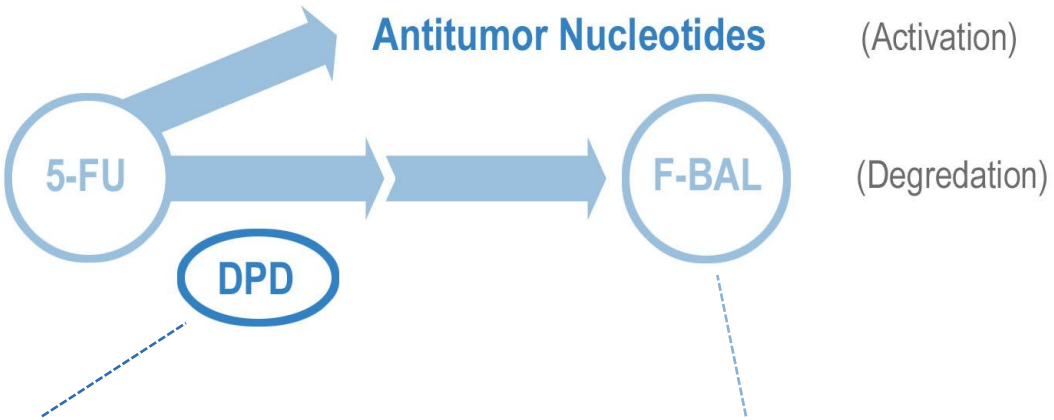
The Eniluracil Story

Eniluracil

Presentation by:
Rosty Raykov, CEO

5-FU Metabolic Pathways

- 5-FU must be activated to kill cancer cells
- The enzyme, DPD, prevents activation and degrades 5-FU to F-BAL



DPD problems:

- Highly Variable levels
- Unpredictable 5-FU PK
- 5-FU $t_{1/2}$ = 10-20 min
- 5-FU MTD correlates with DPD

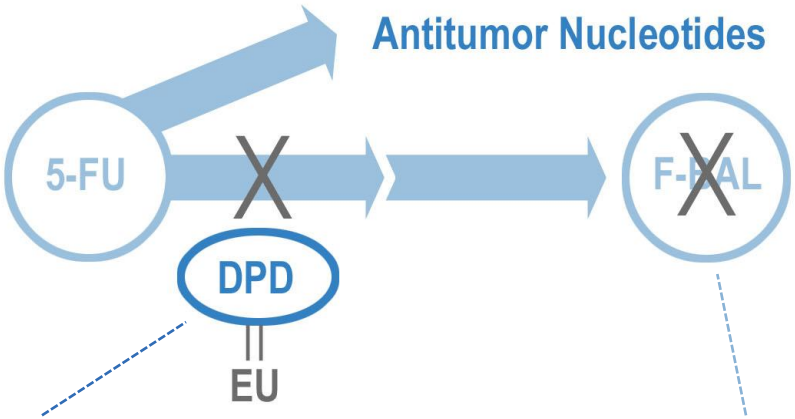
F-BAL problems:

- >80% of dose = F-BAL
- Decreases 5-FU Efficacy
- Neurotoxic
- Hand-foot syndrome (HFS) agent

(PK = pharmacokinetics; measurements of 5-FU in patient's blood. MTD = Maximum Tolerated Dose)

EU Inactivates DPD

EU Eliminates **DPD** & **F-BAL** Problems



5-FU is not destroyed:

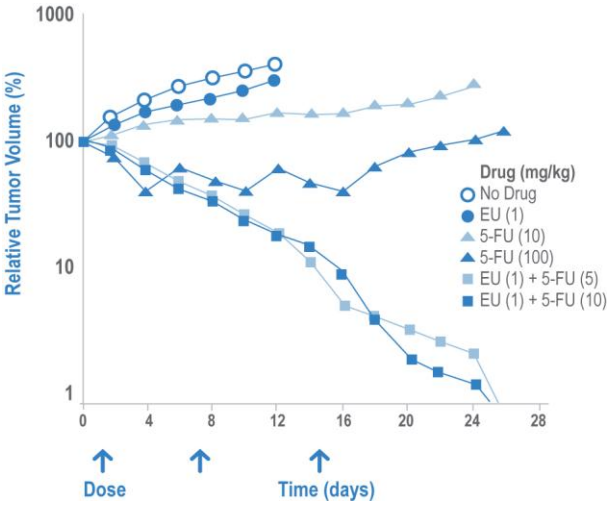
- Half-life = 5 hr.
- Highly predictable linear PK
- Oral dosing

