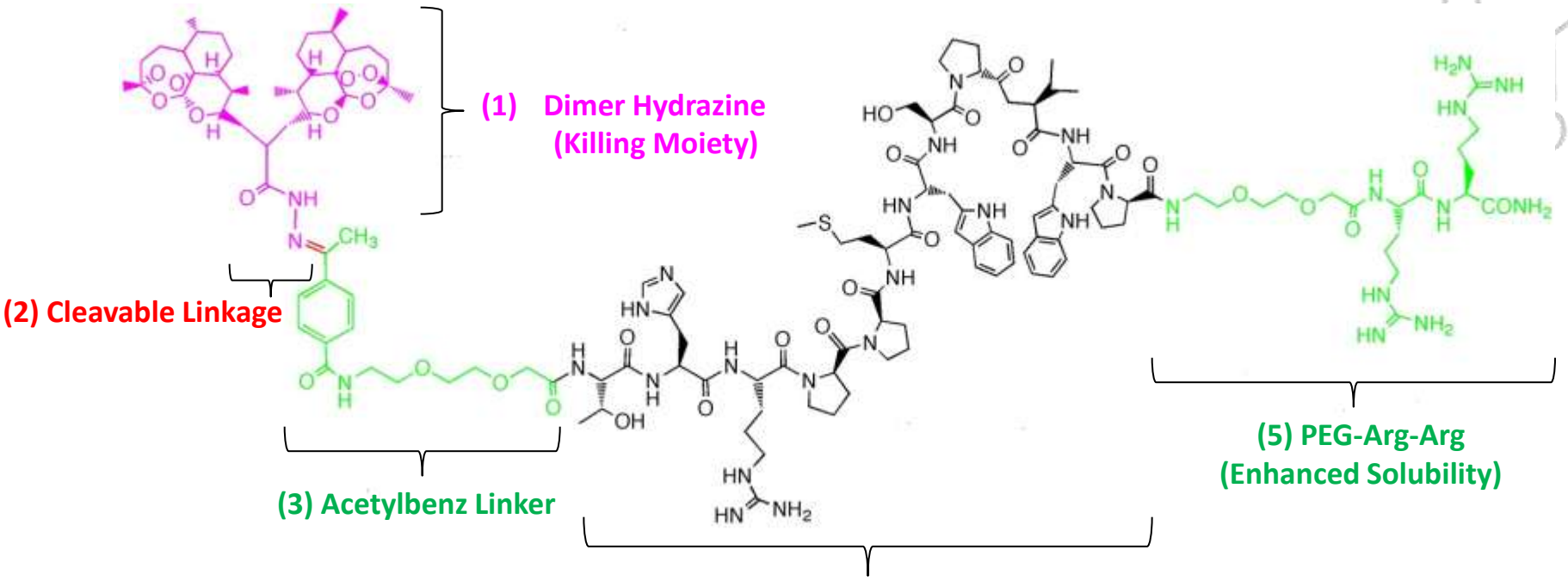
Dimer-Peptides



- Endoperoxide dimers linked to molecules that bind to the cell membrane transferrin receptor (TfR)
- Selective delivery into cells via receptor-mediated endocytosis – tens of thousands times more selective
- *In vivo* efficacy in breast cancer models
- Global exclusive option license to patented peptides from University of Alabama – Birmingham

