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**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**  
Washington, D.C. 20549

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**FORM 8-K**

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**CURRENT REPORT**

**Pursuant to Section 13 or 15(d)  
of the Securities Exchange Act of 1934**

Date of Report (Date of earliest event reported): **June 27, 2012**

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**SYNTA PHARMACEUTICALS CORP.**

(Exact name of registrant as specified in its charter)

**Delaware**  
(State or other jurisdiction  
of incorporation)

**001-33277**  
(Commission File Number)

**04-3508648**  
(IRS Employer  
Identification No.)

**45 Hartwell Avenue**  
**Lexington, MA 02421**  
(Address of principal executive offices and zip code)

Registrant's telephone number, including area code: **(781) 274-8200**

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(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- ☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
  - ☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
  - ☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
  - ☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))
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**ITEM 7.01 Regulation FD Disclosure.**

On June 27, 2012, Synta Pharmaceuticals Corp. (“Synta”) announced results from a planned interim analysis of the GALAXY trial, a randomized Phase 2b/3 study designed to evaluate the efficacy and safety of Synta’s lead Hsp90 inhibitor, ganetespib, in combination with standard-of-care docetaxel vs. docetaxel alone as second-line treatment for advanced non-small cell lung cancer, and held a conference call to present the results. A copy of the presentation used on the conference call is furnished as Exhibit 99.1 to this Current Report on Form 8-K, and shall not be deemed to be “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or otherwise subject to the liabilities under such Section 18, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act except as shall be expressly set forth by specific reference in such filing.

**ITEM 8.01 Other Events.**

On June 27, 2012, Synta issued a press release announcing results from the planned interim analysis of the GALAXY trial described above. A copy of the press release is filed as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference.

**ITEM 9.01 Financial Statements and Exhibits.**

(d) Exhibits.

<b>Exhibit Number</b>	<b>Description</b>
99.1	GALAXY Trial Interim Results Presentation, dated June 27, 2012
99.2	Press Release, dated June 27, 2012

## **SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**SYNTA PHARMACEUTICALS CORP.**

Dated: June 28, 2012

/s/ Keith S. Ehrlich

Keith S. Ehrlich

Vice President, Finance and Administration

Chief Financial Officer

## EXHIBIT INDEX

Exhibit No.	Description
99.1	GALAXY Trial Interim Results Presentation, dated June 27, 2012
99.2	Press Release, dated June 27, 2012

# **Synta Pharmaceuticals**

**(NASDAQ: SNTA)**

## **GALAXY Trial Interim Results June 27 2012 Conference Call**

## Forward-looking statements

This presentation may contain forward-looking statements. These statements reflect our current views with respect to future events and actual results could differ materially from those projected in the forward-looking statements. Factors that could cause actual results to differ are discussed in Synta's 2011 Annual Report on Form 10-K and in our reports on Form 10-Q and Form 8-K. These reports are available on our website at [www.syntapharma.com](http://www.syntapharma.com) in the "Investors—SEC Filings" section. Synta undertakes no obligation to publicly update forward-looking statements, whether because of new information, future events or otherwise, except as required by law.

Ganetespib is an investigational product and has not yet been approved for any use.

# Highlights

## Ganetespib: leading Hsp90 inhibitor in industry

- First to overcome class toxicity challenges
- Active as monotherapy in certain targeted patient populations

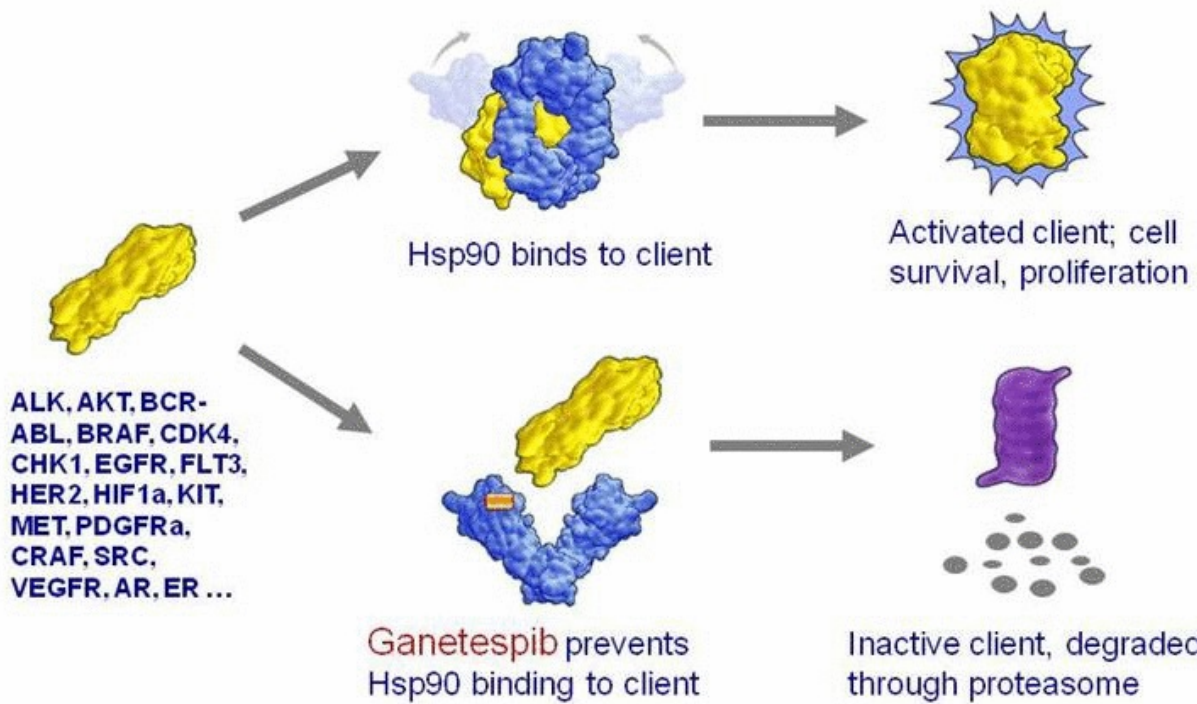
## Positive results from interim GALAXY analysis

- Ganetespib + docetaxel vs. docetaxel, 2<sup>nd</sup> line NSCLC
- 2.5-3x PFS improvement in pts with elevated LDH, pts with mutant KRAS
- PFS and OS improvements in adenocarcinoma patients
- No substantial increase in toxicity to docetaxel, except Gr 1/2 diarrhea

