# How Can Pharmaceutical Companies Facilitate Global Collaboration in Phase 1 Cancer Drug Development in Asia?

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Oncology Therapeutic Area
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# Disclosures

- Employee and stockholder: Johnson & Johnson
- I will not discuss any off label use of any drug or product
- I will describe a Phase 1/2a clinical trial of an experimental oncology therapeutic
- These are my own personal opinions on drug development and do not represent any official company positions

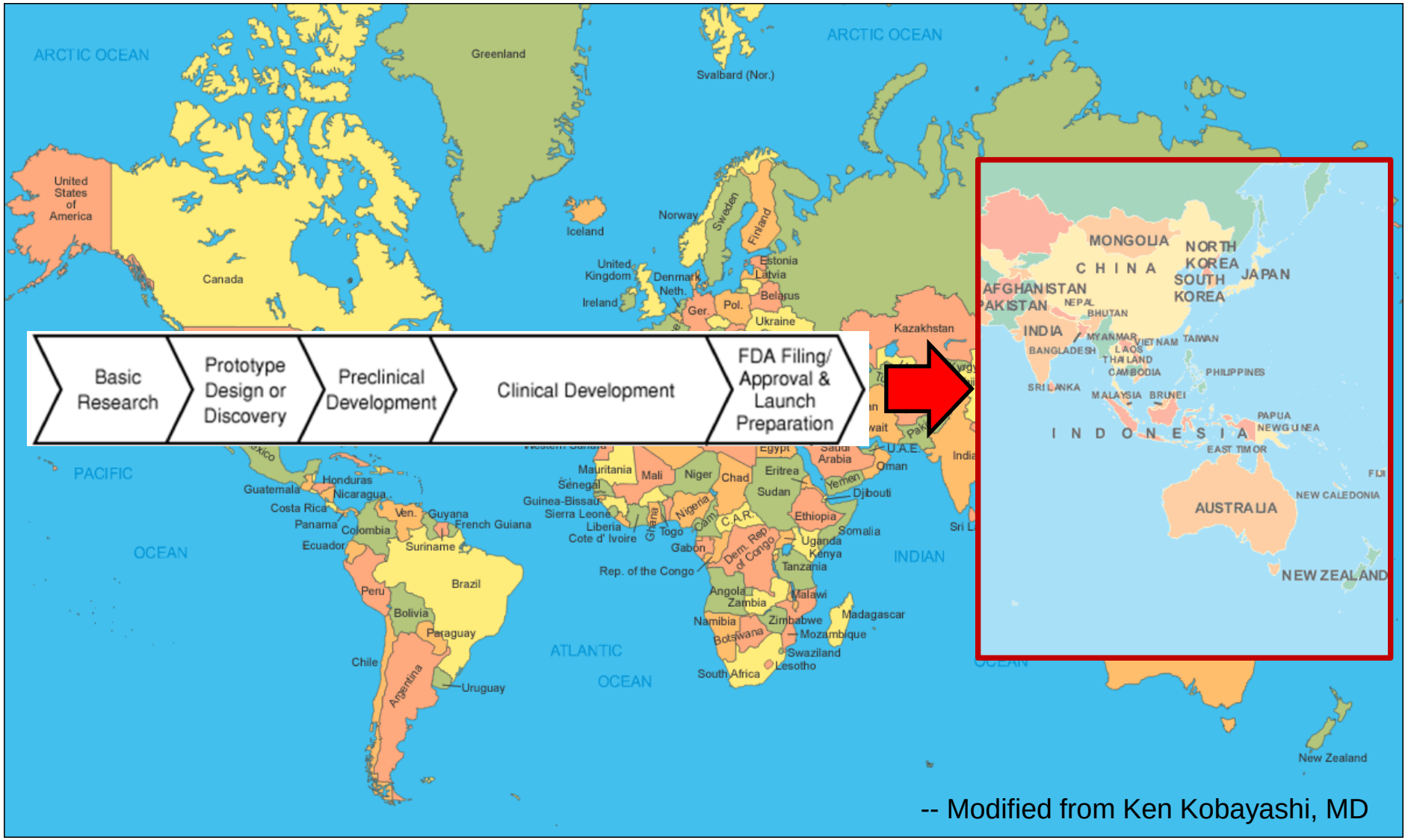
# Warning!! This is an Industry Perspective!

WELCOME TO A VIEW FROM THE "DARK SIDE"!

# Overview

- Historical Approach to ED in Asia: The AP Drug Lag
- Current Vision: Coordinated Global/AP ED strategies
- Why Conduct Early Development Studies in the AP Region?
- Example: FGFRi Phase 1/2a Trial
- AP Early Development Pharma Industry Challenges
- How Can Pharma Facilitate This Effort?