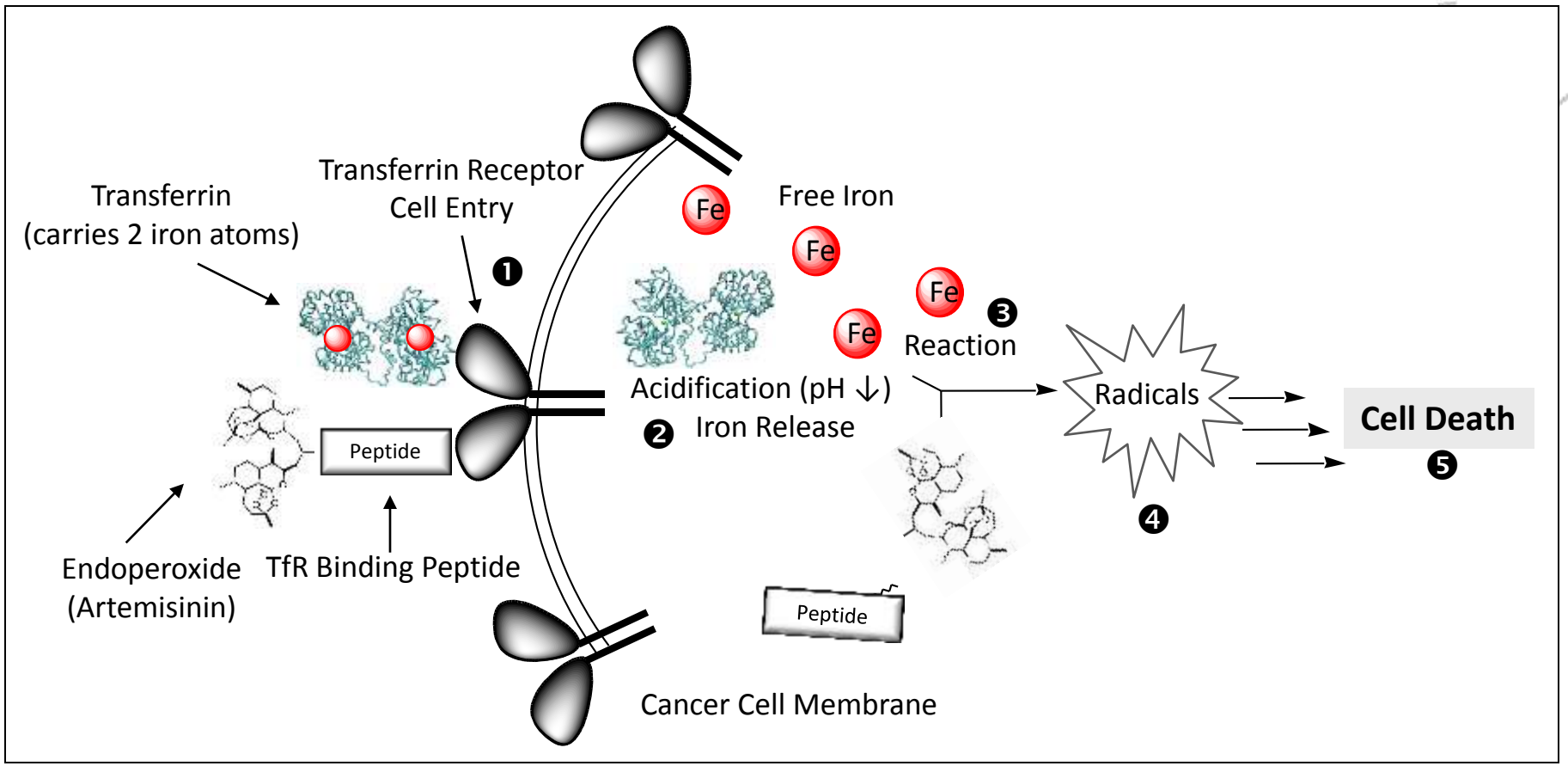
Artemisia BioMedical

Dimer-Acetylbenz-TR14 Conjugate Concept



Artemisia BioMedical

Dimer-Peptide Mechanistic Scheme



"Trojan Horse" Compound

Artemisia BioMedical

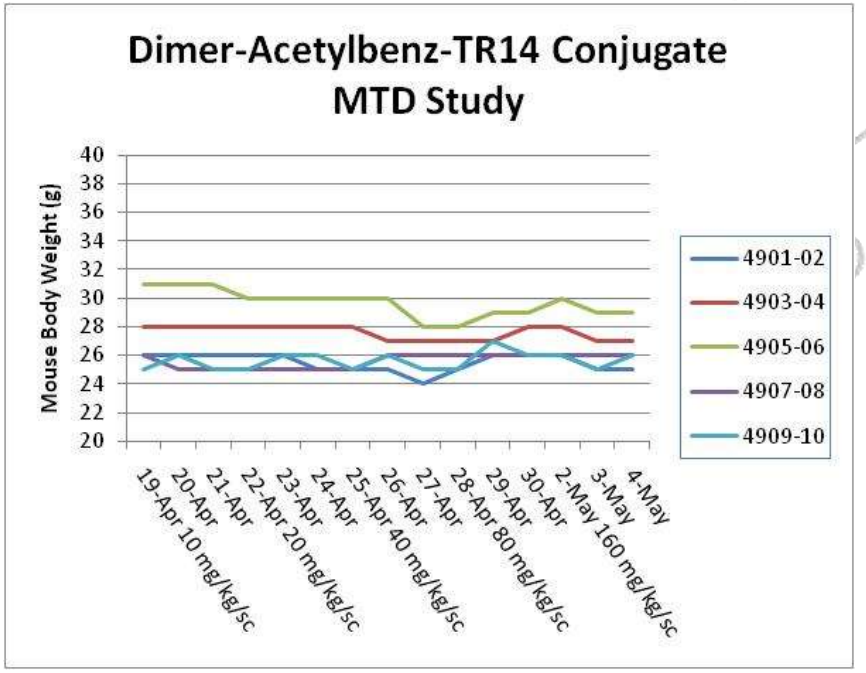
Dimer-Peptide MTD Study

TABLE 1: DOSE ESCALATION

Group	No. Mice	Test Material	ROA	Dose (mg/kg
1	5	dimer peptide	SC*	10 (1X)
3 days following the initial dose the same mice are administered again at 2x initial dose.				
1	5		SC	20 (2X)
1	5		SC	40 (4X)
1	5		SC	80 (8X)

*SC = subcutaneous injection (SOP 1610).

Dose escalation is continued every 3 days until clear evidence of toxicity is observed following administration of a lower dose.



SC mg/kg	10			20			40			80			160		
	19-Apr 10 mg/kg/sc	20-Apr	21-Apr	22-Apr 20 mg/kg/sc	23-Apr	24-Apr	25-Apr 40 mg/kg/sc	26-Apr	27-Apr	28-Apr 80 mg/kg/sc	29-Apr	30-Apr	2-May 160 mg/kg/sc	3-May	4-May
4901-02	26	26	26	26	26	25	25	25	24	25	26	26	26	25	25
4903-04	28	28	28	28	28	28	28	27	27	27	27	28	28	27	27