Aiming for regulatory advice Q3 to discuss Phase 3 plans

Synta owns 100% worldwide rights to ganetespib

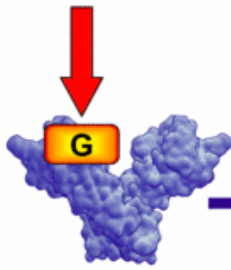
# Chaperones stabilize client proteins; chaperone inhibitors lead to client protein degradation





# Hsp90i: single target, simultaneous inhibition of multiple oncogenic pathways

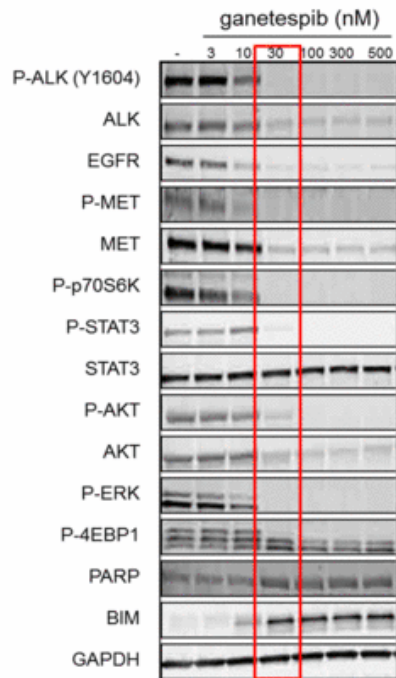
**Ganetespib**



**HSP90**

Hsp90 clients: many key cancer drivers

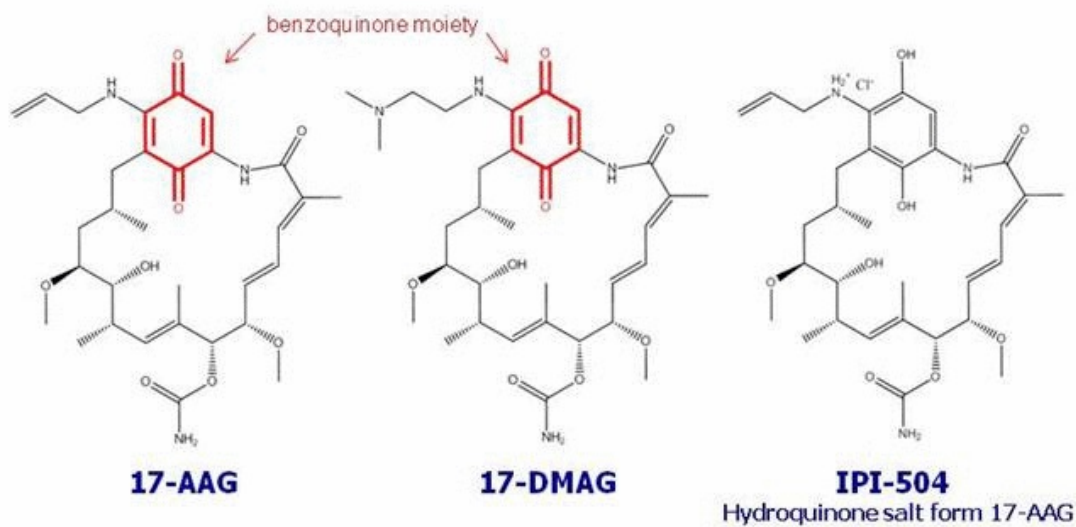
- ~~AXK~~
- ~~AXT~~
- ~~BXR-ABL~~
- ~~FX3~~
- ~~RXF~~
- ~~cXIT~~
- ~~cXMET~~
- ~~EXFR~~
- ~~HXR2~~
- ~~VXGFR~~
- ~~PXGFR~~
- ~~HX-1 $\alpha$~~
- ~~OXers~~



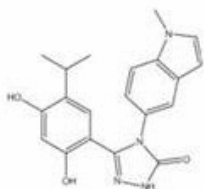
H3122 ALK+ NSCLC cells

## Development of Hsp90i: liver dose-limiting toxicity of 1<sup>st</sup>-gen ansamycins not seen with ganetespib

### 1<sup>st</sup>-gen Ansamycins



### Ganetespib



- Absence of benzoquinone moiety, liver DLTs
- 10-100x more potent

## Common ocular toxicity reported with other Hsp90i not seen with ganetespib

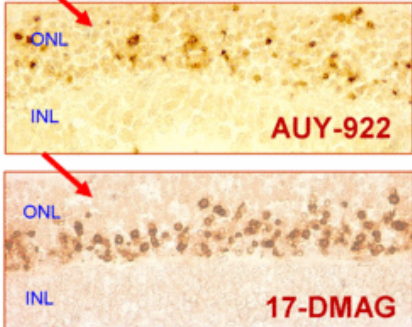
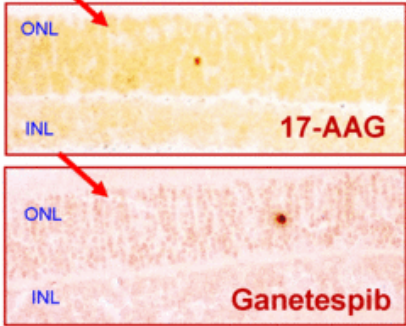
Hsp90i (2 <sup>nd</sup> -gen)	Observed ocular toxicity (at MTD)
Ganetespib Synta	<3%*
AUY-922 Novartis	89% (70 mg/m <sup>2</sup> qw)
AT13387 Astex	>50% (120 mg/m <sup>2</sup> biw)
SNX-5422 Pfizer	Terminated, excessive ocular tox

\* mild, reversible visual impairment symptoms

Source: AUY, AT- ASCO Jun 2010; SNX- Infante et. al., Pos # 375, AACR-EORTC-NCI Nov 2010



# Retinal damage associated with accumulation of Hsp90i in eye; not seen with ganetespiib

Hsp90 inhibitors	17-DMAG, AUY-922, SNX-5422, AT-13387, ...	17-AAG, ganetespiib
Clinical observations	Frequent ocular tox	Little/no ocular tox
Retina, rodent model	 <p>ONL INL <b>AUY-922</b></p> <p>ONL INL <b>17-DMAG</b></p>	 <p>ONL INL <b>17-AAG</b></p> <p>ONL INL <b>Ganetespiib</b></p>
Compound property	<u>Hydrophilic</u> , greater accumulation in retina	<u>Hydrophobic</u> ; reduced accumulation in retina