# Historical Approach to AP Drug Development




-- Modified from Ken Kobayashi, MD

# Historical Approach

- The **Drug Lag**: delayed approval of drugs in AP region
  - Median drug lag in Japan is **~3 years** (Ueno, Clin Pharm Ther 2014)
  - Major cause is new drug applications being "**submitted later** than those submitted in other regions" (Honig, Clin Pharmacol Ther 2014)
  - **Delayed initiation** of clinical programs in Asia is common

- Keys to **shortening the drug lag** (Ueno, CPT 2014)
  - Inclusion of **AP patients in global** clinical registration trials
  - Consideration of **an AP regional development strategy as early as possible**

- AP **participation in global registration** trials is growing
  - Drug lag may be shortening: **Nivolumab** first world-wide approval in Japan in July 2014!

# Why Conduct Early Development Studies in the AP Region?

- Provide rapid access to transformational therapeutics to **57% of the world's** population
- Access **strong regional scientific expertise**
  - Japan, China, Hong Kong, Taiwan, Korea, Singapore, Australia/NZ, and others
- Gain a better understanding of **large and growing markets**
  - China, Japan, Korea, and others
- Recommended Phase 2 **doses for oncology drugs may differ**
  - Japan vs. US dose differences noted in 73 of 190 (38%) approved drugs (Arnold Clin Pharmacol Ther 2014)
  - Unique Asian pharmacogenomic profiles
