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14. ABSTRACT

The current paradigm for detection and treatment of breast cancer is based on clinical evaluation and anatomic imaging, usually with digital mammography or less commonly breast magnetic resonance imaging (MRI), followed by biopsy and surgery or surgery plus radiotherapy. While both mammography and MRI demonstrate excellent sensitivity for detecting tissue abnormalities, they lack sufficient specificity for unequivocally distinguishing malignant from normal tissue, or for discerning highly aggressive from less aggressive neoplasms. Activation of oncogenic signaling nodes occurs prior to the growth of tumors to a size that is anatomically detectable or displaces adjacent tissue, and prior to invasion and metastasis. Detection of these early molecular changes is not possible with existing imaging technologies used for breast cancer screening, but will be possible with the development of a new class of molecular imaging as we propose. We hypothesize that novel PM small molecule inhibitors that selectively target key deregulated intracellular signaling nodes in breast cancer cells can be utilized for detection and molecular characterization of early stage breast cancers using MRI and for subsequent targeted RF-mediated thermal ablation of malignant cells *in vivo*. The goal of this work is to develop multicomponent molecules that deliver PM contrast agents to selected cellular systems through targeted non-covalent interactions with specific enzymes to improve breast cancer detection and treatment. We propose to detect and characterize oncogenic signaling nodes in breast cells *in vivo*, to transform breast cancer diagnosis, characterization, risk stratification, treatment and ultimately prevention

15. SUBJECT TERMS
Breast cancer, HSP90, small molecule inhibitors, lapatinib, oncogenic signaling

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Table of Contents

1. Introduction

A major limitation in the diagnosis and management of breast cancer is a reliance on detectable anatomic changes associated with tumor growth. Our increasing understanding of the characteristic signaling networks perturbed in malignant cells provides an opportunity to identify these early changes associated with malignant behavior. We have exploited the high affinity and specificity of anti-cancer drugs specific for key oncogenic signaling in breast cancer cells to create new molecular entities consisting of the drug linked to a contrast moiety.

The resulting contrast linked drug retains the target specific affinity, and enables non-invasive imaging of the tumor cells that accumulate the drug. In addition, we have demonstrated that contrast linked drugs markedly enhance the potential for intracellular thermal therapy induced by applied near infrared light, and other contrast agents may be used in combination with high (MHz) radiofrequency (RF) energy, enabling selective thermal therapy.

Our contrast linked drugs thus serve as a dual function *intracellular* 'molecular antenna' for both optical, nIR, or MR contrast enhancement *and* nIR or RF mediated intracellular thermal therapy.

We hypothesize that novel contrast linked small molecule inhibitors targeting the intracellular signaling nodes in breast cancer can be utilized for the early detection and characterization using molecular non-invasvie imaging and subsequent nIR or RF mediated thermal therapy of malignant cells *in vivo*.

Phase I Objectives

In phase I, 3 projects supported by cores were proposed. While our initial focus on Hsp90 and HER2 inhibitor serves as "proof of concept" models, we propose to find appropriate PM drugs for specific subtypes of breast cancer.

Project 1 focused on Hsp90, which is a cellular chaperone to a number of proteins involved in oncogenic signaling including estrogen receptor, HER2, EGFR, and HIF1alpha, and significant progress was made using an optical and nIR contrast agent, that the Milestone meeting recommendation was made to concentrate on this agent.

The animal core is used to create in vivo models for the study projects. We prioritize candidates based on their ability to accumulate in subtypes of breast cancer (including triple negative breast cancer [TNBC]), to be detected by non-invasive imaging, and to mediate nIR or RF thermal therapy in preclinical models. We use the pathology and tissue acquisition cores to collect and annotate specific molecular subtypes of breast cancer to accumulate the nIR-Hsp90 inhibitor.

Phase II Objectives

Based on progress in the first phase of the study, we have advanced the most promising candidates to more complete preclinical assessment, screening models of human xengraft representing Triple Negative, HER2+ and ER+ breast cancers. In addition, we used syngenic models of murine tumors to detect more aggressive molecular subclones of the 4T1 model. Furthermore, we screened DCIS cell lines, and demonstrated detection of as few as 10,000

tumor cells in vivo. Finally, we have established and used spontaneous models of breast cancer, in order to model the early event of primary breast cancers, and determine optimal dosing and timing of imaging. We are scheduled for GMP manufacturing, GLP toxicity testing and Phase I clinical testing. We propose to determine the safety and feasibility of contast linked drug administration, with “proof on concept” detection of drug accumulation by nIR imaging. A final “proof of concept” will be based on the optimal dose found in the phase I clinical studies, to combine nIR imaging, and nIR or RF mediated thermal therapy. A long term goal will be identify and prioritize additional lethal oncogenic signaling nodes found in tumors that do not express Hsp90 or HER2 at levels sufficient to allow imaging and thermal therapy.

2. Keywords

Hsp90- Heat Shock Protein 90
Hsp90i- Hsp90 inhibitor
nIR- near infrared
PM- paramagnetic
PM-Hsp90i- paramagnetic Hsp90 inhibitor
TKI- Tyrosine Kinase Inhibitor
ER- Estrogen Receptor
PR- Progesteron Receptor
HER2- Human Epidermal growth factor Receptor 2
MRI- Magnetic Resonance Imaging
PET- Positron Emission Tomography
^{18}FDG-PET- Fludeoxyglucose Positron Emission Tomography
Gd-BOPTA- Gadobenate dimeglumine
GRP94- glucose-regulated protein 94
TRAP1- tumor necrosis factor receptor-associated protein 1
ER- endoplasmic reticulum (ER)
ATP- Adenosine-5'-triphosphate
HIF1a- Hypoxia-inducible factors
EGFR- epidermal growth factor recepto
PI3K- Phosphoinositide (PI) 3-kinase
AKT- member of the non-specific serine/threonine-protein kinase
AQUA- automated quantitative analysis
IHC- immunohistochemical
RF- radiofrequency
MHz- megahertz
kHz- kilohertz
CR- complete response
TNBC- triple negative breast cancers
MTD- maximum tolerated dose
CROs- contract research organizations
GLP- good laboratory practice
IND- investigational new drug
FDA- Food and Drug Administration (United States)
MS- mass spectroscopy
GCP- good clinical practice
ICH- International Conference on Harmonisation
PK- pharmacokinetic
PD- pharamacodynamic
P2D- phase II dose
PRF- proton resonance frequency
TR- relaxation time
GRE- gradient echo
MT- magnetization transfer

FSE- fast spin echo

3. Overall Progress Summary

Project 1-Aim 1: Lead Optimization Studies on Existing PM Hsp90 Inhibitors

While the overall goal of the project was to develop imaging agents that could visualize breast cancer cells in vivo using paramagnetic contrast agents detectable by magnetic resonance scanning, we had difficulties with the stability of our original ferrocene gold – tethered Hsp90 inhibitors. At that time, it became clear that critical in vitro and in vivo imaging could be accomplished using contrast agents that could be detected using high throughput, non-radioactive methods. Therefore, early versions of the contrast agent tethered Hsp90 inhibitors were synthesized using optical and near infrared contrast agents which could be visualized by readily available instruments in the laboratory and in our animal facilities.

To support our decision, we held a formal External Scientific Advisory Committee (ESAC) meeting in January 2014, which concurred with this strategic decision (See appended formal ESAC report as **APPENDIX A**.)

Project 1-Aim 1. Task 1: Define a minimum of 6 bioavailable PM-Hsp90i

Figure 1 summarizes the chemistry efforts for synthesis of tethered inhibitors of Hsp90 targeting the ectopically expressed oncogenic form of Hsp90, with a full list of the synthesized and characterized compounds listed in **APPENDIX B**. The figure illustrates the diversity of imaging probes that have been tested in both cell and animal models of breast cancer.

Figure 1

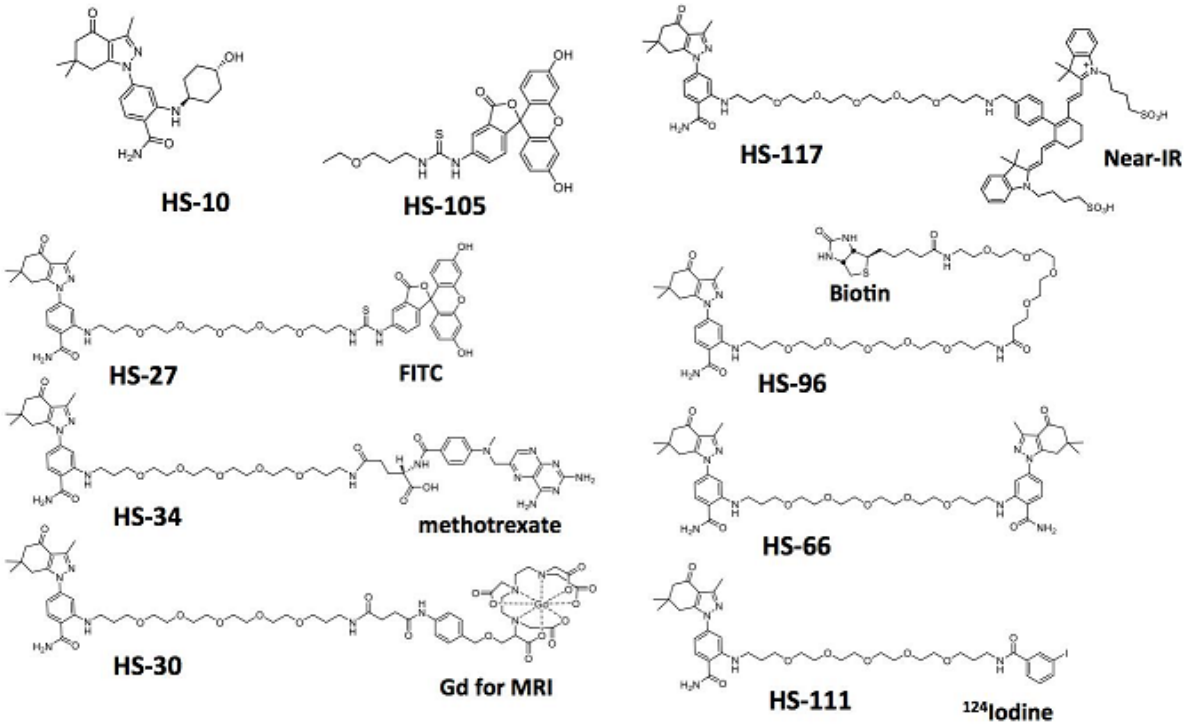


Figure 1. Showing molecular chemistry for the development of multi modal imaging of oncogenically activated Hsp90. (Barrott et al, 2013 Cell Biol.; 20(9):1187-9

Collectively over 60 variants of the compounds have been synthesized. This work has enabled us to not only test the concept of imaging an oncogenic signaling node (such as Hsp90) in vivo, but has potential defined a new cellular pathway that may signify aggressive behavior. Furthermore, this same pathway may be utilized to specifically deliver either MRI active imaging agents for RF studies or toxic payloads such as I^{131}. Much of this work is described in our recent paper Barrott et al. 2013. (Barrott JJ, Hughes PF, Osada T, Yang XY, Hartman ZC, Loiselle DR, Spector NL, Neckers L, Rajaram N, Hu F, Ramanujam N, Vaidyanathan G, Zalutsky MR, Lyerly HK, Haystead TA. Optical and radioiodinated tethered Hsp90 inhibitors reveal selective internalization of ectopic Hsp90 in malignant breast tumor cells. Chem Biol. 2013 Sep 19;20(9):1187-97. doi: 10.1016/j.chembiol.2013.08.004. Epub 2013 Sep 12.)

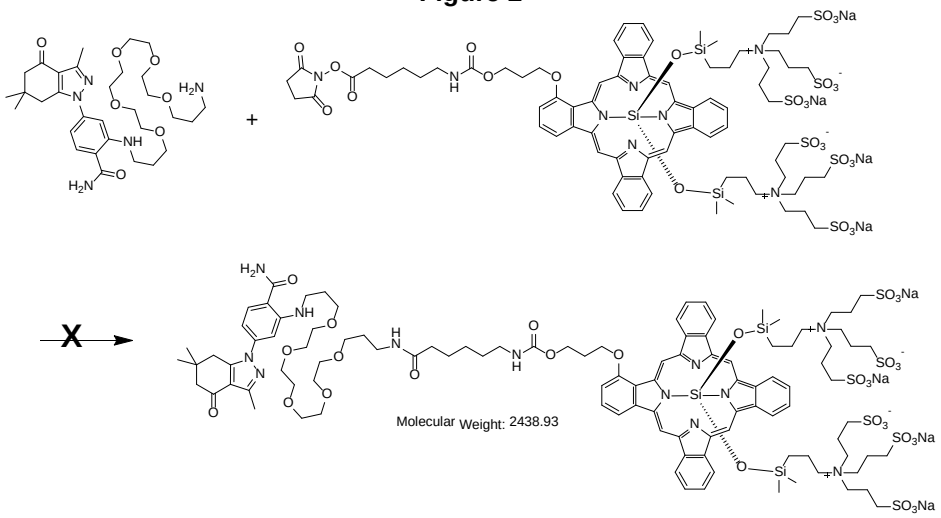
Project 1-Aim 1. Task 2: Demonstrate that our 6 lead molecules promote cell death in response to RF

Due to difficulties with the stability of our original ferrocene gold – tethered Hsp90 inhibitors and a lack of cellular penetrance of the caged gadolinium versions (as measured by the absence of the expected HER2+ knock down and Hsp70 induction in various breast tumor cell lines, indicating that the Hsp90i was not entering the cells) we have been unable to proceed to RF studies. However, from what we have learned from studies with fluorophorotinilated versions it is likely that this goal can be met during the next phase of the project.

To pursue this approach further we have synthesized several nano-gold particle versions and are currently examining their internalization into cells by transmission electron microscopy. Many of the issues with the metal carrying versions appear to be related to either the molecular size of the chelating moiety or chemical stability of the molecule itself in the presence of the metal. We report now that our attention to nIR conjugates has allowed us to create a photodynamic therapeutic, as described below.

We first attempted to conjugate our Hsp90 ligand plus linker with Licor 700DX, a Near IR fluorescent moiety based on different scaffolding from the cyanine dyes used previously. Conjugates of antibodies with Licor 700DX have been reported to be useful in targeted photodynamic therapy. Our standard ligand, HS-23, was reacted in excess with Licor 700DX. Analysis of the reaction mixture showed a large number of peaks containing the blueish color of the dye, but none containing the Hsp90 binding moiety. Generally, this has been a robust type of reaction and the plethora of products suggests some issues with the dye. We were somewhat mystified by the unorthodox bonding of silicon in Licor's structural drawing and perhaps it represents not a single moiety but a generalized structure of some detergent they use to get aqueous solubility.

Figure 2



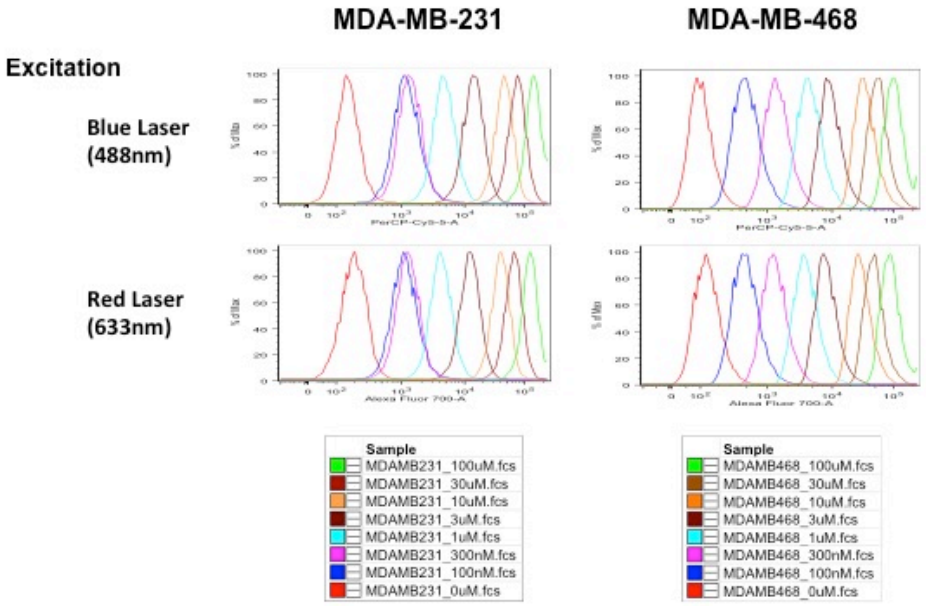
We'll analyze the dye alone to see if it is a single moiety and try to get a mass spectrum to characterize it.

As an alternative, we also generated a cojugate with Verteporfin, which is clinically used phototherapy agent, which when stimulated by nonthermal red light with a wavelength of 689 nm[1] in the presence of oxygen, produces highly reactive short-lived singlet oxygen and other reactive oxygen radicals . It is an attractive option, as it is currently FDA approved for clinical use, and may make the proof of concept clinical trials more feasible, as the parent compound in well known, with a very clear toxicity profile, and clinical instruments are available to provide the appropriate nIR energy to produce the phototherapeutic effects.

After producing this compound, designated HS201, we first tested in vitro uptake and imaging by FACS, as seen below (**Figure 3)**.

Figure 3

Uptake of HS201 (Verteporfin-Hsp90 inhibitor) by Human Breast Cancer Cell Lines



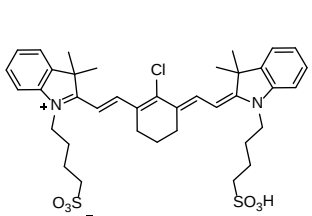
MDA-MB-231 and MDA-MB-468 cells were incubated with/without HS201 (100, 30, 10, 3, 1, 0.3, 0.1, 0 μM) for 30 min at 37°C. Cells were washed with PBS twice and acquired by LSRII flow cytometry machine. Blue Laser (488 nm) or Red Laser (633 nm) were used for excitation and signal was detected with filter 710/50 nm.

Based on the promising in vitro update, we are planning on in vitro toxicity studies in the presence and absence of nIR light, and then will advance these studies to in vivo studies in the primary model of breast cancer, and then extending to the molecular subtypes of breast cancer.

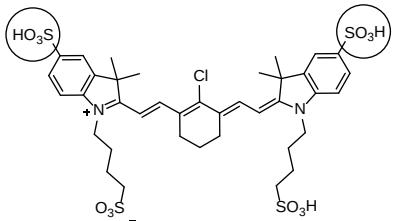
Addition Synthetic Chemistry Efforts

After substantial efforts, a reliable method for the synthesis of the di-sulfonated version of IR783 (shown below) was developed. We were able to make around 730 mg. of the pure dye. It was registered as HS-100200-01. Interestingly, we found a couple of sources claiming to sell this but it would have costs around $250K to get this amount of material.

Figure 4



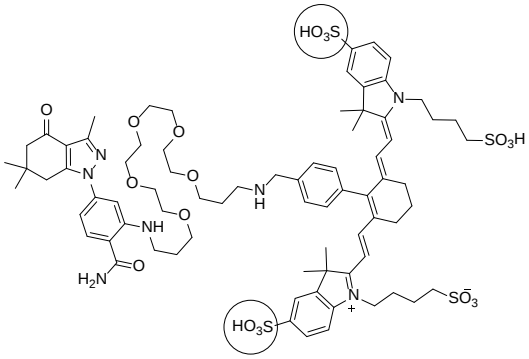
IR-783



PFH-007-027A, HS-200

We were able to use this material to produce a water soluble analog of HS-117. This was registered as HS-100196-01.

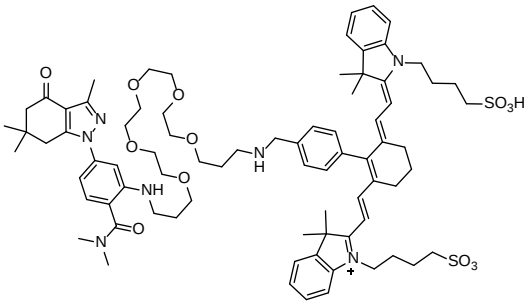
Figure 5



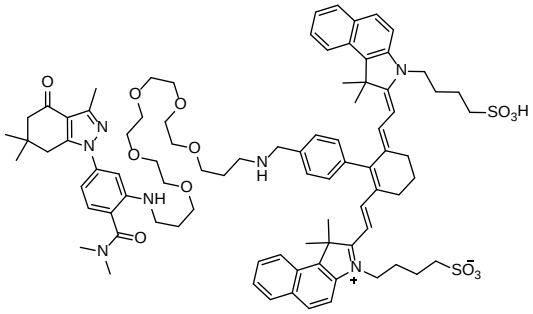
HS-100196-01

There has been considerable debate on the proper control compound to use for studies with these Hsp90 linked nIR dyes. To get perhaps more appropriate controls which incorporated both the dye and most of the structural elements of the Hsp90 inhibitor in a non-binding form, we synthesized dimethyl amide analogs of each of the benzyl amine dyes HS-117, HS-118, HS-131 and HS-196.

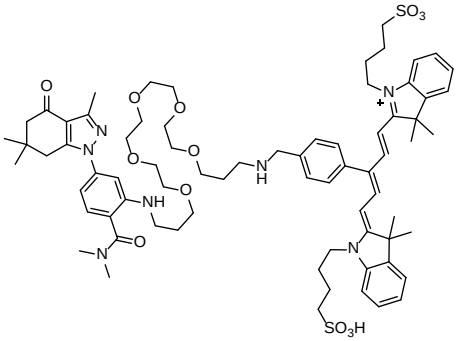
Figure 6



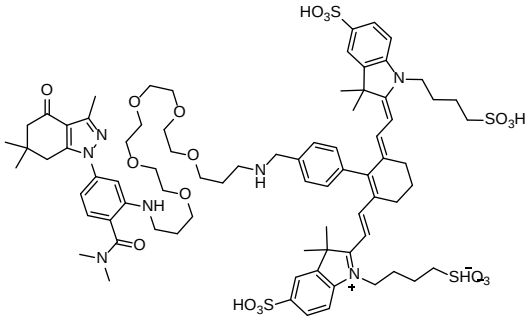
HS-186, control for HS-117



HS-185, control for HS-118



HS-198, control for HS-131

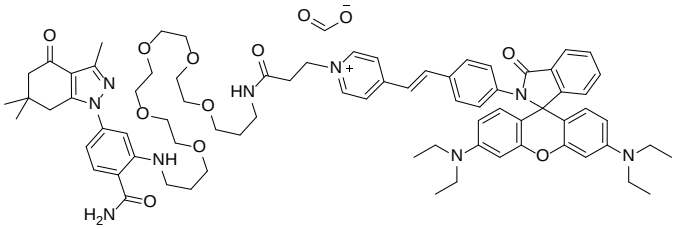


HS-199, control for HS-196

Based on previous SAR of this class of molecules, the dimethyl analogs should have much lower affinity for Hsp90, but these must be tested. We continune to use untethered contols contrast agents.

We have had previous discussions with the Moerner lab at Stanford on using their high resolution imaging technology with the Hsp90 probe. Toward that end, we have made and delivered one analog (HS-100183-01, 120 mg) with our probe connected to their imaging agent. Synthesis of their probe and coupling to our ligand was done in our lab. We have discovered some stability issues with the linking strategy of HS-183, a slow though not surprising retro-Michael reaction leading to cleavage of the dye. We are trying, so far without success, to develop more stable analogs while maintaining the necessary spectral qualities of the quaternary pyridine.

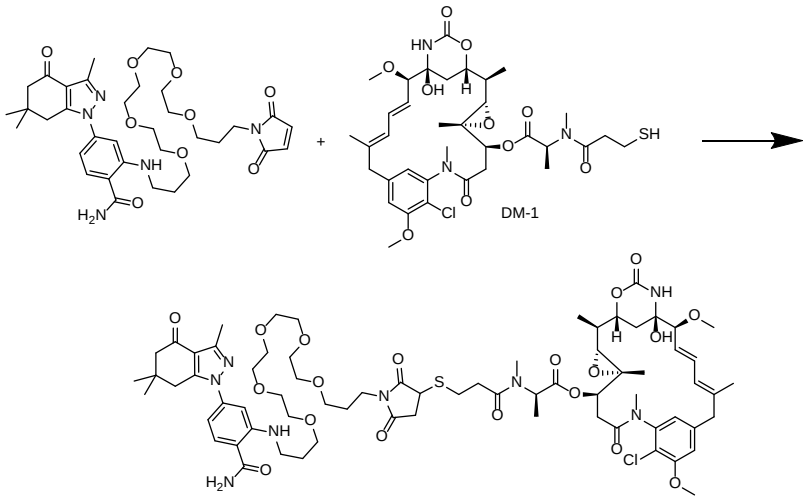
Figure 7



HS-183

As part of our toxin delivery strategy, Dr. Hughes received a supply of DM-1(mertansine) from Genentech and coupled it to his previously prepared maleimide, as shown, to give about 15 mg. the targeted toxin, HS-100184-01.

Figure 8



Preliminary testing in the lab suggested that the compound is stable and maintains its cytotoxicity, so a larger batch (HS-100184-02, 144 mg) was prepared for *in vivo* evaluation. Dr. Hughes has started preparation of the document for the manufacture of HS-118. It will be similar to the document prepared for HS-117 about a year ago.

In addition, HS-106 was resynthesized (HS-100106-02) to give 3.7 g.

Biologic Studies of Hsp90 Internalization

High-resolution confocal microscopy with HS-131 (nrIR tethered Hsp90 inhibitor) suggests that aggressive breast tumor lines actively internalize ectopically expressed Hsp90 through a clathrin dependent pathway. Importantly this pathway does not seems to be active in normal or more benign cells such as MCF10A cells. To understand the potential triggers of this pathway we examined over expression on p110 in MCF10A cells. The induced overexpression of p110-tHER2 in MCF10A cells leads to an increase in Hsp90 internalization and/or surface Hsp90 as visualized with the increased fluorescence of HS131 uptake. We are currently looking to see if a kinase dead mutant of this p110 fragment diminishes this increase. In conjunction with Lyerly group, we have been testing the internalization of HS198, a dimethyl analog of the HS131. This probe was developed as an inactive form of HS-131 and would serve as a control for in vivo animal studies. The dimethyl group significantly reduces the rate at which the drug is internalized (as shown by log and quarter-log dilutions) in both puncta and overall fluorescence. In addition, HS131 is retained in cells at higher levels than HS198. High resolution confocal microscopy shows surface HS131 clusters colocalize with Hsp90, further confirming that these are not non-specific drug aggregates. In looking at the mechanism of internalization of HS131, we have found some evidence that transferrin (a marker for receptor-mediated endocytosis) colocalizes with some HS131 clusters in MDAMB468 cells. To define the molecular mechanism of internalization we have developed stable siRNA lines for AP1g, a clathrin adaptor protein, to observe if Hsp90/HS131 internalization is clathrin-dependent. Because MDAMB468 cells are difficult to transfect (optimized transfection is only ~20%), we chose a scheme that involves creating viruses using the pSUPERIOR system. All shRNAs (3 different ones) have been cloned and are ready (this process took ~2 weeks). The cells have recently been infected with a virus expressing the TetR gene and are under selection - the last round of selection resulted in all cells (infected and control) dying, so this is the second round of TetR infection/selection. Provided successful selection, the shRNA viruses should be ready to be added next week or soon after. In addition, we have been optimizing live imaging of HS131 internalization. Using flow cytometry we have been investigating surface (non-permeabilized) Hsp90 expression in response to treatment with the Hsp70 inhibitor HS72. Our preliminary results suggest that surface Hsp90 may increase in response to overnight treatment with HS72, but further optimization is required to confirm this.

Project 1-Aim 2. Testing -Hsp90i in animal models to demonstrate molecular MRI and RF mediated thermal therapy

As discussed above, the majority of our PK studies have involved our fluorophor versions using the whole body imaging by IVIS, whole organ and tumor analysis by IVIS, and chromatographic analysis are presented below. These studies have shown that the PK and PD properties of our tethered compounds are very much influenced by the structure of the fluorophor and the mode of delivery.

Fluorescein probes

Fluorescein probes were first synthesized as they could be easily detected using microscopes, flow cytometers, and in vivo tumors implanted subcutaneously near the animal's surface could be visualized using readily available instruments.

For example when a fluorescein version (referred to as HS-27) is injected IV, the molecule is cleared rapidly from the serum within 30 minutes, but rapidly accumulates within the tumor to µM level (8-15µM) and is then slowly eliminated from the tumor over 24-48 hours (Tumor T1/2 ~12 hours). When injected interperitoneally (IP), HS-27 accumulation in the tumor peaks at 2 hours and remains at µM levels for up to 72 hours. Serum levels are expected to be constant during this time as the molecule diffuses across the peritoneal cavity into the blood stream.

Near infrared probes

Near infrared versions (nrIR) such as HS-117 and 131 vary significantly in their PK and PD characteristics. Both are eliminated very rapidly from the serum upon IV administration, but rapidly absorbed into human xenografted breast tumors. The molecule HS117 has a tumor T1/2 of ~6 hrs, whereas HS131 has a tumor T1/2 >72 hours and is still detectable in tumors by IVIS after 7 days. Importantly all fluor versions show exquisite recognition of the tumor over all other tissues.

This specificity was determined by harvesting the organs from animals injected with each probe and extracting the tethered probes for chromatographic analysis from each organ, demonstrating the absence of the probe. Much of this work is described in our recently publication (Barrott et al. 2013) More recently, we have developed a more sensitive high through put reverse phase method for quantifying the levels of each probe in serum and tissues. This approach will be utilized for the planed clinical studies with our current lead molecule HS-131. This method will enable sensitive quantitative detection of parent probe and any metabolites at the pmol level in tissue and serum samples.

In vivo imaging

The small animal core is the primary source supplying tumor-bearing SCID mice for tumor imaging experiments performed by investigators in this project. To generate data, we first needed to establish breeding colonies of SCID mice to allow for xenograft generation. Breeding pairs, cages, and daily housing costs were incurred to establish these colonies. Next, we accomplished in vitro expansion of tumor cells to be used for creating the xenograft in order to have a stable collection of cells. These cells were cryopreserved for the establishment of a library of similar passage cells for use. Finally, breast cancer cells lines were tested in vitro for update of the Hsp90 probes. Cell lines that demonstrated in vitro uptake we then tested for in vivo uptake.

In vivo imaging with fluorescein probes

We assessed in vivo labeling of human breast tumors with HS-27 (FITC-tethered HSP90 inhibitor) in the 1st year of the project, and demonstrated the tumor uptake of HS-27 and it's retention at 24 h time point. However, because of the limited penetrance of FITC signals through the tissue, and the high background from fur autoflouresence, signals detected from in vivo tumors were relatively weak.

To further test the possibility of FITC-tethered HSP90 inhibitor localizing to tumor in vivo, we obtained new compound HS-113. HS-27 and HS-113, with control compound (dye with linker) HS-105, were tested for the labeling of in vivo breast cancer xenografts in mice.

HS-27, HS-113, and HS-105 (control compound without HSP90 inhibitor) were injected to a triple negative (MDA-MB-468) tumor-bearing SCID mice via tail vein. Dose of 1 µmol was used

for all the compounds. At multiple time points (3, 6, 12, and 24 hours after injection), FITC signals of HSP90 compound injected mice were analyzed by IVIS imager (Excitation: 465 nm, Emission GFP filter, Exposure 1.0 sec). MDA-MB-468 tumor-bearing mouse without compound/dye injection was used as a negative control for imaging.

As shown in **Figure 9**, at the earlier time point of 3 hours after compound injection, we could detect FITC signals from tumors with the new compound HS-113, while this signal was not so significant with HS-27. The intensities of FITC signals from tumors were the strongest at 3 hour time point, and declined till 24 hour time point. From the normal skin area with hair, we observed significant autofluorescence. Strong background signals with HS-27, HS-113 and HS-105, was observed at earlier time points after compound administration, but the signals diminshed by 24-hours.

In **Figure 10**, the same data set with Figure 9 was aligned to show over time change for each HSP90 inhibitor compound.

Figure 9

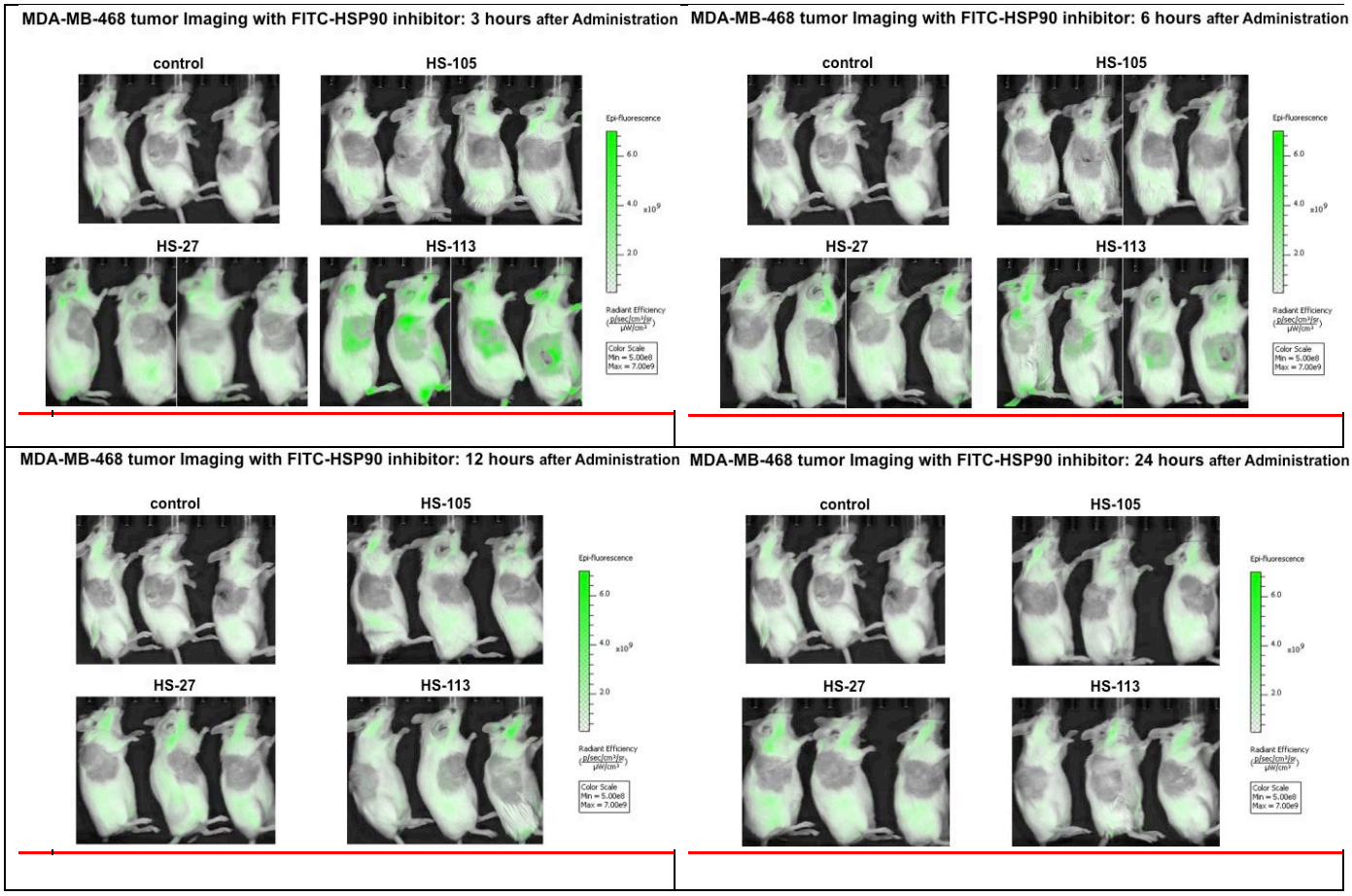


Figure 9. FITC-HSP90 inhibitor Imaging of triple negative MDA-MB-468 tumors in mice. SCID mice were injected with MDA-MB-468 tumor cells (1 M cells/mouse). When tumor size reached ~10 mm in diameter, FITC-HSP90 inhibitors (HS-27, HS-113), control compound (HS-105) was administered (1 µmol

in 50 µL vehicle) via tail vein. FITC signals were detected by IVIS Imager machine (Ex: 465 nm, Em: GFP filter, Exp 1 sec) 3, 6, 12 and 24 hours after administration.