Zhou et al, "Associating retinal drug exposure and retention with the ocular toxicity profiles of Hsp90 inhibitors" ASCO June 2012 Abst. #3086

## Rationale for ganetespib combination therapy

Hsp90 clients involved in cellular **recovery and repair**  
mechanisms: Hsp90 inhibitors **sensitize** cells to anti-cancer  
drugs / radiation

Hsp90 inhibitors **demonstrate synergy** with chemo,  
targeted agents and radiation in preclinical models\*

Rationale for G + D in NSCLC:

- G single-agent activity in NSCLC

- Non-overlapping toxicities

- Synergistic mechanisms

# GALAXY Trial: “Operationally adaptive” design

## Phase 2b/3, NSCLC, Stage IIIB/IV, 2<sup>nd</sup> line

One protocol: two stages

### Phase 2b - “Learn”

N=240 →  
docetaxel  
docetaxel +  
ganetespib

Biomarker-defined  
population



Regulatory input

### Phase 3 - “Confirm”

N~500 →  
docetaxel  
docetaxel +  
ganetespib

Docetaxel 75 mg/m<sup>2</sup> d1 (3-week cycle)

Ganetespib 150 mg/m<sup>2</sup> d1,15 (3-week cycle)

Global trial: 13 countries, ~60 centers

Co-primary endpoints, Phase 2b stage:

PFS in patients with mutant KRAS

PFS in patients with elevated baseline serum LDH



## **Patients stratified to balance key prognostic factors between arms**

1. Histology
2. ECOG Performance Status
3. Baseline serum LDH
4. Smoking status
5. Time since diagnosis of advanced NSCLC

LDH measured in independent, central lab (pre-specified co-primary endpoint)



## Co-primary patient populations for Phase 2b stage: elevated LDH, mutant KRAS

Elevated LDH ~30%, mutant KRAS ~15-30% of all adeno

Both are prognostic variables for poor clinical outcomes<sup>1</sup>

- Patients progress faster and die sooner
- Chemotherapy works less well

Scientific and clinical rationale suggest possible enhanced ganetespib activity in these populations – i.e., predictive variables for G activity, in addition to prognostic

1. Elevated LDH: Schneider, Advan Clin Chem 42:1-41 (2006); Albain et al., J Clin Oncol 9:1618-1626 (1991); Suh and Ahn, Eur J Cancer 43:1051 (2007). Mut KRAS: Johnson, ASCO 2010 Abstr 7541; Socinski, Clinical Lung Cancer 2010



# Why elevated LDH?

## “Oxygen-sensitive agents” (VEGF, mTOR inhibitors)

Study	N	Endpt	Normal LDH	High LDH
Phase 2 carboplatin + paclitaxel +/- <b>bevacizumab</b> 1 <sup>st</sup> line <b>melanoma</b> (BEAM) <sup>1</sup>	214	OS	<b>HR=1.25</b> [0.73-2.13]	<b>HR=0.53</b> [0.32-0.88]
Phase 3 gemcitabine erlotinib +/- <b>bevacizumab</b> 1 <sup>st</sup> line <b>pancreatic</b> <sup>2</sup>	607	OS	<b>HR=0.98</b> [0.78-1.24]	<b>HR=0.59</b> [0.43-0.82]
Phase 3 docetaxel + prednisone +/- <b>bevacizumab</b> 1 <sup>st</sup> line <b>prostate</b> <sup>3</sup>	1050	OS	<b>HR=1.02</b> p=0.87	<b>HR=0.80</b> p=0.029
Phase 3 <b>temsirolimus</b> vs INF- $\alpha$ in <b>advanced RCC</b> (ARCC trial) <sup>4</sup>	404	OS	<b>HR=0.90</b> p=0.5138	<b>HR=0.56</b> p=0.0017

Not significant      Significant

See also **vatalanib** (CONFIRM-1,2): Hecht et al., 29:1997 JCO (2011); van Cutsem et al., 29:2004 JCO (2011)

1. Kim et al., J Clin Oncol 30:34-41 (2012)

2. Van Cutsem et al, J Clin Oncol 27:2231-2237 (2009)

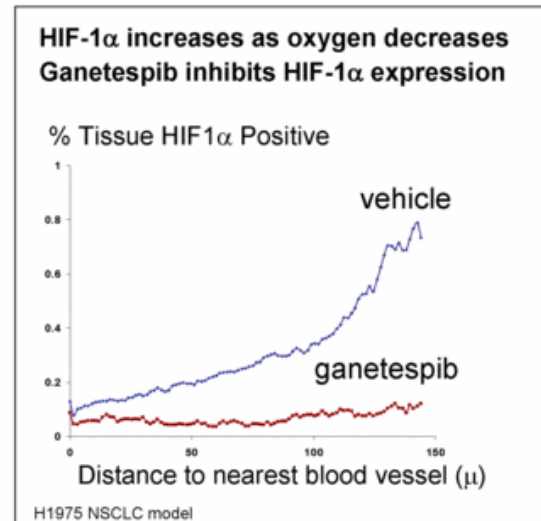
3. Kelly et al, J Clin Oncol 30:1534 (2012)

4. Armstrong et al., ASCO 2010, Abstr 324

# Why elevated LDH?

LDH is **prognostic** in lung and many cancers.<sup>1</sup> In addition:

- LDH-A is a marker of **hypoxia**, regulated by Hypoxia Induced Factor-1 $\alpha$  (**HIF-1 $\alpha$** )<sup>2</sup>
- HIF-1 $\alpha$  also drives metabolic, angiogenesis, cell survival pathways targeted by “oxygen-sensitive” agents (e.g., VEGF, VEGFR, mTOR; low oxygen → need new blood vessels)<sup>2</sup>
- Inhibition of hypoxia pathways **enhances taxane**, chemo activity<sup>3</sup>
- **Ganetespib inhibits HIF-1 $\alpha$**  deep into hypoxic regions of tumors<sup>4</sup> →