F-BAL formation is minimal:

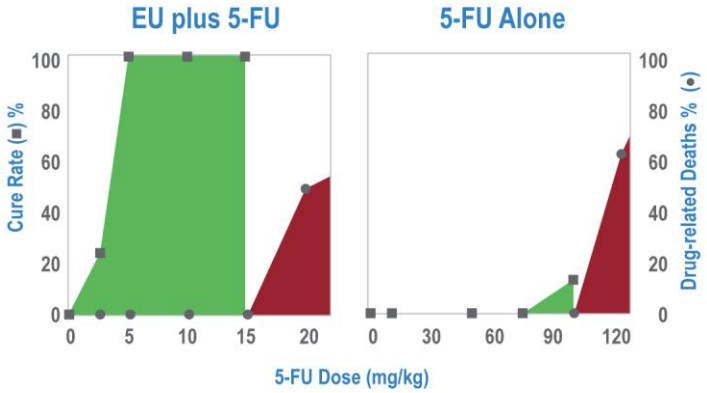
- No interference with efficacy
- Minimize neurotoxicity
- HFS is negligible

Preclinical Studies

Rats Bearing Advanced Colon Carcinoma



EU:5-FU ratio < 1:5



Cure Rate

EU/5-FU = **100**% 5-FU = **13%**

Therapeutic Index

EU/5-FU = **6** 5-FU = **1**

EU improves 5-FU antitumor activity and therapeutic index

Phase III Results

Results of the North American Phase III Trial Colorectal Cancer

EU (10 mg/m^2) + 5-FU (1 mg/m^2) dosed together

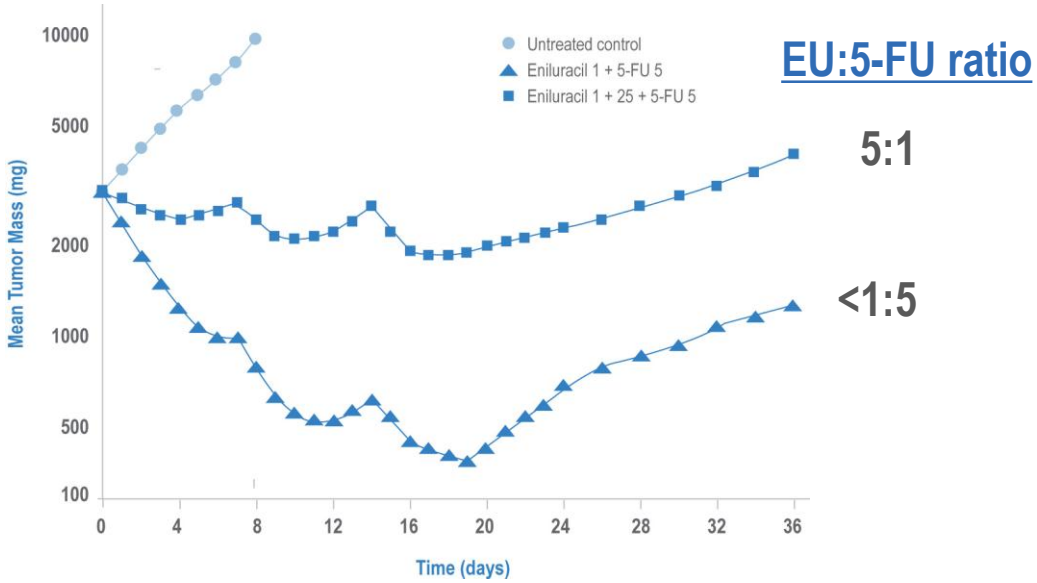
Treatment	Progression-Free Survival	Survival
	(weeks)	(months)
EU:5-FU (10:1) oral: every 12 hr for 28 days	20.0	13.3
5-FU + Leucovorin iv: daily for 5 days	22.7	14.5

(In similar trials, Xeloda® had 18.9 weeks Progression-Free Survival & 13.1 months Survival and the 5-FU/Lv Arm had 18.7 weeks Progression-Free Survival and 12.9 months Survival)

- Although considerably less toxic, oral **EU/5-FU** produced less antitumor activity than iv **5-FU/leucovorin**

Could the 10:1 EU:5-FU ratio have caused the problem?