Figure 10

HS-27 **HS-113** **HS-105**

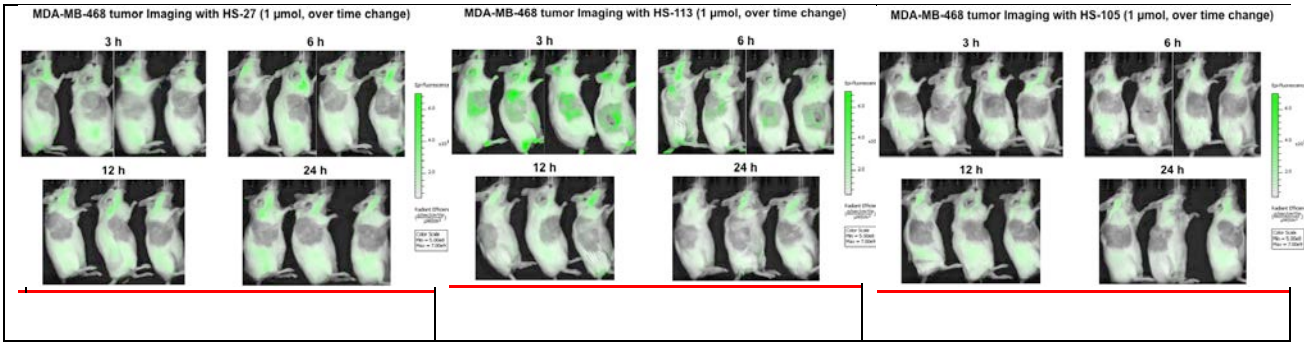


Figure 10. FITC-HSP90 inhibitor Imaging of triple negative MDA-MB-468 tumors in mice (over time change for each compound). FITC signals were detected by IVIS Imager machine (Ex: 465 nm, Em: GFP filter, Exp 1 sec) 3, 6, 12 and 24 hours after administration. Over time change for each HSP90 inhibitor compound (Left: HS-27, Center: HS-113, Right: HS105) is shown.

In **Figure 11**, to compare the detectability of tumor-derived FITC signals, FITC signal levels (Radiant Efficiency) from tumor tissues of individual mice are plotted. Mice injected with HS-113 showed the highest radiant efficiencies at 3 and 6 hour time points, showing better imaging of MDA-MB-468 tumor xenografts compared to HS-27. However, there was an early washout of the compound from the tumor tissues, based on IVIS imaging of mice, and signals decreased to background level by 24 hour time point.

Figure 11

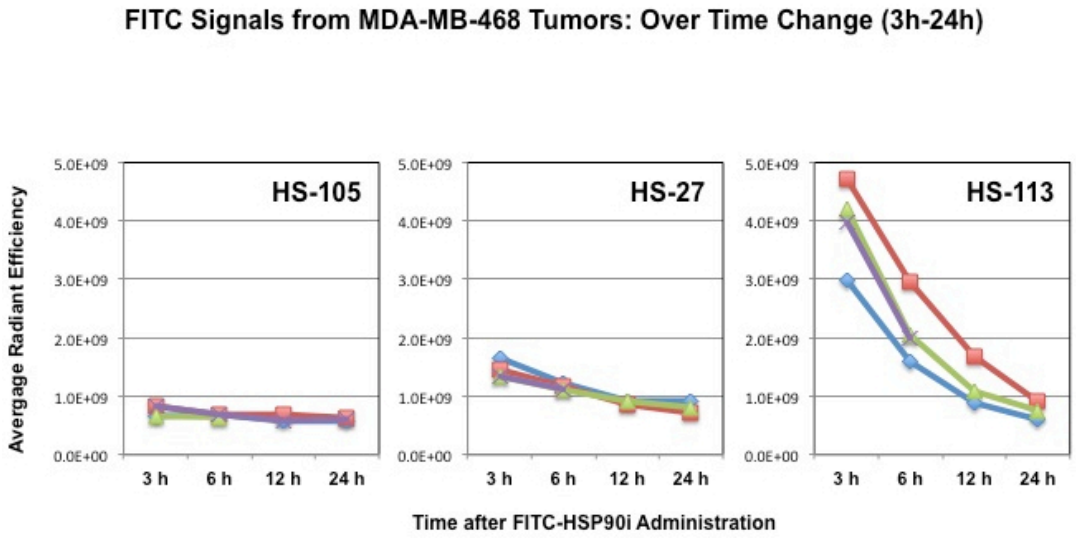


Figure 11. FITC Signals detected from MDA-MB-468 xenograft in mice after FITC-HSP90 inhibitor administration: Comparison of HS-27, HS-113, and HS-105. FITC signals were detected by IVIS

Imager machine (Ex: 465 nm, Em: GFP filter, Exp 1.0 sec) from 3 hours till 24 hours after FITC-HSP90i administration to MDA-MB-468 xenograft-bearing SCID mice. Overtime change of FITC signals (Radiant Efficiency) are shown in the graphs.

To test the accumulation of FITC-HSP90 inhibitor compounds in organs, mice injected with 1 µmol compounds were sacrificed 6 or 24 hours after tail vain injection of compounds, and organs were excised. Emission of FITC signals was analyzed by IVIS imager (465 nm excitation filter, GFP emission filter, 1 sec exposure). Images of each organs/tumors are shown in **Figure 12** (below). Imaging with HS-113 showed the strongest signals in tumor tissue, compared to HS-27. For reasons that are not clear, lung tissue showed significant accumulation of HSP90 inhibitor compound with HS-113.

Figure 12

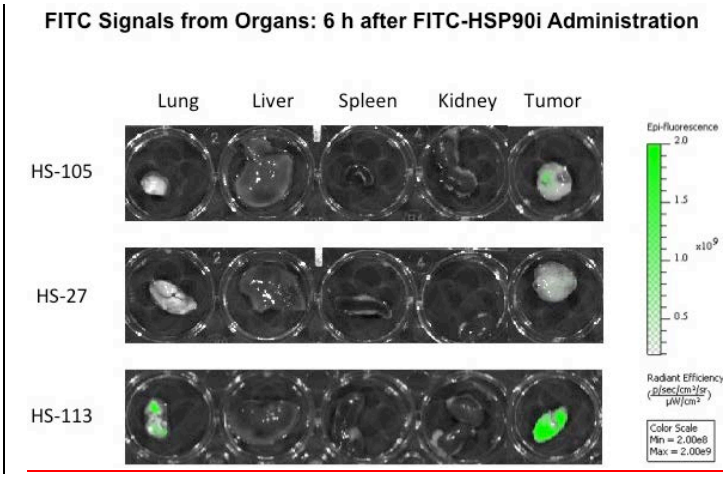


Figure 12. Tissue Distribution of FITC-HSP90 inhibitors: 6 hours after administration. Six hours after the tail vein injection of FITC-HSP90 inhibitor (HS-27, HS-113, HS-105; 1 µmol/mouse), mice are sacrificed and the organs (lung, liver, spleen, kidney) and tumors were excised and put into 24 well plates. FITC signals were analyzed by IVIS Imager machine (Ex: 465 nm, Em: GFP filter, Exp 1.0 sec).

Figure 13A

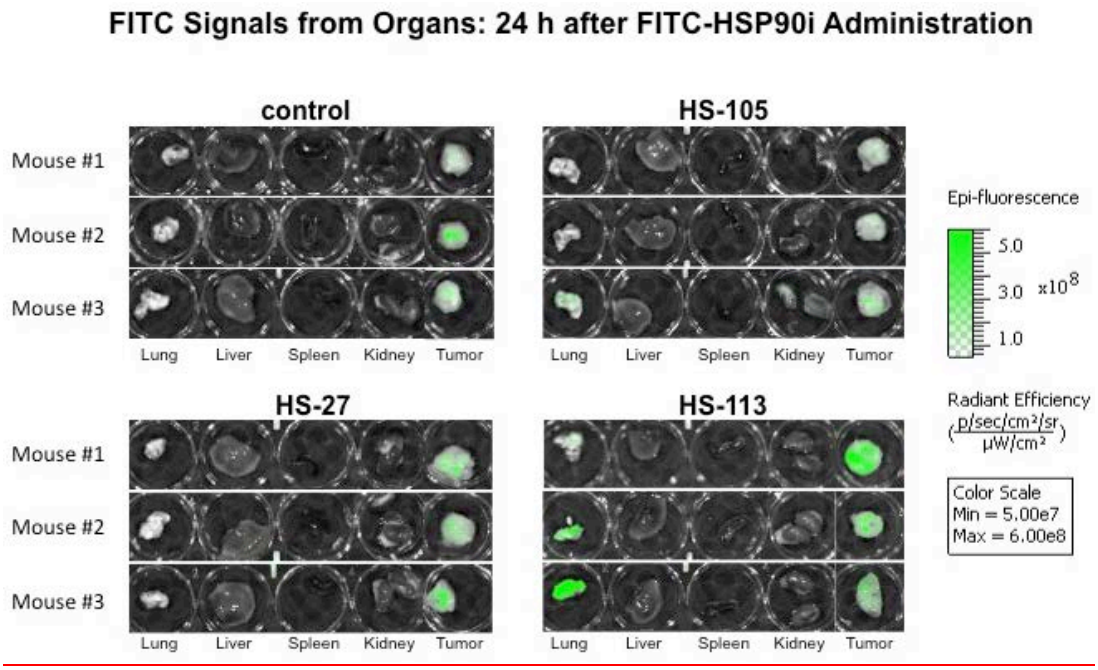


Figure 13A. Tissue Distribution of FITC-HSP90 inhibitors: 24 hours after administration. Twenty-four hours after the tail vein injection of FITC-HSP90 inhibitor (HS-27, HS-113, HS-105; 1 µmol/mouse), mice are sacrificed and the organs (lung, liver, spleen, kidney) and tumors were excised and FITC signals were analyzed by IVIS Imager machine (Ex: 465 nm, Em: GFP filter, Exp 1.0 sec).

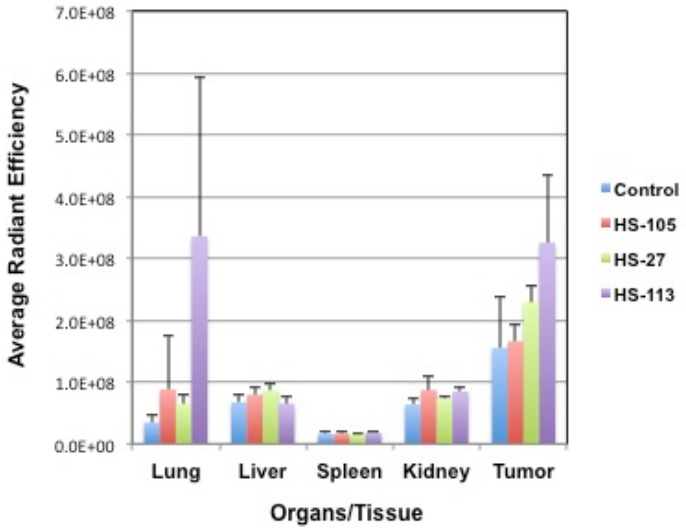


Figure 13B. Tissue Distribution of FITC-HSP90 inhibitors: 24 hours after administration. Twenty-four hours after the tail vein injection of FITC-HSP90 inhibitor (HS-27, HS-113, HS-105; 1 µmol/mouse), mice are sacrificed and the organs (lung, liver, spleen, kidney) and tumors were excised and FITC signals were analyzed by IVIS Imager machine (Ex: 465 nm, Em: GFP filter, Exp 1.0 sec). The graph shows Radiant efficiencies for each organ in each compound administered mouse.

Figure 13A shows imaging of organs/tumor tissues that were excised 24 hours after iv administration of FITC-HSP90 inhibitor. **Figure 13B** shows the average radiant efficiency for each tissue with each compound. At 24 hours, imaging with HS-113 showed stronger FITC signals in tumor tissue compared to HS-27 or HS-105, similar trend with 6 hour time point. Some lungs from HS-113 injected mice showed strong FITC signals. Tumors were put into 24

well plate and FITC signals were detected simultaneously (**Figure 14**). As shown in right figure, HS-113 made stronger signals in tumor tissues.

Figure 14

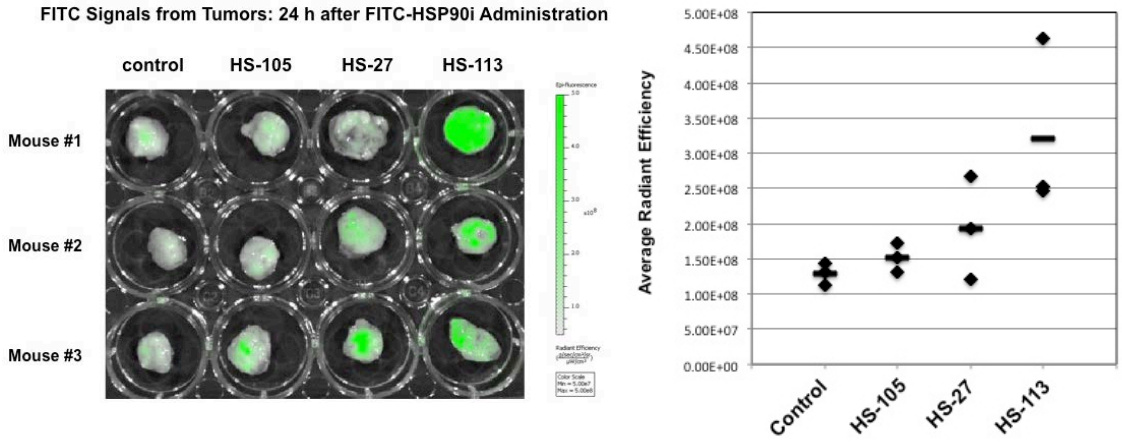


Figure 14. FITC-HSP90 inhibitor Imaging of MDA-MB-468 tumor in vivo: IVIS image analysis (24 h). Twenty four hours after FITC-HSP90 inhibitor compound administration, mice were sacrificed and FITC signals of excised tumors were detected by IVIS Imager machine (Ex: 465 nm, Em: GFP filter, Exp 1 sec). Radiant efficiency for each tumor is shown in the right graph. Control: tumors from mice without HSP90 inhibitor administration.

In summary, based on the earlier time point results of imaging with HS-27, HS-113, and HS-105,

1) HS-113 injection made the strongest FITC signals from tumor tissues by IVIS imager compared to other FITC-HSP90 inhibitor compounds.
2) Radiant Efficiency of tumors with HS-113 imaging showed early peak (3 h or less than 3 h).
3) Although some mice with HS-113 injection showed strong FITC signal in the lungs, other organs were relatively low compared to tumors in these mice.
4) Normal organ uptake of FITC-HSP90 inhibitors was relatively lower in mice injected with HS-27.
5) To make imaging of tumors in vivo, HS-113 was more efficient than HS-27, but on the other hand, lung accumulation was detected with HS-113, which might be negative for tumor imaging.

<u>In vivo imaging with near infrared probes</u>

In our previous preliminary experiment, we tested FITC-HSP90 inhibitors, HS-27 and HS-105 at doses of 1 µmol for injection. Therefore, we tested tumor imaging with NIR-HSP90 inhibitors (HS-117, HS-119, HS-131, 132) and control compounds (HS-124, HS152) in earlier phase until 24-hour time point.

Table 1: NIR-HSP90 Inhibitor Compounds
(See APPENDIX B for detailed structure)

	HS #	Notebook #	mol. Wt.	desc.
a	HS-100117-03	PFH-005-022A	1384.8	780 amine
b	HS-100118-01	PFH-005-007B	1484.9	820 amine
c	HS-100119-01	PFH-005-009C	1398.8	780 amide
d	HS-100120-01	PFH-005-010A	1498.9	820 amide
e	HS-100131-02	PFH-005-037B	1318.7	640 amine
f	HS-100132-01	PFH-005-038A	1332.7	640 amide

1) In vitro and in vivo Imaging with NIR-tethered HSP90 inhibitor compound : HS-117
First, we tested the NIR compound HS117 in vitro. As shown in **Figure 15**, HS117 labeled MDA-MB-468 cells with much higher intensities even without the permeablizing agent, escin treatment in vitro, suggesting that HS117 can enter the cells more easily compared to HS27.

Figure 15

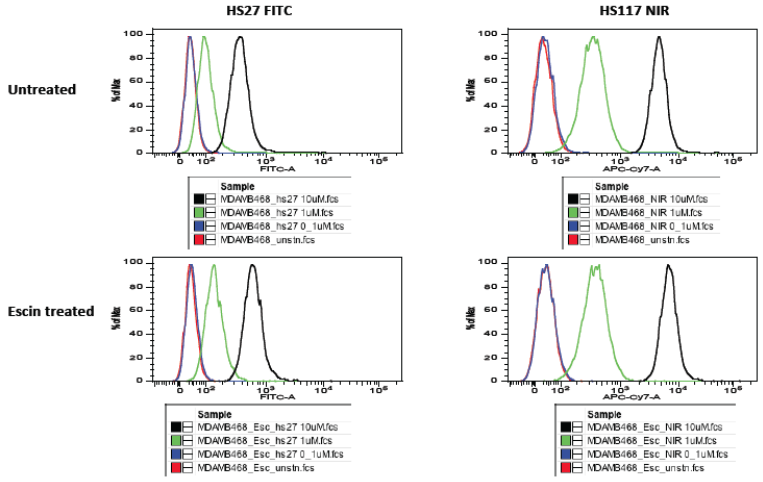


Figure 15. Comparison of MDA-MB-468 breast cancer cell labeling with HS27 and HS117: Flow cytometry assay. In vitro cultured MDA-MB-468 were labeled with HS27 or HS117 (0.1, 1, 10 μM) with/without escin treatment. After 30 min incubation, cells were washed with PBS and acquired by LSRII machine. Red: unstained, Blue: 0.1 μM, Green: 1 μM, Black: 10 μM.

To test the detection limit of tumor cells labeled with HS117, female SCID mice were injected with different number of in vitro HS117-labeled MDA-MB-468 cells. In our previous progress report, we reported that tumor cells in vitro labeled with our previous nIR-tethered HSP90 inhibitor (HS70) could be detected by IVIS imager at the lower number of 100,000 cells/site. As shown in the **Figure 16** (below), with our new nIR-tethered compound (HS117), we could detect the signals from even smaller numbers of the cells (10,000 cells/site). Average Radiant Efficiency for each cell number is shown in the right graph. Linear increase of Radiant Efficiency was observed according to the injected cell numbers, suggesting that larger tumors will have stronger signals.

Figure 16

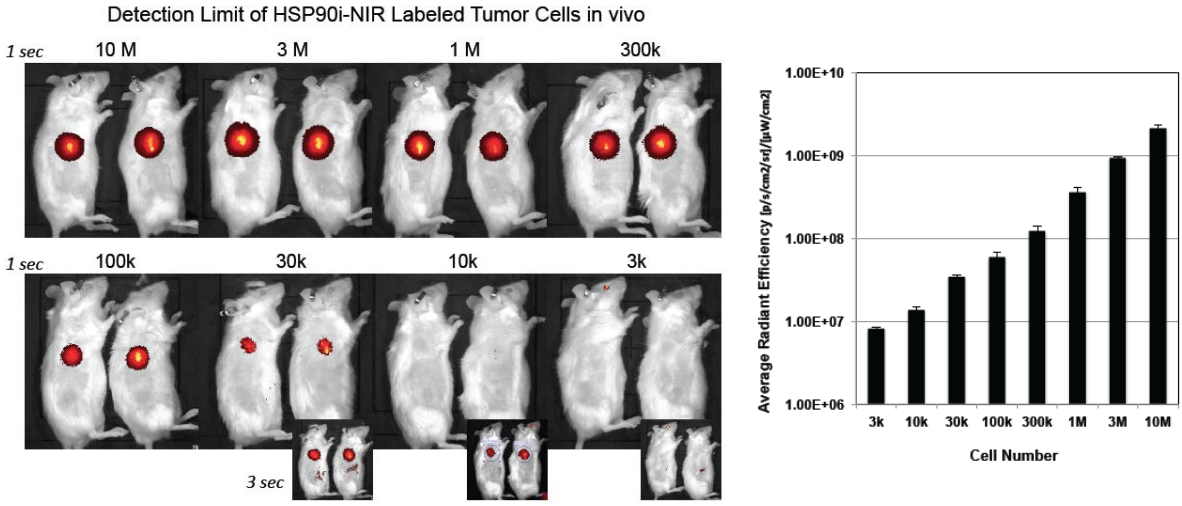


Figure 16. Detection limit of HS117 labeled tumor cells in vivo. BT474M1 cells were labeled with HS117 (10 µM) in vitro for 30 min, and washed with PBS. Different numbers of cells were subcutaneously injected to the upper flank of mice. As a control, unlabeled BT474M1 tumor cells with the same number of cells were injected to the lower flank. After injection of cells, images were taken by IVIS machine to detect nIR signals. Exposure was done for 1 or 3 seconds.

We could detect strong NIR signals from the surface of tumors by using IVIS image analyzer even at low dose injection of HS117 (**Figure 17**). At the dose of 10 nmol or above, clear nIR signals were detected even at 0.1 sec exposure. With longer exposure of 1 sec, even the lowest dose (5 nmol) could show signals in tumor area. The signal detection was confirmed even 5 days after intravenous injection.

Figure 17

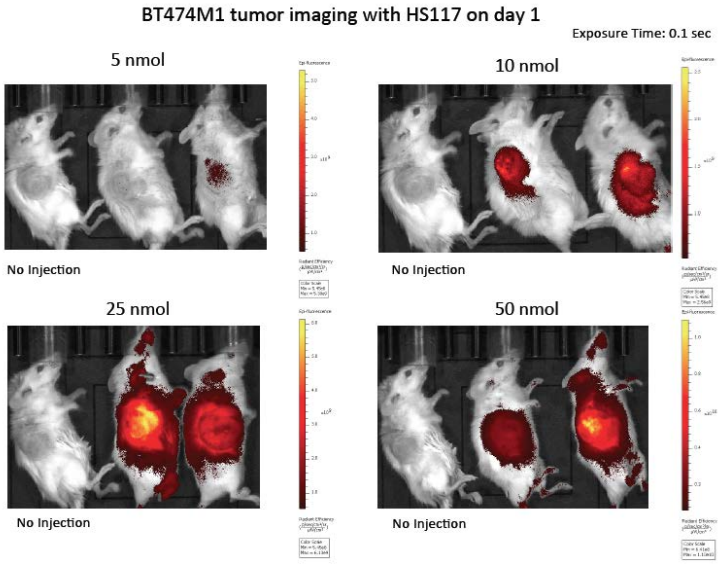


Figure 17. Detection of BT474M1 tumors in mice with different doses of HS117 using IVIS imager. BT474M1 cells were injected to the flank of mice, and when tumors reached over 1 cm in diameter, mice were administered with HS117 (5, 10, 25 or 50 nmol) via tail vein, and 24 hours later images were taken under IVIS machine. The mice in the left side are control mice without HS117 injection.

The small metastatic subcutaneous nodule observed on the back of a mouse showed very intense signals even 5 days after HS117 injection (**Figure 18**), showing the efficacy of HS117 to detect small metastatic lesions. This suggests that HS117 may also be an effective imaging reagent for advanced/metastatic breast cancer.

Figure 18

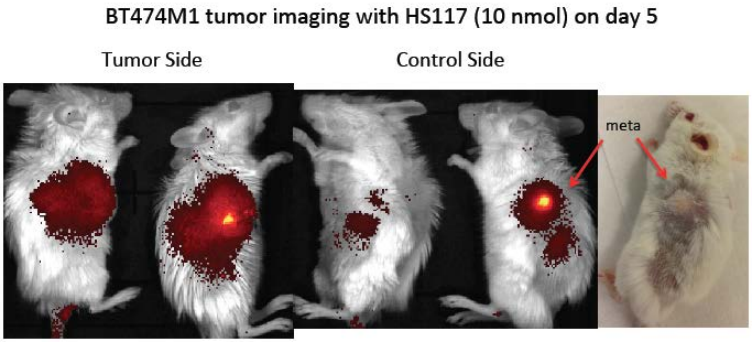


Figure 18. Detection of metastatic breast tumor 5 days after HS117 injection. Two BT474M1 tumor-bearing mice were administered with HS117 (10 nmol) and images of tumor implanted side and opposite side were taken using IVIS machine. Right side mouse had ~6 mm size metastatic nodule (shown in the picture in right: arrow), which showed very strong nIR signal.

2) Testing of second generation NIR-tethered compounds: HS-119, HS-131, HS-132

In the previous section, the efficacy of imaging with our first NIR-tethered compound, HS-117, was tested and it was proved to be an effective compound compared to the FITC-tethered compounds, with strong signals from tumor tissues even 5 days after compound injection to mice. In this section, we further compared the imaging efficacy of a series of second generation NIR-tethered HSP90 inhibitor compounds, HS-119, HS-131 and HS-132.

In Vitro Labeling of MDA-MB-468 cells and Imaging by IVIS Imager

To test the efficacy of labeling tumor cells with these compounds, triple negative MDA-MB-468 tumor cells were labeled with NIR-HSP90i compounds, and imaging analysis was performed by IVIS imager machine. Tumor cells were incubated for 30 min at 37C with NIR-HSP90i at titrated concentrations (0.03 µM ~100 µM), then washed twice with PBS. NIR signals were detected with IVIS machine with 745 nm excitation filter/ICG emission filter for HS-117/118/119/120, and with 640 nm excitation filter/Cy5.5 emission filter for HS-131/132.

Figure 19

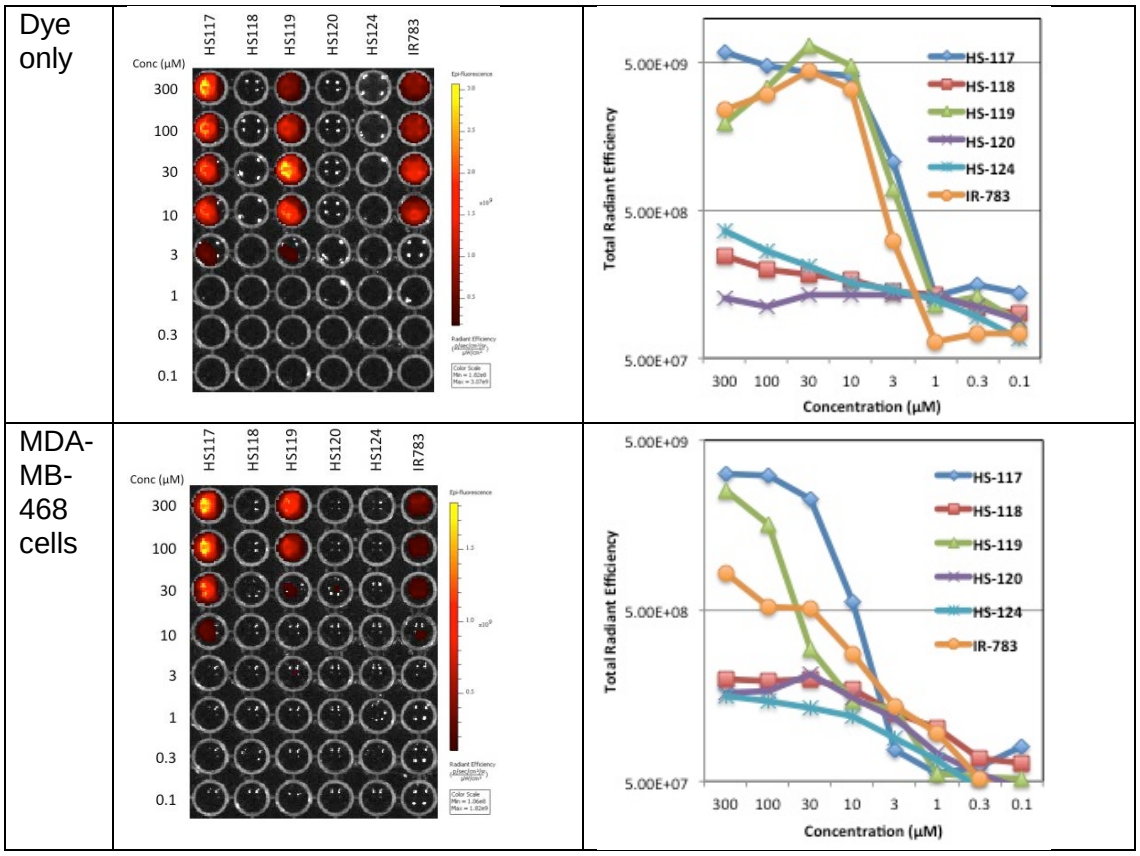


Figure 19. IVIS imaging of NIR-HSP90 inhibitor compound only and MDA-MB-468 cells labeled with NIR-HSP90 inhibitors: HS-117, HS-118, HS-119, HS-120. HS-117, -118, -119, -120, -124 and IR-783 were titrated and added to the plate or used to label MDA-MB-468 cells and incubated for 30 min at 37C. Cells were washed with PBS three times, and image was taken by IVIS machine with 745 nm excitation filter and ICG emission filter. HS-124 consists of dye + linker but without HSP90 inhibitor, used as a negative control compound for HS-117/119. IR-783 is a NIR dye used to generate HS-117 and HS-119. Left pictures show IVIS imaging (exposure 1 sec for dye only, 3 sec for cells). Right graphs show total radiant efficiency for for each compound for each titration. [Upper] Dye only at titration of 300 µM to 0.1 µM (15 nmol/well to 5 pmol/well). [Lower] MDA-MB-468 cells (0.3 M cells/well) were labeled with indicated concentration of NIR compounds, incubated for 30 min, washed three times with PBS, and detected by IVIS machine.

As shown in **Figure 19**, HS-118 and HS-120 were difficult to detect the signals by IVIS imager because higher excitation wavelengths are necessary to activate them (~820 nm). Probably because of poor solubility of HS-124 (control compound) in DMSO or DMSO+ water, HS-124 did not made NIR signals strong enough to be an optimal control (**Figure 19, upper**). Although the signal intensities were almost equivalent when comparing HS-117 and HS-119 compound themselves, HS-117 labeled MDA-MB-468 cells slightly stronger than HS-119 did in vitro.

Figure 20

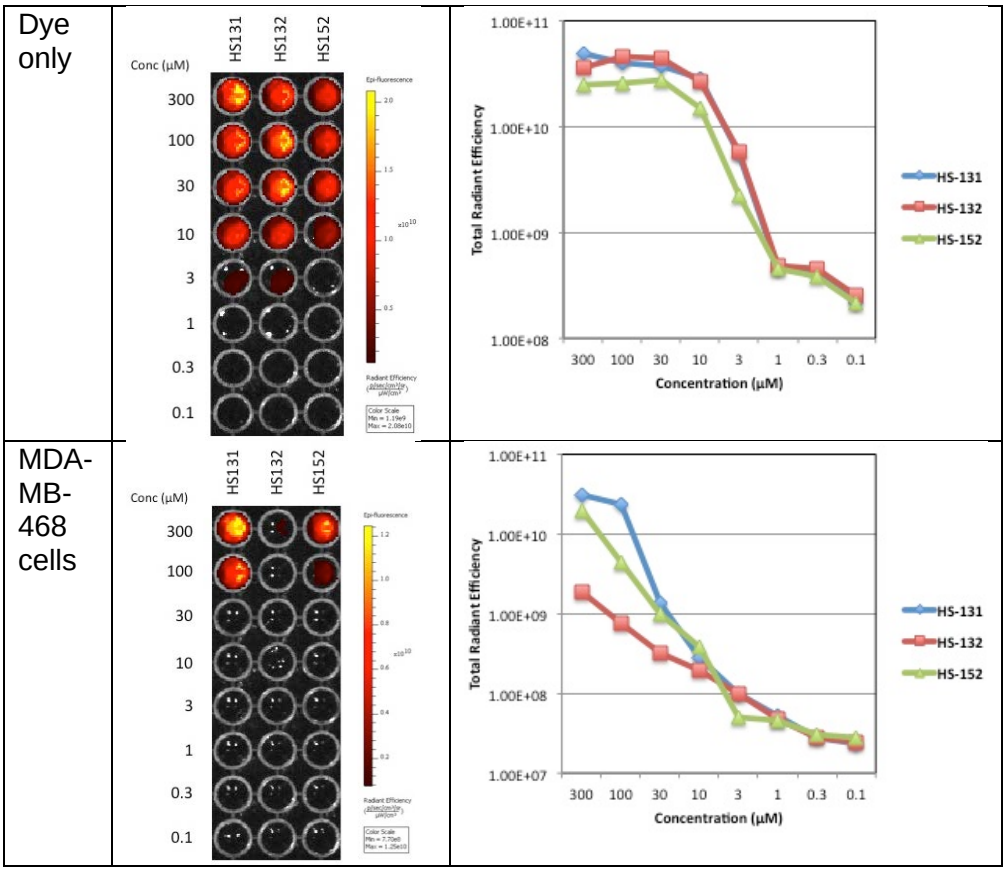


Figure 20. IVIS imaging of NIR-HSP90 inhibitor compound only and MDA-MB-468 cells labeled with NIR-HSP90 inhibitors: HS-131, HS-132. HS-131, HS-132 and HS-152 were titrated and added to the plate or used to label MDA-MB-468 cells and incubated for 30 min at 37C. Cells were washed with PBS three times, and image was taken by IVIS machine with 640 nm excitation filter and Cy5.5 emission filter. HS-152 consists of dye + linker but without HSP90 inhibitor, used as a negative control compound for HS-131/132. Left pictures show IVIS imaging (exposure 0.2 sec for dye only, 0.3 sec for cells). Right graphs show total radiant efficiency for for each compound for each titration. [Upper] Dye only at titration of 300 μM to 0.1 μM (15 nmol/well to 5 pmol/well). [Lower] MDA-MB-468 cells (0.3 M cells/well) were labeled with indicated concentration of NIR-HSP90 inhibitor compounds, incubated for 30 min, washed three times with PBS, and detected by IVIS machine.

As shown in **Figure 20**, HS-131 and HS-132 generated similar level of NIR signals, however, HS-131 showed slightly stronger labeling of MDA-MB-468 tumor cells in vitro compared to HS-132. Based on the IVIS imaging experiment with in vitro tumor cell labeling, HS-117 seems better candidate for in vivo imaging of tumors compared to HS-118, and HS-131 compared to HS-132. HS-118 and HS-120 are difficult to evaluate without current detection system.

In Vivo Labeling of MDA-MB-468 xenograft in mice by IVIS Imager

In our previous preliminary experiment, we tested multiple doses of NIR-HSP90 inhibitor (HS-117), and found 10 nmol to 25 nmol are the optimal dose for the tumor imaging. To compare

multiple different NIR-HSP90i compounds, we set the doses for in vivo administration to 10 nmol and 25 nmol base on the results.