1. Albain, et al., J Clin Oncol 9:1618-1626 (1991); Danner et al., Anticancer Res 30:1347-1352 (2010)
2. Koukourakis et al., Br J Cancer 89:877-885 (2003); Azuma et al. Pharmacogenomics 8:1705-13 (2007)
3. Zhou et al Mol Cancer 9:33 (2010)
- 14 4. Foley et al., AACR April 2010 #2638; Ying et al., Mol Canc Therap Jan 2012; Mahaseth et al, AACR 2012 Abst #2326

**“Lactate dehydrogenase-5 (LDH-5) overexpression in non-small-cell lung cancer tissues is linked to tumour hypoxia, angiogenic factor production and poor prognosis,”**

Koukourakis et al, Br J Cancer 89:877-885 (2003)

**“Serum lactate dehydrogenase levels and glycolysis significantly correlate with tumor VEGFA and VEGFR expression in metastatic CRC patients.”**

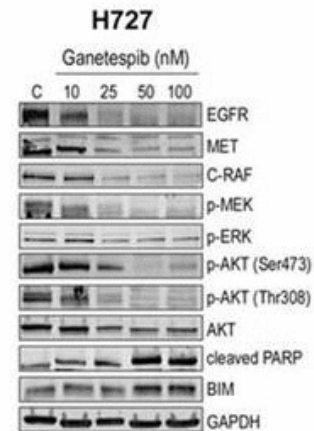
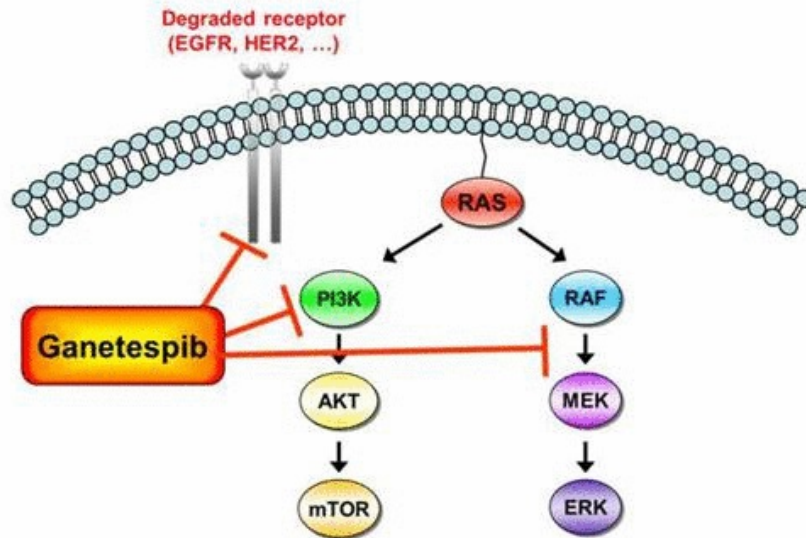
Azuma et al, Pharmacogenomics 8:1705-13 (2007)

**“Warburg effect in chemosensitivity: Targeting LDH-A resensitizes Taxol-resistant cancer cells to Taxol”**

Zhou et al Mol Ca 2010; 9 p33

# Why mutant KRAS?

Ganetespib three-way impact on RAS signaling:  
degrades receptor, PI3K/AKT pathway, and RAF/MEK pathway

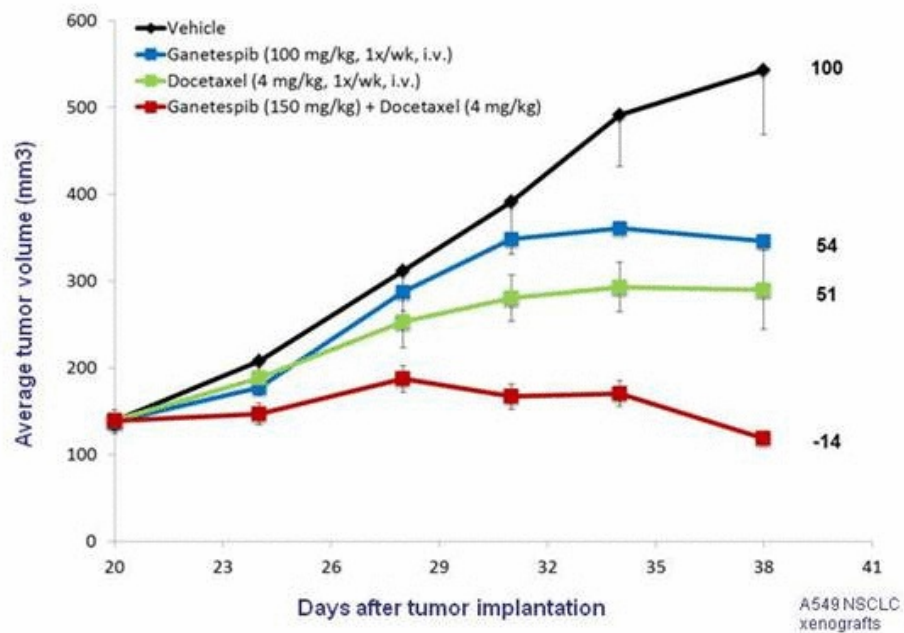


Inhibition of RAS signaling pathway proteins by ganetespib in mutant KRAS NSCLC cell lines

Acquaviva, Proia et al., "Targeting KRAS mutant NSCLC with the Hsp90 inhibitor ganetespib", AACR-IASLC, San Diego Jan 2012 (manuscript submitted)