4905-06	31	31	31	30	30	30	30	30	28	28	29	29	30	29	29
4907-08	26	25	25	25	25	25	25	26	26	26	26	26	26	26	26
4909-10	25	26	25	25	26	26	25	26	25	25	27	26	26	25	26

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New Dimer-Peptide Xenograft Study

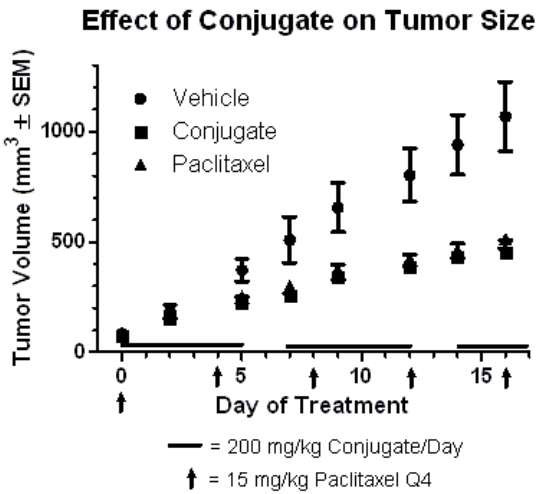
Evaluation of Dimer-Acetylbenz-TR14 Conjugate activity in an MDA-MB-231 (human breast cancer) Xenograft Model

Treatment Regimen.

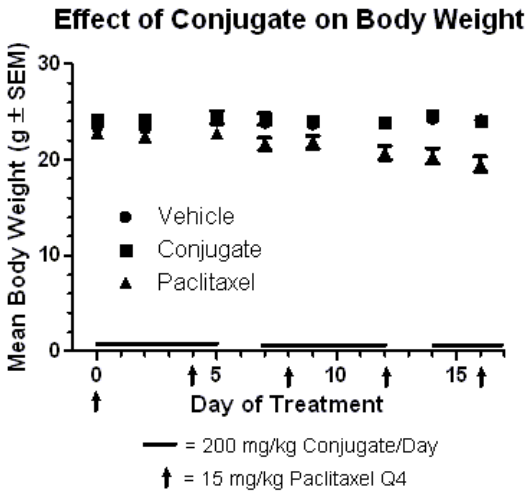
Group No.	No. Mice	Test Material	Dose (mg/kg)	ROA	Regimen
1	8	Vehicle	N/A	SC*	QD**
2	8	Paclitaxel	15	IV	q4x5
3	8	test compound	200	SC	QD**

*SC = subcutaneous injection (SOP 1610)

**QD = once daily for 5 days each week for total 3 weeks (dosing once daily Monday – Friday of each week).



MDA-MB-231 Cells:
Triple-negative breast cancer. Lacks expression of hormone receptors (Estrogen, Progesterone) and HER-2 but does express EGFR.
Associated with early relapse and poor survival.
There is no targeted therapy for triple-negative breast cancer