Figure 21

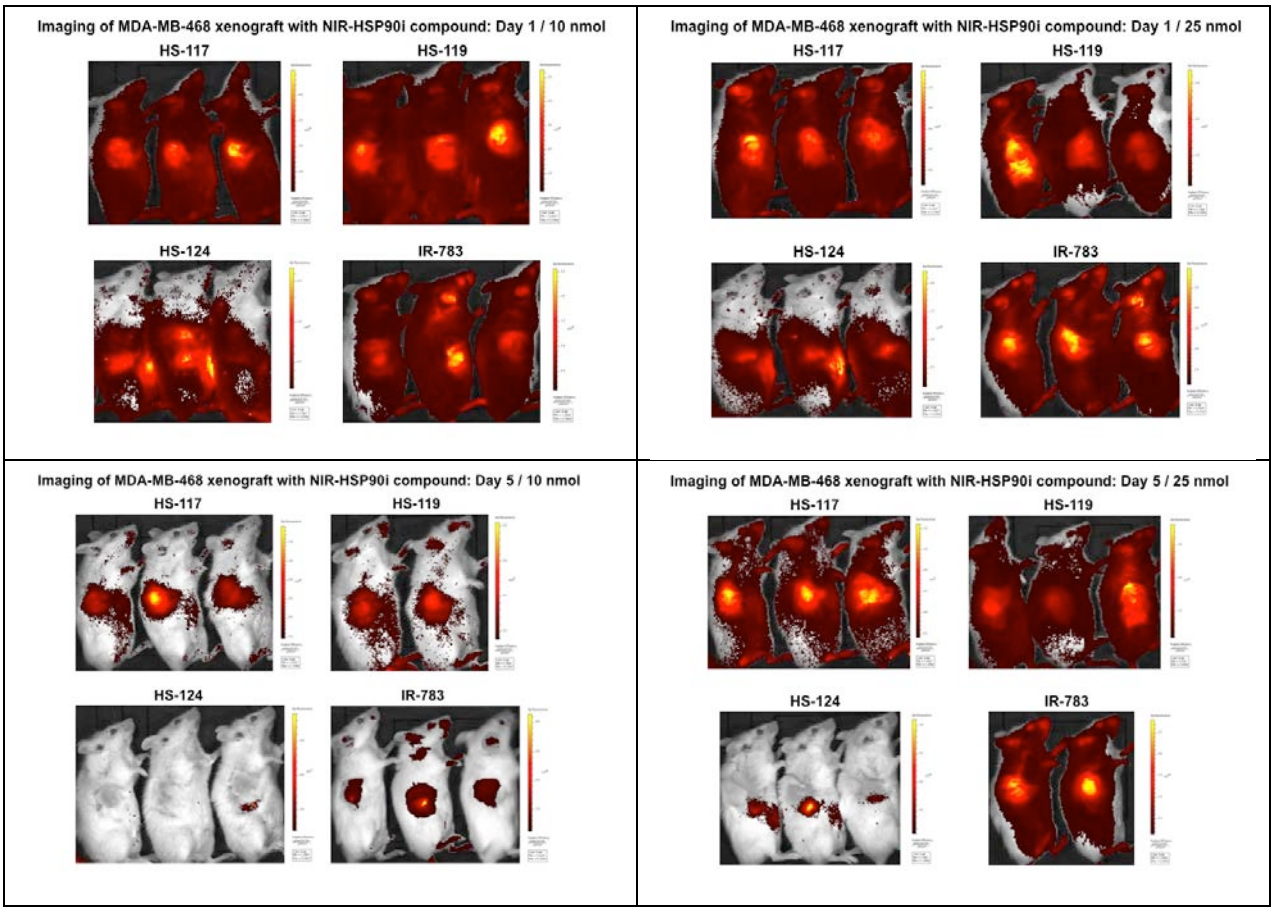


Figure 21. In vivo Imaging of MDA-MB-468 xenografts by NIR-HSP90 inhibitors. Female SCID-beige mice were subcutaneously injected with MDA-MB-468 cells (2M cells/injection) and tumors were allowed to reach 10 mm in diameter. Mice were administered with 10 or 25 nmol of HS-117, HS-117, HS-124, or IR-783 via tail vein. Three mice per group. Twenty-four, 48, 72, 120, and 168 hours later, mice were anesthetized, and NIR signals were detected by IVIS machine (745 nm excitation filter, ICG emission filter, exposure 1 sec). Images of **24 hours (upper)** and **120 hours (lower)** are shown. **Left pictures: 10 nmol injection. Right pictures: 25 nmol injection.**

Figure 22

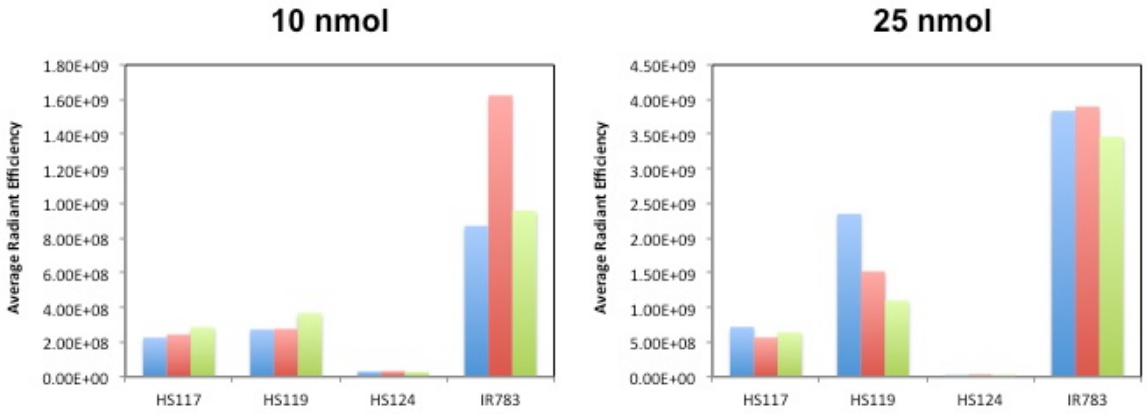


Figure 22. NIR Signals detected from MDA-MB-468 xenograft in mice 1 day after NIR-HSP90 inhibitor administration. SCID-beige mice bearing MDA-MB-468 xenografts were administered with 10 or 25 nmol of HS-117, HS-117, HS-124, or IR-783 via tail vein (three mice/group). Twenty-four later, mice were anesthetized, and NIR signals were detected by IVIS machine (745 nm excitation filter, ICG emission filter, exposure 1 sec). Average radiant efficiencies for the tumor area were measured and plotted individually.

Figure 23A

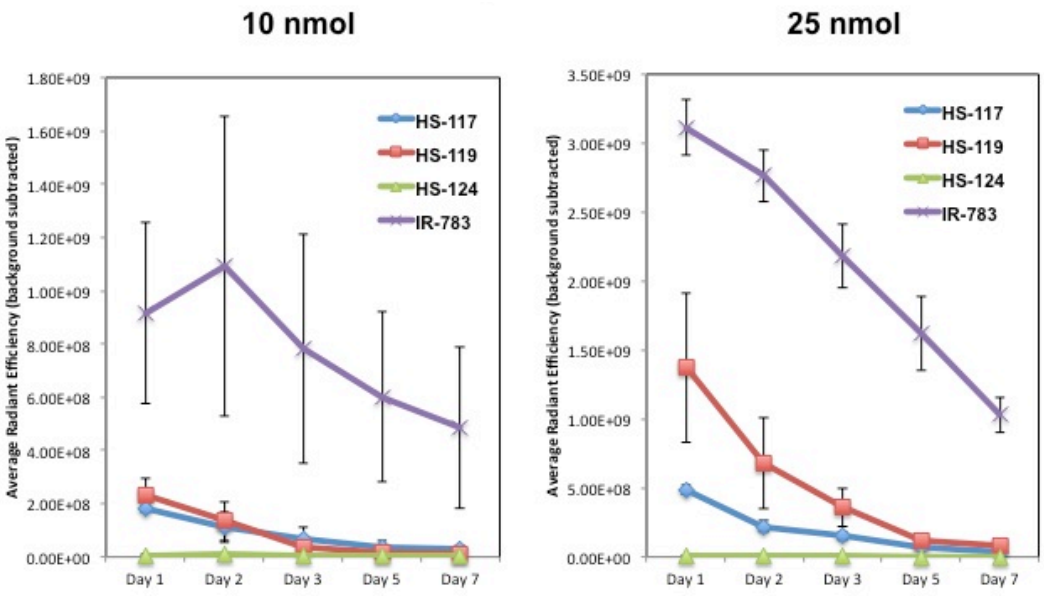


Figure 23A. NIR Signals detected from MDA-MB-468 xenograft in mice after NIR-HSP90 inhibitor administration: over time change with background subtraction. NIR signals were imaged and measured on day 1, 2, 3, 5 and 7 after NIR-HSP90 inhibitor administration. Average radiant efficiencies were measured and the values of distant normal skin areas were subtracted from the values of tumor areas. The average of each group (three mice) are plotted. Error Bar: SD.

Figure 23B

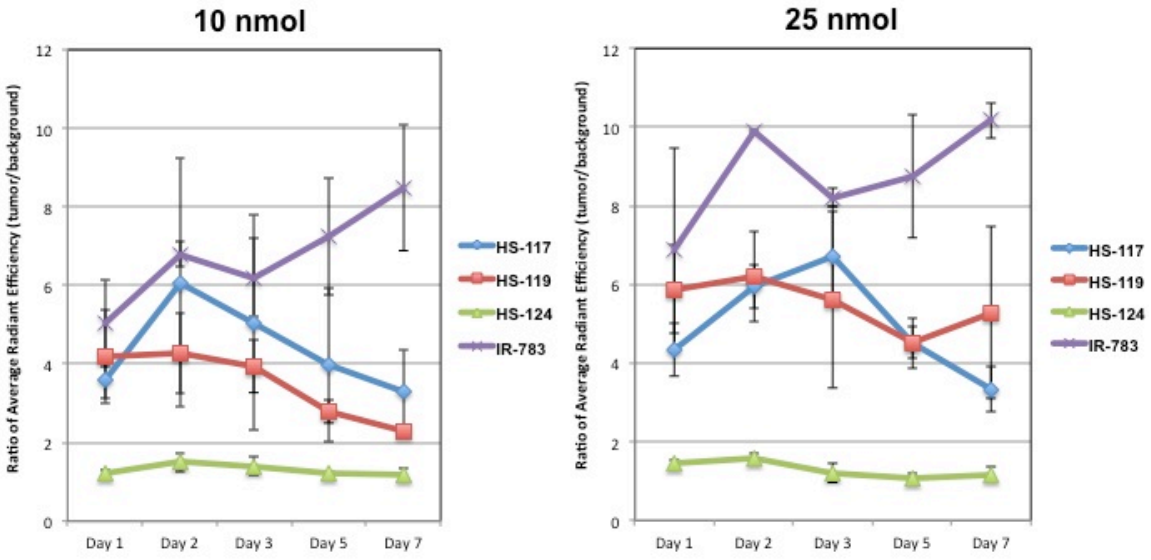


Figure 23B. NIR Signals detected from MDA-MB-468 xenograft in mice after NIR-HSP90 inhibitor administration: over time change of the ratio. NIR signals were imaged and measured on day 1, 2, 3, 5 and 7 after NIR-HSP90 inhibitor administration. Average radiant efficiencies of tumor areas and that of distant skin areas were measured for each mouse and the ratios of these values (tumor value/background value) were calculated. Averages of ratios in each group were plotted in the graphs. Error Bar: SD.

NIR signals from individual mice are shown in **Figure 22**, demonstrating the strongest signals from mice injected with the NIR dye, IR-783, followed by HS-117 and HS-119. At higher dose of 25 nmol, HS-119 showed stronger signals from the tumors compared to HS-119. However, mice injected with IR-783 and HS-119 tended to have stronger background signals (6~10 times and 2~3 times, respectively compared to HS-117), and thus adjustment of radiant efficiency was done by subtracting the background signals in each mouse. **Figure 23A** shows the change over time of these adjusted average radiant efficiencies (average of each group). The trend of gradual decrease in signal intensities was observed until day 7. Stronger signals in HS-119 injected mice was clear until day 3 in 25 nmol injected mice, compared to those in HS-117 injected mice.

In **Figure 23B**, the average ratios of NIR signals (tumor/background) in each group are plotted. In 10 nmol compound injected mice, HS-117 showed slightly higher ratios compared to HS-119, and both showed gradual decrease after day 2. However, in 25 nmol injected mice, both HS-117 and HS-119 showed similar ratios. Interestingly, IR-783, despite its stronger background signals, had higher ratios at each time point, suggesting the greater accumulation of the contrast to the tumor tissue compared to HS-117 and HS-119.

To test the accumulation of NIR-HSP90 inhibitor compounds in organs, some mice injected with 10 nmol compounds were sacrificed 24 hours after tail vain injection of compounds, and organs were excised, and emission of NIR signals was analyzed by IVIS imager (745 nm excitation filter, ICG emission filter, 1 sec exposure). Images and radiant efficiency are shown in **Figure 24** (below).

Figure 24A

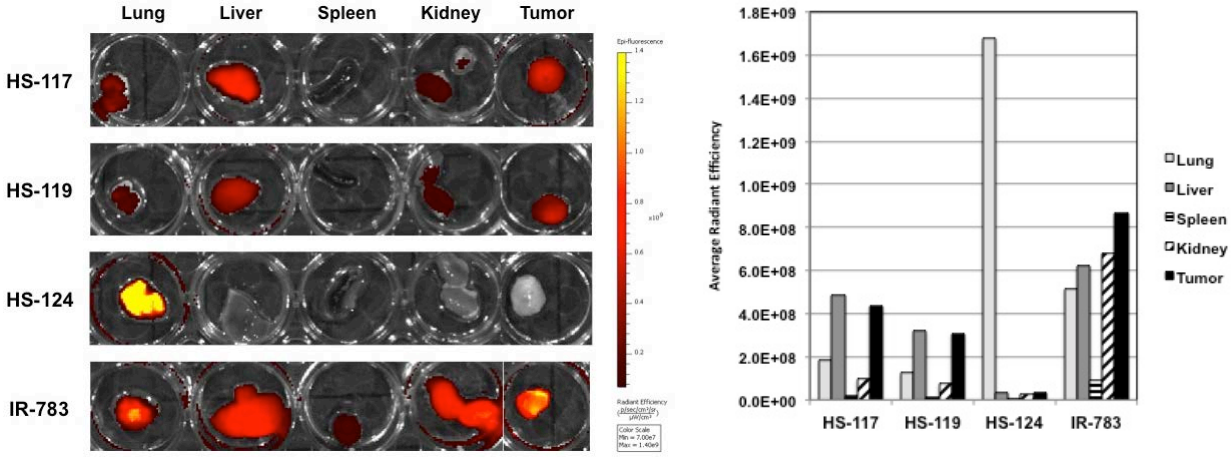
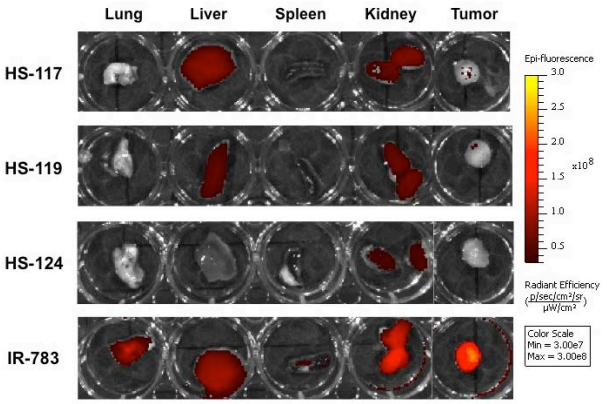


Figure 24A. Tissue Distribution of NIR-HSP90 inhibitors: Day 1. Twenty-four hours after the tail vein injection of NIR-HSP90 inhibitor (10 nmol/mouse), mice are sacrificed and the organs (lung, liver, spleen, kidney) and tumors were excised and NIR signals were analyzed by IVIS Imager machine. Right graph shows average radiant efficiency for each organ in each compound group.

Figure 24B



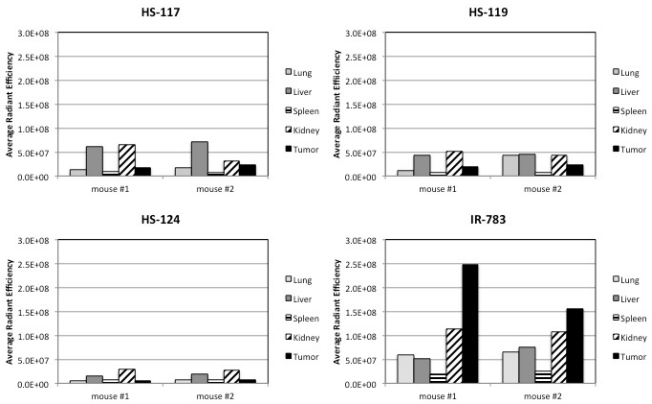


Figure 24B. Tissue Distribution of NIR-HSP90 inhibitors: Day 7. 7 days after the tail vein injection of NIR-HSP90 inhibitor (10 nmol/mouse), mice are sacrificed and the organs (lung, liver, spleen, kidney) and tumors were excised and NIR signals were analyzed by IVIS Imager machine. Lower graphs show average radiant efficiencies of each organ in each compound group.

On day 7, IR-783 administered mice had NIR signals from most of the organs tested except spleen. Especially, accumulation in tumor tissues was still evident, compared to other organs. HS-117 and HS-119 showed residual signals from the liver and kidney, but NIR signals from tumor tissue was very weak on day 7. HS-124 administered mice had only slight NIR signals from kidney at this time point. NIR-HSP90 inhibitors, HS-131 and HS-132, will soon be tested in in vivo imaging experiment using MDA-MB-468 tumor bearing mice.

3) In vivo Imaging with NIR-tethered HSP90 inhibitor compounds: Early time points (~24 hours)
In our previous section, we tested two NIR-HSP90 inhibitors, HS-117 and HS-119 at the doses of 10 nmol and 25 nmol for injection. We tested the NIR signals from the tumors 24 hours to 7 days after tail vein administration. This time, we tested tumor imaging with NIR-HSP90 inhibitors in earlier phase until 24 hour time point.

In Vivo Labeling of MDA-MB-468 xenograft in mice by IVIS Imager
HS-117, HS-119, HS-124 (control compound without HSP90 inhibitor), and IR-783 (dye only) were injected to MDA-MB-468 tumor-bearing SCID mice via tail vein. Dose of 10 nmol was used for all the compounds. At multiple time points (3, 6, 12, and 24 hours after injection), NIR signals of HSP90 compound injected mice were analyzed by IVIS imager (Excitation: 745 nm, Emission ICG filter, Exposure 0.1 and 1.0 sec). MDA-MB-468 tumor-bearing mouse without compound/dye injection was used as a negative control for imaging.

Figure 25

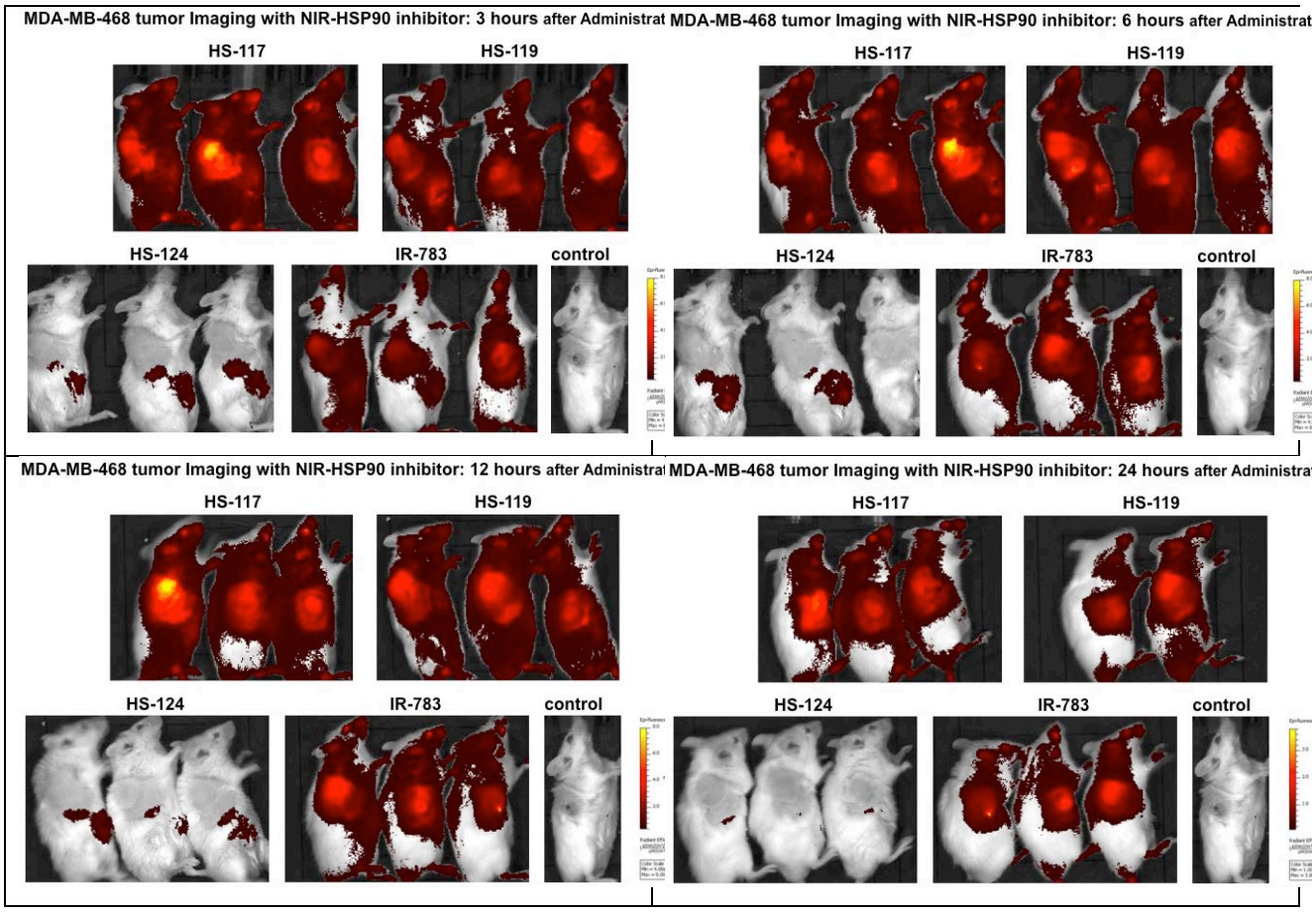


Figure 25. In vivo Imaging of MDA-MB-468 xenografts by NIR-HSP90 inhibitors (HS-117, HS-119, HS-124, IR-783): Earlier Time Points. SCID mice were injected with MDA-MB-468 tumor cells (1 M cells/mouse). When tumor size reached ~10 mm in diameter, NIR-HSP90 inhibitor compound (HS-117, HS-119), control compound (HS-124), or control dye (IR-783) was administered (10 nmol in 20 µL

vehicle) via tail vein. NIR signals were detected by IVIS Imager machine (Ex: 745 nm, Em: ICG filter, Exp 0.1 sec) from 3 hours till 24 hours after NIR-HSP90i administration.

As shown in **Figure 25**, from the earlier time points, such as 3 hours after compound injection, we could detect NIR signals from tumors. The intensities of NIR signals from tumors reached maximum at around 12 hour time point, and slightly declined by 24 hour time point. Also from the normal skin area, we observed strong background signals with HS-117, HS-119 and IR-783 injection (~5.0 x 10^8 radiant efficiency), but the signals got weaker by 24 hour time point. In **Figure 26**, to compare the detectability of tumor-derived NIR signals, NIR signal levels (Radiant Efficiency) from the background (normal skin area) were subtracted from those of the tumors, and plotted. In **Figure 27**, the ratios of NIR signals were calculated (NIR from tumor/NIR from normal skin area) and plotted. Probably because of repeated anesthesia with Ketamine, one mouse in HS-119 group suffered from low body temperature, and thus was euthanized after 12 hour time point.

Figure 26

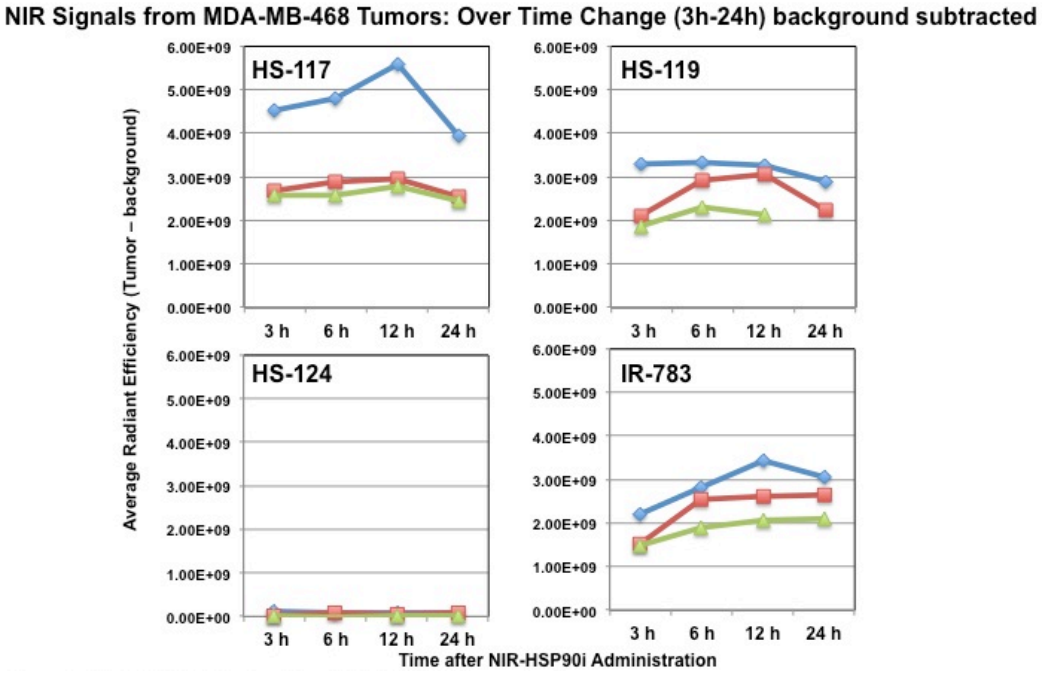


Figure 26. NIR Signals detected from MDA-MB-468 xenograft in mice after NIR-HSP90 inhibitor administration: Comparison of HS-117, HS-119, HS-124, and IR-783. NIR signals were detected by IVIS Imager machine (Ex: 745 nm, Em: ICG filter, Exp 0.1 sec) from 3 hours till 24 hours after NIR-HSP90i administration to MDA-MB-468 xenograft-bearing SCID mice. NIR signals (Radiant Efficiency) from normal skin area (background) were subtracted from those of tumor xenografts in each mouse, and shown in the graphs.

Although HS-117 and HS-119 showed strong NIR signals from tumors in each time point (**Figures 25 & 26**), HS-117 made a little stronger signal during this early time period. Control compound HS-124 did not make significant signals from mice, probably due to low solubility in the vehicle, or early wash out from the body. Interestingly, IR-783 dye alone showed similar accumulation to the tumors, and the similar finding with this dye was already reported by others

(Clinical Cancer Research, 2010, 16(10), 2833-44). Therefore, there is a possibility that the dye (IR-783) used to make NIR-HSP90 inhibitor compounds (HS-117 and HS-119) is playing some role in the accumulation of NIR-HSP90 compounds into tumor xenografts. Therefore, we will confirm the binding of HS-117 and HS-119 to HSP90 protein in the tumor tissues with these tumor samples using monoQ column and HPLC.

Figure 27

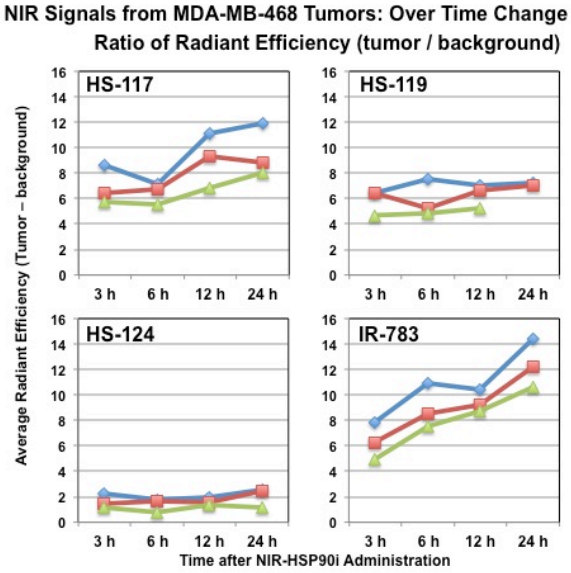


Figure 27. NIR Signals detected from MDA-MB-468 xenograft in mice after NIR-HSP90 inhibitor administration: over time change of the ratio. Average radiant efficiencies of tumor areas and that of distant skin areas were measured for each mouse and the ratios of these values (tumor value/ background value) were calculated, and plotted.

To test the accumulation of NIR-HSP90 inhibitor compounds in organs, some mice injected with 10 nmol compounds were sacrificed 24 hours after tail vain injection of compounds, and organs were excised, and emission of NIR signals was analyzed by IVIS imager (745 nm excitation filter, ICG emission filter, 1 sec exposure). Images and radiant efficiency are shown in **Figure 28** (below).

Figure 28

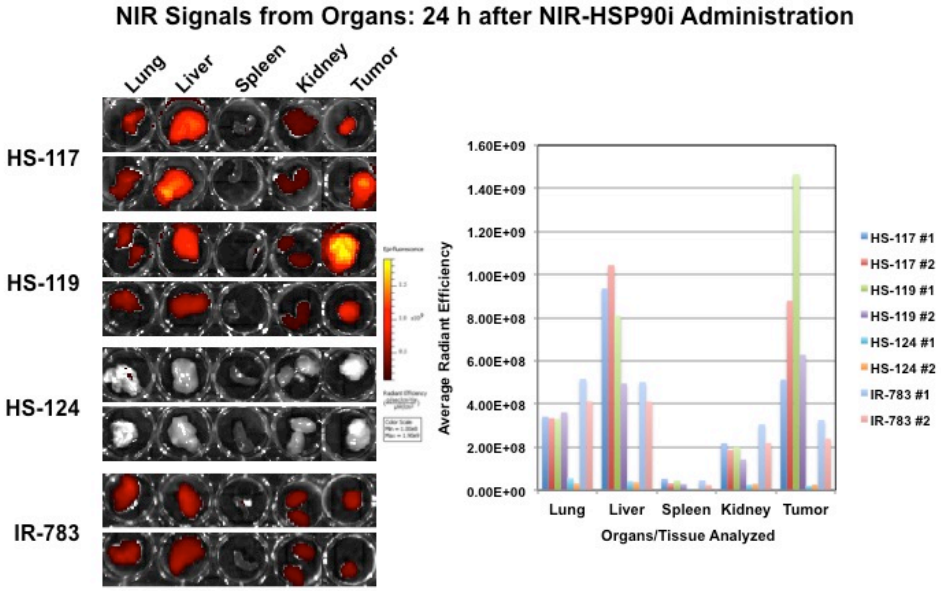


Figure 28. Tissue Distribution of NIR-HSP90 inhibitors: 24 hours after administration. Twenty-four hours after the tail vein injection of NIR-HSP90 inhibitor (10 nmol/mouse), mice are sacrificed and the organs (lung, liver, spleen, kidney) and tumors were excised and NIR signals were analyzed by IVIS Imager machine. Right graph shows average radiant efficiency for each organ in each compound administered mouse.

After 24 hours, MDA-MB-468 breast tumors from mice administered with HS-117 and HS-119 showed strong signals, especially one of HS-119 administered mice had the strongest NIR signal. NIR signals from liver were slightly stronger in HS-117 administered mice compared to HS-119. HS-124 administered mice showed very low level of NIR signals, suggesting that HS-124 may not be an appropriate control compound probably because of poor solubility in the vehicle.

Testing of third generation NIR HSP90 inhibitors- HS-131, HS-132.
Despite the promising results of the second generation NIR HSP90 inhibitor, limitations to their long term development included a lack of structural information about the contrast portion of the compound. To achieve full synthetic control of the compunds, we developed a third generation set of compounds synethesized at Duke. We conducted the same in vivo tumor imaging test with other NIR-HSP90 inhibitor compounds, HS-131 and HS-132, and their control compound HS-152, which has dye and linker but not HSP90 inhibitor.

Figure 29

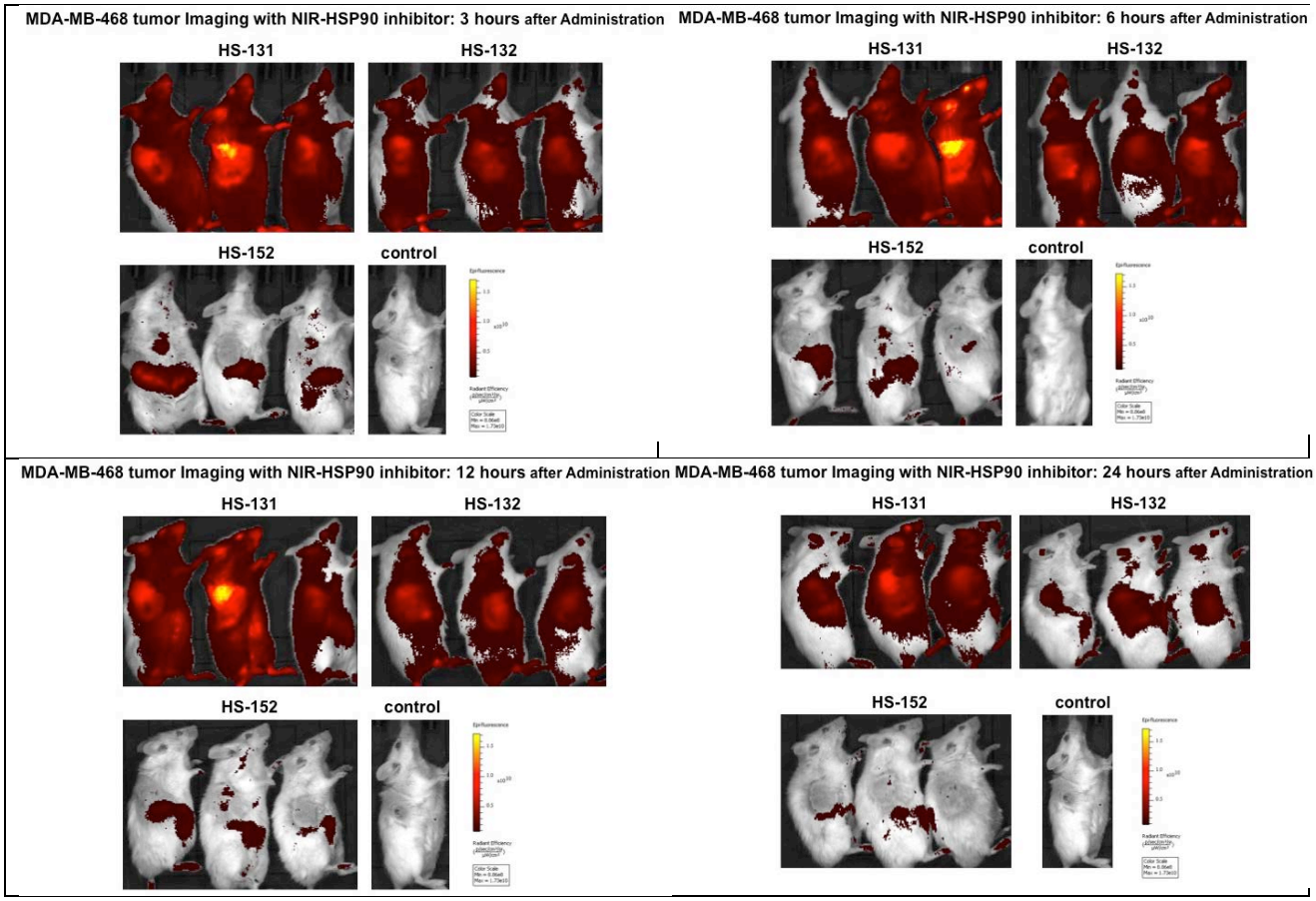


Figure 29. In vivo Imaging of MDA-MB-468 xenografts by NIR-HSP90 inhibitors (HS-131, HS-132, HS-152): Earlier Time Points. SCID mice were injected with MDA-MB-468 tumor cells (1 M cells/mouse). When tumor size reached ~10 mm in diameter, NIR-HSP90 inhibitor compound (HS-131, HS-132), or control compound (HS-152) was administered (10 nmol in 20 µL vehicle) via tail vein. NIR signals were detected by IVIS Imager machine (Ex: 640 nm, Em: Cy5.5 filter, Exp 0.1 sec) from 3 hours till 24 hours after NIR-HSP90i administration.