## Ganetespi and docetaxel show synergy in mutant KRAS NSCLC models



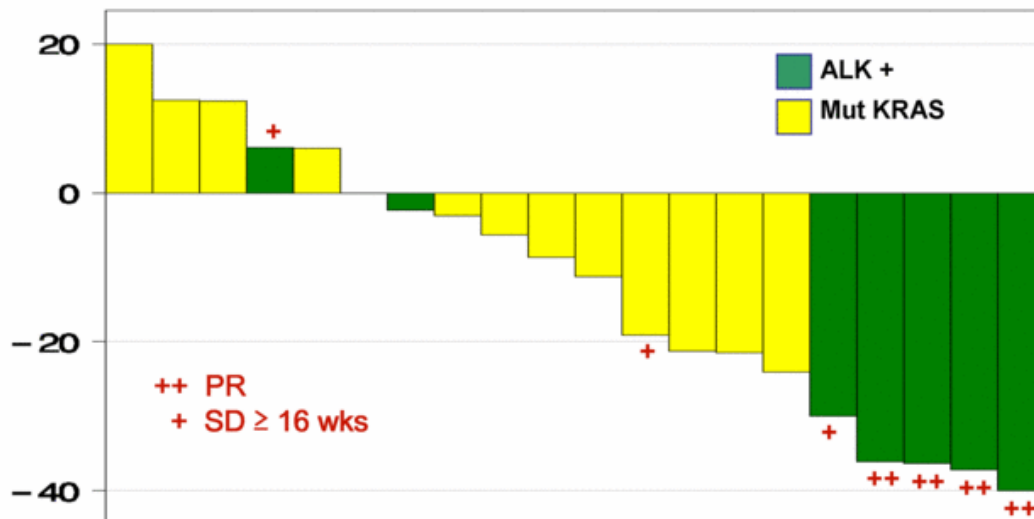
Acquaviva, Proia et al., "Targeting KRAS mutant NSCLC with the Hsp90 inhibitor ganetespi", AACR-IASLC, San Diego Jan 2012 (manuscript submitted)



## Clinical activity observed with ganetespib monotherapy: mutant KRAS, ALK+ patients

Phase 2 NSCLC trial ganetespib monotherapy (ASCO 2011)

Best % change from baseline, target lesions. Crizotinib-naïve ALK+; mut KRAS patients



K. Wong, G. Shapiro, M.A. Socinski et al, ASCO 2011 (manuscript submitted)

6/8 (75%) ALK+ pts, 8/13 (62%) mut KRAS pts show tumor shrinkage; 4/8 (50%) ORR and 7/8 (88%) Disease Control in ALK+ patients; durable responses (average 12mo Rx; 1 ongoing)

# **GALAXY Phase 2b interim analysis**

Planned when  $\approx 50\%$  pts enrolled, one post-baseline follow-up scan

At time of analysis: 114 adenocarcinoma, 69 non-adeno

- Patients well balanced for all key prognostic factors
- Enrollment in non-adeno terminated; lack of activity
- All results reported: adeno only
- N=31 elevated LDH patients; N=20 mutant KRAS patients

## **Key safety findings**

- Increased diarrhea in G+D arm, predominantly grade 1,2
- Other AEs: comparable between two arms
- No evidence of serious liver or common ocular toxicities seen with other Hsp90i

## GALAXY Adverse Event profile

	D (N=59)	D+G (N=55)
% pts w/at least one AE		
All grades	64%	82%
Grade 3 or 4	32	36
% pts w AEs leading to treatment discontinuation	6.8	9.1
% pts w AEs with outcome of death	5.1	5.5
<u>Most common AEs, all grades</u>		
Neutropenia All grades	48	44
Grade 3 or 4	29	33
Fatigue All grades	19	26
Grade 3 or 4	3	0
Diarrhea All grades	10	40
Grade 3 or 4	0	2



## GALAXY interim results

### Primary endpoint populations

	Elevated LDH		Mutant KRAS	
	D (N=15)	G+D (N=16)	D (N=11)	G+D (N=9)
Median PFS	1.4 mo	4.2 mo	1.6 mo	4.2 mo
# PFS events (%)	12 (80)	8 (50)	5 (46)	3 (33)
ORR (%)	0 (0)	2 (13)	1 (9)	2 (22)
# deaths (%)	6 (40)	4 (25)	2 (18)	1 (11)

All response, progression endpoints measured per RECIST 1.1  
PFS: progression-free survival; ORR: best response (CR or PR)  
# events not reached maturity for significance testing



## **GALAXY interim results**

### **PFS, adenocarcinoma patients**

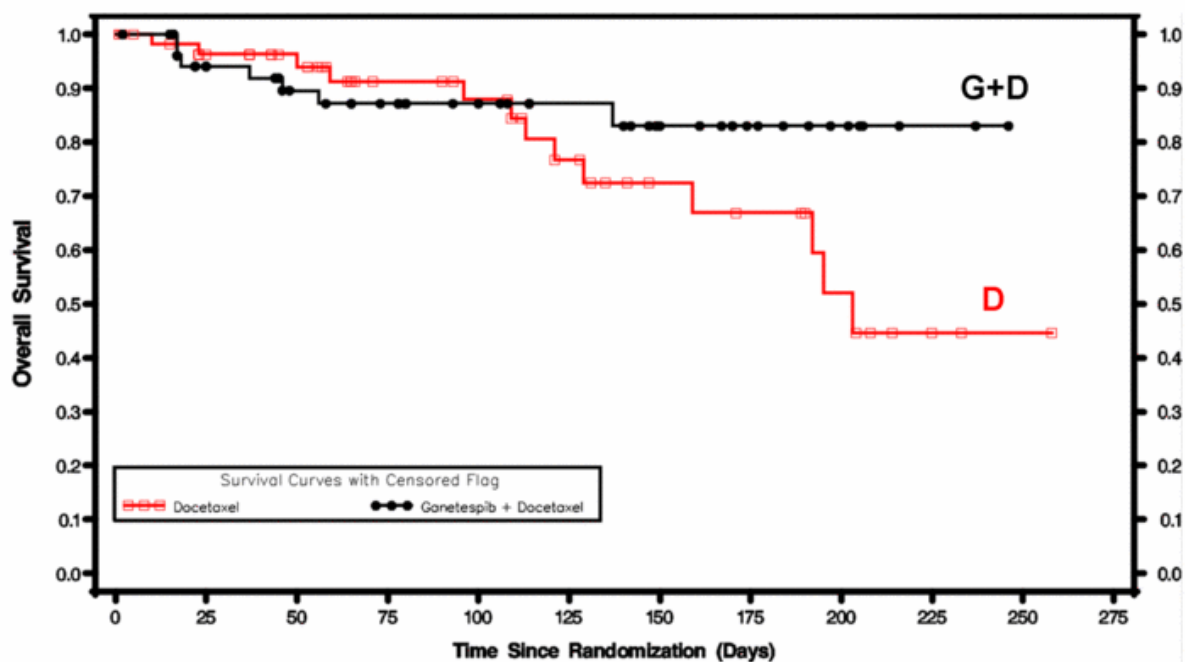
	All adenocarcinoma patients	
	D (N=59)	G+D (N=55)
Median PFS	2.9 mo	4.2 mo
# PFS events (%)	31 (53)	23 (42)
ORR (%)	5 (8)	8 (15)
# deaths (%)	13 (22)	7 (13)