High EU:5-FU Ratio Decreases Efficacy



In rats with large tumors:

A high ratio of EU to 5-FU was less effective than a low ratio.

Data: Spector T, Cao, S. A Possible Cause and Remedy for the Clinical Failure of 5-Fluorouracil plus Eniluracil. Clinical Colorectal Cancer. 2010;9(1):52-4.

Dr. Grem's Weekly Schedule *with* Adherex's Modifications

Aspect	Protocol	
	Dr. Grem's Phase I Study	AHX-03-202 Phase II study
Pretreat with EU	1 hr	11-16 hr
EU Dose	20 mg	40 mg
5-FU Dose	30 mg/m^2	30 mg/m^2
Leucovorin	30 mg (Day 1 & 2)	30 mg (Day 1 & 2)
EU:5-FU Ratio	approx. 1:2-3	<1:10

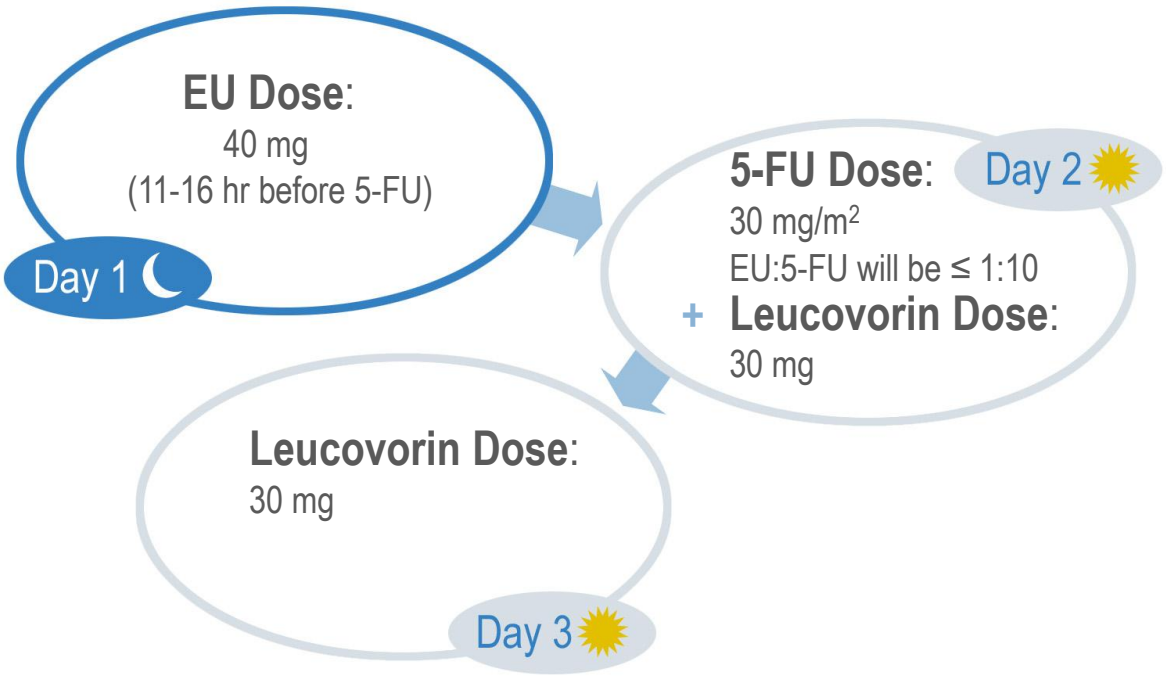
Dr. Grem's Phase I Study: Oral eniluracil/5-FU/leucovorin dosed once per week produced 2 durable responses in 17 advanced colorectal cancer patients who were refractory to iv 5-FU/leucovorin!

Guo XD, Harold N, Saif MW, Schuler B, Szabo E, Hamilton JM, Monahan BP, Quinn MG, Cliatt J, Nguyen D, Grollman F, Thomas RR, McQuigan EA, Wilson R, Takimoto CH, Grem JL**. Pharmacokinetic and pharmacodynamic effects of oral eniluracil, fluorouracil and leucovorin given on a weekly schedule. Cancer Chemother Pharmacol 2003;52:79-85.