In **Figure 29**, in vivo imagings with these compounds are shown until 24 hour time point. 10 nmol of compounds were administered to mice via tail vein, and NIR signals were analyzed by IVIS imager (Excitation: 640 nm, Emission Cy5.5 filter, Exposure 0.1 and 1.0 sec). MDA-MB-468 tumor-bearing mouse without compound/dye injection was used as a negative control for imaging. The range of color scale of each picture was adjusted to be the same for all images, so that different compounds with different time points can be compared easily.

Figure 30

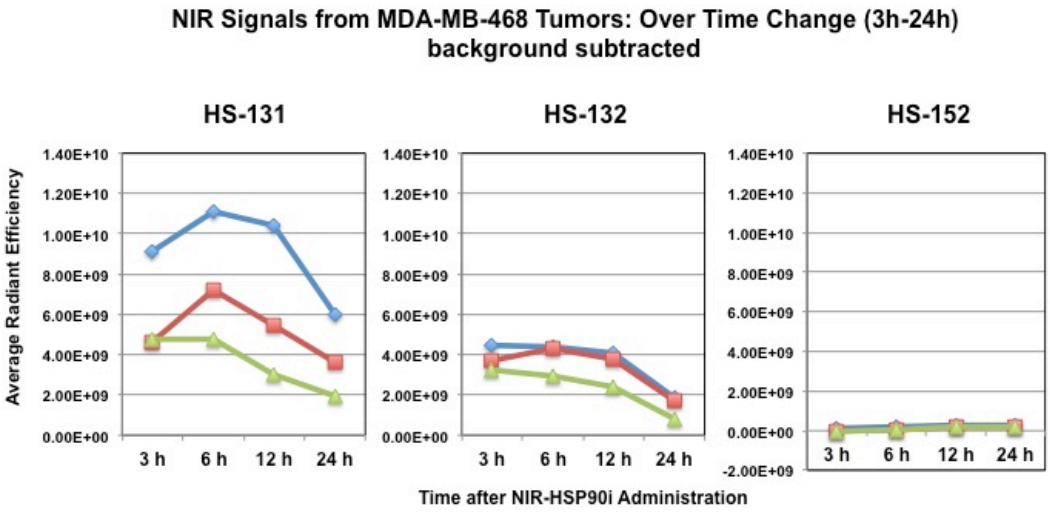


Figure 30. NIR Signals detected from MDA-MB-468 xenograft in mice after NIR-HSP90 inhibitor administration: Comparison of HS-131, HS-132, and HS-152. NIR signals were detected by IVIS Imager machine (Ex: 640 nm, Em: Cy5.5 filter, Exp 0.1 sec) from 3 hours till 24 hours after NIR-HSP90i administration to MDA-MB-468 xenograft-bearing SCID mice. NIR signals (Radiant Efficiency) from normal skin area (background) were subtracted from those of tumor xenografts in each mouse, and shown in the graphs.

Figure 31

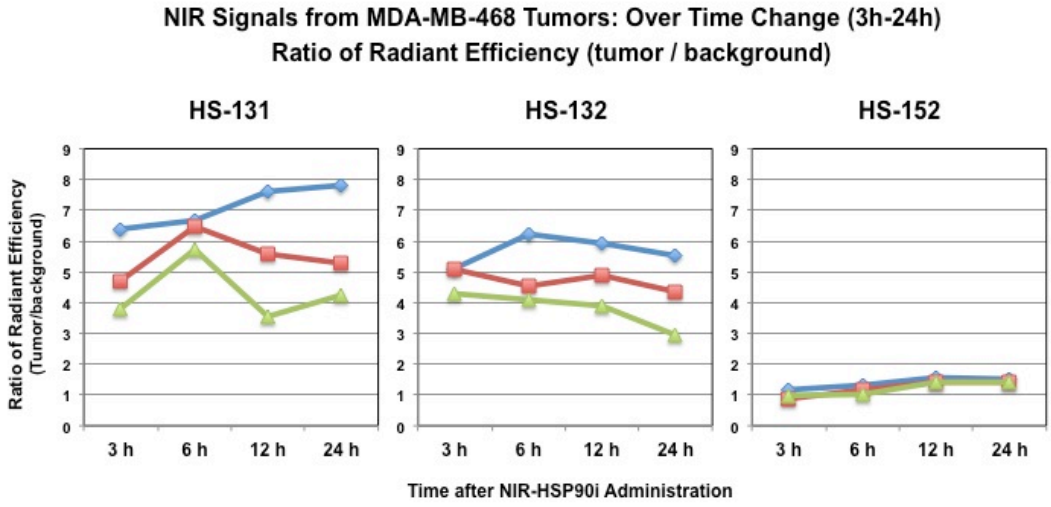


Figure 31. NIR Signals detected from MDA-MB-468 xenograft in mice after NIR-HSP90 inhibitor administration: over time change of the ratio. Average radiant efficiencies of tumor areas and that of distant skin areas (background) were measured for each mouse and the ratios of these values (tumor value/ background value) were calculated, and plotted.

As shown in **Figures 30 and 31**, HS-131 showed stronger NIR signals from tumors compared to HS-132, and reached the peak level at around 6 hour time point, slightly earlier than HS-117

and HS-119. Accumulation of HS-132 was weaker until 24 hours, and the trend was also confirmed by the analysis of organs/tumors in **Figure 32**. NIR signals from organs were relatively low with HS-131 and HS-132 administration, except one lung from the mouse injected with HS-131. Control HS-152 showed no accumulation to the tumors, and only weak NIR signals were detected from excised organs/tumors as shown in **Figure 32**.

Figure 32

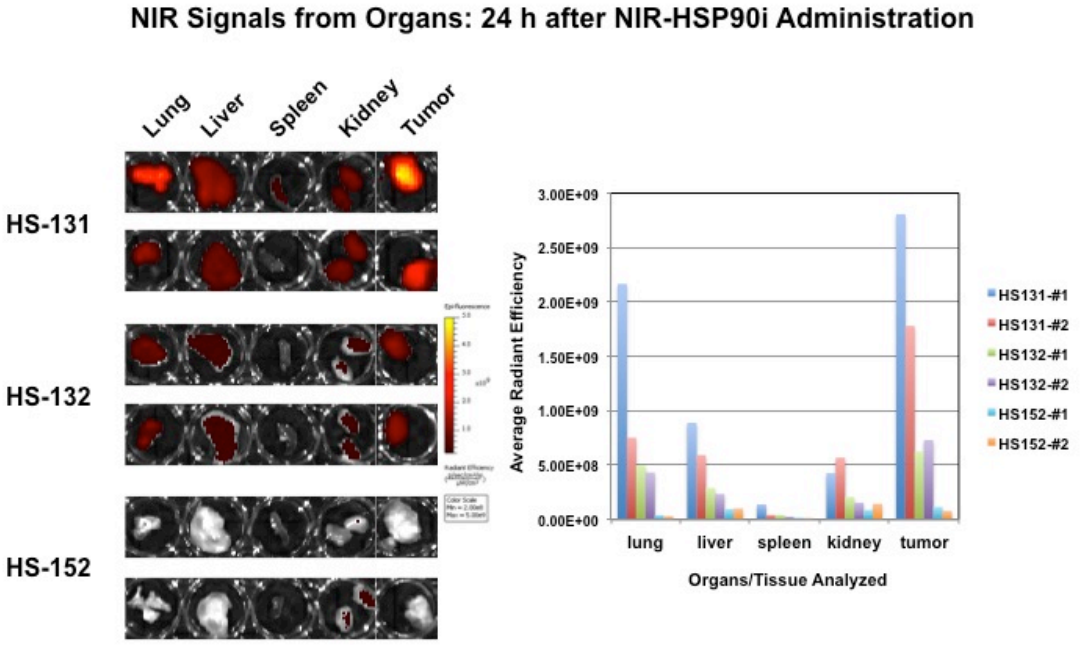


Figure 32. Tissue Distribution of NIR-HSP90 inhibitors: 24 hours after administration. Twenty-four hours after the tail vein injection of NIR-HSP90 inhibitor (10 nmol/mouse), mice are sacrificed and the organs (lung, liver, spleen, kidney) and tumors were excised and NIR signals were analyzed by IVIS Imager machine. Right graph shows average radiant efficiency for each organ in each compound administered mouse.

We have advanced our efforts in nIR imaging, and a recommendation to acquire a more useful instrument that would allow us to detect longer wavelength lights was made. This would allow us to develop a probe that would be clinically useful for breast imaging, as the superior and inferior aspect of a breast could be visualized using instruments developed at Dartmouth. Therefore, using institutional support, we aquired a LiCOR PEARL instrument.

Project 1-Aim 2. Task 2: Demonstrate PM Hsp90 accumulation in tumor xenografts derived from luminal, HER2+ and triple negative human breast cancer cell lines.

Extensive studies have been performed to investigate the uptake of various tethered Hsp90 inhibitors into BT474 (HER2+) or MDA MB 468 (triple negative) derived xenographs are described above. In general selective uptake can be observed within 2 hour IV or IP and detected for up to 72 hours post injection (IP). Several imaging modalities have been tested

including whole body imaging by IVIS in the optical and nr IR range or with a spectral pen (Ramanujam lab).

Project 1-Aim 2. Task 3: Demonstrate nIR detection of PM Hsp90 accumulation in human breast cancer xenografts. Perform PK/PD analysis of two different dose schedules to correlate plasma and tumor drug levels with imaging.

This work will be described in the small animal core.

Project 1-Aim 2. Task 4: Demonstrate MR detection of PM Hsp90 accumulation in tumor xenografts derived from luminal, HER2+ and triple negative human breast cancer cell lines.

This work will be described in the small animal core.

Project 1-Aim 2. Task 5: Demonstrate thermal changes and antitumor effects of RF mediated thermal therapy in human breast cancer xenograft models, then test antitumor effects.

The compounds have been synthesized, and in vitro uptake experiments have been performed as reported above. We are planning in vitro photodynamic therapy, and will proceed to start these experiments in Year 3.

Project 1-Aim 3. Confirming Hsp90 Expression in specific molecular subtypes of human breast cancer

To get an initial perspective of the role of Hsp90 in breast cancer, we compiled a collection of 4,010 breast tumor gene expression data derived from 23 datasets that have been posted on the National Center for Biotechnology Information (NCBI) Gene Expression Omnibus (GEO) database. We performed a genome-scale survival analysis using Cox-regression survival analyses, and validated using Kaplan-Meier Estimates survival and Cox Proportional-Hazards Regression survival analyses. We conducted a genome-scale analysis of chromosome alteration using 481 breast cancer samples obtained from The Cancer Genome Atlas (TCGA), from which combined expression and copy number data were available. We assessed the correlation between somatic copy number alterations and gene expression using analysis of variance (ANOVA).

We found increased expression of each of the heat shock protein (HSP) 90 isoforms, as well as HSP transcriptional factor 1 (HSF1), was correlated with poor prognosis in different subtypes of breast cancer. High-level expression of HSP90AA1 and HSP90AB1, two cytoplasmic HSP90 isoforms, was driven by chromosome coding region amplifications and were independent factors that led to death from breast cancer among patients with triple-negative (TNBC) and HER2-/ER+ subtypes, respectively. Furthermore, amplification of HSF1 was correlated with higher HSP90AA1 and HSP90AB1 mRNA expression among the breast cancer cells without amplifications of these two genes. A collection of HSP90AA1, HSP90AB1 and HSF1 amplifications defined a subpopulation of breast cancer with up-regulated HSP90 gene expression, and up-regulated HSP90 expression independently elevated the risk of recurrence of TNBC and poor prognosis of HER2-/ER+ breast cancer.

Therefore, we concluded that up-regulated HSP90 mRNA expression represents a confluence of genomic vulnerability that renders HER2 negative breast cancers more aggressive, resulting in poor prognosis. Targeting breast cancer with up-regulated HSP90 may potentially improve the effectiveness of clinical intervention in this disease. (Cheng Q, Chang JT, Geradts J, Neckers LM, Haystead T, Spector NL, Lyerly HK. Breast Cancer Res. 2012 Apr 17;14(2):R62.)

To date we have consented 165 patients. Of these 165 cases, we have pathologically processed 318 tissue samples from 152 individual patients (range 1-6 samples per patient). None of the reviewed research samples contain pathologic features that were not present in the paired diagnostic biopsies. In regards to blood samples collected, we continue to collect blood in 40-50% of the consented patients to date.

Project 1-Aim 3. Task 1: Confirm protein expression levels of Hsp90 in breast cancer subtypes including TNBC. We have used commercially available Hsp90 antibodies for IHC staining, and have mixed results.

We tried a variety of commercially available Hsp90 specific antibodies for IHC analysis. Results from staining a single tumor sample with three different antibodies are shown below.

Figure 33

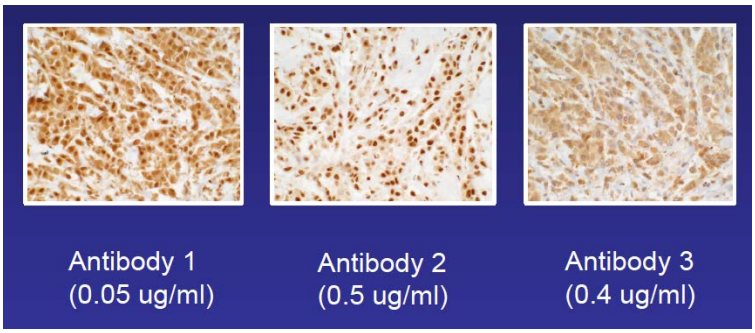


Figure 33. Immunohistochemical straining of breast cancer using three different commercial Hsp90 antibodies.

We haven't assayed a larger number of TNBC cases yet because it's still unclear which antibody we should use for IHC staining. It is not clear that any commercial antibody can detect differnces in HSP90 expression in breast cancer. Based on these results, we continue to analyze other available Hsp90 antibodies, and will continue to test them.

Project 1-Aim 3. Task 2: Analyze the breast cancer tissues for additional markers of Hsp90 activity including Hsp70 and caspase 3.

We have not yet assayed additional biomarkers, but continue to collect and annotate mammographically detected breast cancers.

Project 1-Aim 3. Task 3: Begin collection of an annotated tissue bank representing mammographically detected breast cancer

We have established a tissue bank for mammographically detected cancers. All women or men undergoing an image-guided (ultrasound or stereotactic mammogram) core needle biopsy for diagnosis of a breast lesion are eligible to participate. Patients with mammographically concerning lesions returning for biopsy are screened. If deemed appropriate by the attending radiologist for additional research biopsies the eligible patients are introduced by the radiology staff to our Clinical Research Coordinator. The research coordinator reviews the study with the eligible patients in order to ascertain if they would be interested in having research tissue and blood collected in addition to the clinical planned biopsy. If the patients are willing to participate in the study, then informed consent to obtain tissue for research is obtained from patients by our Clinical Research Coordinator prior to the biopsy procedure. The informed consent for this study allows for the continued access to information on clinical treatment and follow up status to make the collected tissue maximally useful in studies of treatment response and prognosis. The Clinical Research Coordinator informs the radiologist obtaining the biopsies of the patient's consent to donate tissue. The physician then has the study coordinator alerted to come to the biopsy suite once the clinical biopsy procedure begins so they are present when the biopsy is obtained. Typically patients will have 5-10 passes of an 8 to 14-gauge needle during a biopsy procedure. For this study the radiologists will perform up to 4 additional passes to obtain cores for research (this will be about 0.5 gram of tissue). These passes will occur without additional breast incisions and are essentially a continuation of the biopsy procedure. There is added risk to the patient, which involves a small additional risk of hematoma from the extra passes. In regards to the collection of research tissue, research blood is obtained on the same day as the research biopsies in the radiology suite by our Clinical Research Coordinator. The blood tubes that are collected are for PBMCs, serum, plasma, and Paxgene tubes.

To date we have consented 165 patients to date, see below graph (**Figure 34)**. Of these 165 cases, we have pathologically processed 318 tissue samples from 152 individual patients (range 1-6 samples per patient). None of the reviewed research samples contain pathologic features that were not present in the paired diagnostic biopsies. Of the pathologically verified biopsies, 26% of the tissue samples contain invasive carcinoma, 5% of the samples contain DCIS only, and 10% of the samples contain atypical breast lesions. In regards to blood samples collected, we continue to collect blood in 40-50% of the consented patients to date.

Figure 34

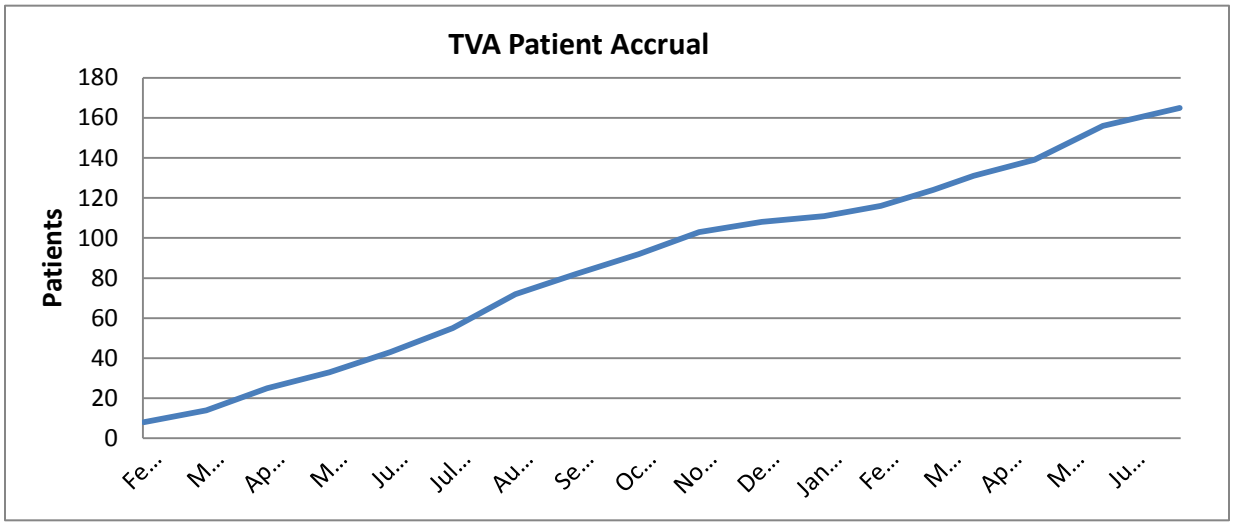


Figure 34. Accrual graph of consented patients under the mammographically detected breast cancer tissue bank protocol.

We have also established a clinical database for annotation of the specimens. To date, the first 100+ cases consented for the tissue collection have been clinically annotated in this clinical annotation database.

Figure 35

Clinical Database Details

- Housed on server at Cedar-Sinai Medical Center
  - No PHI
- Platform is REDCap (includes full functionality of REDCap)
- Accessible on the web via https (no VPN required)
- Database adheres to CSMC Enterprise Information Services (EIS) research database security standards
- Database consists of:
  - 9 Baseline forms (125 Clinical fields)
  - 4 Follow-up forms (65 Clinical fields)

Figure 36

Demographics

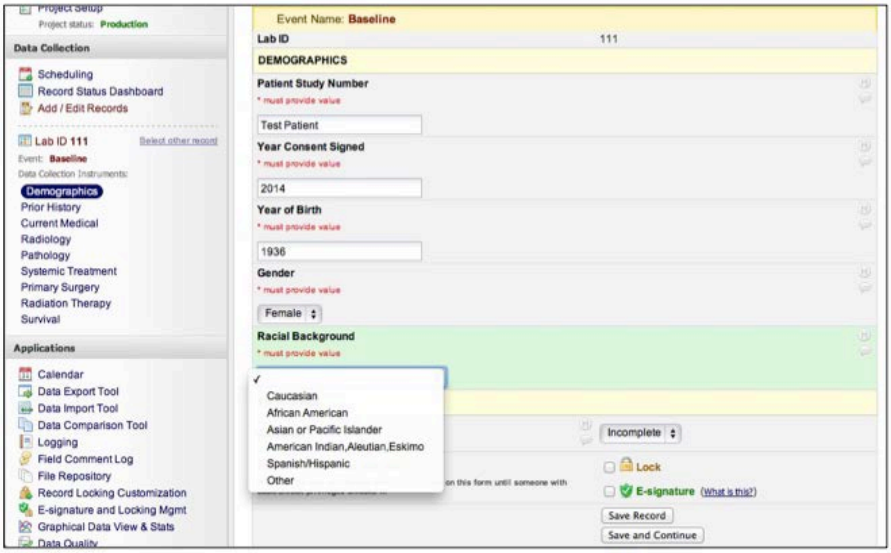


Figure 37

Searching of the Database

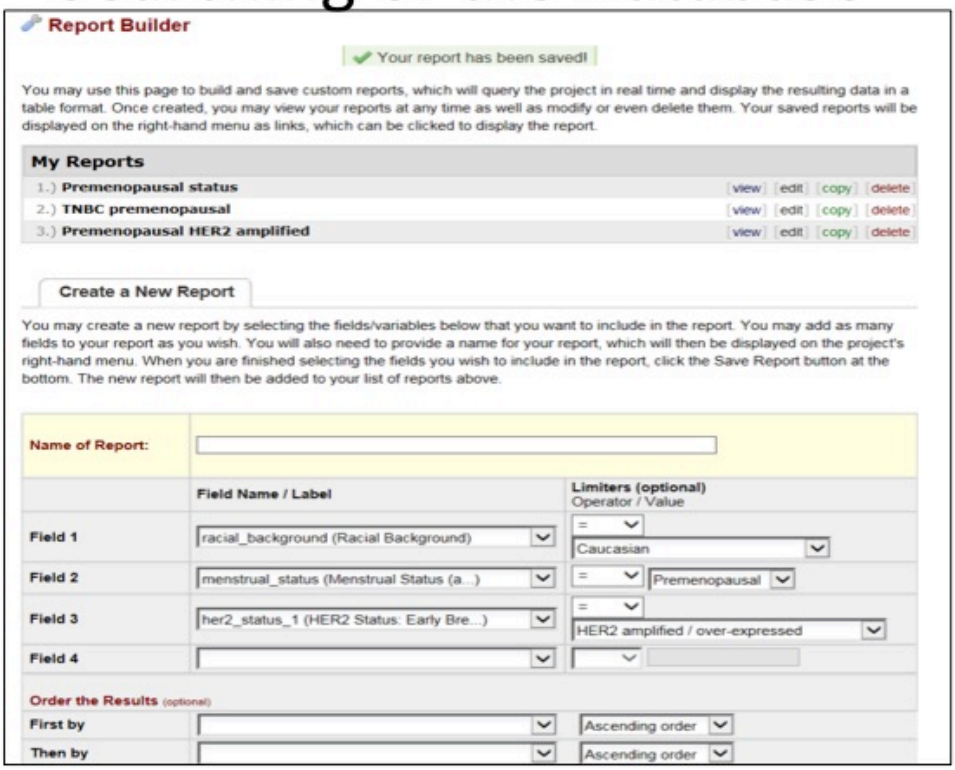


Figure 38

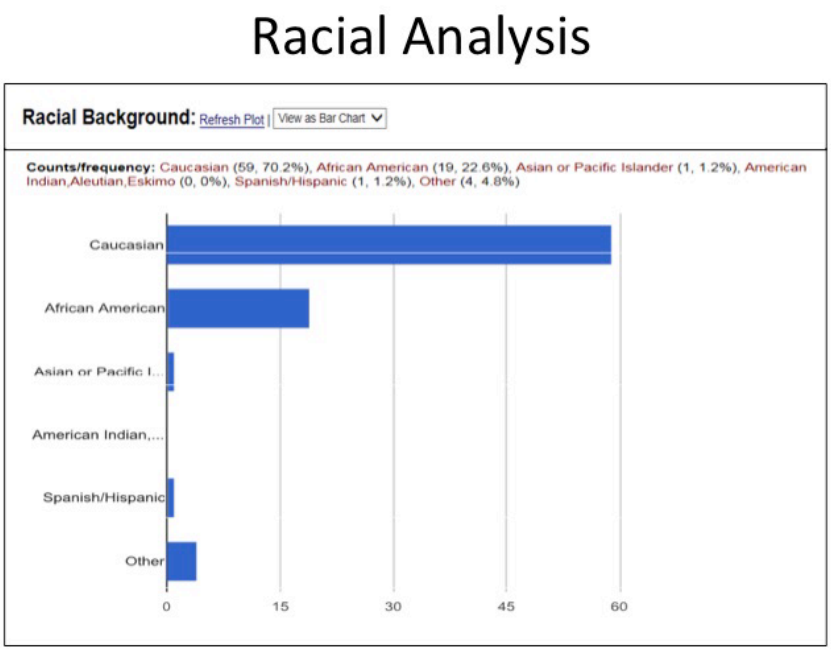
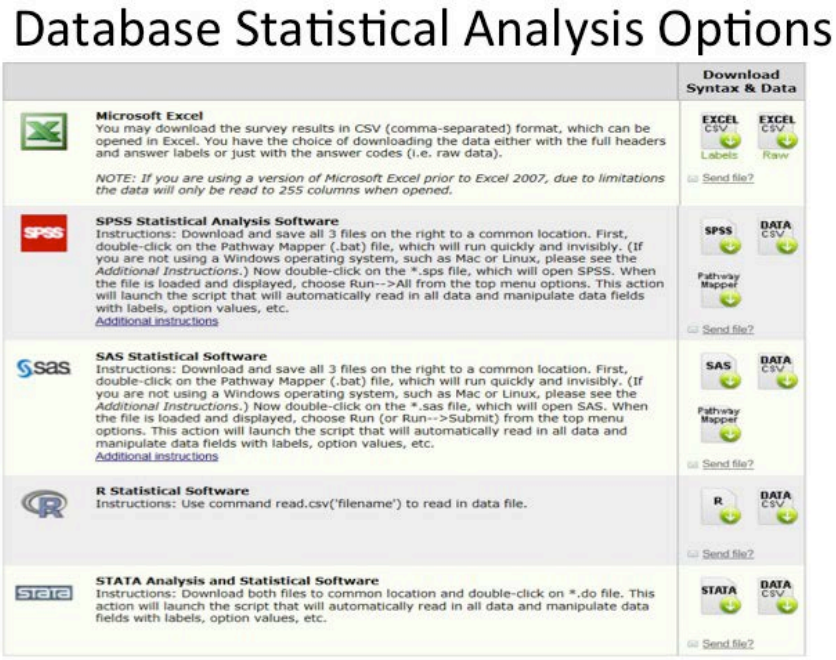


Figure 39



Project 1-Aim 3. Task 4: Perform pilot feasibility studies to determine the association of Hsp90 expression with patient outcomes.

We will perform this task as we develop a reliable assessment of Hsp90 high expression.

Project 1-Aim 4. GMP Manufacturing of PM Hsp90 Inhibitor

Project 1-Aim 4. Task 1: Establish synthetic pathways and SOPs for lead molecule

Studies with various cell and animal models with near infrared (NIR) versions of our tethered inhibitors identified HS-117, HS-131 and HS-118 as lead molecules for testing in human subjects. Of these molecules we had prioritized HS-131 over HS-117, based upon the structural influence of the NIR imaging moiety on the PK and PD of the complete molecule. Our ESAC suggested that HS-118 would be much more useful clinically.

Importantly, we have full synthetic control over the synthesis of these molecules and have therefore developed an SOP for their synthesis. Our lead chemist, Dr. Philip Hughes has developed protocols for the synthesis of the NIR component and its attachment to the tether. We also have full synthetic control over the ligand portion of the molecule as described in earlier reports to the DOD. These are important milestones and enable us to contact a pharmaceutical contractor for the production of GMP material prior to clinical studies.

Project 1-Aim 4. Task 2: Engage a private pharmaceutical contractor for synthesis of GMP material.

Albany Molecular Research Inc., NJ (AMRI) has been contacted as a potential contractor for the GMP synthesis of HS118. Currently an MTA is being put in place between Duke and AMRI to enable our molecule and methods of synthesis to be transferred to the contractor. A quote for the synthesis for the GMP manufacture of HS118 will be generated.

Project 1-Aim 4. Task 2: Produce GMP material. Based on our SOW, this will be produced this year.

Project 1-Aim 5. Required GMP Preclinical Toxicology Studies for Phase I Testing

Project 1-Aim 5. Task 1: Define an MTD value for our lead candidate in 3 species. Typically, a total of **220** mice to be used (110 per treatment group, 55 of each sex)
Preliminary MTD studies have been carried out with none GMP material with HS27 compared with the clinical candidate SNX5422 (the ligand portion of HS27 is derived from this drug). MTD values in mice were determined to be 80mg/Kg for HS27 compared with 30mg/Kg with SNX5422 showing the tethered molecules are likely to be better tolerated than free drug. MTD studies are underway with HS131.

Based on our SOW, this will be produced in Year 3.
Project 1-Aim 5. Task 2: If lead fails, repeat the MTD studies with other PM compounds tested in preclinical studies.

Based on our SOW, this will be produced in Year 3.

Project 1-Aim 5. Task 3: Perform appropriate GLP toxicology to support the IND

Based on our SOW, this will be produced in Year 3.

Project 1-Aim 6. Regulatory Pathway to Phase I Study

Project 1-Aim 6. Task 1: Pre-IND meeting with the FDA

Based on progress with HS-118 Dr Lyerly has requested a pre-IND meeting with the FDA to help guide development of HS-118 for Phase 0 clinical studies in human subjects.
Prior to filing our IND for the Phase I study, we have requested a Pre-IND meeting with FDA which was expected to occur August 19, 2014, however the FDA changed the date to September 19, 2014 which allowed to determine the expected requirement for the material and for the clinical trial.

Project 1-Aim 6. Task 2: Filing of an investigational new drug (IND) application with the FDA.
Our question and issues that we dicussed for HS131 were identical for HS118, therefore, we will produce GMP 118, and file our IND for HS118.

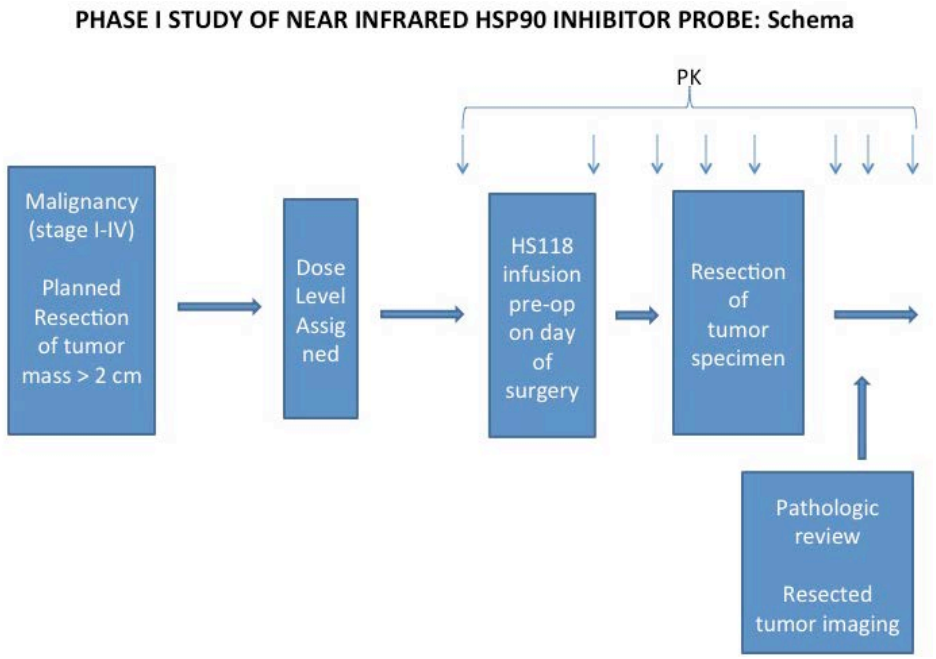
Based on our SOW, this will be produced in Year 3.

Project 1-Aim 6. Task 3: Obtain other regulatory approval including IRB and DOD approval for Phase I testing

Based on our SOW, this will be produced in Year 3.

Project 1- Aim 7. Begin Phase I Study with Lead PM HSP90 Inhibitor
Project 1-Aim 7. Task 1: Begin the Phase I study

Figure 40



Based on our SOW, this will be started in Year 3. In support of the clinical trial, we had been advised to include an expert on imaging clinical trials. Therefore, we asked Dr. Dan Sullivan to join as a co-investigator (see Changes to Key Personnel Section for biographical information).

Project 1-Aim 7. Task 2: Define the safety and PK profiles of the clinical PM lead compound in the phase I study.

Based on our SOW, this will be started in Year 3.

Project 1-Aim 7. Task 3: Identify a dose and schedule (single or daily x 3) for Phase II trials

Based on our SOW, this will be started in Year 3.

Project 1-Aim 7. Task 4: Perform PK and imaging studies to measure nIR-Hsp90i accumulation in tumors

Based on our SOW, this will be started in Year 3.

Project 1-Aim 7. Task 5: Perform PD analysis of tumor biopsies to verify the effects of the nIR inhibitor on the Hsp90 signaling node

Based on our SOW, this will be started in Year 3.

Project 1- Aim 8. Phase I Study: Begin Phase I Study of nIR-Hsp90i with nIR or RF mediated thermal therapy

Project 1-Aim 8. Task 1: Obtain regulatory approval of a Phase I study

Based on our SOW, this will be started in Year 4.

Project 1-Aim 8. Task 2: Begin Phase I study

Based on our SOW, this will be started in Year5.

Project 1-Aim 8. Task 3: Define MTD of combination of P2D from Phase I study with nIR or RF mediated thermal therapy

Based on our SOW, this will be started in Year5.

Project 1-Aim 8. Task 4: Define therapy related toxicities

Based on our SOW, this will be started in Year5.

Project 1-Aim 8. Task 5: Perform imaging studies to measure nIR-Hsp90i accumulation and indicators of temperature change

Based on our SOW, this will be started in Year5.