  - Different social and cultural tolerance limits for drug-related toxicities

# Why Conduct Early Development Studies in the AP Region?

- Accelerate the impact on unmet medical needs in key AP tumor types
  - Adenocarcinoma of the Lung
  - Gastric/Esophageal cancer
  - Hepatocellular cancer
  - Nasopharyngeal cancer

- Foster a global oncology drug development perspective
  - Broaden thinking about global indications and opportunities

# Current Vision: Coordinated AP Early Development Programs

- Coordinated early clinical development
  - Selective AP participation in oncology early development programs
  - AP regional strategy teams choose from Global R&D projects

- Example
  - Preclinical translational studies initiated in AP region to evaluate potential
  - Staggered or parallel AP Phase 1 studies conducted simultaneously with Global studies
  - Rapid advancement to Phase 2 proof of concept studies in key AP tumor types (Lung, liver, gastric cancers)

- Goals
  - Contribute to clinical programs in indications of global interest
  - Address unmet medical needs in AP region with the potential for global application

# First in Human Study of JNJ-42756493, A Potent Pan Fibroblast Growth Factor Receptor (FGFR) Inhibitor, in Patients with Advanced Solid Tumors

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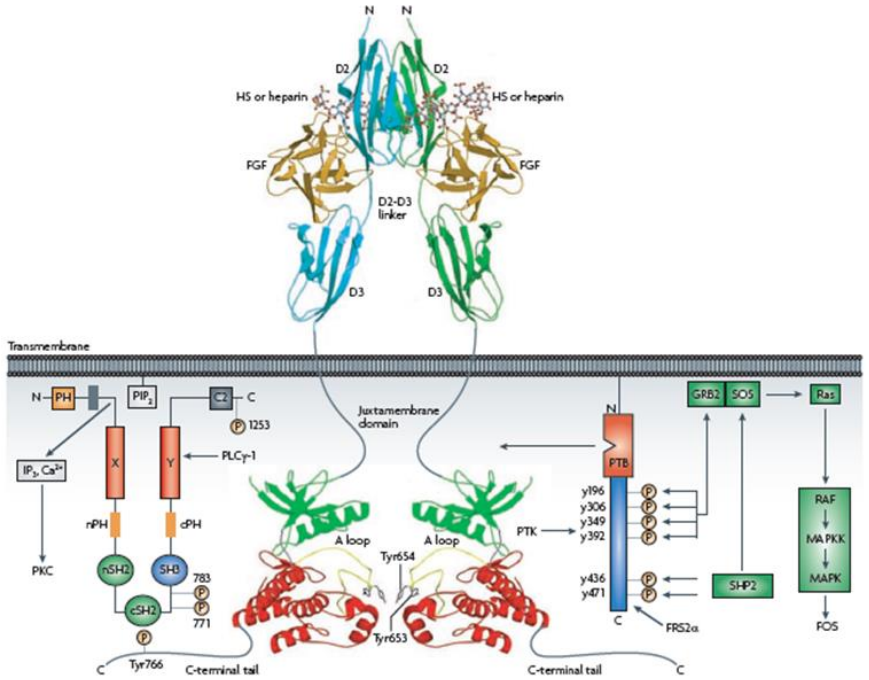
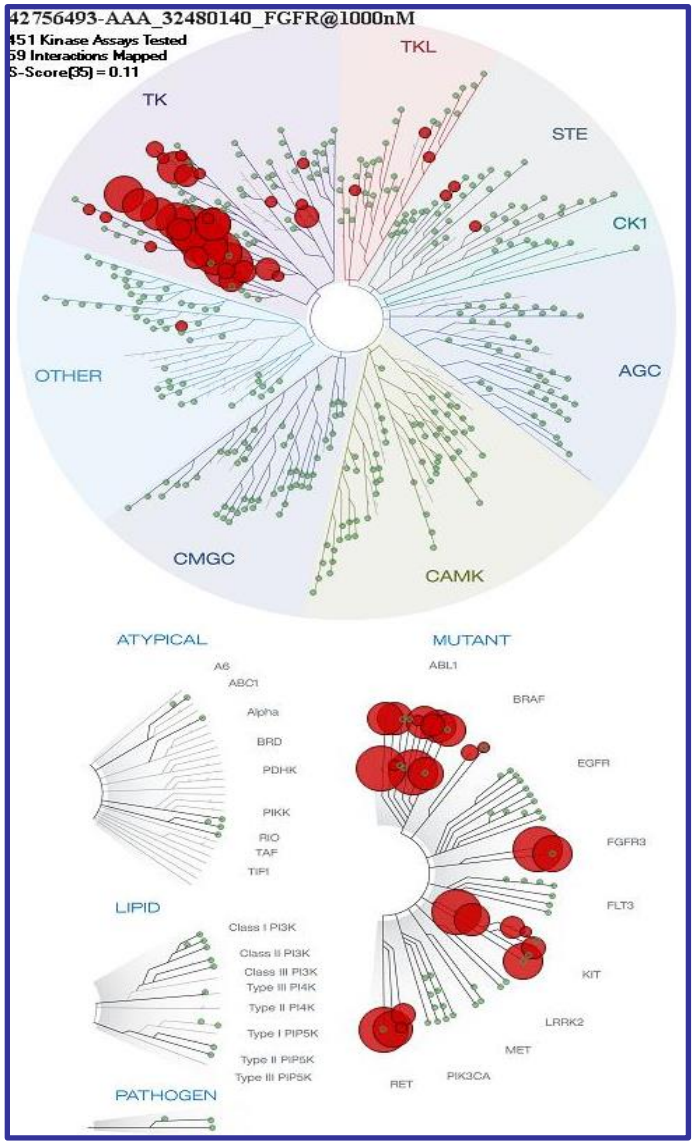
[3]Janssen Research and Development, LLC