All response, progression endpoints measured per RECIST 1.1  
PFS: progression-free survival; ORR: best response (CR or PR)  
# events not reached maturity for significance testing



# GALAXY interim results

## Overall Survival, adenocarcinoma patients



	D	G+D	.
N	59	55	
# events	13 (22%)	7 (13%)	

## Next Steps

- Complete enrollment, N=240 adenocarcinoma patients (ongoing)
- Expand # sites NA, Europe, Asia in preparation for transition to Phase 3 (ongoing)
- Additional interim analysis, medical meeting presentation (2H 2012)
- Regulatory advice for Phase 3 design (Q3)

**Focus on GALAXY, 2<sup>nd</sup>-line NSCLC as most immediate path to registration**

# References

## Elevated LDH in cancer

Albain et al., "Survival determinants in extensive-stage non-small-cell lung cancer: the Southwest Oncology Group experience," J Clin Oncol 9:1618-1626 (1991)

Armstrong et al. "Serum lactate dehydrogenase (LDH) is a predictive biomarker for mTOR inhibition in patients with metastatic renal cell carcinoma (RCC)," ASCO 2010, Abstr 324

Azuma et al., "Serum lactate dehydrogenase levels and glycolysis significantly correlate with tumor VEGFA and VEGFR expression in metastatic CRC patients," Pharmacogenomics 8:1705-13 (2007)

Danner et al. "Long-term survival is linked to serum LDH and partly to tumour LDH-5 in NSCLC," Anticancer Res 30:1347-1352 (2010)

Kelly et al. "Randomized, Double-Blind, Placebo-Controlled Phase III Trial Comparing Docetaxel and Prednisone With or Without Bevacizumab in Men With Metastatic Castration-Resistant Prostate Cancer: CALGB 90401," J Clin Oncol 30:1534 (2012)

Kim et al., "BEAM: A Randomized Phase II Study Evaluating the Activity of Bevacizumab in Combination With Carboplatin Plus Paclitaxel in Patients With Previously Untreated Advanced Melanoma," J Clin Oncol 30:34-41 (2012)

## References (continued)

Koukourakis et al., "Lactate dehydrogenase-5 (LDH-5) overexpression in non-small-cell lung cancer tissues is linked to tumour hypoxia, angiogenic factor production and poor prognosis," Br J Cancer 89:877-885 (2003)

Suh and Ahn, "Lactate dehydrogenase as a prognostic factor for survival time of terminally ill cancer patients: a preliminary study," Eur J Cancer 43:1051 (2007)

Van Cutsem et al., "Phase III Trial of Bevacizumab in Combination With Gemcitabine and Erlotinib in Patients With Metastatic Pancreatic Cancer," J Clin Oncol 27:2231-2237 (2009)

Zhou et al., "Warburg effect in chemosensitivity: targeting lactate dehydrogenase-A re-sensitizes taxol-resistant cancer cells to taxol," Mol Cancer 9:33 (2010)

### **Mutant KRAS in cancer**

Acquaviva et al., "Targeting KRAS mutant NSCLC with the Hsp90 inhibitor ganetespib," AACR-IASLC, San Diego Jan 2012 (manuscript submitted)

Douillard et al., "Molecular Predictors of Outcome With Gefitinib and Docetaxel in Previously Treated Non-Small-Cell Lung Cancer: Data From the Randomized Phase III INTEREST Trial," J Clin Oncol 28:744-752 (2010)

Janne et al. "Phase II double-blind, randomized study of selumetinib (SEL) plus docetaxel (DOC) versus DOC plus placebo as second-line treatment for advanced KRAS mutant non-small cell lung cancer (NSCLC)," ASCO abstr 7503 (2012)

## References (continued)

Johnson et al., "Association of KRAS and EGFR mutations with survival in patients with advanced lung adenocarcinoma," ASCO Jun 2010 Abstr 7541

Schneider, "Tumor markers in detection of lung cancer," Advan Clin Chem 42:1-41 (2006)

Socinski, "The emerging role of biomarkers in advanced non-small-cell lung cancer," Clin Lung Can 11:149-159 (2010)

### **Hsp90 inhibition**

Foley et al., "Hsp90 inhibitor STA-9090 induces HIF-1 $\alpha$  degradation in the hypoxic regions of solid tumors," AACR April 2010 Abstr 2638

Infante et al. "A Phase 1 Dose-Escalation Study of the Oral Heat Shock Protein 90 Inhibitor PF-04929113 (SNX5422) and its Associated Ocular Toxicity," AACR-EORTC-NCI Nov 2010 Pos # 375

Mahaseth et al., "Antiangiogenic Effects Associated with the Inhibition of HSP90 in Colorectal Cancer," AACR 2012 Abstr 2326

Samuel et al., "AUY922, a novel HSP90 inhibitor: Final results of a first-in-human study in patients with advanced solid malignancies," ASCO Jun 2010 Abstr 2528

Shapiro et al., "Phase I pharmacokinetic and pharmacodynamic study of the heat shock protein 90 inhibitor AT13387 in patients with refractory solid tumors," ASCO Jun 2010 Abstr 3069

## References (continued)

Socinski et al., "Phase II study of ganetespib monotherapy in patients with advanced stage IIIB/IV NSCLC," ASCO 2011 (manuscript submitted)

Ying et al., "Ganetespib, a unique triazolone-containing Hsp90 inhibitor, exhibits potent antitumor activity and a superior safety profile for cancer therapy," Molec Canc Therap 11:475 (2012)

Zhou et al., "Associating retinal drug exposure and retention with the ocular toxicity profiles of Hsp90 inhibitors," ASCO June 2012 Abstr 3086





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**Synta Announces Results from Interim Analysis of the  
Randomized Phase 2b/3 GALAXY Trial Evaluating Ganetespib plus Docetaxel  
in Second-Line Non-Small Cell Lung Cancer**

*—2.5 to 3-fold improvement in PFS observed in co-primary endpoints: mutant KRAS and elevated LDH patients—*

*—Improvements in PFS, response rate, and survival events observed in all adenocarcinoma patients—*

*—Results support advancing to Phase 3 stage of GALAXY trial in 2H 2012—*

*—Synta to host conference call and webcast today at 5:00 pm EST—*

**LEXINGTON, MA — June 27, 2012** — Synta Pharmaceuticals Corp. (NASDAQ: SNTA) today announced encouraging results from a planned interim analysis of the GALAXY trial, a randomized Phase 2b/3 study designed to evaluate the efficacy and safety of the Company's lead Hsp90 inhibitor, ganetespib, in combination with standard-of-care docetaxel vs. docetaxel alone as second-line treatment for advanced non-small cell lung cancer (NSCLC).