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R&D Pipeline

Product	Preclinical					IND	Phase I
	Lead Validation		Lead Optimization & Formulation	Efficacy & Safety			
	In Vitro	In Vivo		In Vitro	In Vivo		
Cancer	**2010**		**2011**			**2012**	
ART Dimer-Peptide							
ART Dimer							
ART Dimer-Iron Chelator							
Proliferative & Inflammatory Disorders (BPH, RA, Lupus, AMD, etc)							
ART Dimer							
ART Dimer-Peptide							
ART Dimer-Iron Chelator							
Infectious & Parasitic Diseases (Malaria, TB, HIV, Leishmaniasis, Trypanosomiasis, etc)							
ART Dimer, Monomer							
ART Dimer-Peptide							
ART Dimer-Iron Chelator							

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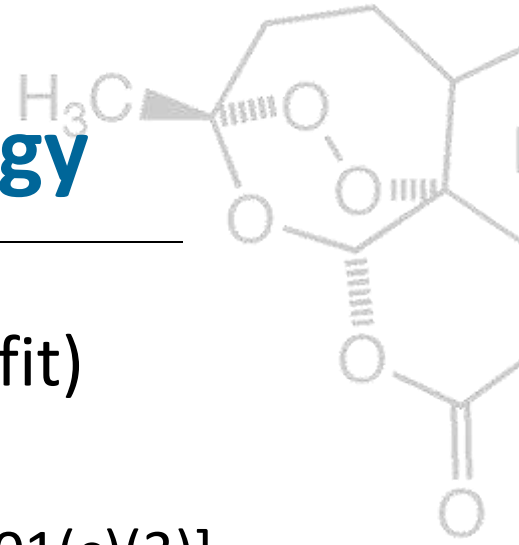
Technology Development Strategy



- Dual development track (profit/non-profit)
  - Cancer/Inflammation
  - Malaria and neglected diseases [separate 501(c)(3)]
- Cancer and Malaria first, then other diseases based on screening results and partnerships
- Co-develop compounds to PII proof of concept
- Collaborate with major partner/foundation

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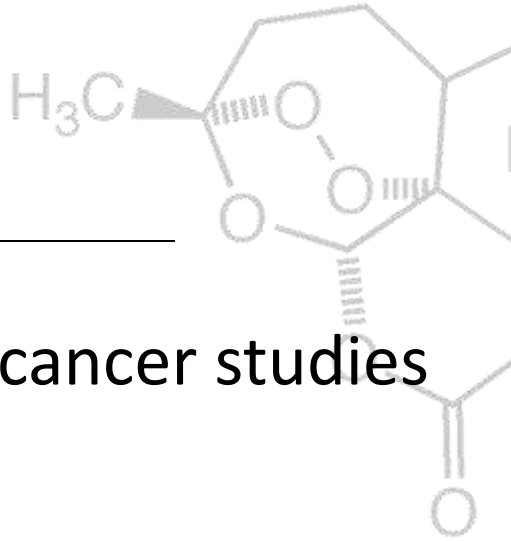
R&D Collaborations



- University of Washington/FHCRC *in vivo* cancer studies
- Johns Hopkins novel dimer synthesis
- Duke Cancer Center CNS tumor xenograft studies
- Brown University gynecologic tumor xenograft studies
- University of Vermont CNS tumor xenograft studies
- Ohio State University canine cancer studies
- Washington State University canine cancer studies
- NCI Developmental Therapeutics Program

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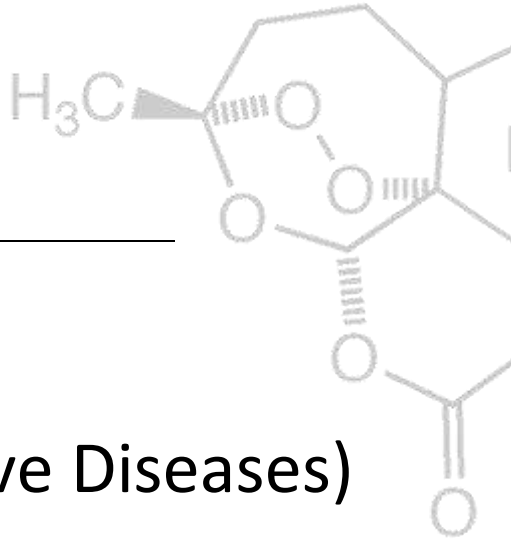
Business Development Strategy



- Specialty pharmaceutical company
- For-Profit Business (Cancer & Proliferative Diseases)
  - R&D partnership with major companies to co-develop with co-promotion option in North America
  - Out-license in RoW
- Non-Profit Business (Malaria & Neglected Diseases)
  - 501(c)(3)
  - Co-develop compounds with partners through PII PoC
  - Out-license to distributors for global health