-- Presented at AACR 2014

# JNJ-42756493 FGFR Inhibitor in Ph 1 Trials




| | JNJ-42756493 $IC_{50}$ (nM) | BGJ398 $IC_{50}$ (nM) | AZD4547 $IC_{50}$ (nM) |
|---|---|---|---|
| FGFR1 | <1 | 4.55 | <1 |
| FGFR2 | <1 | 28.1 | <1 |
| FGFR3 | 1.05 | 19.5 | 2.52 |
| FGFR4 | <1 | 376 | 40.6 |
| FGFR3 (G697C) | 1.90 | 28.8 | 5.25 |

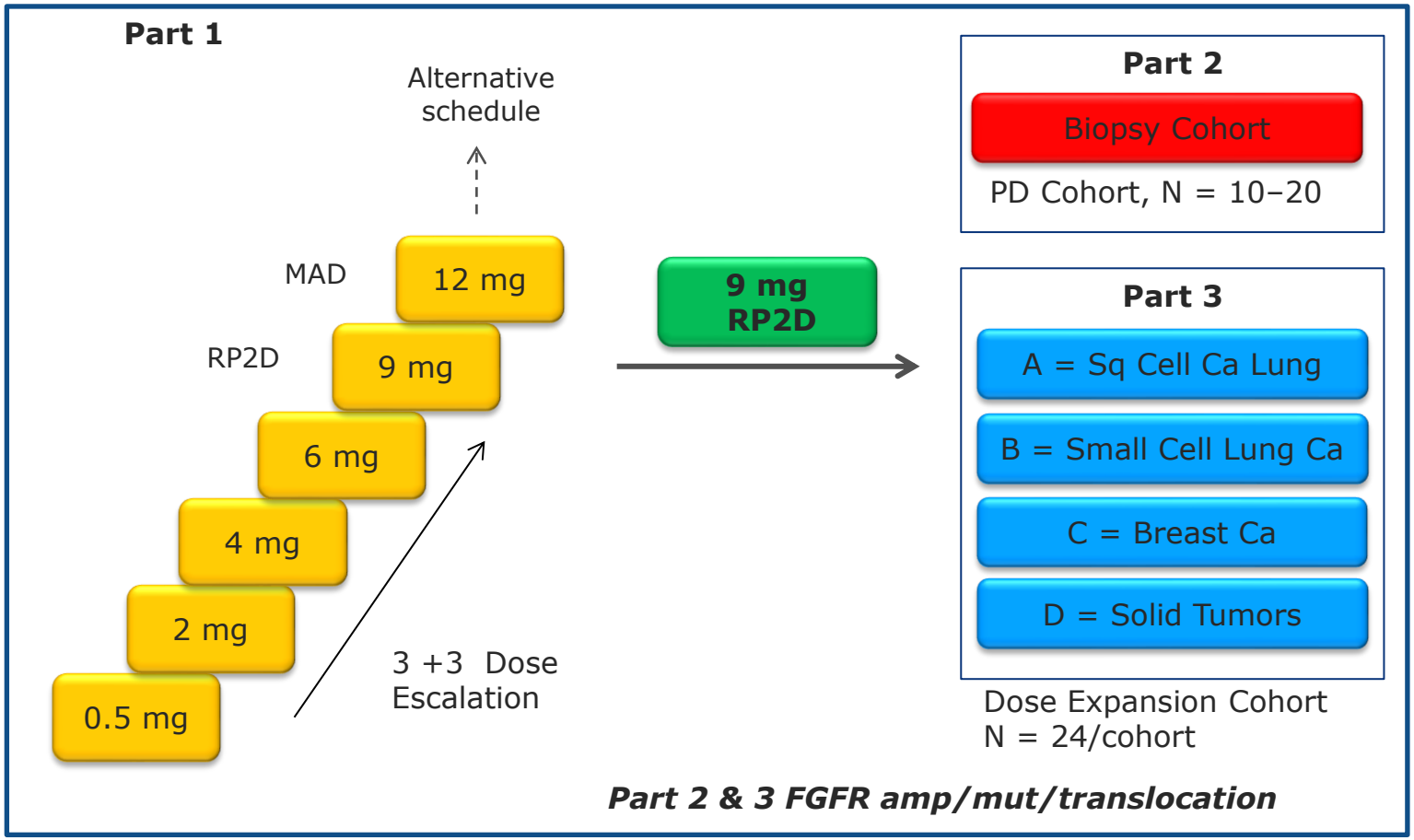



- JNJ-42756493 is a highly potent FGFR 1, 2, 3 and 4 inhibitor that was designed using structure based drug approach coupled to a fragment based approach
- JNJ-42756493 is a selective FGFR inhibitor



-- Presented at AACR 2014

# JNJ-42756493 Global FIH Phase 1/2 Study

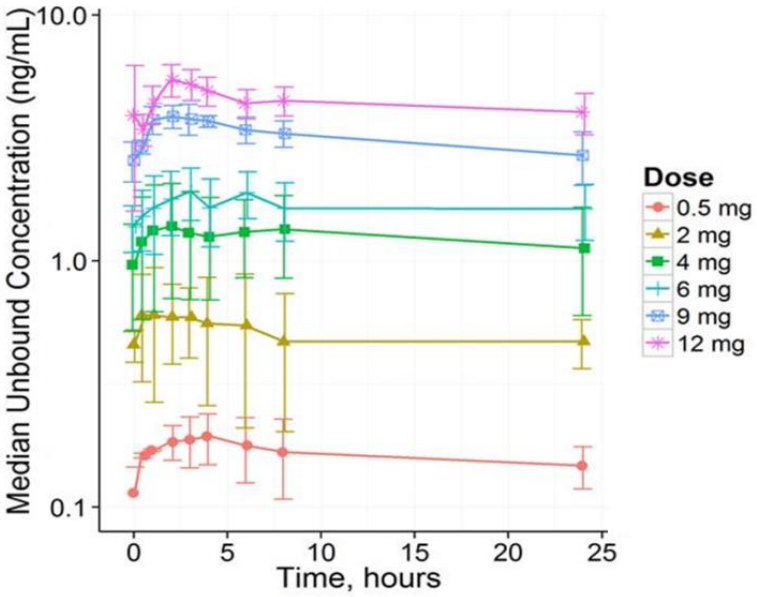



- Primary Objectives : Safety and RP2D, Clinical activity in select cohorts
- Secondary Objectives: PK and PD for JNJ-42756493