Project 1-Aim 8. Task 6: Perform analysis of cell viability and Hsp90 expression in samples obtained pre and post therapy.

Based on our SOW, this will be started in Year 5.

Project 2-Aim 1. Synthesis of PM-TKI: Development of Chemistry Plan for Synthesis of Novel PM Tyrosine kinase Inhibitors.

This project was discontinued after the year 2 Milestone meeting

a. Summary of the status of the U.S. Food and Drug Administration (FDA) approvals of Investigational New Drugs (INDs) and Investigational Device Exemptions (IDEs)

We are planning on filing our IND this year, as noted in the Milestone figure.

b. Discussion of changes to key personnel

As recommended, we have stopped work on Projects 2 and 3, and minimized efforts of Drs. Neil Spector and Chris Lascola.

We have also added more professional support for project management, added an experience imaging clinical trials expert, Dr. Dan Sullivan, and replaced Dr. Joe Geradts, our pathologist, who recently left Duke for a position with AstraZeneca in London.

Dan C. Sullivan, M.D.

Dr. Sullivan is Professor Emeritus of Radiology at Duke University Medical Center and has 35 years of experience in clinical and academic radiology, as well as developing and leading complex, cooperative organizations. He is considered a nationally recognized expert in imaging as a biomarker. Particularly relevant to this project, he was involved in the initiation of many imaging biomarker activities, including the Quantitative Imaging Biomarkers Alliance, and was Chair of QIBA from its formation in 2007 until 2015. As Chair-Emeritus of QIBA, he is in a unique position to facilitate dissemination and implementation of QIBA deliverables (e.g., Profiles, physical and virtual test objects, protocols, etc.) by diverse entities such as cooperative clinical trial groups, industry and academic institutions. In his current role with QIBA Dr. Sullivan is responsible for facilitating interactions between QIBA and many external organizations. These QIBA responsibilities will interface particularly well with the activities of CITARS. In addition, in QIBA he is also the Vice Chair of the QIBA Process Committee, to improve uniformity of procedures and activities across the QIBA committees. Dr. Sullivan also facilitates the emerging international activities of QIBA in Europe, Asia and South America.

Dr. Sullivan was an undergraduate at Brown University and then received his medical degree from the University of Vermont. After radiology residency and nuclear medicine fellowship at Yale, he practiced nuclear medicine as an assistant professor at Yale and then at Duke, where he was on faculty from 1978 to 1994. While at Duke, Dr. Sullivan did a part-time “sabbatical” in psychiatry—he completed a psychiatry residency and passed the board exam, he says, “so I could better understand why the world worked the way it did.” Returning to radiology in 1984, Dr. Sullivan developed an expertise in breast imaging, leading Duke’s Division of Mammography until 1991, when he assumed a larger administrative role as Director of Imaging. In 1994, he accepted a position at Penn to more fully pursue his interests in breast imaging.

In 1997, when the National Cancer Institute (NCI) decided that the time to address medical imaging had finally arrived, Dr. Sullivan competed for and won the position of Associate Director, Division of Cancer Treatment and Diagnosis, and head of what became the Cancer Imaging Program (CIP). During his 10 years at NCI, Dr. Sullivan grew the CIP “from the ground up” to a productive organization that took medical imaging research at NCI from a sleepy $47 million in grants and contracts in 1997 to more than $180 million when he left NCI in 2007. Examples of successful programs Dan developed and pushed through the competitive NCI environment included basic and translational research programs like the In Vivo Cellular and Molecular Imaging Centers and the Small Animal Imaging Resource Program project grants. He was responsible for the initiation of core funding for the Imaging Response Assessment Teams (IRATs), intended to better involve radiologists with cancer centers. By securing funding for key conferences on imaging sponsored by the National Institutes of Health (NIH) and by leading the development of initiatives like the Interagency Council for Biomedical Imaging in Oncology (ICBIO) and the NIH Biomarkers Consortium, Dr. Sullivan raised the profile of medical imaging throughout the NIH.

Edgardo Parrilla Castellar, M.D., Ph.D.

Dr. Parrilla Castellar received his combined, M.D./Ph.D. degree from the University of Puerto Rico School of Medicine and Mayo Clinic Graduate School. His post-graduate training in Anatomic Pathology was at the National Institutes of Health, Laboratory of Pathology, after which time he completed Surgical Pathology and Molecular Genetic Pathology fellowships at

the Mayo Clinic. He is currently Board Certified in Molecular Genetic Pathology, is an Assistant Professor with the UW Department of Pathology, and is a member of the Gynecologic and Breast Pathology service.

The focus of Dr. Parrilla Castellar's research is on the molecular genetics of gynecologic tract malignancies using massively parallel next generation sequencing approaches for diagnostic, therapeutic, and biomarker discovery applications. His research seeks to contribute more broadly to the development of high-throughput molecular genetics and precision diagnostics for personalized care within oncology.

BOARD CERTIFICATIONS

Board Certified in Anatomic Pathology

ACADEMIC/MEDICAL APPOINTMENTS

Assistant Professor, Department of Pathology, University of Washington, Seattle, WA, 2013-December 2014

Staff, University of Washington Medical Center, Seattle, WA, 2013-December 2014

Staff, Harborview Medical Center, Seattle, WA, 2013-December 2014

Staff, Seattle Cancer Care Alliance, Seattle, WA, 2013-December 2014

Assistant Professor, Department of Pathology, Duke University, Durham, NC, January 2015 - present

c. Discussion of significant budgetary changes

None

Small Animal Core and In vivo Imaging

Section I
The Small Animal Core is responsible for providing human and murine breast cancer cell lines representing molecular subtypes of early breast cancer for in vitro studies and imaging. In addition, the Small Animal Core will provide mouse models of breast cancer representing molecular subtypes for in vivo imaging.

Section II
Near infrared red (NIR)-tethered HSP90 inhibitors were generated by Haystead Lab, and intense NIR signals from tumors with less background noise level was confirmed in tumor-bearing mice using IVIS imager machine. In year 2, we performed in vivo labeling of breast tumors with NIR-tethered HSP90 inhibitor (HS-117, HS-119, HS-131, HS-132), and demonstrated the tumor uptake of NIR-Hsp90 inhibitors at 6 h time point and it's retention at 24 h time point. However, because these NIR-Hsp90i compounds have relatively shorter wavelengths for excitation and emission as NIR dye (HS-131/HS-132; emission 640 nm, HS-117/HS-119; emission 745 nm), the penetrance of NIR signals through the tissue might be limited. Imaging efficacy can be enhanced more with longer wavelength NIR-Hsp90 inhibitor compounds, such as HS-118 and HS-120 (emission wave lengths: 820 nm). Thus in year 3, using the FMT2500 imager machine (PerkinElmer) that can detect NIR signals around 800 nm, we performed imaging test of MDA-MB-468 breast cancer xenografts with HS-118, HS-120 and HS-165 (dye with linker as a negative control). We performed imaging test at the dose of 10 nmol and analyzed the signals after the tail vein injection, and NIR signals were detected from the tumor area in HS-118/HS-120 injected mice, and much weaker NIR signal in HS-165 injected mice. Strong NIR signals were confirmed in excised tumor tissues.

To get more sensitive detection of longer wavelength NIR signals, we obtained LI-COR Pearl Trilogy Imager machine, which has two lasers to detect the NIR signals at emission wavelength of 700 nm and 800 nm. In the previous quarter, we confirmed the very strong NIR signals (800 nm channel) from the tumors could be detected after i.v. injection of HS118.

Imaging of MDA-MB-468 xenograft with HS118

To test the over time change of NIR signals from tumors after the administration of HS118, MDA-MB-468 tumors in SCID mice were tested. Based on the imaging test with LI-COR Pearl machine in the previous quarter, we confirmed that 1 nmol of HS118 compound is sufficient to label MDA-MB-468 tumors in vivo, and thus we used 1 nmol dose for imaging with HS118. MDA-MB-468 cells (1 x 10E6 cells/mouse) in 50% Matrigel were implanted subcutaneously to the right flank of mice. When tumor size reached about 10 mm in diameter, mice were used in imaging test. Images were taken for individual mice at pre-injection, immediate, 3 h, 6 h, 12 h, 24 h, 48 h, and 120 h after NIR-HSP90i compound injection. NIR signals detected at 800 nm channel are shown in Figure 41.

Figure 41A

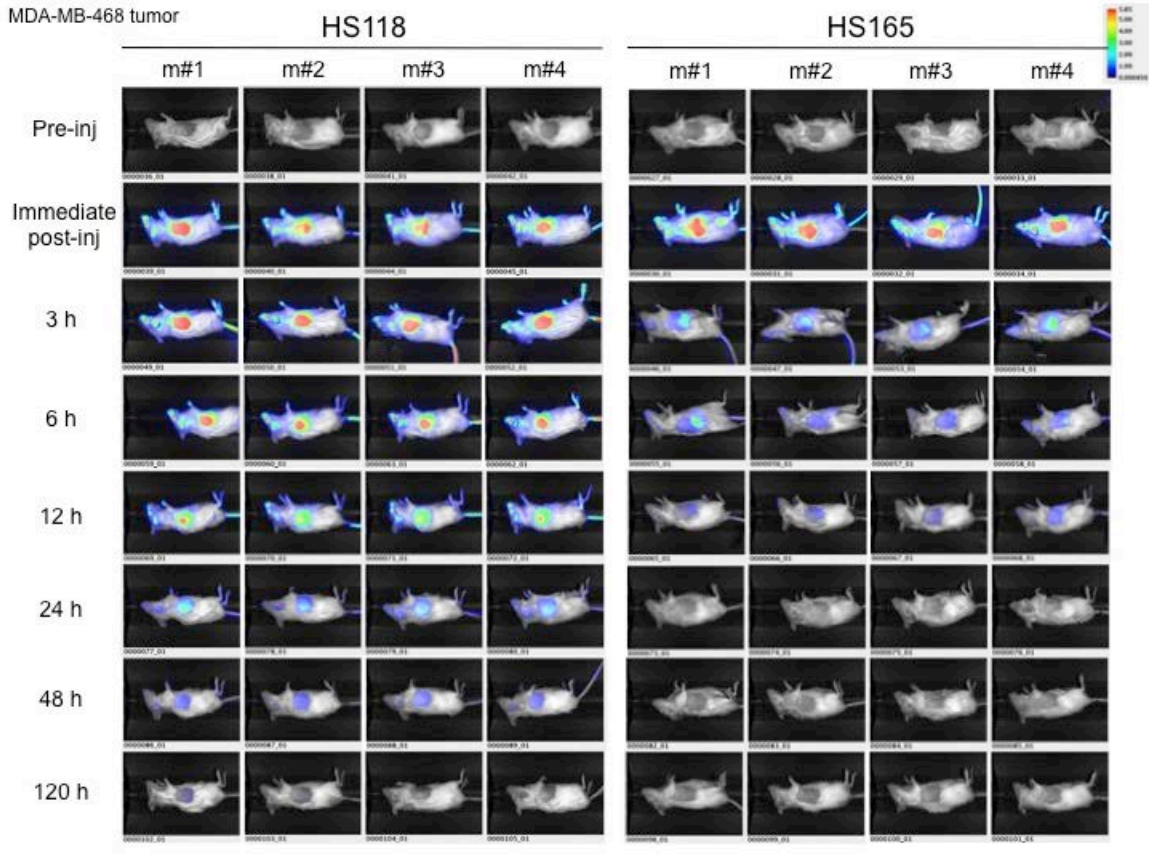


Figure 41A. MDA-MB-468 tumor imaging with HS-118 and HS165: nIR Signals
HS118 or HS165 (control compounds) were injected via tail vein (1 nmol /injection). Immediate after, 6 h, 24 h, 48 h, and 120 h after injection, NIR signals (800 nm channel) from tumor area were detected by Pearl Imager.

Figure 41B

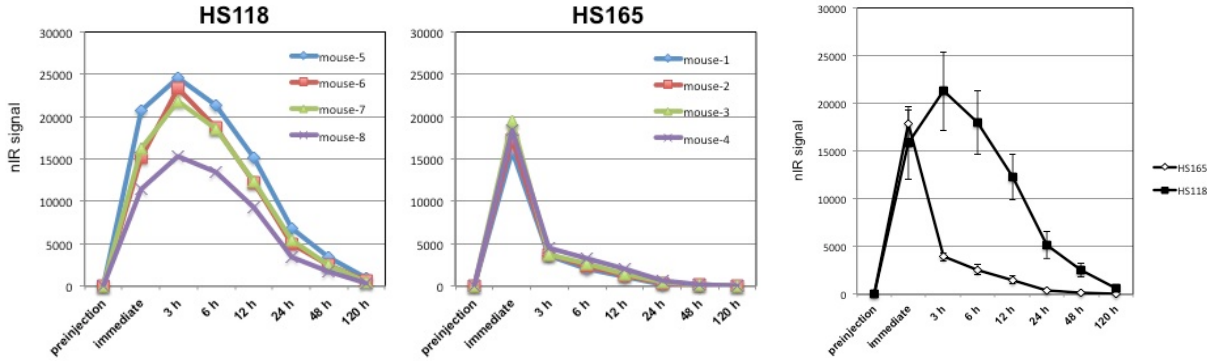


Figure 41B. Over time change of nIR signals from MDA-MB-468 Tumors: HS118 vs. HS165. NIR signals (800 nm channel) from tumor areas are shown for each mice (left, middle panel) and in average (right panel). Error Bar: SD.

As shown in Figure 41A, 4 mice in each group showed similar imaging pattern and clearly the retention of the nIR signals in tumors were stronger and longer in HS118 compared to control HS165. In Figure 1B, nIR signals from tumor areas were graphed, which shows the clear trend of longer retention in HS118 injected mice compared to HS165 injected mice. In HS165 injected mice, the strength of nIR signals fell quickly even at 3 h after tail vein injection, and almost completely washed out by 24 h time point. HS118 compound, however, showed the peak signal intensities at 3 h, and then gradually decreased. The signals were still detectable at 24 h, and even at 48 h time point after injection.

We plan to test NIR-HSP90 inhibitor compounds in multiple different breast cancer xenograft models with different molecular subtypes as shown in Table 2. For luminal, HER2+, triple negative, DCIS, and spontaneous breast cancer (GEMM) model, we will have 2 cancer cell lines or mouse strains for each molecular subtype.

Table 2

Molecular Subtype	Cell Line
Luminal	MCF7
	T-47D
HER2	BT474M1
	KPL4
Triple Negative	MDA-MB-468
	MDA-MB-231
DCIS	MCF10.DCIS.COM
	SUM225
GEMM	MMTV-neu
	MMTV-tTA

Table 2. Breast cancer models to be tested for imaging with NIR-HSP90 inhibitor.

In this quarter, imaging with HS118 was tested for most of the breast cancer models listed in Table 2, except SUM225 and MMTV-rTA. Imaging tests were performed in the same setting with MDA-MB-468 tumor model.

LUMINAL TYPE BREAST CANCER
MCF-7 Tumor

Figure 42A

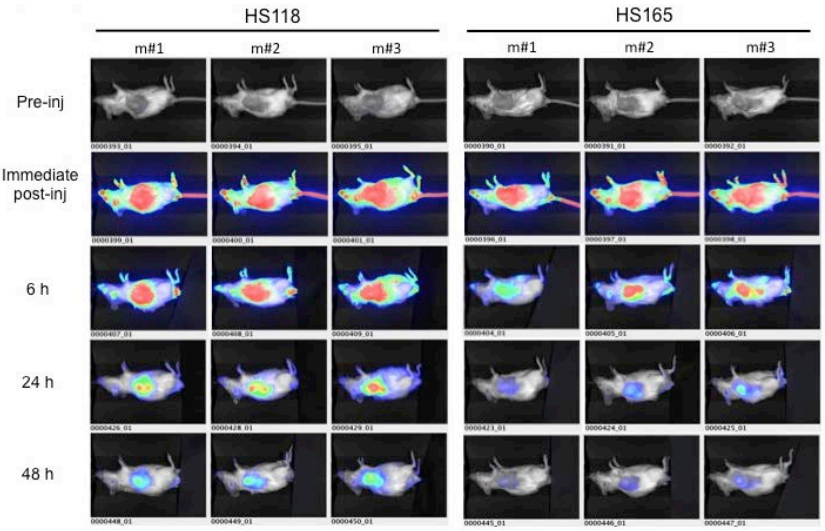


Figure 42A. MCF7 tumor imaging with HS-118 and HS165: nIR Signals. HS118 or HS165 (control compounds) were injected via tail vein (1 nmol /injection). Immediate after, 6 h, 24 h, and 48 h after injection, NIR signals (800 nm channel) from tumor area were detected by Pearl Imager.

Figure 42B

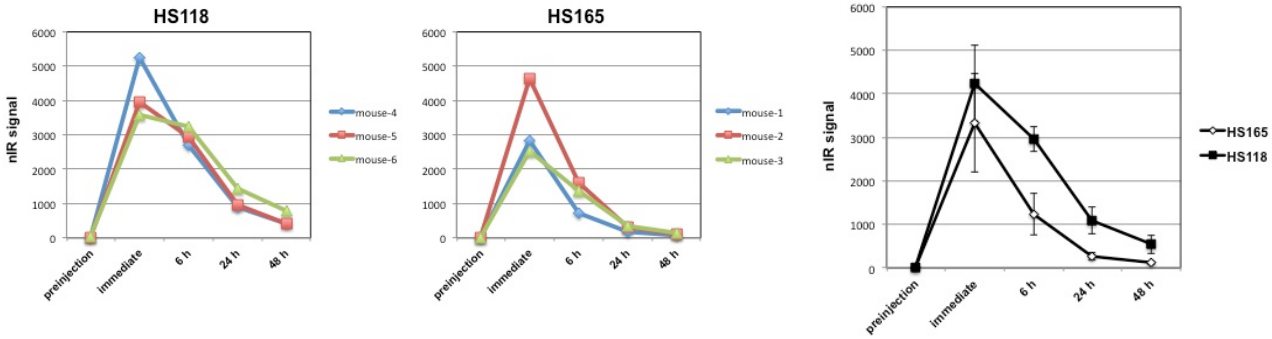


Figure 42B. Over time change of nIR signals from MCF7 Tumors: HS118 vs. HS165. NIR signals (800 nm channel) from tumor areas are shown for each mice (left, middle panel) and in average (right panel). Error Bar: SD.

As shown in Figure 42A and 42B, HS118 made stronger nIR signals from MCF7 tumors compared to control HS165, and the difference was evident at 6 h or 24 h time point. Anther luminal type breast cancer, T-47D tumor, was also tested. As shown in Figures 43A and 43B, similar imaging pattern with previous 2 tumor models was obtained. Although the difference in nIR signal intensities was not so large (Figure 43B), the difference between HS118 and HS165 was still detectable at 48 h time point as shown in Figure 43C.

T-47D Tumor

Figure 43A

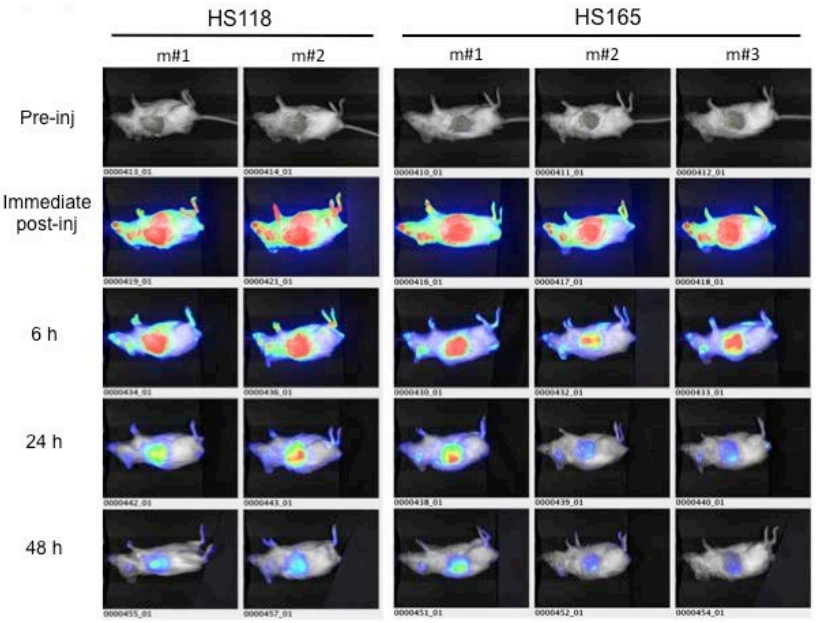


Figure 43A. T-47D tumor imaging with HS-118 and HS165: nIR Signals. HS118 or HS165 (control compounds) were injected via tail vein (1 nmol /injection). Immediate after, 6 h, 24 h, and 48 h after injection, NIR signals (800 nm channel) from tumor area were detected by Pearl Imager.

Figure 43B

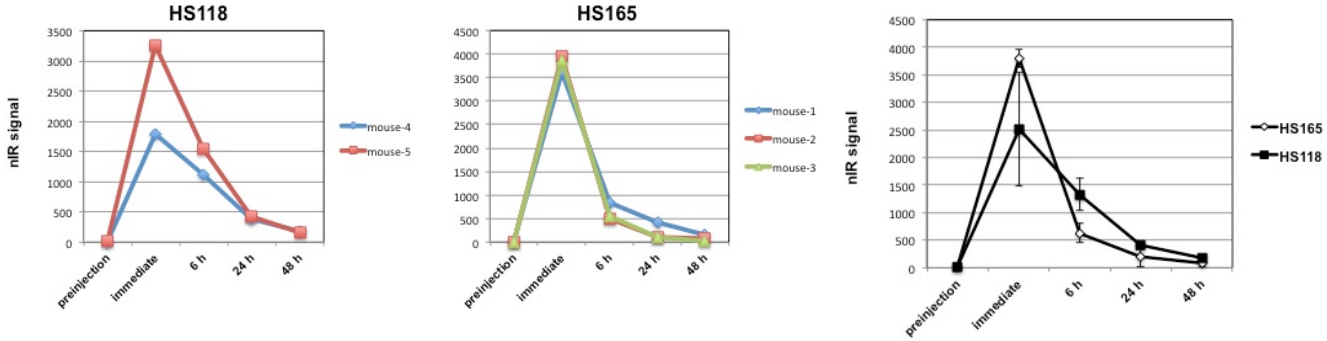


Figure 43B. Over time change of nIR signals from T-47D Tumors: HS118 vs. HS165. NIR signals (800 nm channel) from tumor areas are shown for each mice (left, middle panel) and in average (right panel). Error Bar: SD.

Figure 43C

HS118 **HS165**

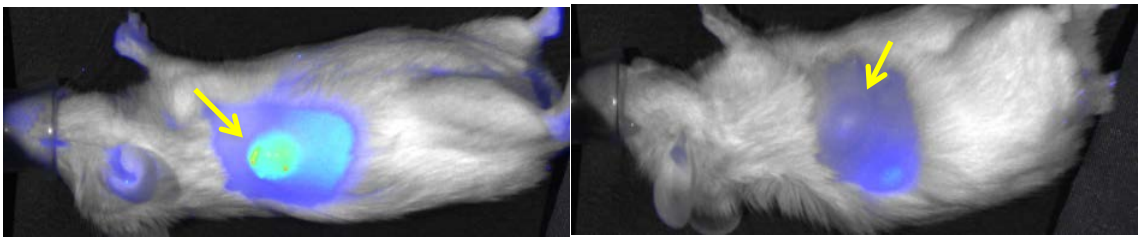


Figure 43C. Representative Images of T-47D Tumor at 48 h. For HS118 imaging, tumors are detectable even at 48 h after injection, while HS165 makes negative at tumor area (shown by yellow arrows).

HER2 POSITIVE BREAST CANCER
BT474M1 Tumor

Figure 44A

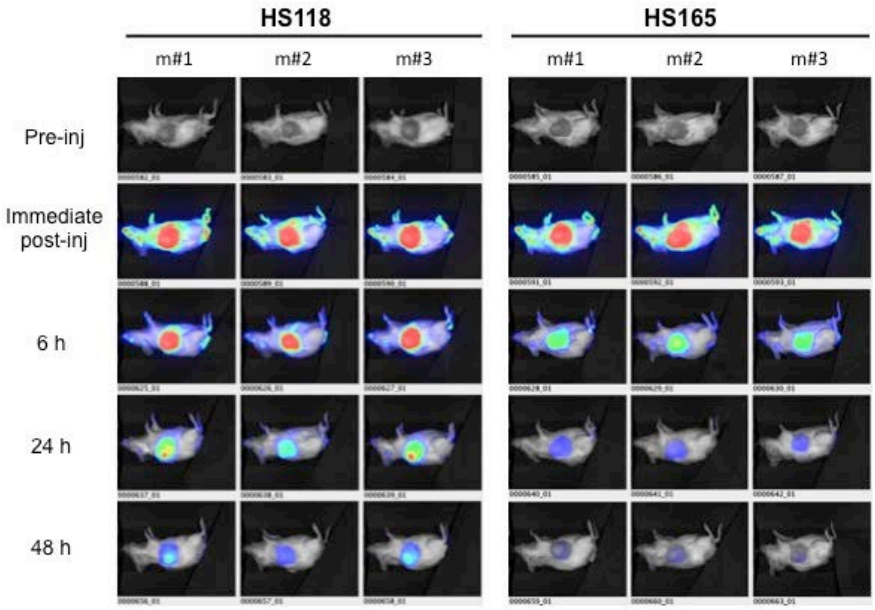


Figure 44A. BT474M1 tumor imaging with HS-118 and HS165: nIR Signals. HS118 or HS165 (control compounds) were injected via tail vein (1 nmol /injection). Immediate after, 6 h, 24 h, and 48 h after injection, NIR signals (800 nm channel) from tumor area were detected by Pearl Imager.

Figure 44A

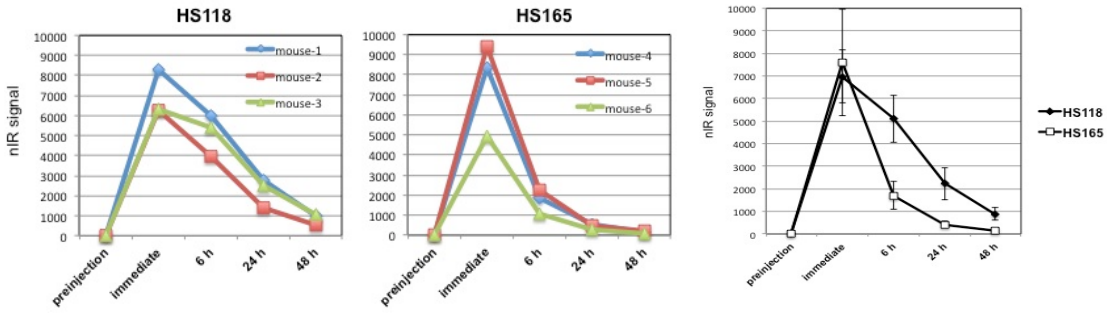


Figure 44B. Over time change of nIR signals from BT474M1 Tumors: HS118 vs. HS165. NIR signals (800 nm channel) from tumor areas are shown for each mice (left, middle panel) and in average (right panel). Error Bar: SD.

KPL4 Tumor

Figure 45A

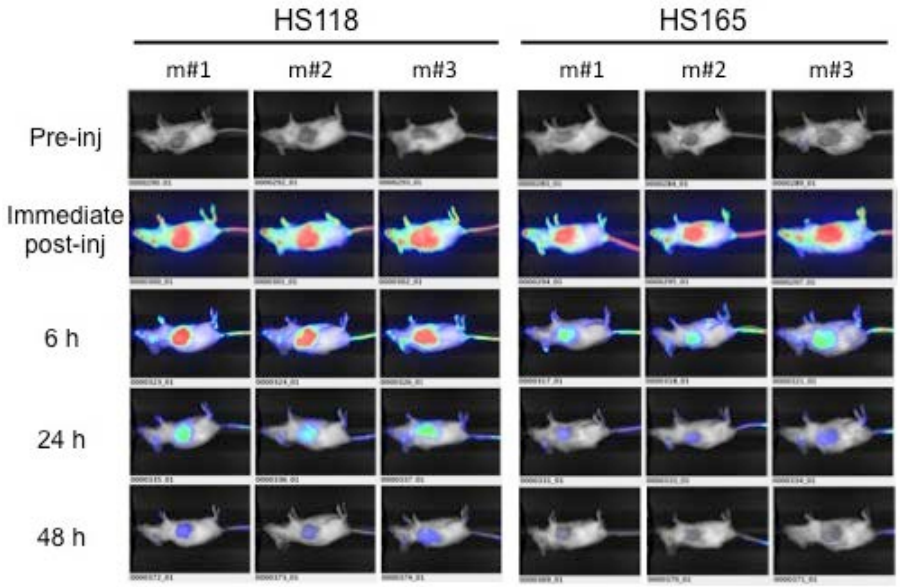


Figure 45A. KPL4 tumor imaging with HS-118 and HS165: nIR Signals. HS118 or HS165 (control compounds) were injected via tail vein (1 nmol /injection). Immediate after, 6 h, 24 h, and 48 h after injection, NIR signals (800 nm channel) from tumor area were detected by Pearl Imager.

At 6 h and 24 h time points, the difference of nIR signal intensities were clear between HS118 injected mice and HS165 injected mice. Three mice in each arm showed similar uptake and release of the compounds. For HS118 group, nIR signals were still detectable at 48 h time point.

Figure 45B

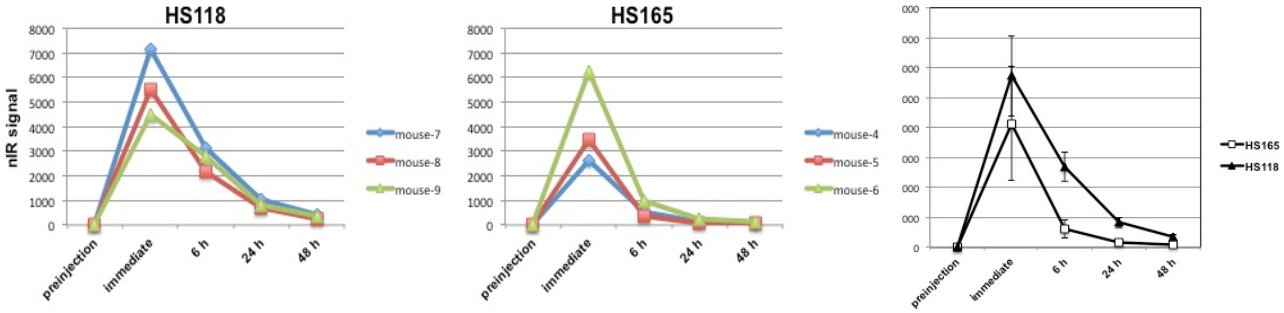


Figure 45B. Over time change of nIR signals from KPL4 Tumors: HS118 vs. HS165. NIR signals (800 nm channel) from tumor areas are shown for each mice (left, middle panel) and in average (right panel). Error Bar: SD.

TRIPLE NEGATIVE BREAST CANCER

MDA-MB-231 Tumor

Figure 46A

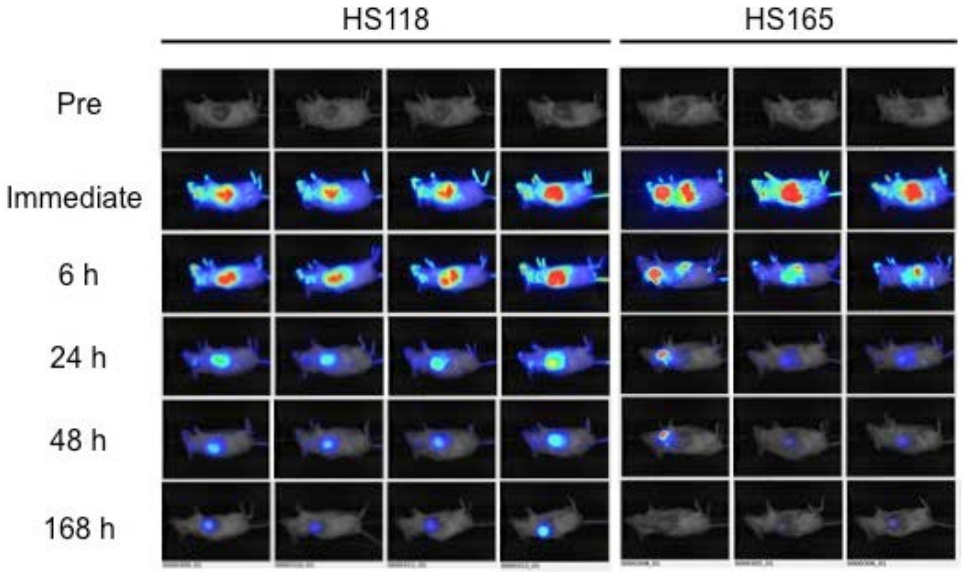


Figure 46A. MDA-MB-231 tumor imaging with HS-118 and HS165: nIR Signals. HS118 or HS165 (control compounds) were injected via tail vein (1 nmol /injection). Immediate after, 6 h, 24 h, 48 h and 168 h after injection, NIR signals (800 nm channel) from tumor area were detected by Pearl Imager.

Figure 46B

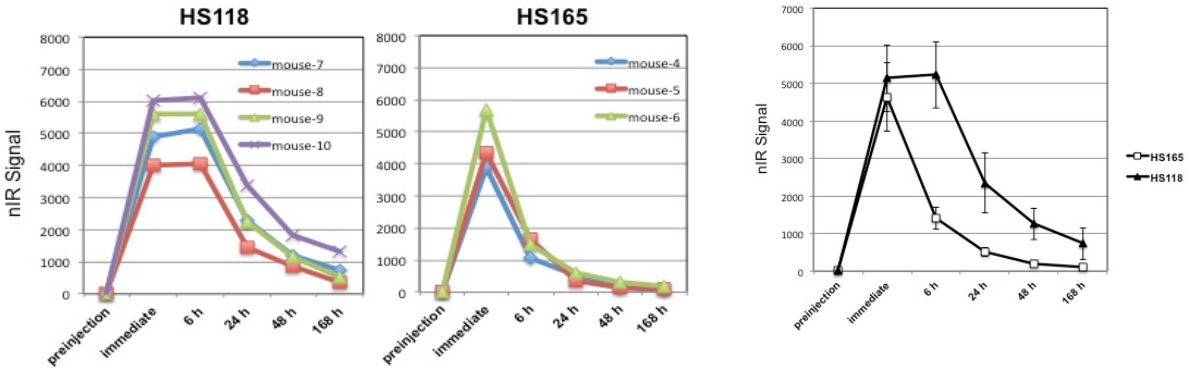


Figure 46B. Over time change of nIR signals from MDA-MB-231 Tumors: HS118 vs. HS165. NIR signals (800 nm channel) from tumor areas are shown for each mice (left, middle panel) and in average (right panel). Error Bar: SD.