The GALAXY trial is based on a two-stage, operationally adaptive design. The first-stage, randomized, open-label, 240-patient Phase 2b portion of the trial is designed to enroll Stage IIIB/IV NSCLC patients who have progressed following one prior line of therapy, with the goal of determining biomarkers predictive of ganetespib activity. Results will be used to guide choice of patient population for the Phase 3 stage of the trial.

Patients in the GALAXY trial are randomized 1:1 to receive ganetespib plus docetaxel or docetaxel alone. Patients in both arms receive a standard regimen of docetaxel 75 mg/m<sup>2</sup> on day 1 of a 21-day cycle; patients in the combination arm receive in addition ganetespib 150 mg/m<sup>2</sup> on days 1 and 15. Treatment continues until disease progression per RECIST 1.1 criteria.

The co-primary endpoints of GALAXY are PFS (progression-free survival) in patients with elevated baseline level of serum LDH (lactate dehydrogenase), and PFS in the mutant KRAS population. PFS and OS (overall survival) in all adenocarcinoma patients are key secondary endpoints. Serum LDH levels and tumor KRAS mutation status are assessed by independent central laboratories.

*Elevated LDH:* Elevated baseline LDH occurs in approximately one quarter to one third of advanced cancer patients in clinical trials and is prognostic of poor clinical outcomes in many cancer types, including lung cancer.(1)-(3) While elevated LDH can result from several conditions, in cancer patients elevated levels of LDH and its isoforms have been associated with tumor hypoxia (lack of oxygen).(4),(5) Inhibition of hypoxia pathways has been shown to enhance anti-cancer activity of taxanes and other chemotherapies.(6) Recent results from trials evaluating

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agents that target hypoxia-related pathways, including VEGF and mTOR inhibitors, have shown correlation between elevated LDH and improved clinical activity.(7)-(10) In laboratory experiments, treatment with ganetespib potentially suppresses HIF-1alpha, a critical regulator of hypoxic pathways(11) — supporting potential application for ganetespib in combination with taxanes in this patient population.

**KRAS mutation:** Activating KRAS mutations, estimated to occur in 15-30% of NSCLC patients, are also associated with poor clinical outcomes and limited therapeutic options.(12),(13) Hsp90 is required for the proper function of a number of key signaling proteins in the KRAS pathway, while inhibition of Hsp90 by ganetespib has shown promising activity in laboratory models of this disease.(14) Recent results from trials evaluating ganetespib monotherapy in lung, colon, and gastric cancers have further suggested promising potential in patients with KRAS mutations.

Based on a target enrollment of 240 adenocarcinoma patients, GALAXY is 90% powered to detect a PFS improvement from 6 to 12 weeks in elevated LDH patients and from 5 weeks to 10 weeks in the mutant KRAS patients. For the key secondary endpoints: in all adenocarcinoma patients, GALAXY is 88% powered to detect an improvement in PFS from 3 to 4.5 months, and 73% powered to detect an improvement in OS from 6 to 8.5 months. All powering assumptions are based on a 1-sided alpha of 0.05. An interim analysis was planned when approximately 50% of patients had been enrolled and had sufficient follow up, defined as one post-baseline scan.

## GALAXY Interim Results

At the time of this interim analysis, a total of 114 adenocarcinoma and 69 non-adenocarcinoma patients had been enrolled. Following a review earlier this year that determined low likelihood of benefit in the non-adenocarcinoma population, the trial was modified to enroll only adenocarcinoma patients. Results reported below are for adenocarcinoma patients only.

### Activity

The table below lists primary and key secondary endpoints relating to the two co-primary patient populations, as well as the all adenocarcinoma population. Partial response (PR), stable disease (SD), and progressive disease (PD) are assessed per RECIST 1.1 criteria; N/E indicates not available or evaluated at time of analysis. There have been no complete responses (CR) in the trial.

	Elevated LDH (N=31)		Mutant KRAS (N=20)		All adeno (N=114)	
	D (N=15)	G+D (N=16)	D (N=11)	G+D (N=9)	D (N=59)	G+D (N=55)
Primary endpoint						
median PFS	1.4 mo	4.2 mo	1.6 mo	4.2 mo	2.9 mo	4.2 mo
# events (%)	12 (80)	8 (50)	5 (46)	3 (33)	31 (53)	23 (42)
Best response						
PR (%)	0	2 (13)	1 (9)	2 (22)	5 (8)	8 (15)
SD (%)	6 (40)	7 (44)	5 (46)	6 (67)	31 (53)	27 (49)
PD (%)	5 (33)	2 (13)	3 (27)	0	13 (22)	7 (13)
N/E (%)	4 (27)	5 (31)	2 (18)	1 (11)	10 (17)	13 (24)
Overall survival events						
# deaths (%)	6 (40)	4 (25)	2 (18)	1 (11)	13 (22)	7 (13)

The sample size in each of these populations is small compared to the total planned sizes. Event rates have not yet achieved maturity for meaningful significance testing.

### ***Safety***

The adverse event profile was comparable between both arms. The proportion of adenocarcinoma patients with at least one adverse event (AE) was 64% vs. 82%; with grade 3 or 4 AEs was 32% vs. 36%; with AEs leading to treatment discontinuation was 7% vs. 9%; and with AEs with outcome of death were 5.1% vs. 5.5%, for D (N=59) vs. G+D (N=55), respectively. The most common AEs, all grades were neutropenia (48% vs. 44%), diarrhea (10% vs. 40%) and fatigue (19% vs. 26%), for D vs. G+D, respectively. Diarrhea and fatigue were predominantly grade 1 and grade 2; the incidence of grade 3 or 4 diarrhea was 0% vs. 2% and grade 3 or 4 fatigue was 3% vs. 0% in D vs. G+D, respectively. The most common grade 3 or 4 AEs were neutropenia (29% vs. 33%), leukopenia (5% vs. 4%), and nausea (3% vs. 4%).