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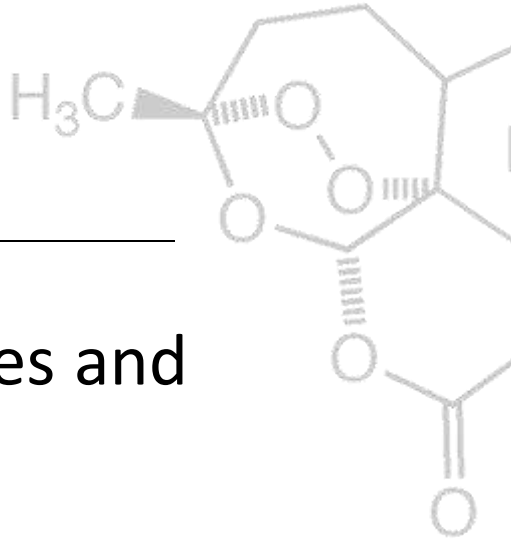
Licenses and IP



- University of Washington (Dimer-Peptides and Dimer-Chelators)
  - 1 issued, 4 pending US/foreign patents
- Johns Hopkins University (ART Trioxane Dimers and Monomers)
  - 11 issued, 5 pending US/foreign patents
- University of Alabama – Birmingham (TfR Peptides)
  - 1 issued, 1 pending US/foreign patents

Artemisia BioMedical

Leadership

Michael Kuran, Founder & CEO

Mr Kuran founded Artemisia BioMedical, Inc in 2006, and has over 20 years of years of senior management experience in the biopharma industry. He is concurrently CEO of ACLIRES International Ltd, a global boutique CRO service provider with GCP-certified clinical units in Latin America and Southeast Asia. Prior to establishing Artemisia BioMedical, he held senior management positions with C3, Inc (Los Angeles, CA), Fulcrum Ventures (Bellevue, WA), ZymoGenetics, Inc (Seattle, WA) and Novo Nordisk and IMS Health in Tokyo, Japan. Mr Kuran speaks Japanese and holds a BA degree from the University of Michigan, Ann Arbor. He has participated in the Biotechnology Project Management Certificate Program managed jointly by the University of Washington, Seattle and University of California at San Diego, and he attended the Executive MBA program at Temple University, Tokyo campus.

Woerner P. Meehan, PhD, President

Dr Meehan is a physiologist with over 20 years of experience in managing studies of animal models of disease for drug development. He previously worked at ZymoGenetics, Inc to develop models of vascular occlusion and evaluated the efficacy of drugs in maintaining blood flow through blood vessels. He has analyzed preclinical models required for FDA approval and formulated potential clinical pathways for drug development. At the University of Southern California and University of California, Los Angeles, Dr Meehan investigated drugs designed to inhibit the proliferative stages of atherosclerosis. He devised murine models of accelerated atherosclerosis and investigated the effect on the whole animal of preventing the formation of fatty plaques. Dr Meehan received a PhD in Physiology and Biophysics from the University of Southern California.

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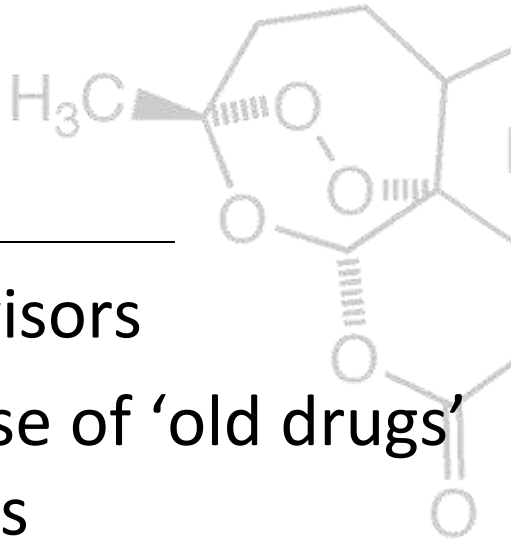
Company Highlights



- Experienced management team and advisors
- Lower risk model – re-design and new use of 'old drugs' with excellent therapeutic/safety profiles
- Significant Profit and Non-Profit business opportunities
- Low cost, effective and safe breakthrough therapeutics
- Favorable responses from oncologists/researchers at leading US and EU cancer/global health centers
- Solid IP position
- Multiple product opportunities in cancer and other proliferative/inflammatory diseases

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