MDA-MB-468 Tumor: Shown above (Figure 41A & 41B)

DUCTAL CARCINOMA IN SITU

MCF10DCIS.COM Tumor

Figure 47A

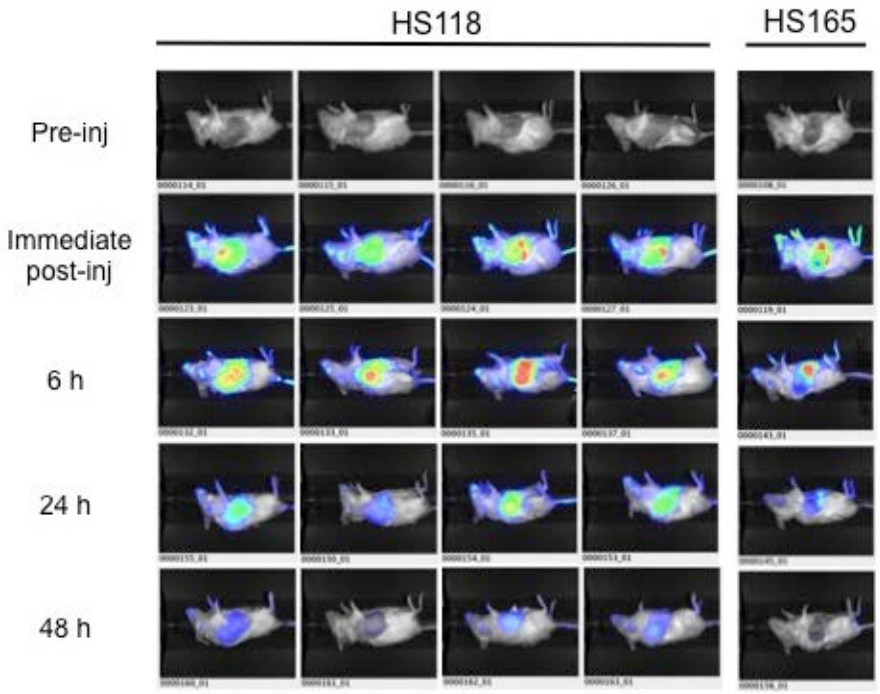


Figure 47A. MCF10DCIS.COM tumor imaging with HS-118 and HS165: nIR Signals. HS118 or HS165 (control compounds) were injected via tail vein (1 nmol /injection). Immediate after, 6 h, 24 h, and 48 h after injection, NIR signals (800 nm channel) from tumor area were detected by Pearl Imager.

Figure 47B

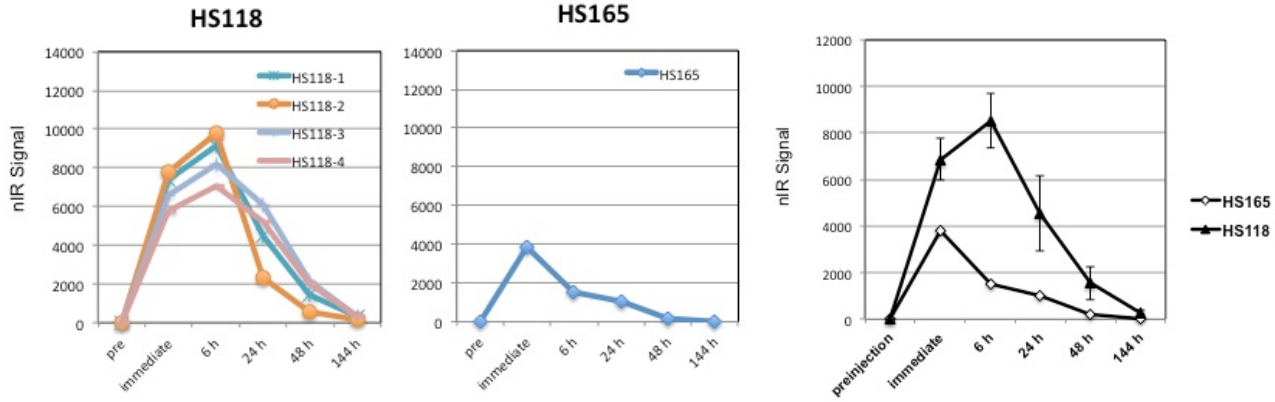


Figure 47B. Over time change of nIR signals from MCF10DCIS.COM Tumors: HS118 vs. HS165. NIR signals (800 nm channel) from tumor areas are shown for each mice (left, middle panel) and in average (right panel). Error Bar: SD.

Figure 47C

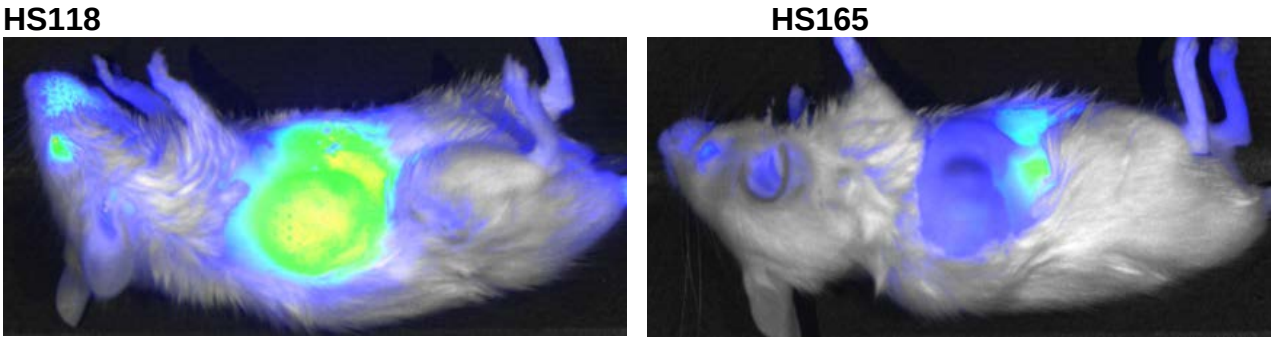


Figure 47C. Representative Images of MCF10DCIS.COM Tumor at 24 h. By imaging with HS118, tumors are detectable at 24 h after injection, while HS165 makes negative at tumor area.

Importantly, even for the DCIS type breast tumor, uptake of HS118 by tumors was stronger than that of HS165. The peak of nIR signals from tumors in HS118 injected mice were coming around 6 h time point and the signal decreased by 24 h to almost a half intensity, and decreased to a quarter level at 48 h time point.

GENETICALLY ENGINEERED MOUSE MODEL
MMTV-neu

Figure 48A

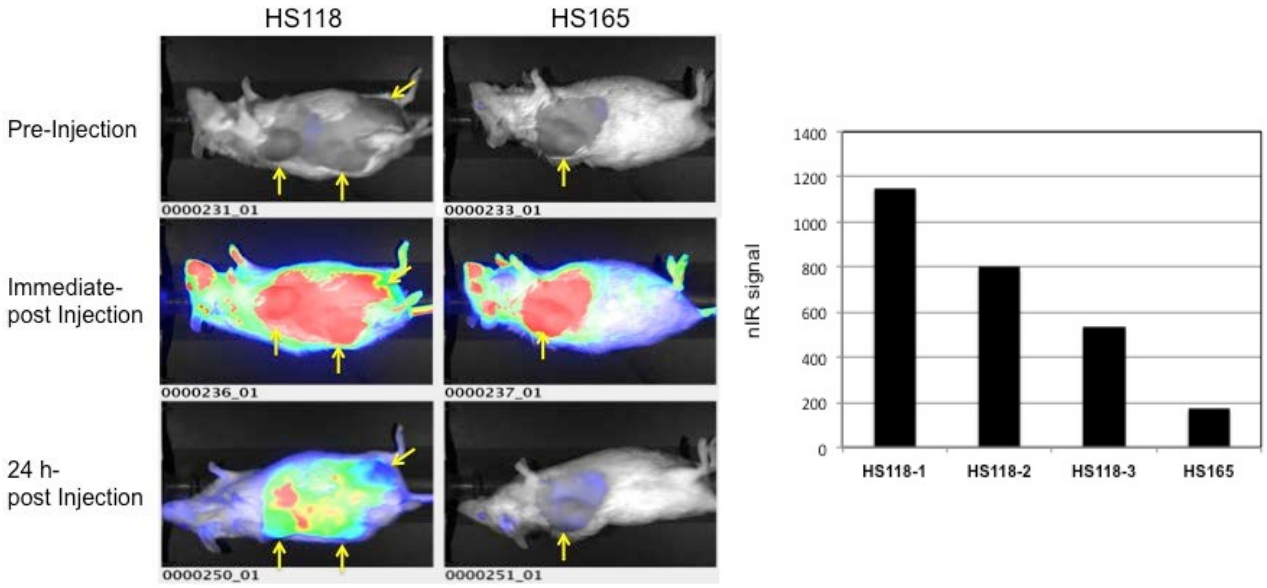


Figure 48A. nIR-Hsp90i imaging of Spontaneous Breast Tumors in MMTV-neu mice. Female MMTV-neu mice developed spontaneous breast tumors in 2nd~4th mammary glands with the size of around 1 cm in diameter. HS118 or HS165 (control compounds) were administered via tail vein (1 nmol/mouse) and 24 h later, mouse images were taken by Pearl Imager. Yellow arrows indicate the tumors (Left panel). nIR signals from spontaneous tumors at 24 h after iv injection of HS118 or HS165 are shown in the right panel. One of MMTV-neu mice developed 3 spontaneous tumors simultaneously and imaging test with HS118 was done at once.

Figure 48B

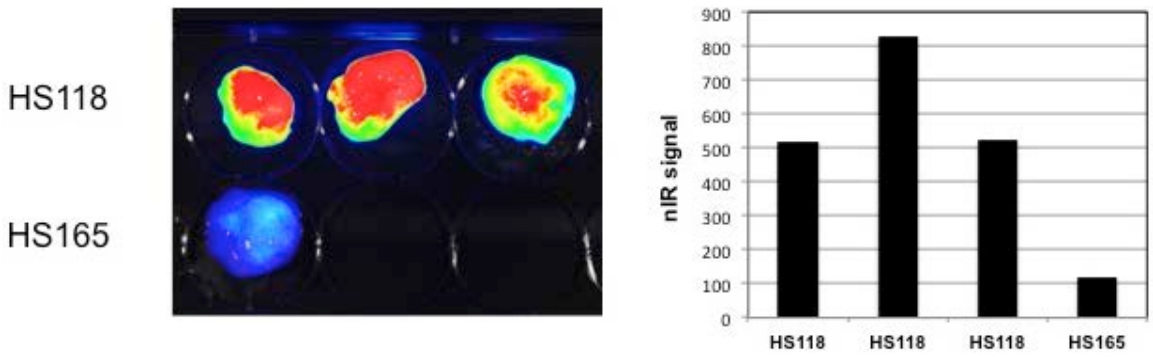


Figure 48B. nIR Signals of Spontaneous Breast Tumors in MMTV-neu mice. HS118 or HS165 (control compounds) were administered via tail vein (1 nmol/mouse) to female MMTV-neu mice bearing spontaneous breast tumors with the size of around 1 cm in diameter. Twenty-four hours later, tumors were excised and nIR signals detected by Pearl Imager.

Although the number of mice are still limited for the imaging of MMTV-neu spontaneous tumor, HS118 injection made strong nIR signals at 24 h time point, which was approximately 5 times stronger than that with HS165. Although nIR signals of tumors detected by whole body imaging

was relatively weak for MMTV-neu tumors (nIR signals 534~1150) compared to other implanted human breast cancer xenografts shown above (around 1000 or above at 24 h time point), nIR signals were still detectable with LI-COR Pearl Imager.

Simultaneous Imaging of MDA-MB-468 Tumors

HS118 vs. HS152: To confirm the different pharmacokinetic of HS118 and control compound (HS152), these compounds (10 nmol each/20 µL vehicle) were mixed before injection and administered via tail vein. nIR signals were assessed by LI-COR Pearl Imager soon after injection till 7 day time point. HS152 is a control compound for HS131 with emission wavelength of 640 nm, consists of nIR dye with linker but without HSP90 inhibitor. HS118 signal (800 nm channel, green color) was overlaid with HS152 signal (700 nm channel, red color).

Figure 49A

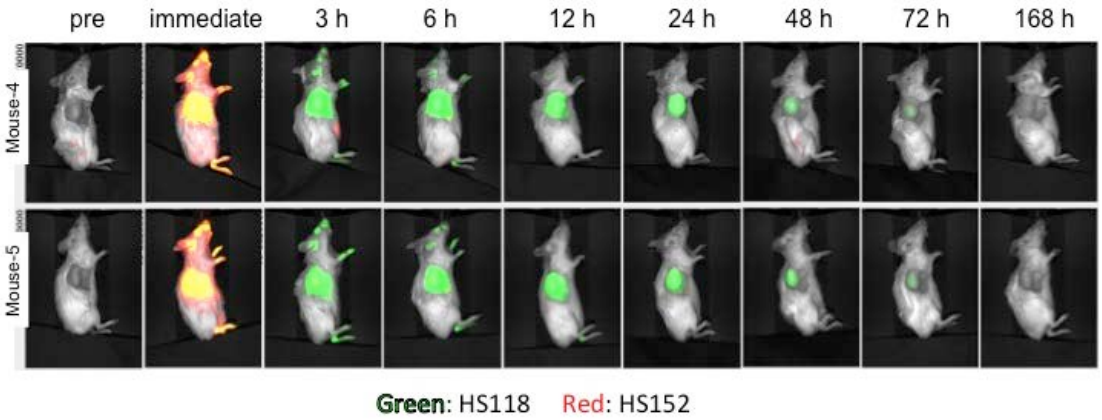


Figure 49A. Simultaneous Imaging of MDA-MB-468 Tumor: HS118 vs. HS152
MDA-MB-468 tumor bearing SCID mice were injected with mixture of HS118 and HS152 compounds (10 nmol each/20 µL vehicle). Over time change of the nIR signals were detected at 700 nm (Red) and 800 nm (Green) channels, and signals were overlaid.

Figure 49B

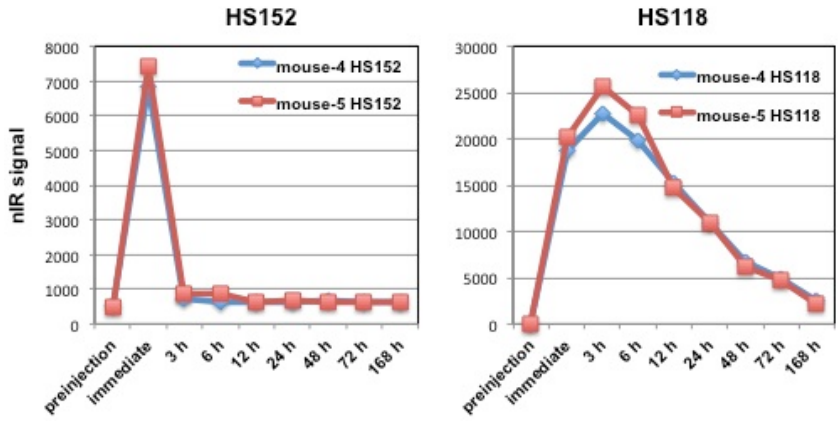


Figure 49B. Simultaneous Imaging of MDA-MB-468 Tumor: nIR signals from tumors. MDA-MB-468 tumor bearing SCID mice (n=2) were injected with mixture of HS118 and HS152 compounds. Over time change of the nIR signals were detected at 700 nm (Red) and 800 nm (Green) channels, and shown in the graphs.

Co-administration of two different compounds to MDA-MB-468 tumor bearing mice showed different kinetics of these compounds in the tumors. Immediate images after co-administration showed yellow color in whole bodies, suggesting the distribution of both compounds by blood flow. Especially, skin exposed area, such as legs and nose, and tumor area showed yellow color. However as early as 3 h time point, most of red color signal weakened. HS118 clearly showed longer retention inside the tumors compared to control HS152 which will not bind to Hsp90 protein and thus do not make strong uptake by tumor tissues. In this experiment, by the simultaneous imaging of nIR-HSP90 inhibitor compound (HS118) and control compound (HS152) in the same tumors, we confirmed that HS118 has longer retention inside the tumors than control compound.

Summary of Breast Cancer Imaging with HS118

1) Luminal, HER2+, Triple Negative, and DCIS xenograft models as well as spontaneous breast cancers (MMTV-neu) were tested for the imaging with HS118.
2) Over time change of the nIR signals from tumors were analyzed, which showed the peak intensity around 3~6 hours after nIR-HSP90 inhibitor injection. nIR signals deceased significantly by 24 hours, but mostly they were still detectable by LI-COR imager until 48 h time point, and even at 168 h time point for some tumors (MDA-MB-231).
3) Compared to control HS165, retention of HS118 in tumors was longer for all breast cancers analyzed in this study, and therefore, the differences in nIR signals from tumors were detectable at 6 ~ 24 h or 6 ~ 48 h time points depend on cancer cell lines.
4) Imaging of tumors with HS118 was applicable to all the breast cancers with different molecular subtypes.

Plan

1) Accumulate more MMTV-neu mice with spontaneous breast tumors for imaging test with HS118/HS165.
2) Accumulate more MMTV-rTA mice with spontaneous breast tumors as another GEMM model for imaging test with HS118/HS165.
3) Conduct imaging test with SUM225 tumor bearing mice as another model of DCIS type tumor.

Administrative Updates

None

4. Key Research Accomplishments

- Demonstrated high Hsp90 mRNA expression and breast outcome relationship- published.
- Established mammographic tumor sampling program for mammogram detected breast cancer bank.
- Design and synthesized multiple small molecule Hsp90 inhibitors linked to contrast agents- published.
- Tested Hsp90i-nIR contrast in vitro in triple negative, and HER2+ breast cancers.
- Tested Hsp90i-nIR contrast in vivo models of triple negative and HER2+ breast cancers.
- Held a second External Scientific Advisory Committee meeting at Duke.
- Prepared pre-IND package for FDA review, held pre-IND teleconference with FDA.
- Planning GMP manufacturing and regulatory approval for FIH testing.
- Design and synthesized small molecule Hsp90 inhibitors linked to nIR contrast agents for phototherapy.

5. A description of work to be performed during the next reporting period

See Appendix C, “2016 Milestones and Future SOW.”

6. Administrative Comments

Project management: VSolvit contracted to support project.

- SBA certified 8(a)/Small Disadvantaged Business, HUBZone, and 8(m)/Economically Disadvantaged Woman owned, technology services provider that specializes in business intelligence (BI) systems, data warehousing, geographic information systems (GIS), custom application development, health analytics, project/program management, and hosting and cloud services.

- Serves clients such as the Department of Defense (DOD), the U.S. Department of Agriculture (USDA), the Department of Housing and Urban Development (HUD), and the Bill & Melinda Gates Foundation.

- Custom technology solutions for federal and health industry clients and partners have won awards for innovation, been launched from the U.S. White House, and are being used to solve complex problems ranging from improving national security to optimizing vaccine supply chains and breast cancer screening and treatment programs.

VSolvit personnel have previously been part of the large biopharma supporting program / project management function.

Mr. Ashish Shah has been part of the R&D Program Management group to advance Oncology Therapeutic product candidates through the pipeline. He has supported team in strategy identification, and execution for various oncology indications, supported Capacity Planning & Resourcing activities, performed gap analysis, and executed other program level support. He has facilitated program risk management, issue identification and issues resolution, and maintained timelines. He has supported / instituted tools such as Community Portal, and EDM Teams to support collaboration among team members. He has a strong experience managing projects for Pharma – R&D /Clinical / Commercialization domain. He is experienced in end to end project management including managing project finances, managing business stakeholders and project sponsors across multiple disciplines such as commercial, development, operations, and regulatory.

Project 2 and Project 3.
These projects were discontinued following the year 2 Milestone meeting.

7. Conclusion

We have synthesized a variety of compounds**,** and have tested them in vitro and in vivo in a variety of models representing the molecular subtypes of breast cancer, non-invasive breast cancer, and spontaneous breast cancer in murine models.

We had our yearly External Scientific Advisory Committee meeting. They recommended that the “proof of principle” of visualizing malignant cells by detecting HSP90 uptake by malignant cells could be achieved by using near infrared probes, rather that MRI probes at this time. We are currently addressing the options of optical, near infrared, radioisotope, or MRI probes for our first in human and proof of concept studies for visualization, but the strong recommendation was for a nIR probe that was in the 700-800 range. For this reason, we developed additional probes, acquired an instrument to screen animals in this range, and repeated studies with newly synthesized probes that could be detected with light in this range. Furthermore, our choice of nIR probes allowed for the generation of near 700 nm probes that would be useful to tissue ablation, and a second generation probe looks promising.

Based on current findings, we are in process to produce GMP probe for first in human and proof of concept studies to be started this year. We have addition an expert, Dr. Sullivan in imaging studies to aid this work.

Several nrIR probes have also been sent to Brian Pogue the Dartmouth group which may well offer a opportunity to test our probes patients with breast cancer. We anticipated that studies with this group will also aid in candidate selection, but is more likely that we will collaborate with them using their breast specific detectors.

We will continue to prospectively collect and clinically annotate research tissue and blood from consented patients with mammographically detected breast lesions undergoing diagnostic breast biopsies. We project that we will consent approximately 120 patients each calendar year for this tissue and blood collection study.

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8. Publications, Abstracts and Presentations

Cheng Q, Chang JT, Geradts J, Neckers LM, Haystead T, Spector NL, Lyerly HK. Breast Cancer Res. 2012 Apr 17;14(2):R62.

Barrott JJ, Hughes PF, Osada T, Yang XY, Hartman ZC, Loiselle DR, Spector NL, Neckers L, Rajaram N, Hu F, Ramanujam N, Vaidyanathan G, Zalutsky MR, Lyerly HK, Haystead TA. Optical and radioiodinated tethered Hsp90 inhibitors reveal selective internalization of ectopic Hsp90 in malignant breast tumor cells. Chem Biol. 2013 Sep 19;20(9):1187-97. doi: 10.1016/j.chembiol.2013.08.004. Epub 2013 Sep 12.

Matthew K. Howe, Khaldon Bodoor, Philip F. Hughes, David R. Loiselle, Alex M. Jaeger, David B. Darr, Jamie L. Jordan, Lucas M. Hunter, Eileen T. Molzberger, Theodore A. Gobillot, Dennis J. Thiele, Jeffrey L. Brodsky, Neil L. Spector and Timothy A. J. Haystead. Identification of a Novel Allosteric Small Molecule Inhibitor of the Inducible Form of Heat Shock Protein 70. 2014 submitted

9. Inventions, Patents and Licenses

Patent application to tethered Hsp90 inhibitors filed by Duke and Dr. T. Haystead

10. Reportable Outcomes

None

11. Other Achievements

None

12. References

Barrott JJ, Hughes PF, Osada T, Yang XY, Hartman ZC, Loiselle DR, Spector NL, Neckers L, Rajaram N, Hu F, Ramanujam N, Vaidyanathan G, Zalutsky MR, Lyerly HK, Haystead TA. Optical and radioiodinated tethered Hsp90 inhibitors reveal selective internalization of ectopic Hsp90 in malignant breast tumor cells. Chem Biol. 2013 Sep 19;20(9):1187-97. doi: 10.1016/j.chembiol.2013.08.004. Epub 2013 Sep 12.

Cheng Q, Chang JT, Geradts J, Neckers LM, Haystead T, Spector NL, Lyerly HK. Amplification and high-level expression of heat shock protein 90 marks aggressive phenotypes of human epidermal growth factor receptor 2 negative breast cancer. Breast Cancer Res. 2012 Apr 17;14(2):R62.

13. Appendices

A. ESAC Report

B. Inventory of Synthesized Compounds

C. 2016 Milestones and Future SOW

D. Gantt Charts

External Scientific Advisory Committee (ESAC) Report

Duke University DOD TVA Award

"Detection and Elimination Of Oncogenic Signaling Networks In Premalignant And Malignant Cells With Magnetic Resonance Imaging"

Principal Investigator- Herbert K. Lyerly, MD

Meeting Date: January 20, 2015

ESAC Members:

1. **Len Neckers, PhD**
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2. **A. Dean Sherry, PhD**
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*Absent

Summary and ESAC Comments on Project Direction

The Duke DoD TVA Award team made significant progress during phase I of the supported research period and is much closer to a formal test of their hypothesis to detect breast cancer using molecularly targeted imaging agents. In response to prior reviews by the ESAC and the recent DoD Milestone assessment, the team focused its effort on detecting breast cancer that is characterized by ectopically expressed HSP90 using synthetic NIR probes consisting of a HSP90 binding domain linked to a NIR excitable moiety. Given the time and resources available to this research group as well as recent progress with the HSP90 NIR probes, this is an appropriate decision.

The research team prepared by chemical synthesis six HSP90-targeting NIR probes with interesting potential. These agents have yet to undergo rigorous pharmacologic investigation as will be necessary to select a single agent (and possibly a backup candidate) for clinical evaluation.

Although HS-131 looks very interesting in the laboratory, its NIR excitation/emission spectrum renders it an unlikely agent for clinical application. It appears to have been selected, in part, for its compatibility with the group's existing imaging equipment. However, sensitivity and other parameters of this imaging technology are not optimal for clinical application. A major concern of the ESAC is that the investigators plan to move forward with pre-IND studies and first in human studies without having identified the optimal NIR agent for human imaging and without the proper clinical trial design suitable to evaluate an imaging agent.

- Comparisons were done using various linker molecules between the HSP targeting moiety and a Cy5.5 probe that absorbs light at 640 nm. Based on comparisons of HS-131, HS-132 and HS-152 in animals bearing MDA-MB-468 tumors using an IVIS system for detection (Ex = 640 nm, certainly not optimal for human breast imaging), HS-131 was chosen as the best NIR probe to move

forward toward clinical trials. The ESAC believes this is premature, in that HS-131 is not optimized for human breast imaging. A NIR probe that emits light in the 800-900 nm region would have been a better choice for pre-clinical experiments but these were apparently not attempted because of instrument limitations. ESAC recommends that a scientific priority should be placed on the practical need for an imaging device appropriate to the wavelength most suitable for breast imaging, whether obtained via purchase, lease or collaboration. It seems possible that combining the proper NIR probe with various linkers to the HSP targeting moiety could in fact lead to a different conclusion.

- There seems to have been little thought given as to how to proceed toward a clinical trial in breast imaging. How will the imaging be done? Why have investigators not considered working with a company (or companies) with expertise in optical breast imaging designs? We suggest that a feasible strategy would be to combine the group's expertise in building HSP targeting probes with relevant optical breast imaging equipment so that they could match the optimal wavelengths of the probe with the equipment that will ultimately be used clinically.

- The ESAC recommends that the group refocus priorities as necessary to move as quickly as possible into collaborations with one or more companies building optical breast imaging equipment.

- Should the Duke team need suggestions as to whom to partner with to identify an optimal probe and imaging equipment, the ESAC suggests contacting Brian Pogue (Dartmouth, presenter at the ESAC meeting) and/or John Frangioni, a PhD/clinician who recently left his job at Harvard to start a company (http://curadel.com/home/) that produces both NIR imaging devices and NIR probes that could be connected to their HSP-targeting moiety.

In summary, the team should articulate a set of design parameters to guide both the optimization of the chemical SAR and the selection of an agent to move forward to IND-enabling studies. These critical success factors (CSFs) should include, but not be limited to, the following parameters:

- Excitation/emission wavelength
- HSP90 affinity
- HSP90 binding kinetics
- Cellular potency
- Plasma stability
- Metabolic stability
- Pharmacokinetic properties
- In vivo activity in mouse models
- Biodistribution

- Solubility and ease of developing an acceptable clinical formulation
- Minimum observable imaging dose
- Maximum tolerated dose

Appropriate design of the first clinical trials of the new imaging agent is also critically important with respect to the allocation of preclinical investment (safety studies, GMP synthesis, etc.). Should these studies be phase 1 or phase 0 studies? Should the first trial be more translational in scope? What are realistic objectives given the time and resources available to the project? To help with these deliberations, the research team should identify an individual with extensive imaging trial experience to serve as an advisor, possibly joining the ESAC.

With these caveats in mind, the Duke team has made significant progress in advancing these early breast cancer detection ideas to a formal proof of concept. It may be possible to move to clinical studies within 1-2 years, but this will be largely dependent on a robust decision process requiring additional information (CSFs and clinical trial design) while balancing available time and resources with opportunity.

Patient Advocate Comments (Liz Frank and Carol Matyka)

The patient advocates continue to be excited about the goal of this project – namely early detection and characterization of breast cancer using molecularly targeted imaging. Identifying these cancers could significantly impact clinical diagnosis, treatment options and outcomes. However, their comments/concerns mirror those of the other ESAC members.

- HS-131 seems like a reasonable starting point, but if it fails, there is no obvious back-up plan. Consideration should be given to testing 2 candidates instead of just one.

- The choice of HS-131 is probably reasonable, but it was not obvious how it compared to other candidates across a number of dimensions, including PK data. Do other candidates need to be developed or is there adequate data to move ahead with what we have?

- A strategic plan for advancing the top candidate or two top candidates should be more clearly articulated.

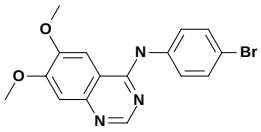
- The current project team appears to lack experience with phase 0/1 studies focused on testing diagnostics as opposed to therapeutics. Consideration should be given to adding someone with expertise in early stage diagnostics testing to the team.

- There was a fair amount of discussion around identifying the equipment needed to do fulfill the goals of the grant. Gaining access to such equipment should be a research priority moving forward.

- Opportunities for collaboration with Brian Pogue (Dartmouth) should be further explored.

In summary, success of the proposed study depends on identification of appropriate NIR imaging agent(s) coupled with the use of clinically optimal imaging equipment. At this point, there is insufficient confidence in selection of HS-131 to move forward successfully and there is concern about appropriate trial design able to best evaluate translation of such an imaging agent into clinical application. The researchers are urged to obtain both appropriate expertise in imaging trials and the appropriate imaging equipment before committing to HS-131.

1. **HS-100001-01**



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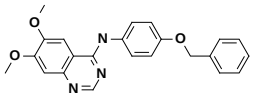
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Tom Barta	TB1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.070	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				

2. **HS-100002-01**



chemical registry				
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chirality	origin	chemist	notebook	salt form
	Internal synthesis	Tom Barta	TB4	None: Free base
amount available	program	primary target	percent purity	elemental analysis
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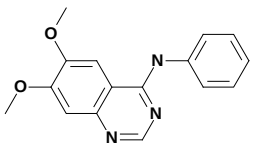
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				

3. **HS-100003-01**



chemical registry				
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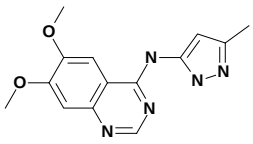
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Tom Barta	TB2	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.210	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
LCMS datafile				

4. **HS-100004-01**



chemical registry				
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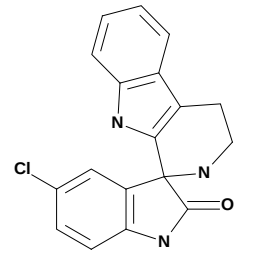
HS-100004-01	285.303	O2N5C14H15	2010-07-09	O(C)c1cc2ncnc(c2cc1OC)Nc3[nH]nc(C)c3
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Tom Barta	TB8	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.130	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				

5. **HS-100005-01**



chemical registry				
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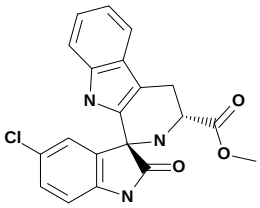
HS-100005-01	323.778	Cl1O1N3C18H14	2010-08-27	Clc1ccc2NC(C3(c2c1)NCCc4c3[nH]c5ccccc45)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-001-002A	C: TsOH
amount available	program	primary target	percent purity	elemental analysis
0.114			95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
	on	on	Toluene sulfonic acid salt; anti-malarial J Med Chem 2010; 53; 5155.	yes
LCMS datafile				

6. **HS-100006-01**



chemical registry

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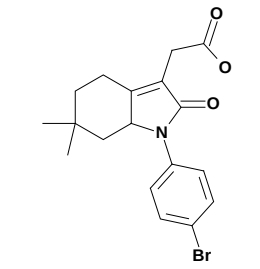
HS-100006-01	381.814	Cl1O3N3C20H16	2010-09-20	Clc1ccc2NC(C3(c2c1)NC(Cc4c3[nH]c5ccccc45)C(OC)=O)=O
chirality	origin	chemist	notebook	salt form
{8R;12R;}	Internal synthesis	Philip Hughes	PFH-001-004A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.310	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
	on	on	anti-malarial J Med Chem 2010; 53; 5155.	yes
LCMS datafile				

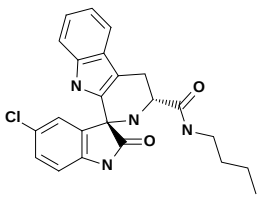
7. **HS-100007-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100007-01	378.262	Br1O3N1C18H20	2010-10-29	Brc1ccc(cc1)N2C(C(CC(O)=O)=O)=C3CCC(CC23)(C)C)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-001-018A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.201	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		yes
LCMS datafile				

8. **HS-100008-01**



chemical registry

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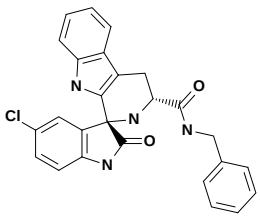
HS-100008-01	422.910	Cl1O2N4C23H23	2010-10-29	Clc1ccc2NC(C3(c2c1)NC(Cc4c3[nH]c5ccccc45)C(NCCCC)=O)=O
chirality	origin	chemist	notebook	salt form
{8R;12R;}	Internal synthesis	Philip Hughes	PFH-001-019A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.013	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
	on		anti-malarial J Med Chem 2010; 53; 5155.	yes
LCMS datafile				

9. **HS-100009-01**



chemical registry

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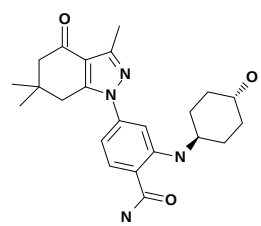
HS-100009-01	456.926	Cl1O2N4C26H21	2010-10-29	Clc1ccc2NC(C3(c2c1)NC(Cc4c3[nH]c5ccccc45)C(NCc6ccccc6)=O)=O
chirality	origin	chemist	notebook	salt form
{8R;12R;}	Internal synthesis	Philip Hughes	PFH-001-021A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.042	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
	on		anti-malarial J Med Chem 2010; 53; 5155.	yes
LCMS datafile				

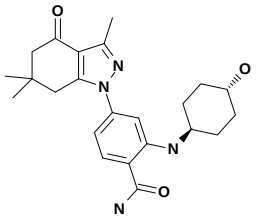
10. **HS-100010-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100010-01	410.512	O3N4C23H30	2010-11-11	O=C(c1ccc(cc1NC2CCC(CC2)O)n3nc(C)c4c3CC(CC4=O)(C)C)N
chirality	origin	chemist	notebook	salt form
{10-13T;}	Internal synthesis	Philip Hughes	PFH-001-027A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.400	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
	on			yes
LCMS datafile				
yes				

11. **HS-100010-02**



chemical registry

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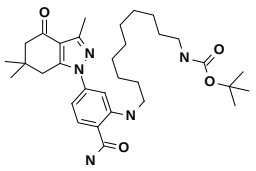
HS-100010-02	410.512	O3N4C23H30	2011-02-15	O=C(c1ccc(cc1NC2CCC(CC2)O)n3nc(C)c4c3CC(CC4=O)(C)C)N
chirality	origin	chemist	notebook	salt form
{10-13T;}	Internal synthesis	Dave Carlson	1dac046-1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
10.5	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
				yes
LCMS datafile				

