

# Ganetespib Clinical Summary

## March 2011

# Content

- Ganetespib Clinical Development Program
- Summary Clinical Safety and Activity
- Preliminary data from the NSCLC study
- Clinical cases

# Ganetespiib Clinical Development Overview

|  | LEAD OP | PRECLIN | PHASE 1 | PHASE 2 | PHASE 3 |
|--|---------|---------|---------|---------|---------|
| <b>Ganetespiib (Hsp90i)</b>  |         |         |         |         |         |
| <i>Ph 2b/3 NSCLC</i>   |         |         | Q2 2011 |         |         |
| <i>NSCLC</i>   |         |         |         |         |         |
| <i>Colorectal</i>  |         |         |         |         |         |
| <i>Breast</i>  |         |         |         |         |         |
| <i>Prostate</i>  |         |         |         |         |         |
| <i>Others (SCLC, gastric, GIST, heme, HCC, pancreatic, melanoma)</i> |         |         |         |         |         |
| <i>Docetaxel combination</i>   |         |         |         |         |         |
| <i>Solid/heme (3 trials)</i>   |         |         |         |         |         |

# Ganetespib Clinical Development Strategy

|           | Objective  |
|-----------|--|
| 2008-2009 | Determine dose, schedule<br>Characterize safety profile in solid and hematologic malignancies  |
| 2010      | Initiate robust activity signal detection program  |
| 2011 -    | Initiate registration-enabling study for lead indication<br>Identify additional activity signals<br>Optimize single agent path forward |

# Clinical Safety Profile Highlights

- Well tolerated in >350 patients treated so far
  - Tolerability better than chemotherapy and many targeted drugs
- Absence of dose-limiting liver toxicity
- Absence of ocular toxicity
- Diarrhea
  - Easily manageable with supportive care

# Summary Phase 1 Clinical Safety

## Treatment-related AEs in >10% of subjects

|                    | All Grades<br>N=198 | Grade ≥3<br>N=198 |
|--------------------|---------------------|-------------------|
| Diarrhea           | 137 (70%)           | 16 (8%)           |
| Fatigue            | 65 (33%)            | 11 (6%)           |
| Nausea             | 62 (31%)            | -                 |
| Vomiting           | 30 (15%)            | -                 |
| Abdominal pain     | 22 (11%)            | -                 |
| Decreased appetite | 19 (10%)            | -                 |
| Anemia             | 15 (8%)             | 2 (1%)            |

# Summary of Clinical Activity

- First positive activity signal in NSCLC
  - Correlation with specific genetic profiles underway
- Additional signs of ganetespib single agent activity in
  - GIST
  - Gastric cancer
  - Breast cancer
- Hsp90 inhibitors activity associated with specific genetic profiles
  - ALK-EML4 translocation
  - HER2-neu overexpression
  - PDGFRA- $\alpha$  mutations (ganetespib)
  - BRAF mutations (ganetespib)
  - Certain other mutations under investigation

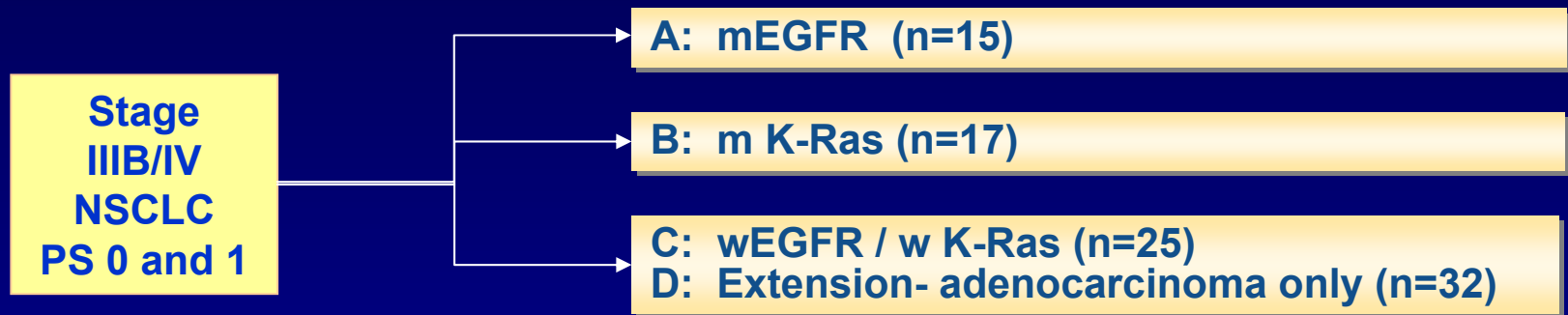
***Phase 2 Study of Ganetespib (STA-9090)  
in Subjects with Stage IIIB or IV Non-Small  
Cell Lung Cancer – A Preliminary Report***