New Protocol: Phase II Trial
(Metastatic Breast Cancer)

Adherex

Weekly Schedule*



*Based on Dr. Grem's encouraging regimen with these modifications:

- EU dosed the night before 5-FU to aid efficacy
- EU dose is increased to minimize neurotoxicity

DPD Inactivation

Adequate DPD Inactivation Ensures EU's Advantages

Higher EU doses will:

1. Consistently preserve 5-FU; half-life = 5 hr
2. Ensure consistent 5-FU PK, MTD, & Safety
3. Enable leucovorin's* safe use
4. Minimize F-BAL formation
5. Minimize hand-foot syndrome
6. Minimize neurotoxicity (Adherex **Patent** Filed 9/09)

40 mg EU should adequately inactivate DPD in nervous and non-nervous tissues

* Leucovorin (LV) improves 5-FU antitumor activity, but adds risk if blood levels of 5-FU are variable. LV cannot be used with Xeloda® (capecitabine).

Clinical Plan

Disease Target: Metastatic Breast Cancer

- The daily schedule with 10:1 EU:5-FU was active and well tolerated in five previous Metastatic Breast Cancer Studies
- Our revised weekly protocol avoids high EU:5-FU ratios and includes leucovorin

Study Design: Eniluracil/5-FU/leucovorin vs. Xeloda®

- Eniluracil/5-FU/leucovorin has promise of improved efficacy:
  - It is efficacious in 5-FU/Leucovorin-refractory patients
- Eniluracil/5-FU/leucovorin is less toxic:
  - The occurrence of hand-foot syndrome is 0-6% vs. about 60% (HFS may be painful, debilitating, & dose-limiting)
  - The occurrence of neurotoxicity is minimized

Encouraging Comparison

Dr. Grem's Phase I vs. Xeloda®'s Phase II Results in Advanced Colorectal* Cancer Refractory to iv 5-FU/LV

Outcome	EU/5-FU/LV	Xeloda®
Treatment	20mg/29mg/m^2/30mg **weekly** for 3 weeks	1,250mg/m^2 **every 12 hr** for 14 days
Tumor Responses	**2/17**	**0/22**
Diarrhea total (*severe*)	**65** (*17*) **%**	**74** (*26*) **%**
Hand-Foot-Syndrome total (*severe*)	**0** (*0*) **%**	**87** (*13*) **%**

*These studies in 5-FU-refractory colorectal cancer provide encouragement for improved efficacy vs. Xeloda® in metastatic breast cancer. The tolerability advantage is evident.

New Management and Consulting Team

Robert Butts – Chairman
- Former principal of Southpoint Capital, LP the Company's largest shareholder

Rostislav Raykov – CEO
- Existing shareholder with over 13 years corporate finance, investment and management experience including Bear Stearns, Tiedemann Group, John Levin & Co., Alchem and DCML Co.

Robert Andrade – CFO
- Existing shareholder with over 13 years corporate finance, investment and management experience including Bear Stearns, JP Morgan, CIBC, Caxton Associates, Millenium Partners and DCML Co.

Tom Spector, PhD – Chief Scientific Officer
- Principal inventor on original and recent eniluracil/5-fluoruracil patents with over 35 years drug research experience, including International VP of Cancer Research at GlaxoWellcome (now GSK)

Anne McKay– Regulatory and Project Management Consultant
- Over 30 years of regulatory and quality assurance experience primarily with Triangle Pharmaceuticals and Burroughs Wellcome Co. leading all regulatory programs for over 100 NDAs and INDs

Millie Van Ness– Clinical Operations Consultant
- Over 15 years of managing global clinical trials predominantly in oncology at Biocryst Pharmaceuticals, Invaresk, Celgene Corp. and Imclone Systems

Lex Smith– CMC Consultant
- Over 25 years in technical product development, API, and drug product sourcing. Managed the chemistry manufacturing and controls activities of over 10 NDAs and 100 INDs for Burroughs Wellcome, Triangle Pharmaceuticals, Fulcrum Pharma, and Serenex, Inc.

Jack Spira, MD, PhD – Medical Consultant
- Over 25 years of clinical drug development experience for Kabi-Pharmacia, Pharmacia & Upjohn, Serono Nordic, Tripep and Oncopeptides (currently serves as Chief Executive)

Lei Fang – Statistics Consultant
- Senior statistician with over 15 years of clinical trial design/implementation/programming support and analysis at Pharstat Inc., Trimeris, Triangle Pharmaceuticals, and Quintiles

Steven Littlefield – Data Management Consultant
- Senior data.manager with expertise in data capture, analysis, mining, viewing, and regulatory submissions serving numerous pharma companies with own business and self-developed EDC system.

Dedication

George Hitchings
and Trudy Elion