12. **HS-100011-01**



chemical registry

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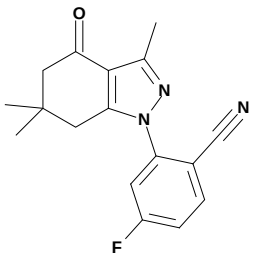
HS-100011-01	567.766	O4N5C32H49	2010-11-11	O=C(NCCCCCCCCCCNc1cc(ccc1C(N)=O)n2nc(C)c3c2CC(CC3=O)(C)C)OC(C)(C)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-001-031A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.040	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
LCMS datafile				

13. **HS-100012-01**



chemical registry

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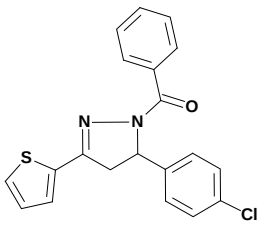
HS-100012-01	297.328	F1O1N3C17H16	2010-11-11	Fc1cc(c(C#N)cc1)n2nc(C)c3c2CC(CC3=O)(C)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-001-024B	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.250	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
			yellow needles; isomeric synthetic byproduct	
LCMS datafile				

14. **HS-100013-01**



chemical registry

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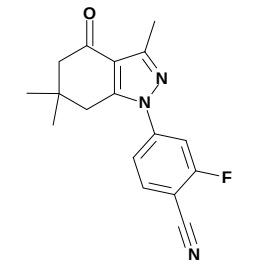
HS-100013-01	366.866	Cl1S1O1N2C20H15	2011-01-03	Clc1ccc(C2N(C(c3ccccc3)=O)N=C(C2)c4sccc4)cc1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	1dac032_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
500	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
	on		J.Med.Chem 2006; 2127-2137	yes
LCMS datafile				

15. **HS-100014-01**



chemical registry

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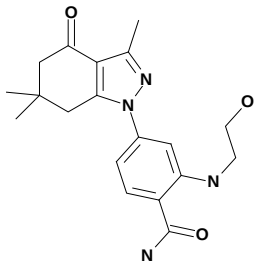
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	1dac040_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
300	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
	on			yes
LCMS datafile				

16. **HS-100015-01**



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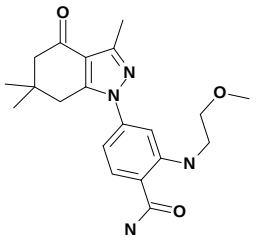
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-001-071A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.233	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
	on			yes
LCMS datafile				

17. **HS-100016-01**



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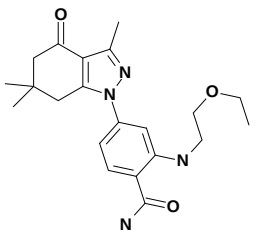
HS-100016-01	370.447	O3N4C20H26	2011-02-14	O=C(c1ccc(cc1NCCOC)n2nc(C)c3c2CC(CC3=O)(C)C)N
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-001-072A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.226	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
				yes
LCMS datafile				

18. **HS-100017-01**



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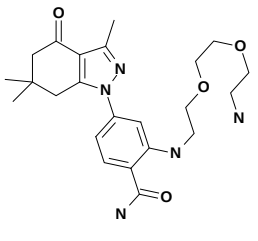
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-001-073A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.222	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
				yes
LCMS datafile				

19. **HS-100018-01**



chemical registry				
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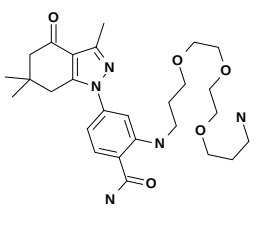
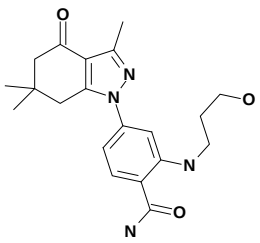
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	1DAC048-1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
.200	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
				yes
LCMS datafile				
yes				

20. **HS-100019-01**



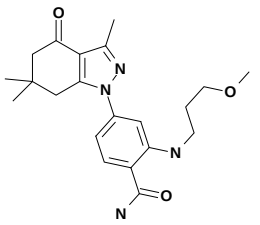
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100019-01	515.648	O5N5C27H41	2011-02-15	O=C(c1ccc(cc1NCCCOCCOCCOCCCN)n2nc(C)c3c2CC(CC3=O)(C)C)N
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	1DAC049-1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
			See Dave Carlson for compound	yes
LCMS datafile				
yes				

21. **HS-100020-01**



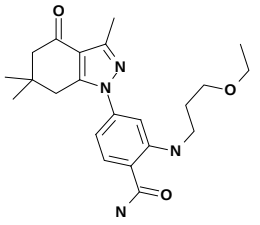
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100020-01	370.447	O3N4C20H26	2011-02-24	O=C(c1ccc(cc1NCCCO)n2nc(C)c3c2CC(CC3=O)(C)C)N
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-001-075A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.238	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
				yes
LCMS datafile				

22. **HS-100021-01**



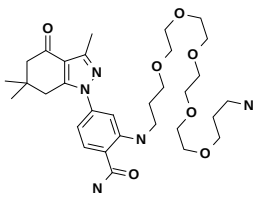
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100021-01	384.474	O3N4C21H28	2011-02-24	O=C(c1ccc(cc1NCCCOC)n2nc(C)c3c2CC(CC3=O)(C)C)N
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-001-075B	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.260	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
				yes
LCMS datafile				

23. **HS-100022-01**



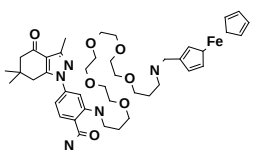
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100022-01	398.501	O3N4C22H30	2011-02-24	O=C(c1ccc(cc1NCCCOCC)n2nc(C)c3c2CC(CC3=O)(C)C)N
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-001-075C	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.234	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
				yes
LCMS datafile				

24. **HS-100023-01**



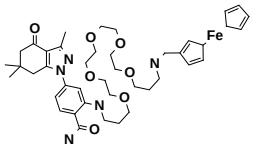
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100023-01	603.753	O7N5C31H49	2011-02-25	O=C(c1ccc(cc1NCCCOCCOCCOCCOCCOCCCN)n2nc(C)c3c2CC(CC3=O)(C)C)N
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-001-063A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.01	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
			See chemist for sample	yes
LCMS datafile				

25. **HS-100024-01**



chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100024-01	801.797	Fe1O7N5C42H59	2011-03-22	O=C(c1ccc(cc1NCCCOCCOCCOCCOCCOCCCNCC2C=CC([Fe]C3C=CC=C3)=C2)n4nc(C)c5c4CC(CC5=O)(C)C)N
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-001-080A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.046	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
			See P Hughes for Sample	yes
LCMS datafile				
yes				

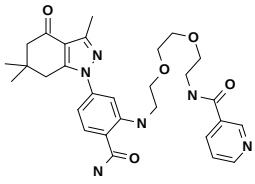
26. **HS-100024-02**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100024-02	801.797	Fe1O7N5C42H59	2011-11-04	O=C(c1ccc(cc1NCCCOCCOCCOCCOCCOCCCNCC2C=CC([Fe]C3C=CC=C3)=C2)n4nc(C)c5c4CC(CC5=O)(C)C)N
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-002-018C	None: Free base
amount available	program	primary target	percent purity	elemental analysis
.490	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
			See P Hughes for Sample	
LCMS datafile				
yes				

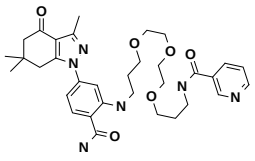
27. **HS-100025-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100025-01	548.636	O5N6C29H36	2011-04-07	O=C(c1cnccc1)NCCOCCOCCNc2cc(ccc2C(N)=O)n3nc(C)c4c3CC(CC4=O)(C)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	1DAC056-1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
.101	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
LCMS datafile				
yes				

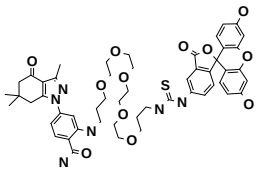
28. **HS-100026-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100026-01	620.742	O6N6C33H44	2011-04-07	O=C(c1cnccc1)NCCCOCCOCCOCCCNc2cc(ccc2C(N)=O)n3nc(C)c4c3CC(CC4=O)(C)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	1DAC057-1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.080	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
LCMS datafile				
yes				

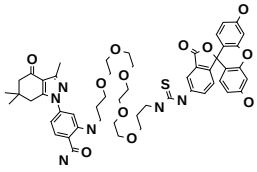
29. **HS-100027-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100027-01	993.137	S1O12N6C52H60	2011-04-10	S=C(NCCCOCCOCCOCCOCCOCCCNc1cc(ccc1C(N)=O)n2nc(C)c3c2CC(CC3=O)(C)C)Nc4ccc5c(C(OC56c7ccc(cc7Oc8cc(ccc68)O)O)=O)c4
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-001-091A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.010	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
			See chemist for sample	yes
LCMS datafile				
yes				

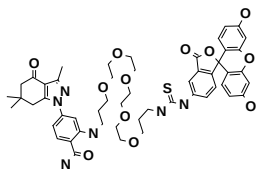
30. **HS-100027-02**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100027-02	993.137	S1O12N6C52H60	2012-02-10	S=C(NCCCOCCOCCOCCOCCOCCCNc1cc(ccc1C(N)=O)n2nc(C)c3c2CC(CC3=O)(C)C)Nc4ccc5c(C(OC56c7ccc(cc7Oc8cc(ccc68)O)O)=O)c4
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-002-094C	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.084	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				
yes				

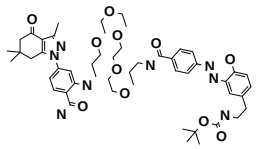
31. **HS-100027-03**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100027-03	993.137	S1O12N6C52H60	2012-02-10	S=C(NCCCOCCOCCOCCOCCOCCCNc1cc(ccc1C(N)=O)n2nc(C)c3c2CC(CC3=O)(C)C)Nc4ccc5c(C(OC56c7ccc(cc7Oc8cc(ccc68)O)O)=O)c4
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-002-094D	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.180	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				
yes				

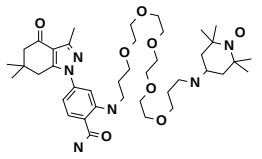
32. **HS-100028-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100028-01	971.154	O11N8C51H70	2011-04-12	O=C(NCCc1ccc(c(c1)N=Nc2ccc(C(NCCCOCCOCCOCCOCCOCCCNc3cc(ccc3C(N)=O)n4nc(C)c5c4CC(CC5=O)(C)C)=O)cc2)O)OC(C)(C)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-001-090B	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.184	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
			See chemist for sample	yes
LCMS datafile				
yes				

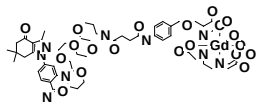
33. **HS-100029-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100029-01	758.992	O8N6C40H66	2011-05-16	O=C(c1ccc(cc1NCCCOCCOCCOCCOCCOCCCNC2CC(C)(C)N(C(C2)(C)C)O)n3nc(C)c4c3CC(CC4=O)(C)C)N
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-001-093A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.025	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
	on		In the refridgerator; -O radical; not -OH; MW 1 high	yes
LCMS datafile				
yes				

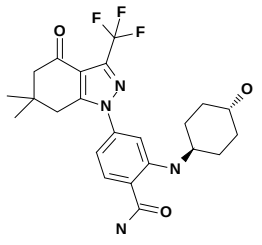
34. **HS-100030-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100030-01	1366.537	Gd1O20N9C57H78	2011-05-23	O=C1O[Gd]234567OC(CN2(C1COCc8ccc(cc8)NC(CCC(NCCCOCCOCCOCCOCCOCCCNc9cc(ccc9C(N)=O)n10nc(C)c11c10CC(CC11=O)(C)C)=O)=O)CCN3(CC(O4)=O)CCN5(CC(O6)=O)CC(O7)=O)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	1DAC92-1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.100	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Diammonium salt	
LCMS datafile				
yes				

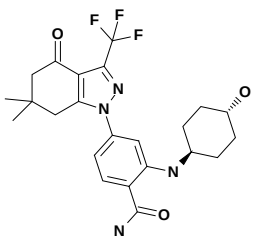
35. **HS-100031-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100031-01	464.483	F3O3N4C23H27	2011-06-08	FC(c1nn(c2c1C(CC(C2)(C)C)=O)c3ccc(C(N)=O)c(c3)NC4CCC(CC4)O)(F)F
chirality	origin	chemist	notebook	salt form
{25-28T;}	Internal synthesis	Philip Hughes	PFH-002-011A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.089	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
LCMS datafile				

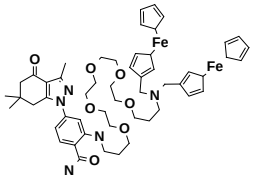
36. **HS-100031-02**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100031-02	464.483	F3O3N4C23H27	2011-10-05	FC(c1nn(c2c1C(CC(C2)(C)C)=O)c3ccc(C(N)=O)c(c3)NC4CCC(CC4)O)(F)F
chirality	origin	chemist	notebook	salt form
{25-28T;}	Internal synthesis	Philip Hughes	PFH-002-053C	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.247	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
LCMS datafile				

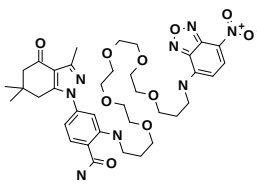
37. **HS-100032-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100032-01	999.840	Fe2O7N5C53H69	2011-07-11	O=C(c1ccc(cc1NCCCOCCOCCOCCOCCOCCCN(CC2C=CC([Fe]C3C=CC=C3)=C2)CC4C=CC([Fe]C5C=CC=C5)=C4)n6nc(C)c7c6CC(CC7=O)(C)C)N
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-002-018Ap	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.080	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	See P Hughes for Sample	
LCMS datafile				
yes				

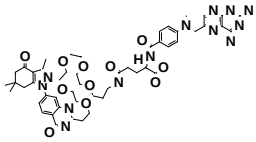
38. **HS-100033-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100033-01	766.844	O10N8C37H50	2011-08-16	o1nc2c(c(ccc2NCCCOCCOCCOCCOCCOCCCNc3cc(ccc3C(N)=O)n4nc(C)c5c4CC(CC5=O)(C)C)[N+](=O)=[O-])n1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-002-028A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.036	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	See P Hughes for Sample	
LCMS datafile				
yes				

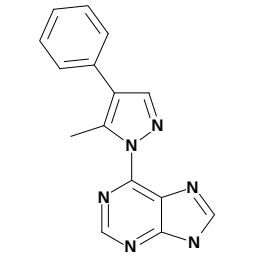
39. **HS-100034-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100034-01	1040.179	O11N13C51H69	2011-08-23	OC(C(CCC(NCCCOCCOCCOCCOCCOCCCNc1cc(ccc1C(N)=O)n2nc(C)c3c2CC(CC3=O)(C)C)=O)NC(c4ccc(cc4)N(Cc5nc6c(nc(N)nc6N)nc5)C)=O)=O
chirality	origin	chemist	notebook	salt form
{3S;}	Internal synthesis	Philip Hughes	PFH-002-029A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.020	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
			tentative assignment for amide regiochemistry HS23plusMTX	
LCMS datafile				

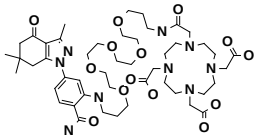
40. **HS-100035-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100035-01	276.297	N6C15H12	2011-09-08	n1n(c(C)c(c1)c2ccccc2)c3ncnc4[nH]cnc34
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	2DAC008_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.070	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		yes
LCMS datafile				
yes				

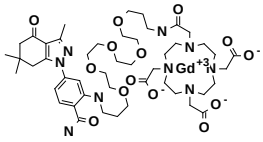
41. **HS-100036-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100036-01	990.155	O14N9C47H75	2011-10-03	OC(CN1CCN(CC(NCCCOCCOCCOCCOCCOCCCNc2cc(ccc2C(N)=O)n3nc(C)c4c3CC(CC4=O)(C)C)=O)CCN(CC(O)=O)CCN(CC(O)=O)CC1)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	2DAC007_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				

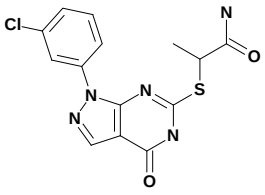
42. **HS-100037-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100037-01	1144.385	Gd1O14N9C47H72	2011-10-03	[Gd+3].[O-]C(CN1CCN(CC(NCCCOCCOCCOCCOCCOCCCNc2cc(ccc2C(N)=O)n3nc(C)c4c3CC(CC4=O)(C)C)=O)CCN(CC([O-])=O)CCN(CC([O-])=O)CC1)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	2DAC011_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.052	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				

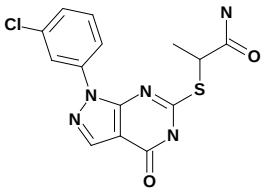
43. **HS-100038-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100038-01	349.797	Cl1S1O2N5C14H12	2011-11-18	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SC(C)C(N)=O)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-002-068B	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.020	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Sample given to Doug W. Same structure as HS-206012-1	
LCMS datafile				
yes				

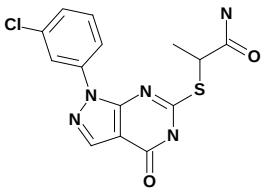
44. **HS-100038-02**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100038-02	349.797	Cl1S1O2N5C14H12	2011-12-06	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SC(C)C(N)=O)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-002-077A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.127	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Same structure as HS-206012-1	
LCMS datafile				
yes				

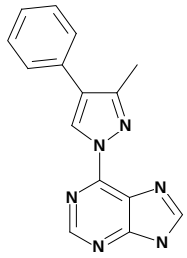
45. **HS-100038-03**



chemical registry

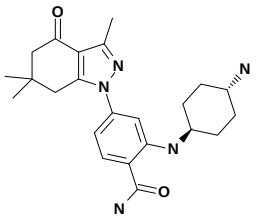
registry id	mol wt	formula	date	SMILES
HS-100038-03	349.797	Cl1S1O2N5C14H12	2011-12-06	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SC(C)C(N)=O)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-002-077B	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.061	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Same structure as HS-206012-1	
LCMS datafile				
yes				

46. **HS-100039-01**



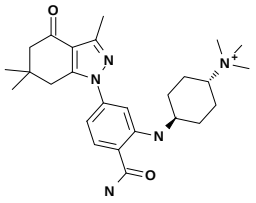
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100039-01	276.297	N6C15H12	2012-01-26	n1n(cc(c1C)c2ccccc2)c3ncnc4[nH]cnc34
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	2DAC013_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.5	Purine_inhib		80-90	
melting point	NMR data	LCMS data	comment	NMR datafile
			contains 25% HS-100035	
LCMS datafile				

47. **HS-100040-01**



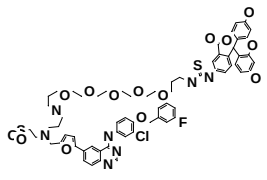
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100040-01	409.527	O2N5C23H31	2012-02-23	O=C(c1ccc(cc1NC2CCC(CC2)N)n3nc(C)c4c3CC(CC4=O)(C)C)N
chirality	origin	chemist	notebook	salt form
{10-13T;}	Internal synthesis	Philip Hughes	PFH-002-097A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.689	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	contains a trace of bis product	
LCMS datafile				
yes				

48. **HS-100041-01**



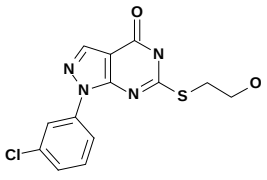
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100041-01	452.615	O2N5C26H38	2012-03-12	O=C(c1ccc(cc1NC2CCC(CC2)[N+](C)(C)C)n3nc(C)c4c3CC(CC4=O)(C)C)N
chirality	origin	chemist	notebook	salt form
{10-13T;}	Internal synthesis	Philip Hughes	PFH-003-002A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.027	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				
yes				

49. **HS-100042-01**



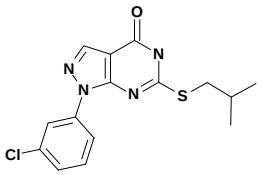
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100042-01	1318.924	C1S2F1O14N7C67H73	2012-03-14	Clc1cc(ccc1OCc2cccc(c2)F)Nc3ncnc4ccc(cc34)c5oc(CN(CCCNCCCOCCCOCCOCCOCCOCCCNC(Nc6ccc7c(C(OC78c9ccc(cc9Oc10cc(ccc810)O)O)=O)c6)=S)CCS(C)(=O)=O)cc5
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-003-010A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.014	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
			see chemist	
LCMS datafile				

50. **HS-100043-01**



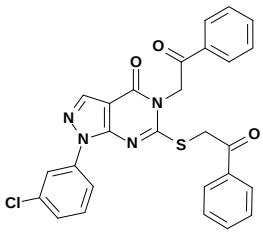
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100043-01	322.772	Cl1S1O2N4C13H11	2012-03-20	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SCCO)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC023_2	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.027	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

51. **HS-100044-01**



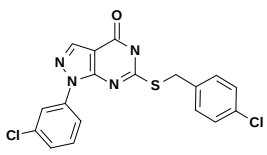
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100044-01	334.826	Cl1S1O1N4C15H15	2012-03-20	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SCC(C)C)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC023_3	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.010	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

52. **HS-100045-01**



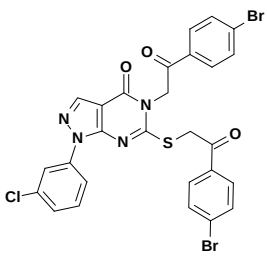
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100045-01	514.986	Cl1S1O3N4C27H19	2012-03-20	Clc1cc(ccc1)n2ncc3c(n(CC(c4ccccc4)=O)c(nc23)SCC(c5ccccc5)=O)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC023_5	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.036	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

53. **HS-100046-01**



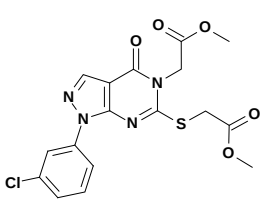
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100046-01	403.288	Cl2S1O1N4C18H12	2012-03-20	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SCc4ccc(cc4)Cl)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC023_12	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.022	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

54. **HS-100047-01**



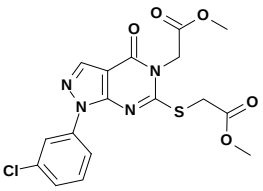
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100047-01	672.778	Br2Cl1S1O3N4C27H17	2012-03-20	Brc1ccc(C(CSc2nc3n(c4cccc(c4)Cl)ncc3c(n2CC(c5ccc(cc5)Br)=O)=O)=O)cc1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC023_13	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.039	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

55. **HS-100048-01**



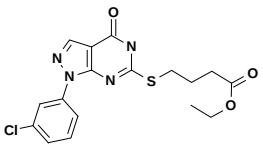
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100048-01	422.845	Cl1S1O5N4C17H15	2012-03-20	Clc1cc(ccc1)n2ncc3c(n(CC(OC)=O)c(nc23)SCC(OC)=O)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC023_14A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.018	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor. Regioisomer of HS-49	
LCMS datafile				
yes				

56. **HS-100048-02**



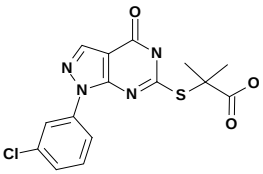
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100048-02	422.845	Cl1S1O5N4C17H15	2012-03-20	Clc1cc(ccc1)n2ncc3c(n(CC(OC)=O)c(nc23)SCC(OC)=O)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC023_14B	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.021	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor. Regioisomer of HS-48	
LCMS datafile				
yes				

57. **HS-100049-01**



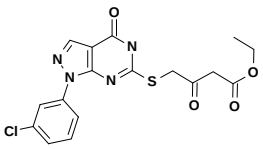
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100049-01	392.862	Cl1S1O3N4C17H17	2012-03-20	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SCCCC(OCC)=O)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC023_15	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.016	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

58. **HS-100050-01**



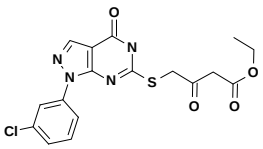
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100050-01	364.809	Cl1S1O3N4C15H13	2012-03-20	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SC(C)(C)C(O)=O)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC023_16	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.032	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				

59. **HS-100051-01**



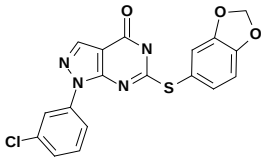
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100051-01	406.846	Cl1S1O4N4C17H15	2012-03-20	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SCC(CC(OCC)=O)=O)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC023_17	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.031	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

60. **HS-100051-02**



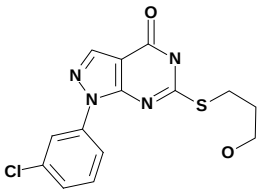
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100051-02	406.846	Cl1S1O4N4C17H15	2012-08-15	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SCC(CC(OCC)=O)=O)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC057_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.114	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38.	
LCMS datafile				
yes				

61. **HS-100052-01**



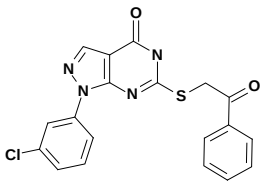
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100052-01	398.825	Cl1S1O3N4C18H11	2012-03-20	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)Sc4ccc5OCOc5c4)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC025_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.020	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

62. **HS-100053-01**



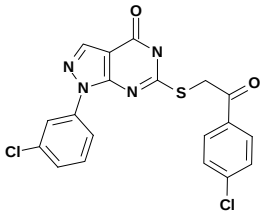
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100053-01	336.799	Cl1S1O2N4C14H13	2012-03-20	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SCCCO)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC026_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.044	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

63. **HS-100054-01**



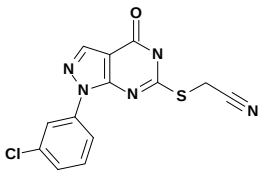
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100054-01	396.853	Cl1S1O2N4C19H13	2012-03-20	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SCC(c4ccccc4)=O)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC026_2	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.046	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

64. **HS-100055-01**



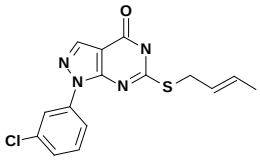
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100055-01	431.298	Cl2S1O2N4C19H12	2012-03-20	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SCC(c4ccc(cc4)Cl)=O)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC026_3	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.055	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

65. **HS-100056-01**



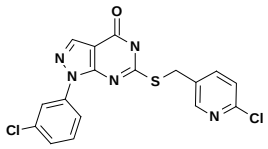
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100056-01	317.755	Cl1S1O1N5C13H8	2012-03-20	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SCC#N)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC026_4	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.022	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

66. **HS-100057-01**



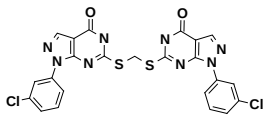
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100057-01	332.810	Cl1S1O1N4C15H13	2012-03-20	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SCC=CC)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC026_5	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.034	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

67. **HS-100058-01**



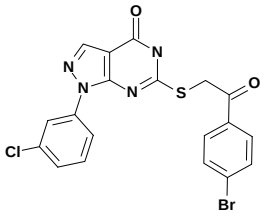
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100058-01	404.276	Cl2S1O1N5C17H11	2012-03-20	Clc1ncc(CSc2nc3n(c4cccc(c4)Cl)ncc3c([nH]2)=O)cc1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC026_6	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.026	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

68. **HS-100059-01**



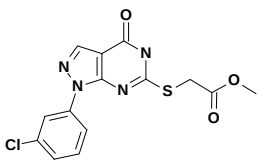
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100059-01	569.449	Cl2S2O2N8C23H14	2012-03-20	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SCSc4nc5n(c6cccc(c6)Cl)ncc5c([nH]4)=O)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC026_7	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.040	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

69. **HS-100060-01**



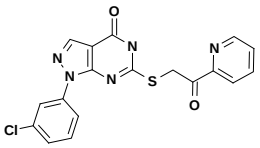
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100060-01	475.749	Br1Cl1S1O2N4C19H12	2012-03-20	Brc1ccc(C(CSc2nc3n(c4cccc(c4)Cl)ncc3c([nH]2)=O)=O)cc1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC026_8	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.052	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

70. **HS-100061-01**



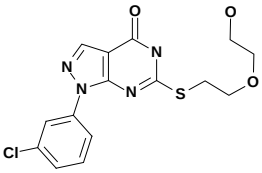
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100061-01	350.782	Cl1S1O3N4C14H11	2012-03-20	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SCC(OC)=O)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC026_9	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.028	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

71. **HS-100062-01**



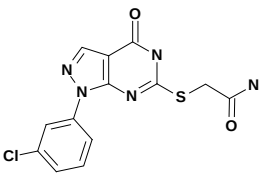
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100062-01	397.841	Cl1S1O2N5C18H12	2012-03-20	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SCC(c4ncccc4)=O)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC026_10	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.024	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

72. **HS-100063-01**



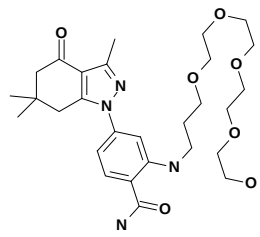
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100063-01	366.825	Cl1S1O3N4C15H15	2012-03-20	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SCCOCCO)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC028_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.010	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

73. **HS-100064-01**



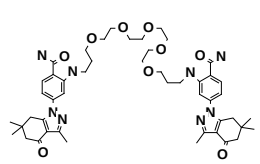
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100064-01	335.771	Cl1S1O2N5C13H10	2012-03-20	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SCC(N)=O)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC029_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.008	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

74. **HS-100065-01**



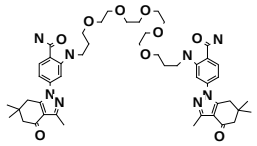
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100065-01	546.659	O7N4C28H42	2012-03-20	O=C(c1ccc(cc1NCCCOCCOCCOCCOCCO)n2nc(C)c3c2CC(CC3=O)(C)C)N
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-003-013A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.041	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	glass	
LCMS datafile				
yes				

75. **HS-100066-01**



chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100066-01	899.091	O9N8C48H66	2012-03-20	O=C(c1ccc(cc1NCCCOCCOCCOCCOCCOCCCNc2cc(ccc2C(N)=O)n3nc(C)c4c3CC(CC4=O)(C)C)n5nc(C)c6c5CC(CC6=O)(C)C)N
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-003-013B	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.026	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	glass	
LCMS datafile				
yes				

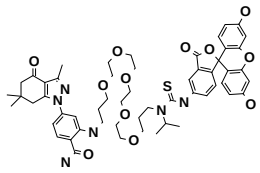
76. **HS-100066-02**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100066-02	899.091	O9N8C48H66	2012-05-17	O=C(c1ccc(cc1NCCCOCCOCCOCCOCCOCCCNc2cc(ccc2C(N)=O)n3nc(C)c4c3CC(CC4=O)(C)C)n5nc(C)c6c5CC(CC6=O)(C)C)N
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-003-043A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.043	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	glass sample dissolved in DMSO at 10mM	
LCMS datafile				
yes				

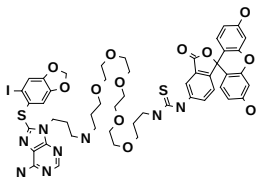
77. **HS-100067-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100067-01	1035.217	S1O12N6C55H66	2012-04-02	S=C(N(C(C)C)CCCOCCOCCOCCOCCOCCCNc1cc(ccc1C(N)=O)n2nc(C)c3c2CC(CC3=O)(C)C)Nc4ccc5c(C(OC56c7ccc(cc7Oc8cc(ccc68)O)O)=O)c4
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-003-019A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.0043	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	3 mg in DMSO (10 mM) put in Khaldon box.	yes
LCMS datafile				
yes				

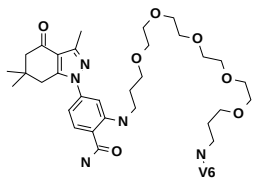
78. **HS-100068-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100068-01	1151.059	I1S2O12N8C50H55	2012-04-23	Ic1cc2OCOc2cc1Sc3nc4c(N)ncnc4n3CCCNCCCOCCOCCOCCOCCOCCCNC(Nc5cc6c(C7(c8ccc(cc8Oc9cc(ccc79)O)O)OC6=O)cc5)=S
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-003-029A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.0071	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
LCMS datafile				

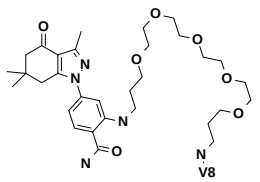
79. **HS-100069-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100069-01	602.745	O7N5C31H48X1	2012-05-18	O=C(c1ccc(cc1NCCCOCCOCCOCCOCCOCCCCN[V6])n2nc(C)c3c2CC(CC3=O)(C)C)N
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-002-082A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.002	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
			v6=VivoTag645 near-IR probe; negative ion mass 1577.5	
LCMS datafile				

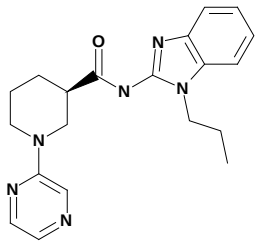
80. **HS-100070-01**



chemical registry

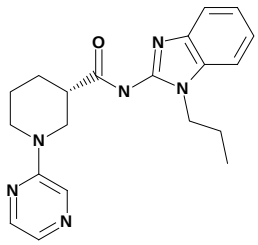
registry id	mol wt	formula	date	SMILES
HS-100070-01	602.745	O7N5C31H48X1	2012-05-18	O=C(c1ccc(cc1NCCCOCCOCCOCCOCCOCCCCN[V8])n2nc(C)c3c2CC(CC3=O)(C)C)N
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-002-090A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.005	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
			V8=VivoTag800 near-IR probe; negative ion mass 1648	
LCMS datafile				

81. **HS-100071-01**



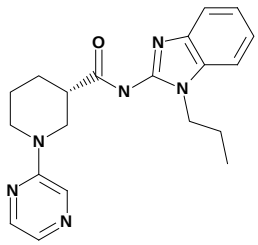
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100071-01	364.446	O1N6C20H24	2012-05-22	O=C(C1CN(CCC1)c2nccnc2)Nc3nc4ccccc4n3CCC
chirality	origin	chemist	notebook	salt form
{3R;}	Internal synthesis	Philip Hughes	PFH-003-044A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.031	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Derived from (R) enantiomer	
LCMS datafile				
yes				

82. **HS-100072-01**



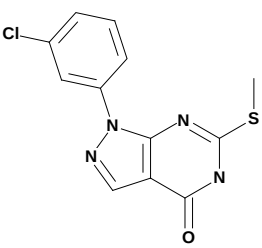
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100072-01	364.446	O1N6C20H24	2012-05-22	O=C(C1CN(CCC1)c2nccnc2)Nc3nc4ccccc4n3CCC
chirality	origin	chemist	notebook	salt form
{3S;}	Internal synthesis	Philip Hughes	PFH-003-050A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.0092	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Derived from (S)-enantiomer	
LCMS datafile				
yes				

83. **HS-100072-02**



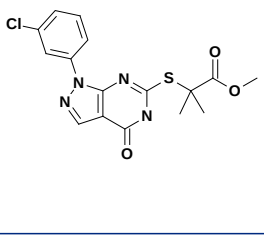
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100072-02	364.446	O1N6C20H24	2012-07-31	O=C(C1CN(CCC1)c2nccnc2)Nc3nc4ccccc4n3CCC
chirality	origin	chemist	notebook	salt form
{3S;}	Internal synthesis	Philip Hughes	PFH-003-050B	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.021	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
			Derived from (S)-enantiomer	
LCMS datafile				

84. **HS-100073-01**



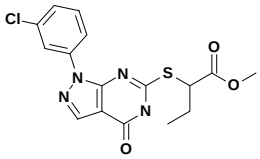
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100073-01	292.746	Cl1S1O1N4C12H9	2012-06-13	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SC)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	2DAC033_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.035	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				
yes				