*Jonathan Goldman, MD*

**11th Annual Targeted Therapies of the  
Treatment of Lung Cancer Meeting  
Feb 26, 2011, Santa Monica, CA**

# Study Design

Ganetespib 200 mg/m<sup>2</sup> qw 3 weeks on, 1 week off

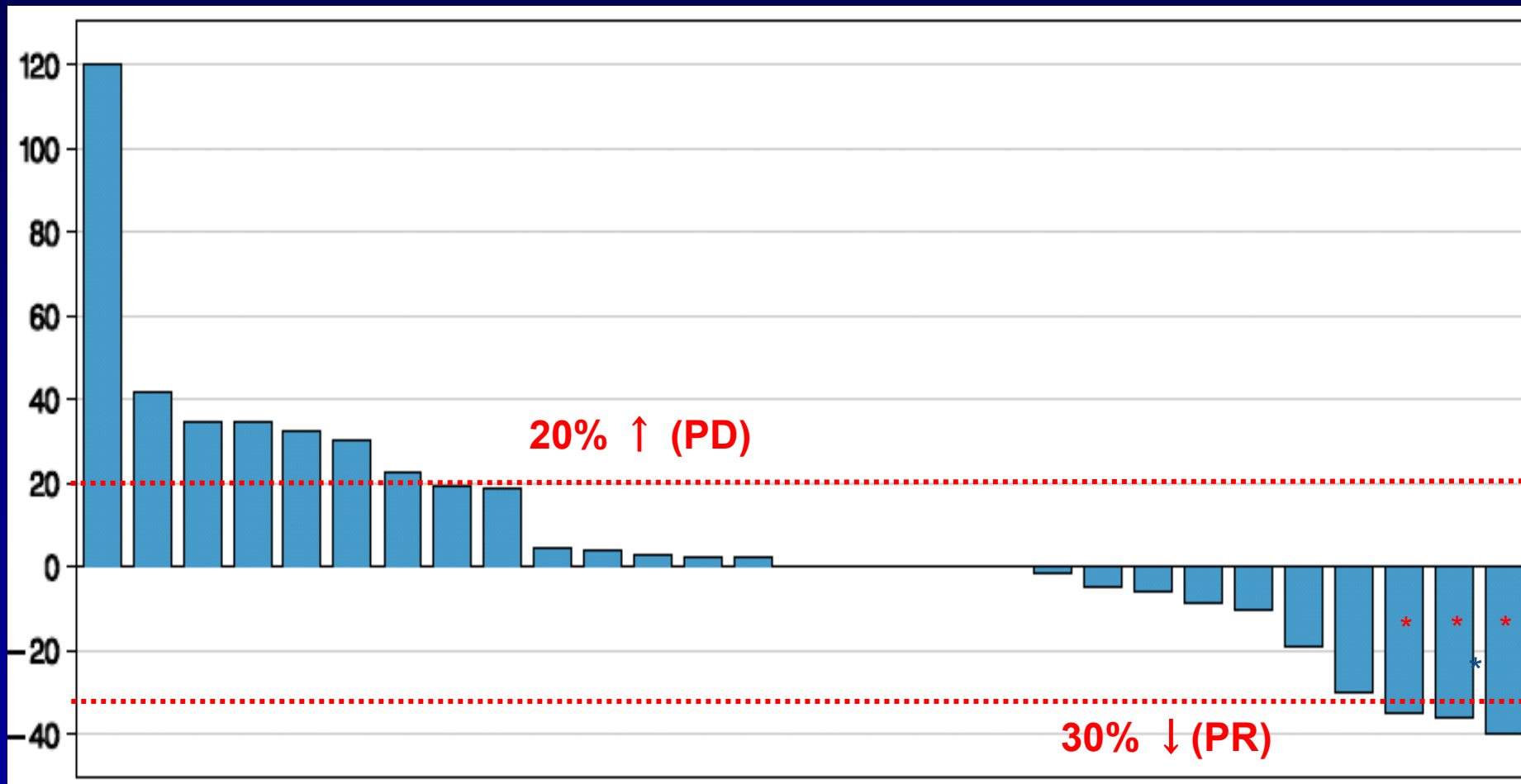


- Genotyping required for all patients
- Primary endpoint : PFS at 16 wks
- Patients who progressed on single agent but had some clinical benefit were allowed to roll over to Cohort E: weekly ganetespib + docetaxel (n=5)