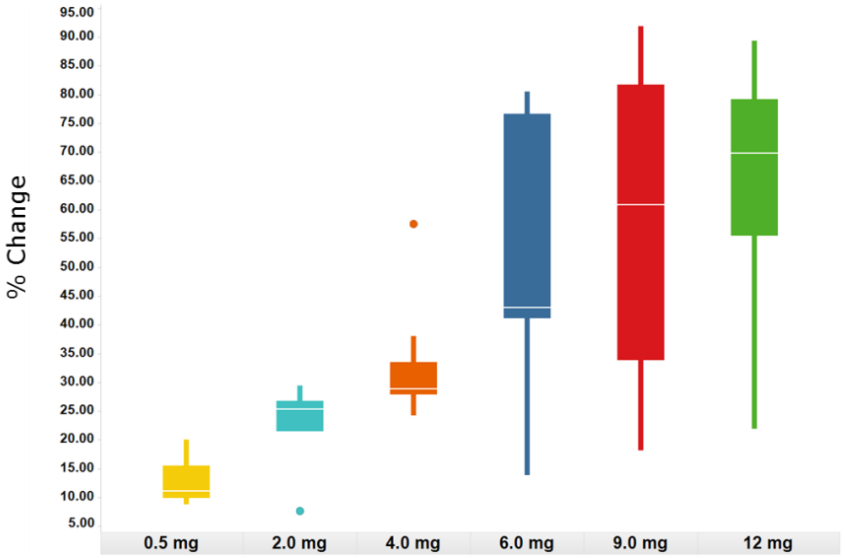
-- Presented at AACR 2014

# JNJ’493 Data Highlights from Dose Escalation

**Pharmacokinetics**




**PD Serum Biomarkers: Phosphate**
**Percent Change from Baseline to Cycle 1 D8**

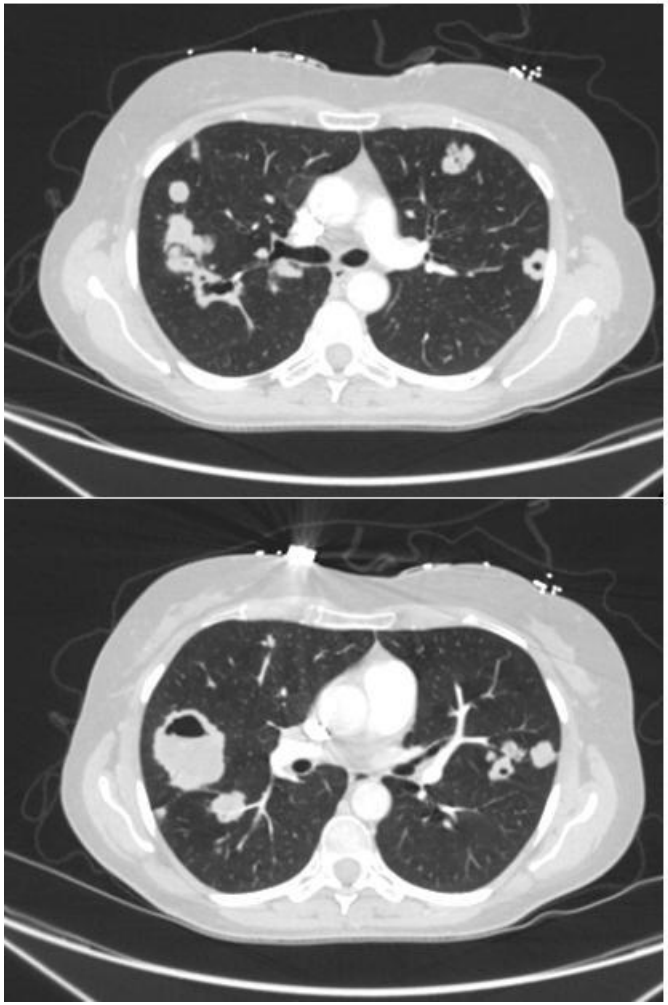



-- Presented at AACR 2014

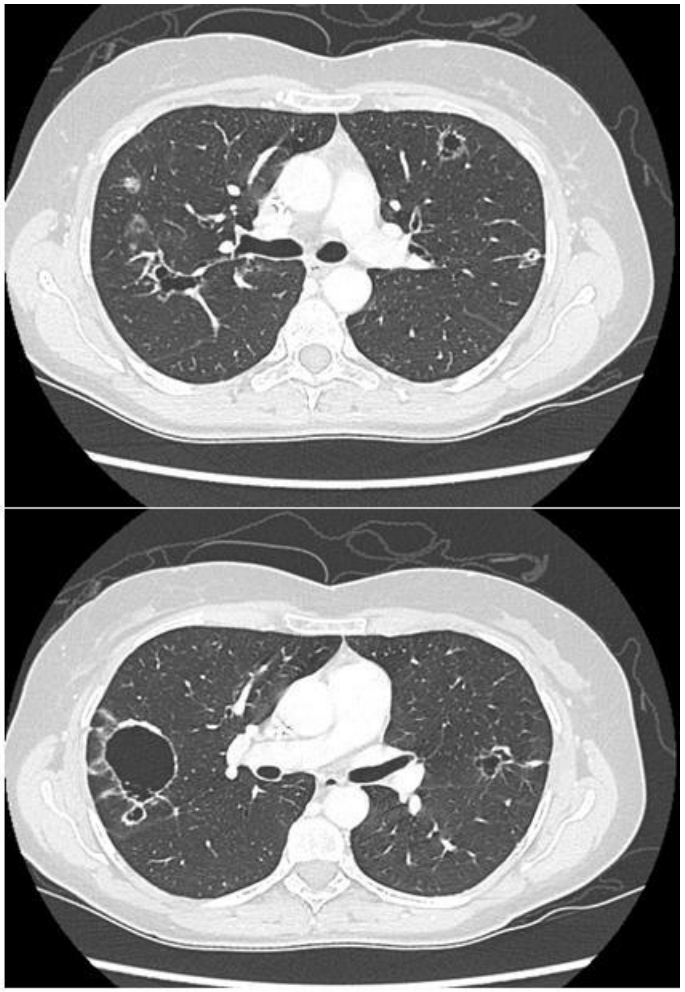
# Metastatic Bladder Cancer with Partial Response at 9 mg