Trials with some other Hsp90 inhibitors have reported a high incidence of ocular toxicities. In the GALAXY trial to date, there has been one report of ocular-related adverse event (grade 2, blurred vision, transient) in the G+D arm (2%) vs. no reports in the D arm.

### **GALAXY Trial Next Steps**

Enrollment completion of the Phase 2b stage and transition to the Phase 3 stage are expected later this year. An additional interim analysis of the Phase 2b portion of the trial, presentation of results at a medical meeting, and a more detailed announcement of plans for the Phase 3 stage of this trial are also anticipated for later this year.

“Ganetespib was designed by our scientists almost ten years ago to improve the potency and safety seen with other Hsp90 compounds, and be the first compound to realize the full potential of chaperone inhibition for treating cancer,” said Safi R. Bahcall, Ph.D., President and CEO of Synta. “The complex biology and broad potential of this new therapeutic class present both an opportunity and a challenge: how can we identify as efficiently as possible which patients, defined by underlying disease biology, are most likely to benefit? In response, our team designed an innovative trial — a highly-powered, Phase 2b ‘learning’ stage followed, in an operationally continuous manner, by a Phase 3 ‘confirming’ stage. We believe that the encouraging results reported today support the therapeutic potential of ganetespib, and the operationally adaptive approach allows us to advance quickly to the next step. We are hopeful that additional development will lead to a new treatment option for patients with this devastating disease.”

“We are encouraged by both the safety profile and the signals of activity seen in the interim results announced today,” said Vojo Vukovic, M.D., Ph.D., Chief Medical Officer of Synta. “The results show that ganetespib can overcome the liver and common ocular safety concerns seen with other Hsp90 inhibitors, can be added to docetaxel without substantial toxicity, and has

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potential to enhance the activity of this standard of care treatment. We are excited to advance this program to the next stage of development.”

#### **Conference Call**

Synta management will be hosting a conference call today at 5:00 p.m. (ET) to discuss this announcement. The call can be accessed by dialing (877) 407-8035 or (201) 689-8035 prior to start. A slide presentation will be referenced on the call, which can be found on the Synta homepage at [www.syntapharma.com](http://www.syntapharma.com). The live, listen-only webcast of the conference call can be accessed by visiting the “Investors” section of the Synta Pharmaceuticals website, prior to the event.

For those unable to join the live conference call, a replay will be available approximately two hours after the completion of the call, and can be accessed by dialing (877) 660-6853 or (201) 612-7415, and by referring to both account number 286 and conference ID 396810. A replay of the webcast will be archived on the Company’s website for two weeks following the call.

#### **About Ganetespib**

Ganetespib is a potent inhibitor of heat shock protein 90 (Hsp90) that is structurally unrelated to first-generation, ansamycin-related Hsp90 inhibitors. In preclinical experiments, ganetespib has shown activity in multiple tumor models both as a single agent and in combination with certain widely used cancer agents. Company-sponsored clinical trials with ganetespib include 1) the GALAXY Phase 2b/3 trial evaluating ganetespib in combination with docetaxel as second-line treatment of non-small cell lung cancer (NSCLC), 2) the CHIARA Phase 2 trial evaluating ganetespib monotherapy in ALK+ NSCLC, and 3) the ENCHANT Phase 2 trial evaluating ganetespib as first-line treatment for HER2+ and triple-negative metastatic breast cancer. In addition, ganetespib is being evaluated in investigator-sponsored trials including lung, breast, prostate, gastric, pancreatic, and colorectal cancers as well as ocular melanoma, acute myeloid leukemia and multiple myeloma. Information on these trials can be found at [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

#### **About the GALAXY Trial™**

The GALAXY (Ganetespib Assessment in Lung cAncer with docetaXel) trial is a randomized Phase 2b/3 trial comparing the combination of ganetespib and docetaxel versus docetaxel alone in patients with Stage IIIB/IV NSCLC who have received one prior systemic therapy. More information about the GALAXY trial can be found at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (NCT01348126).

#### **About Hsp90**

Hsp90 is a molecular chaperone required for the proper folding and activation of many cancer-promoting proteins, and is recognized as a key facilitator of cancer cell growth and survival. Many of the “client proteins” of Hsp90 — such as ALK, AKT, BCR-ABL, BRAF, KIT, MET, EGFR, FLT3, HER2, HIF-1alpha, PDGFRA, VEGFR are the targets of clinically validated cancer drugs. In preclinical studies, inhibiting Hsp90 causes the degradation of multiple client proteins and leads to cancer cell death.

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## About Synta Pharmaceuticals

Synta Pharmaceuticals Corp. is a biopharmaceutical company focused on discovering, developing, and commercializing small molecule drugs to extend and enhance the lives of patients with severe medical conditions, including cancer and chronic inflammatory diseases. Synta has a unique chemical compound library, an integrated discovery engine, and a diverse pipeline of clinical- and preclinical-stage drug candidates with distinct mechanisms of action and novel chemical structures. All Synta drug candidates were invented by Synta scientists using our compound library and discovery capabilities. For more information, please visit [www.syntapharma.com](http://www.syntapharma.com).

## Safe Harbor Statement

This media release contains forward-looking statements about Synta Pharmaceuticals Corp. Such forward-looking statements can be identified by the use of forward-looking terminology such as “will”, “would”, “should”, “expects”, “anticipates”, “intends”, “plans”, “believes”, “may”, “estimates”, “predicts”, “projects”, or similar expressions intended to identify forward-looking statements. Such statements, including statements relating to the timing, developments and progress of our GALAXY trial and our clinical development plans for ganetespib, reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such forward-looking statements. Those risks and uncertainties include whether the results from the interim analysis of the Phase 2b portion of the GALAXY trial will be consistent with future data from the Phase 2b portion and the Phase 3 stage of the trial; whether the results at the conclusion of the Phase 2b portion of the trial will demonstrate safety and statistically significant efficacy; challenges with respect to patient enrollment or other delays in our clinical development plans; as well as other risks and uncertainties described in the “Risk Factors” section of our Form 10-K for the year ended December 31, 2011, as filed with the Securities and Exchange Commission, including those under the heading “Risks Related to the Development and Regulatory Approval of our Drug Candidates.” Synta undertakes no obligation to publicly update forward-looking statements, whether because of new information, future events or otherwise, except as required by law.

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