# Treatment-related AEs occurring in $\geq 10\%$ of patients

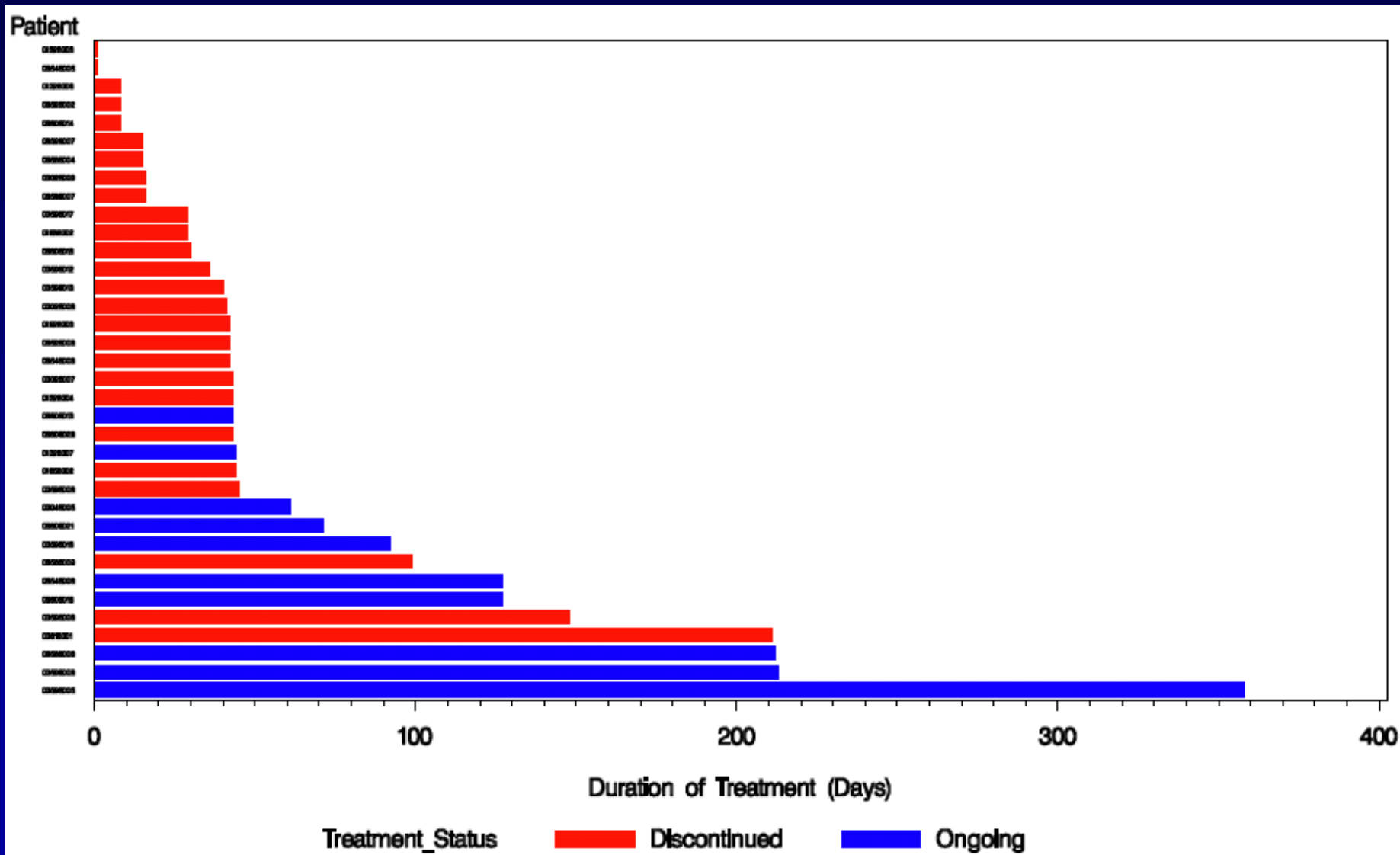
|                           | <b>AEs<br/>N (%)<br/>N=36</b> | <b><math>\geq</math> Grade 3 AEs<br/>N (%)<br/>N=36</b> |
|---------------------------|-------------------------------|---|
| <b>Diarrhea</b>           | <b>29 (81)</b>                | <b>2 (6)</b>  |
| <b>Fatigue</b>            | <b>11 (31)</b>                | <b>3 (8)</b>  |
| <b>Nausea</b>             | <b>11 (31)</b>                | <b>0</b>  |
| <b>Insomnia</b>           | <b>6 (17)</b>                 | <b>2 (6)</b>  |
| <b>Increased Alk Phos</b> | <b>5 (14)</b>                 | <b>0</b>  |
| <b>Decreased appetite</b> | <b>5 (14)</b>                 | <b>0</b>  |