(-38% decrease)

Screening



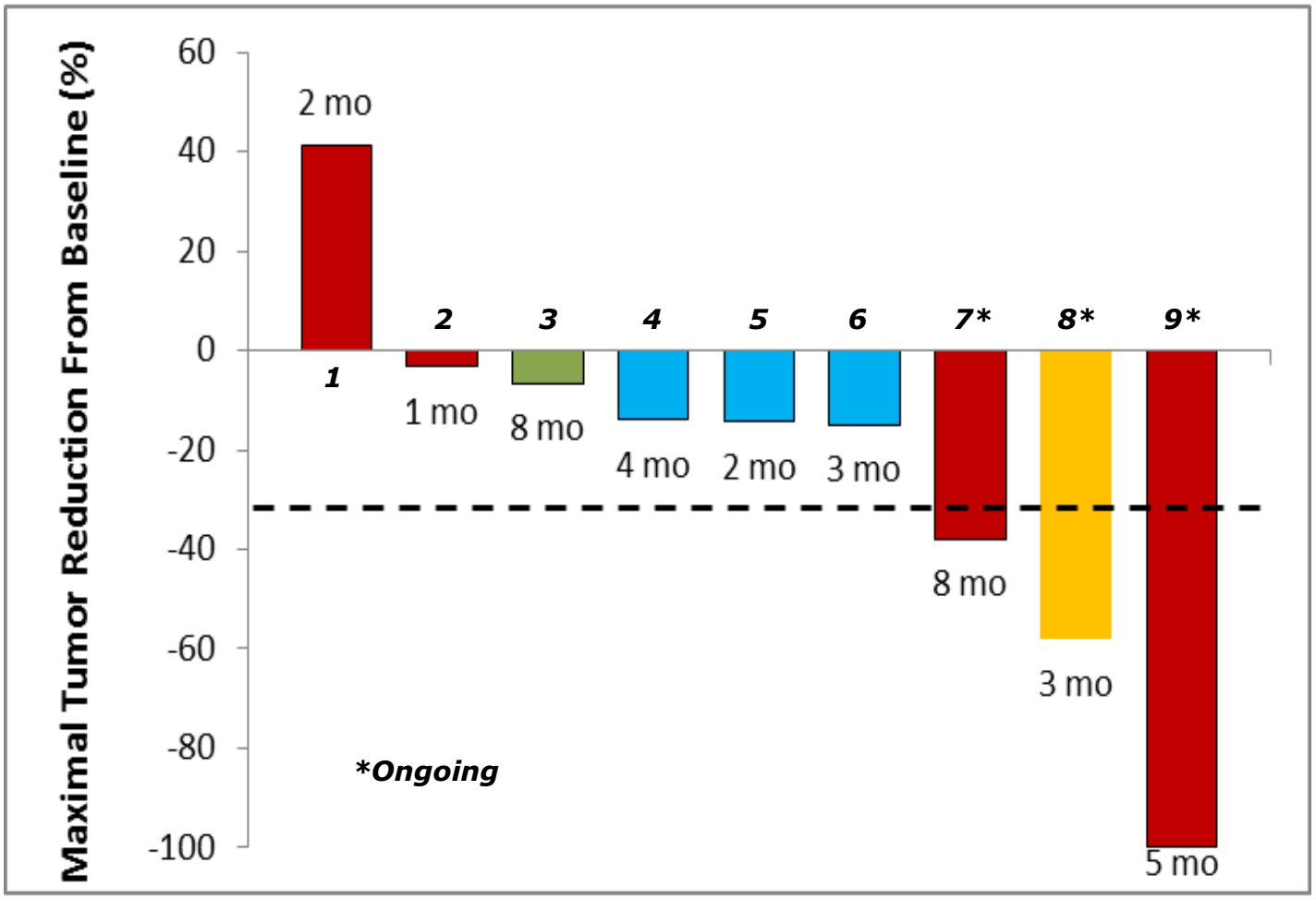
Week 6



Tumor tissue positive for FGFR3-TACC3 translocation

-- Presented at AACR 2014

# Clinical Activity of JNJ-42756493 in Patients with FGFR Aberrations Treated at ≥ 6mg Dose




***1*** – Intrahepatic Cholangiocarcinoma: FGFR2-CCDC6 fusion

***2*** – Breast Cancer: FGF3/4 amp

***3*** – Adrenal Carcinoma: FGFR3-TAC3/FGFR2-CCDC6 fusion

***4*** – NSCLC: FGFR1 amp

***5*** – Breast cancer: FGFR1 amp

***6*** – NSCLC: FGF6/23 amp

***7*** – Urothelial CA: FGFR3-TACC3 fusion

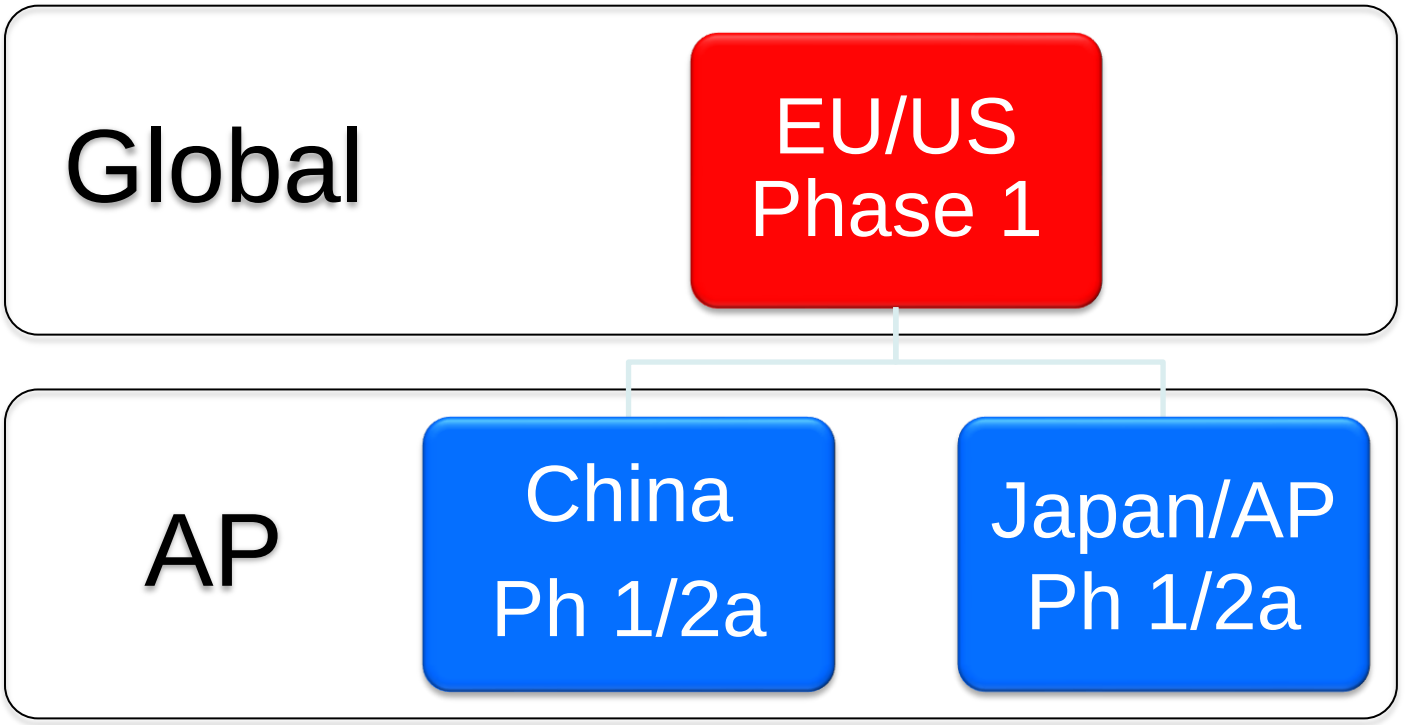
***8*** – GBM: FGFR3-TACC3 fusion

***9*** – Urothelial CA: FGFR2-BICC1 fusion

6 mg daily | 9 mg daily | 12 mg daily | 12 mg 7 on/7 off

-- Presented at ASCO 2014

# JNJ493 FGFR Inhibitor: Global Early Development!




Pre-POC Trials in the Asia-Pacific Region!

# AP Early Development Pharma Industry Challenges

- Establish and sustain a strong and stable AP R&D presence (Japan, China and elsewhere)
  - Build **clinical research expertise** beyond Phase 3
    - Enhance experience in oncology Phase 1 trials
  - Build **translational science** expertise
    - Preclinical investigations to support indications of regional interest
    - Example: Molecular profiling on local tissue specimens
  - Establish AP translational and clinical **research collaborations and networks**

- Build **AP Regional strategic teams** that work across countries
  - Global >> AP Regional >> Country organizations
  - History of autonomous R&D activities in AP countries

# AP Early Development Pharma Industry Challenges

- Promote **strong mutual respect** and good lines of **communication**
  - Execute integrated strategies that create value for the AP regional and global portfolios
  - Provide insight and feedback on clinical data interpretation
- Cultivate an **ED culture**: calculated risk-taking and considered risk management
- AP Countries are **scientifically and economically diverse**
- **Regulatory** environment can be unpredictable
- **Restrictions on specimen shipping** can impact biomarker screening strategies

# AP Early Development Pharma Industry Challenges

- Personnel challenges
  - Build and **sustain** a **diverse and expert professional workforce**
  - **High turnover** of individuals
  - Invest regional teams with an **appropriate independence**

- Must proactively address key issues
  - Cultural **differences in defining dose limiting toxicities**
  - Regional **differences in disease management** and standards of care
  - Unexpected **safety findings**
  - Population specific **differences in drug pharmacokinetics**
  - Possible racial or ethnic **differences in dosing**
    - Is the "**One World-One Dose**" concept outdated?

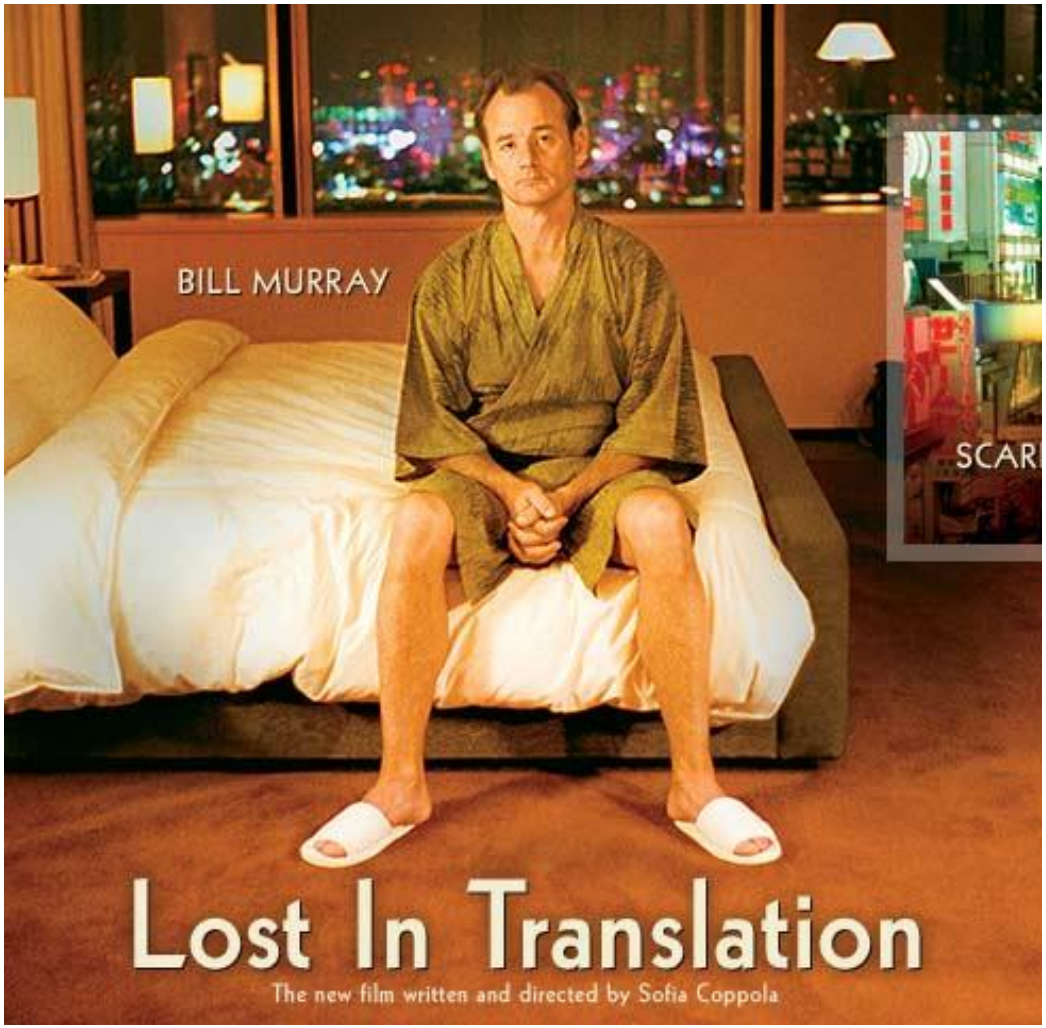
-- Adapted from Ken Kobayashi, MD

# How Can Pharma Facilitate This Effort?

- **Commit** to early drug development in the region
- Build **experienced AP teams**
  - Collaborate with dedicated Phase 1 and Ph 2 centers
  - Establish translational research networks
- Strive for **two way integration** of discovery and development
  - Not a one way flow of drugs to Asia
  - AP can lead translational/Phase 1 programs that expand globally

# The Future Approach to AP Drug Development

# And we cannot allow our key messages to be…



# Remember! Oncology Drug Development…


# is a Global Enterprise!

# Thank You!