# Waterfall plot of best change in sum of longest diameter



•\*3 confirmed PRs: 1 ongoing at 14 months, 2 ongoing at 6 months

# Duration of Treatment



# Clinical Cases

## 79 y, adenocarcinoma NSCLC

- Progressed on 4 prior regimens including Carboplatin/Paclitaxel/Bevacizumab, Bevacizumab, Erlotinib, Carboplatin/Pemetrexed
- Enrolled Jan 2010 – single-agent ganetespib
- Achieved PR (RECIST, 36%)
- On study for 14 cycles (13 months)
- PD in Feb 2011; continues on ganetespib single agent agent
- Significant symptom improvement

## 53 y, Gastric cancer

- Diagnosed in Feb 2008 with metastatic gastroesophageal junction carcinoma; KRAS mutation positive
- Progressed on cisplatin/docetaxel/irinotecan and leucovorin/fluorouracil
- Enrolled Sep 2010 – single-agent ganetespib
- Achieved PR (RECIST, 32% reduction of TL)
- Duration of treatment, 7 cycles, ongoing

## 39 y, triple-negative Breast Cancer

- Diagnosed in March 2007 with Stage III invasive ductal carcinoma, triple negative (ER/PR/HER2 negative)
- Progressed on 6 prior regimens including adriamycin/cytosine, paclitaxel, bevacizumab/capecitabine, cisplatin, capecitabine, cediranib/olaparib
- Enrolled Nov 2010
- Achieved PR (RECIST, 31%)
- Currently undergoing WBRT for treatment of brain metastases, will continue treatment with ganetespib

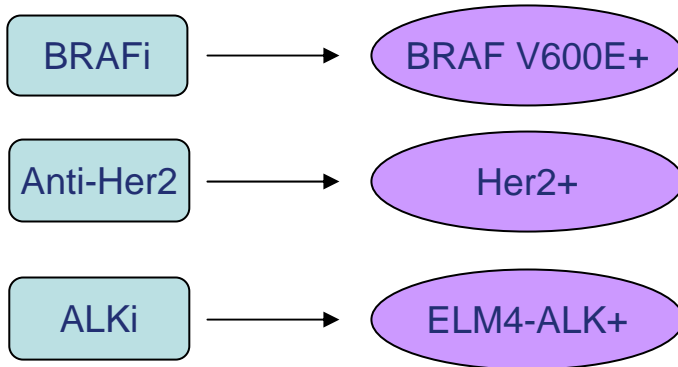
## 49 y, GIST

- Diagnosed with GIST in May 2006; PDGFR A exon 18 D842V mutation
- Progressed on Imatinib (adjuvant), docetaxel + gemcitabine, sunitinib, IPI 504, sunitinib
- Enrolled July 2009
- Best response SD (18%TL shrinkage)
- Duration of treatment 8 cycles (8 months)

# Different paradigm

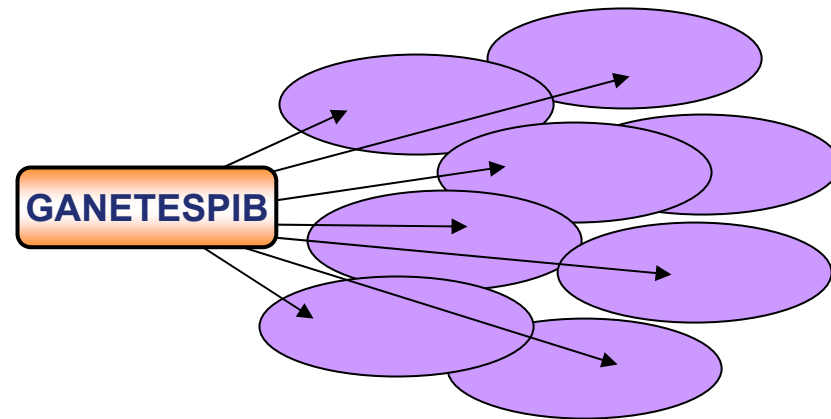
Targeting  
Oncoprotein

Unique high-response  
gene profile



Targeting  
Chaperone

Multiple high-response  
gene profiles



# Summary

- Favorable safety profile
  - Good tolerability key to successful combinations
- Clinical activity in NSCLC
  - Signs of activity in multiple tumor types
- Correlation with specific genetic profiles, single agent administration