85. **HS-100074-01**



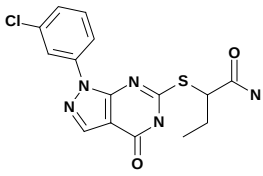
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100074-01	378.836	Cl1S1O3N4C16H15	2012-06-13	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SC(C)(C)C(OC)=O)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	2DAC033_2	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.030	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				
yes				

86. **HS-100075-01**



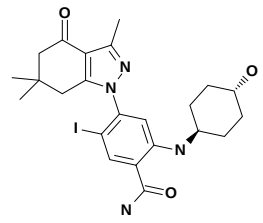
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100075-01	378.836	Cl1S1O3N4C16H15	2012-06-13	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SC(CC)C(OC)=O)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	2DAC033_3	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.023	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				
yes				

87. **HS-100076-01**



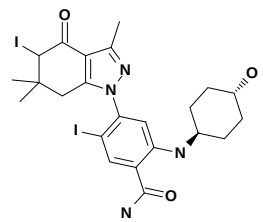
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100076-01	363.824	Cl1S1O2N5C15H14	2012-06-13	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SC(CC)C(N)=O)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	2DAC042_2	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.012	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				
yes				

88. **HS-100077-01**



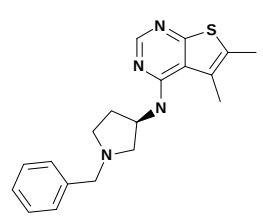
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100077-01	536.408	I1O3N4C23H29	2012-06-13	Ic1c(cc(c(C(N)=O)c1)NC2CCC(CC2)O)n3nc(C)c4c3CC(CC4=O)(C)C
chirality	origin	chemist	notebook	salt form
{12-15T;}	Internal synthesis	Dave Carlson	2DAC043_MONO	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.048	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				
yes				

89. **HS-100078-01**



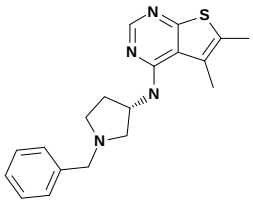
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100078-01	662.305	I2O3N4C23H28	2012-06-13	Ic1c(cc(c(C(N)=O)c1)NC2CCC(CC2)O)n3nc(C)c4c3CC(C(C4=O)I)(C)C
chirality	origin	chemist	notebook	salt form
{12-15T;}	Internal synthesis	Dave Carlson	2DAC043_BIS	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.074	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				
yes				

90. **HS-100079-01**



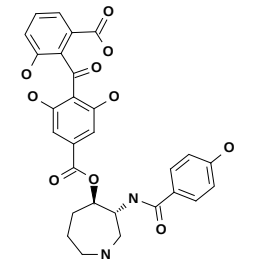
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100079-01	338.472	S1N4C19H22	2012-06-13	s1c2ncnc(c2c(C)c1C)NC3CN(CC3)Cc4ccccc4
chirality	origin	chemist	notebook	salt form
{13R;}	Internal synthesis	Philip Hughes	PFH-003-058A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.134	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		yes
LCMS datafile				
yes				

91. **HS-100080-01**



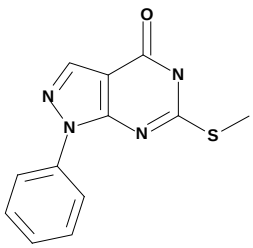
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100080-01	338.472	S1N4C19H22	2012-06-13	s1c2ncnc(c2c(c1C)C)NC3CN(Cc4ccccc4)CC3
chirality	origin	chemist	notebook	salt form
{13S;}	Internal synthesis	Philip Hughes	PFH-003-059A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.101	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				
yes				

92. **HS-100081-01**



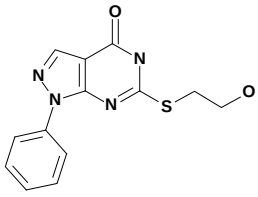
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100081-01	550.516	O10N2C28H26	2012-06-14	OC(c1cccc(c1C(c2c(cc(C(OC3CCCNCC3NC(c4ccc(cc4)O)=O)cc2O)O)=O)O)=O)=O
chirality	origin	chemist	notebook	salt form
{16R;22R;}	Internal synthesis	Philip Hughes	PFH-003-039A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.0099	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Gift of Sphinx Pharmaceuticals; LC impurity from previous injection	
LCMS datafile				
yes				

93. **HS-100082-01**



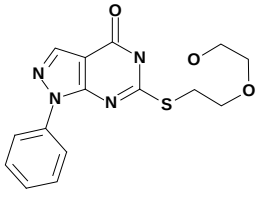
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100082-01	258.301	S1O1N4C12H10	2012-08-15	S(C)c1nc2n(c3ccccc3)ncc2c([nH]1)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC054_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.019	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

94. **HS-100083-01**



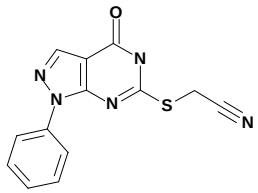
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100083-01	288.327	S1O2N4C13H12	2012-08-15	S(CCO)c1nc2n(c3ccccc3)ncc2c([nH]1)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC054_2	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.021	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

95. **HS-100084-01**



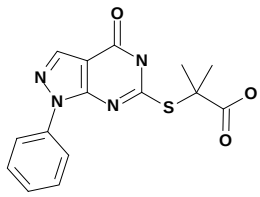
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100084-01	332.380	S1O3N4C15H16	2012-08-15	S(CCOCCO)c1nc2n(c3ccccc3)ncc2c([nH]1)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC054_3	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.045	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

96. **HS-100085-01**



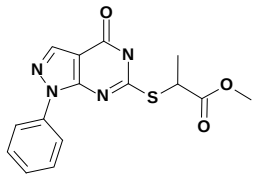
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100085-01	283.310	S1O1N5C13H9	2012-08-15	S(CC#N)c1nc2n(c3ccccc3)ncc2c([nH]1)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC054_4	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.060	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				

97. **HS-100086-01**



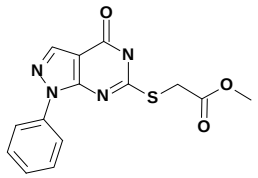
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100086-01	330.364	S1O3N4C15H14	2012-08-15	S(C(C)(C)C(=O)O)c1nc2n(c3ccccc3)ncc2c([nH]1)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC054_5	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.044	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

98. **HS-100087-01**



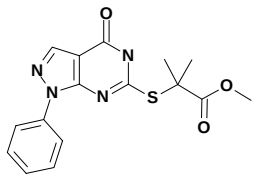
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100087-01	330.364	S1O3N4C15H14	2012-08-15	S(C(C)C(OC)=O)c1nc2n(c3ccccc3)ncc2c([nH]1)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC054_6	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.038	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

99. **HS-100088-01**



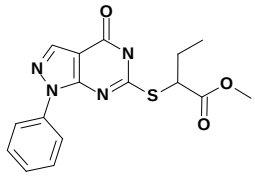
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100088-01	316.337	S1O3N4C14H12	2012-08-15	S(CC(OC)=O)c1nc2n(c3ccccc3)ncc2c([nH]1)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC054_7	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.063	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

100. **HS-100089-01**



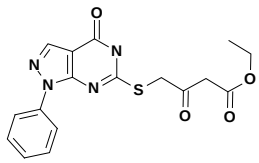
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100089-01	344.390	S1O3N4C16H16	2012-08-15	S(C(C)(C)C(OC)=O)c1nc2n(c3ccccc3)ncc2c([nH]1)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC054_8	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.048	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

101. **HS-100090-01**



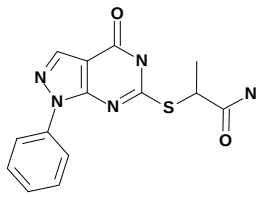
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100090-01	344.390	S1O3N4C16H16	2012-08-15	S(C(CC)C(OC)=O)c1nc2n(c3ccccc3)ncc2c([nH]1)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC054_9	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.036	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

102. **HS-100091-01**



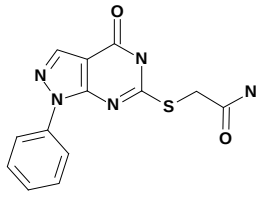
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100091-01	372.401	S1O4N4C17H16	2012-08-15	S(CC(CC(OCC)=O)=O)c1nc2n(c3ccccc3)ncc2c([nH]1)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC054_10	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.075	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38.	
LCMS datafile				
yes				

103. **HS-100092-01**



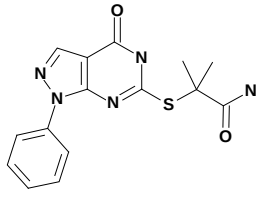
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100092-01	315.352	S1O2N5C14H13	2012-08-15	S(C(C)C(N)=O)c1nc2n(c3ccccc3)ncc2c([nH]1)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC056_2	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.017	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

104. **HS-100093-01**



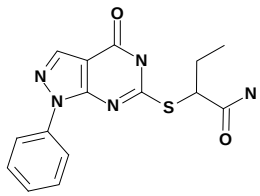
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100093-01	301.326	S1O2N5C13H11	2012-08-15	S(CC(N)=O)c1nc2n(c3ccccc3)ncc2c([nH]1)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC056_3	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.017	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

105. **HS-100094-01**



chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100094-01	329.379	S1O2N5C15H15	2012-08-15	S(C(C)(C)C(N)=O)c1nc2n(c3ccccc3)ncc2c([nH]1)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC056_4	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.016	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

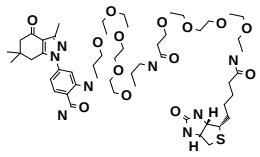
106. **HS-100095-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100095-01	329.379	S1O2N5C15H15	2012-08-15	S(C(CC)C(N)=O)c1nc2n(c3ccccc3)ncc2c([nH]1)=O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC056_5	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.016	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				
yes				

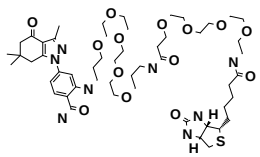
107. **HS-100096-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100096-01	1077.340	S1O14N8C52H84	2012-09-27	S1C(C2NC(=O)NC2C1)CCCCC(=O)NCCOCCOCCOCCOCCC(=O)NCCCOCCOCCOCCOCCOCCCNc3c(ccc(n4nc(c5c4CC(CC5=O)(C)C)C)c3)C(=O)N
chirality	origin	chemist	notebook	salt form
{2S;3S;8R;}	Internal synthesis	Philip Hughes	PFH-003-074A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.011	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	See chemist for sample	
LCMS datafile				
yes				

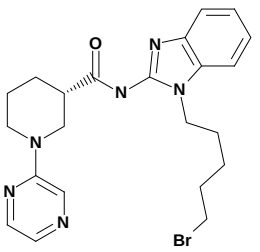
108. **HS-100096-02**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100096-02	1077.340	S1O14N8C52H84	2014-06-11	S1C(C2NC(=O)NC2C1)CCCCC(=O)NCCOCCOCCOCCOCCC(=O)NCCCOCCOCCOCCOCCOCCCNc3c(ccc(n4nc(c5c4CC(CC5=O)(C)C)C)c3)C(=O)N
chirality	origin	chemist	notebook	salt form
{2S;3S;8R;}	Internal synthesis	Philip Hughes	PFH-006-015A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	See Lauren for sample	
LCMS datafile				
yes				

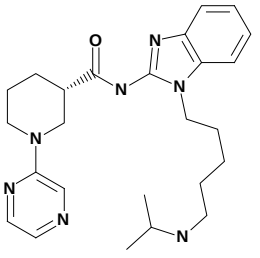
109. **HS-100097-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100097-01	471.396	Br1O1N6C22H27	2012-11-27	BrCCCCCn1c(nc2c1cccc2)NC(=O)C3CN(c4nccnc4)CCC3
chirality	origin	chemist	notebook	salt form
{19S;}	Internal synthesis	Philip Hughes	PFH-003-079A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.108	Purine_inhib	Hsp70	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
			Derived from (S)-enantiomer; see PFH for sample	
LCMS datafile				
yes				

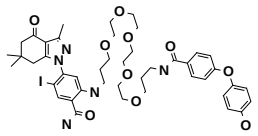
110. **HS-100098-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100098-01	449.594	O1N7C25H35	2012-11-27	O=C(Nc1n(c2c(n1)cccc2)CCCCCNC(C)C)C3CN(c4nccnc4)CCC3
chirality	origin	chemist	notebook	salt form
{22S;}	Internal synthesis	Philip Hughes	PFH-003-080A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.0095	Purine_inhib	Hsp70	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
			Derived from (S)-enantiomer; see PFH for sample	
LCMS datafile				
yes				

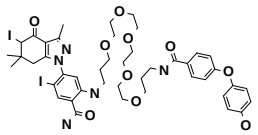
111. **HS-100099-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100099-01	941.852	I1O10N5C44H56	2012-12-03	Ic1c(n2nc(c3c2CC(CC3=O)(C)C)C)cc(c(c1)C(=O)N)NCCCOCCOCCOCCOCCOCCNC(=O)c4ccc(cc4)Oc5ccc(cc5)O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-003-062A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.013	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Iodine position is speculative; based on lack of eluting power	
LCMS datafile				
yes				

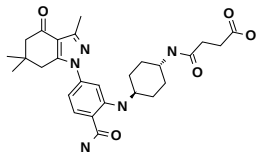
112. **HS-100100-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100100-01	1067.748	I2O10N5C44H55	2012-12-03	Ic1c(n2nc(c3c2CC(C(I)C3=O)(C)C)C)cc(c(c1)C(=O)N)NCCCOCCOCCOCCOCCOCCOCCNC(=O)c4ccc(cc4)Oc5ccc(cc5)O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-003-062B	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.023	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Iodine positions are speculative; based on lack of Hsp90 eluting power	
LCMS datafile				
yes				

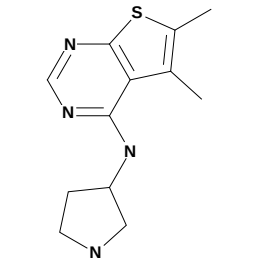
113. **HS-100101-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100101-01	509.600	O5N5C27H35	2012-12-03	O=C(O)CCC(=O)NC1CCC(Nc2c(ccc(n3nc(c4c3CC(CC4=O)(C)C)C)c2)C(=O)N)CC1
chirality	origin	chemist	notebook	salt form
{9-12T;}	Internal synthesis	Philip Hughes	PFH-003-099A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.062	Purine_inhib	Hsp90	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				
yes				

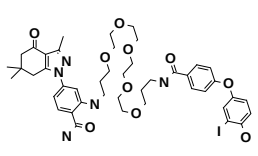
114. **HS-100102-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100102-01	248.349	S1N4C12H16	2012-12-13	s1c2ncnc(c2c(c1C)C)NC3CNCC3
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-004-014A	A: HCL
amount available	program	primary target	percent purity	elemental analysis
0.090	Purine_inhib	FAS		
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				
yes				

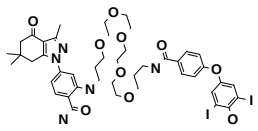
115. **HS-100103-01**



chemical registry

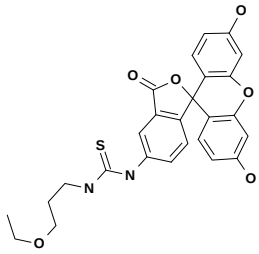
registry id	mol wt	formula	date	SMILES
HS-100103-01	941.852	I1O10N5C44H56	2012-12-20	Ic1c(ccc(c1)Oc2ccc(cc2)C(=O)NCCCOCCOCCOCCOCCOCCOCCNc3c(ccc(n4nc(c5c4CC(CC5=O)(C)C)C)c3)C(=O)N)O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-004-016A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.046	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
			Iodine position is speculative; made under basic conditions and different from 100099.	
LCMS datafile				

116. **HS-100104-01**



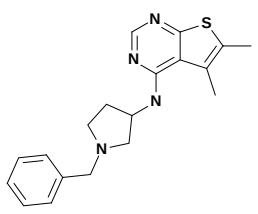
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100104-01	1067.748	I2O10N5C44H55	2012-12-20	Ic1c(c(cc(c1)Oc2ccc(cc2)C(=O)NCCCOCCOCCOCCOCCOCCCNc3c(ccc(n4nc(c5c4CC(CC5=O)(C)C)C)c3)C(=O)N)I)O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-004-016B	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.023	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
	on	on	Iodine position are speculative; made under basic conditions.	yes
LCMS datafile				
yes				

117. **HS-100105-01**



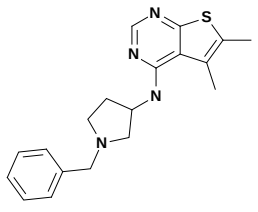
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100105-01	492.547	S1O6N2C26H24	2013-01-17	S=C(Nc1cc2c(cc1)C3(OC2=O)c4c(cc(cc4)O)Oc5cc(ccc35)O)NCCCOCC
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-004-022A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.062	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	non targeted fluorescein analog	
LCMS datafile				
yes				

118. **HS-100106-01**



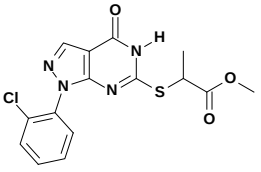
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100106-01	338.472	S1N4C19H22	2013-02-08	s1c2ncnc(c2c(c1C)C)NC3CN(Cc4ccccc4)CC3
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-004-033B	C: TsOH
amount available	program	primary target	percent purity	elemental analysis
3.51	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
			Racemic; TsOH salt	
LCMS datafile				

119. **HS-100106-02**



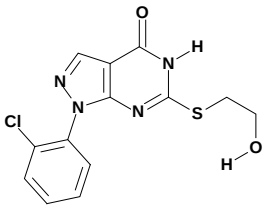
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100106-02	338.472	S1N4C19H22	2015-06-25	s1c2ncnc(c2c(c1C)C)NC3CN(Cc4ccccc4)CC3
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-007-034A	C: TsOH
amount available	program	primary target	percent purity	elemental analysis
3.7	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Racemic; TsOH salt	
LCMS datafile				
yes				

120. **HS-100107-01**



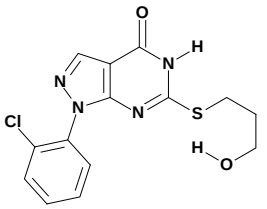
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100107-01	364.809	Cl1S1O3N4C15H13	2013-02-18	Clc1c(n2ncc3c(=O)[nH]c(nc23)SC(C(=O)OC)C)cccc1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC070_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

121. **HS-100108-01**



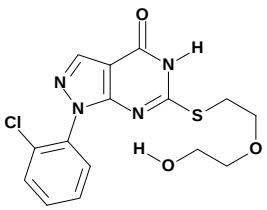
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100108-01	322.772	Cl1S1O2N4C13H11	2013-02-19	Clc1c(n2ncc3c(=O)[nH]c(nc23)SCCO)cccc1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC071_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.020	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				

122. **HS-100109-01**



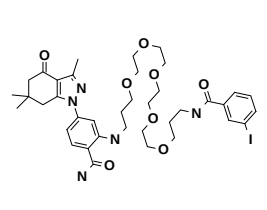
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100109-01	336.799	Cl1S1O2N4C14H13	2013-02-19	Clc1c(n2ncc3c(=O)[nH]c(nc23)SCCCO)cccc1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC071_2	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.020	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				

123. **HS-100110-01**



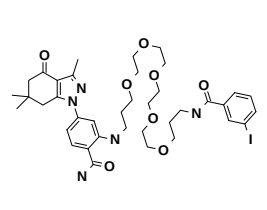
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100110-01	366.825	Cl1S1O3N4C15H15	2013-02-19	Clc1c(n2ncc3c(=O)[nH]c(nc23)SCCOCCO)cccc1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC071_3	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.020	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				

124. **HS-100111-01**



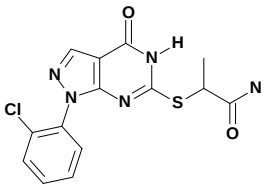
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100111-01	833.757	I1O8N5C38H52	2013-02-22	Ic1cc(ccc1)C(=O)NCCCOCCOCCOCCOCCOCCCNc2c(ccc(n3nc(c4c3CC(CC4=O)(C)C)C)c2)C(=O)N
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-004-027A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.0103	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Made up as 10 mM and given to Jared	
LCMS datafile				
yes				

125. **HS-100111-02**



chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100111-02	833.757	I1O8N5C38H52	2013-06-18	Ic1cc(ccc1)C(=O)NCCCOCCOCCOCCOCCOCCCNc2c(ccc(n3nc(c4c3CC(CC4=O)(C)C)C)c2)C(=O)N
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-004-069A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.0198	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				

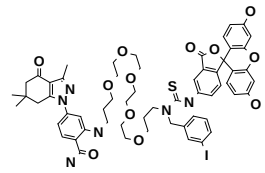
126. **HS-100112-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100112-01	349.797	Cl1S1O2N5C14H12	2013-02-26	Clc1c(n2ncc3c(=O)[nH]c(nc23)SC(C(=O)N)C)cccc1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	002DAC070_2	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.048	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

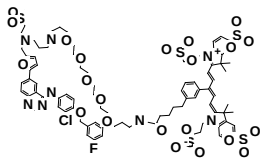
127. **HS-100113-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100113-01	1209.156	I1S1O12N6C59H65	2013-03-27	Ic1cc(ccc1)CN(C(=S)Nc2cc3c(cc2)C4(OC3=O)c5c(cc(cc5)O)Oc6cc(ccc46)O)CCCOCCOCCOCCOCCOCCNc7c(ccc(n8nc(c9c8CC(CC9=O)(C)C)C)c7)C(=O)N
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-004-038A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.028	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	See chemist for sample	
LCMS datafile				
yes				

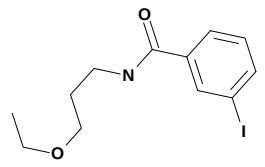
128. **HS-100114-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100114-01	1846.643	Cl1S5F1O22N8C88	2013-03-27	Clc1c(ccc(c1)Nc2ncnc3ccc(c4oc(cc4)CN(CCS(=O)(=O)C)CCCNCCCOCCOCCOCCOCCOCCOCCNC(=O)CCCCc5cc(ccc5)C(=CC=C6N(c7c(cc(cc7)S(=O)(=O)O)C6(C)C)CCCS(=O)(=O)[O-])C=CC8=[N+](c9c(cc(cc9)S(=O)(=O)O)C8(C)C)C
chirality	origin	chemist	notebook	salt form
	Internal synthe	Philip Hughes	PFH-004-047A	None: Free base
amount availa	program	primary target	percent purity	elemental analysis
0.002	Purine_inhib	Her2	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Maybe a Hunig`s base salt. See chemist	
LCMS datafile				
yes				

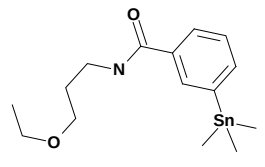
129. **HS-100115-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100115-01	333.167	I1O2N1C12H16	2013-06-11	Ic1cc(ccc1)C(=O)NCCCOCC
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-004-065A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.114	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	gave 4 mg to Ganesan	
LCMS datafile				
yes				

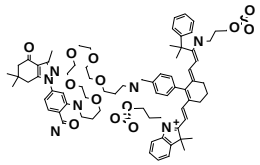
130. **HS-100116-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100116-01	370.077	Sn1O2N1C15H25	2013-06-11	Sn(c1cc(ccc1)C(=O)NCCCOCC)(C)(C)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-004-066A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.174	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	gave 21 mg to Ganesan	
LCMS datafile				
yes				

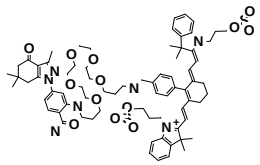
131. **HS-100117-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100117-01	1384.793	S2O13N7C76H101	2013-09-04	S(=O)(=O)([O-])CCCC[N+]1=C(C=CC2=C(C(=CC=C3N(c4c(cccc4)C3(C)C)CCCCS(=O)(=O)O)CCC2)c5ccc(cc5)CNCCCOCCOCCOCCOCCOCCOCCNc6c(ccc(n7nc(c8c7CC(CC8=O)(C)C)C)c6)C(=O)N)C(c9c1cccc9)(C)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-005-003B	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.031	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
LCMS datafile				

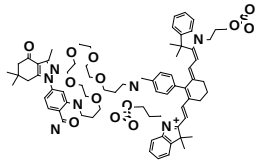
132. **HS-100117-02**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100117-02	1384.793	S2O13N7C76H101	2013-09-13	S(=O)(=O)([O-])CCCC[N+]1=C(C=CC2=C(C(=CC=C3N(c4c(cccc4)C3(C)C)CCCCS(=O)(=O)O)CCC2)c5ccc(cc5)CNCCCOCCOCCOCCOCCOCCOCCNc6c(ccc(n7nc(c8c7CC(CC8=O)(C)C)C)c6)C(=O)N)C(c9c1cccc9)(C)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-005-003C	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		yes
LCMS datafile				
yes				

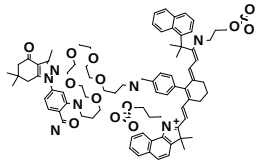
133. **HS-100117-03**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100117-03	1384.793	S2O13N7C76H101	2014-03-12	S(=O)(=O)([O-])CCCC[N+]1=C(C=CC2=C(C(=CC=C3N(c4c(cccc4)C3(C)C)CCCCS(=O)(=O)O)CCC2)c5ccc(cc5)CNCCCOCCOCCOCCOCCOCCOCCNc6c(ccc(n7nc(c8c7CC(CC8=O)(C)C)C)c6)C(=O)N)C(c9c1cccc9)(C)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-005-022A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.320	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
			See Chemist for sample	
LCMS datafile				

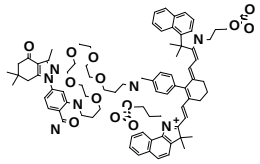
134. **HS-100118-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100118-01	1484.911	S2O13N7C84H105	2013-10-01	S(=O)(=O)([O-])CCCC[N+]1=C(C=CC2=C(C(=CC=C3N(c4c(c5c(cccc5)cc4)C3(C)C)CCCCS(=O)(=O)O)CCC2)c6ccc(cc6)CNCCCOCCOCCOCCOCCOCCOCCNc7c(ccc(n8nc(c9c8CC(CC9=O)(C)C)C)c7)C(=O)N)C(c1c1c1c(cccc1)cc1)(C)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-005-007B	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.074	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		yes
LCMS datafile				
yes				

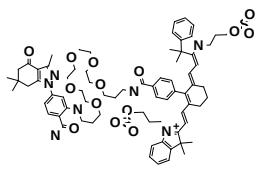
135. **HS-100118-02**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100118-02	1484.911	S2O13N7C84H105	2015-04-01	S(=O)(=O)([O-])CCCC[N+]1=C(C=CC2=C(C(=CC=C3N(c4c(c5c(cccc5)cc4)C3(C)C)CCCCS(=O)(=O)O)CCC2)c6ccc(cc6)CNCCCOCCOCCOCCOCCOCCOCCNc7c(ccc(n8nc(c9c8CC(CC9=O)(C)C)C)c7)C(=O)N)C(c1c1c1c(cccc1)cc1)(C)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-005-029A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.239	Purine_inhib	Hsp90	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				
yes				

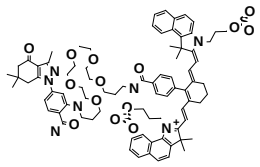
136. **HS-100119-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100119-01	1398.776	S2O14N7C76H99	2013-10-10	S(=O)(=O)([O-])CCCC[N+]1=C(C=CC2=C(C(=CC=C3N(c4c(cccc4)C3(C)C)CCCCS(=O)(=O)O)CCC2)c5ccc(cc5)C(=O)NCCCOCCOCCOCCOCCOCCNc6c(ccc(n7nc(c8c7CC(CC8=O)(C)C)C)c6)C(=O)N)C(c9c1cccc9)(C)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-005-009C	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.036	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
	on	on	See PFH for sample	yes
LCMS datafile				
yes				

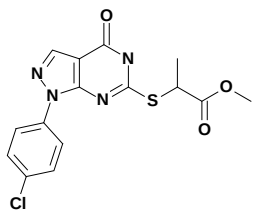
137. **HS-100120-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100120-01	1498.894	S2O14N7C84H103	2013-10-10	S(=O)(=O)([O-])CCCC[N+]1=C(C=CC2=C(C(=CC=C3N(c4c(c5c(cccc5)cc4)C3(C)C)CCCCS(=O)(=O)O)CCC2)c6ccc(cc6)C(=O)NCCCOCCOCCOCCOCCOCCNc7c(ccc(n8nc(c9c8CC(CC9=O)(C)C)C)c7)C(=O)N)C(c1c1c1c(cccc1)cc1)(C)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-005-010A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.065	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
	on	on	See PFH for sample	yes
LCMS datafile				
yes				

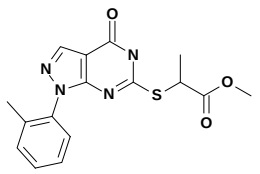
138. **HS-100121-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100121-01	364.809	Cl1S1O3N4C15H13	2013-11-05	Clc1ccc(n2ncc3c(=O)[nH]c(nc23)SC(C(=O)OC)C)cc1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC003_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

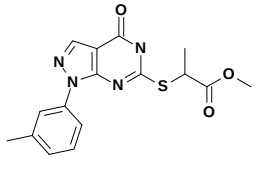
139. **HS-100122-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100122-01	344.390	S1O3N4C16H16	2013-11-07	S(c1[nH]c(=O)c2c(n(nc2)c3c(cccc3)C)n1)C(C(=O)OC)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC003_2	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

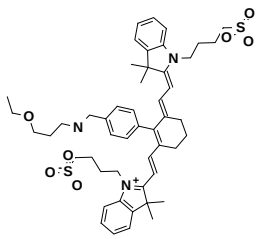
140. **HS-100123-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100123-01	344.390	S1O3N4C16H16	2013-11-07	S(c1[nH]c(=O)c2c(n(nc2)c3cc(ccc3)C)n1)C(C(=O)OC)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC003_3	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

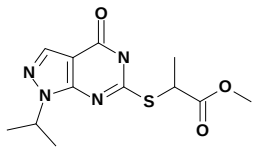
141. **HS-100124-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100124-01	884.203	S2O7N3C50H65	2013-11-11	S(=O)(=O)([O-])CCCC[N+]1=C(C=CC2=C(C(=CC=C3N(c4c(cccc4)C3(C)C)CCCCS(=O)(=O)O)CCC2)c5ccc(cc5)CNCCCOCC)C(c6c1cccc6)(C)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-005-030A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.021	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				
yes				

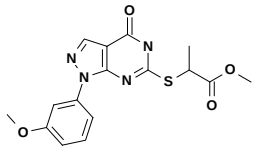
142. **HS-100125-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100125-01	296.347	S1O3N4C12H16	2013-11-12	S(c1[nH]c(=O)c2c(n(nc2)C(C)C)n1)C(C(=O)OC)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC004_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.100	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

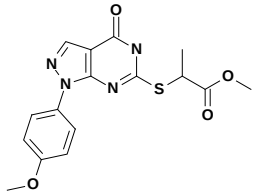
143. **HS-100126-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100126-01	360.390	S1O4N4C16H16	2013-11-12	S(c1[nH]c(=O)c2c(n(nc2)c3cc(ccc3)OC)n1)C(C(=O)OC)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC004_2	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

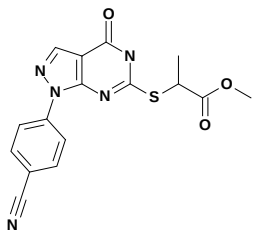
144. **HS-100127-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100127-01	360.390	S1O4N4C16H16	2013-11-12	S(c1[nH]c(=O)c2c(n(nc2)c3ccc(cc3)OC)n1)C(C(=O)OC)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC004_3	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

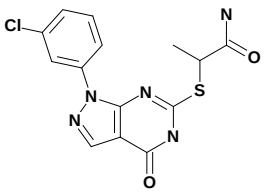
145. **HS-100128-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100128-01	355.373	S1O3N5C16H13	2013-11-12	S(c1[nH]c(=O)c2c(n(nc2)c3ccc(cc3)C#N)n1)C(C(=O)OC)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC004_4	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

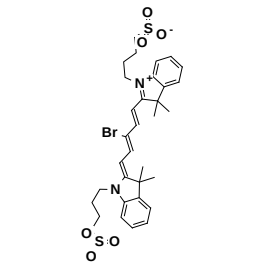
146. **HS-100129-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100129-01	349.797	Cl1S1O2N5C14H12	2013-11-25	Clc1cc(n2ncc3c(=O)[nH]c(nc23)SC(C(=O)N)C)ccc1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC005_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
2 g	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				

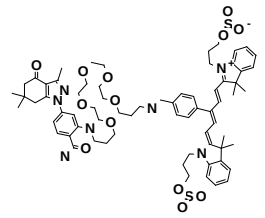
147. **HS-100130-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100130-01	705.727	Br1S2O6N2C33H41	2013-12-04	BrC(=CC=C1N(c2c(cccc2)C1(C)C)CCCCS(=O)(=O)O)C=CC3=[N+](c4c(cccc4)C3(C)C)CCCCS(=O)(=O)[O-]
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-005-036A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.144	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	See PFH for sample	
LCMS datafile				
yes				

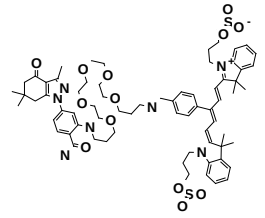
148. **HS-100131-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100131-01	1318.691	S2O13N7C71H95	2013-12-04	S(=O)(=O)([O-])CCCC[N+]1=C(C=CC(=CC=C2N(c3c(cccc3)C2(C)C)CCCCS(=O)(=O)O)c4ccc(cc4)CNCCCOCCOCCOCCOCCOCCOCCNc5c(ccc(n6nc(c7c6CC(CC7=O)(C)C)C)c5)C(=O)N)C(c8c1cccc8)(C)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-005-037A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.061	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	See PFH for sample; impure; may be resubmitted after purifica	
LCMS datafile				
yes				

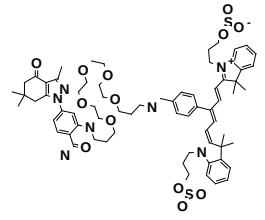
149. **HS-100131-02**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100131-02	1318.691	S2O13N7C71H95	2013-12-05	S(=O)(=O)([O-])CCCC[N+]1=C(C=CC(=CC=C2N(c3c(cccc3)C2(C)C)CCCCS(=O)(=O)O)c4ccc(cc4)CNCCCOCCOCCOCCOCCOCCOCCNc5c(ccc(n6nc(c7c6CC(CC7=O)(C)C)C)c5)C(=O)N)C(c8c1cccc8)(C)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-005-037B	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.045	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	See PFH for sample; This sample is purified HS-100131-	
LCMS datafile				
yes				

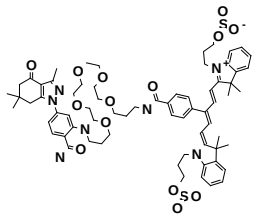
150. **HS-100131-03**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100131-03	1318.691	S2O13N7C71H95	2014-08-07	S(=O)(=O)([O-])CCCC[N+]1=C(C=CC(=CC=C2N(c3c(cccc3)C2(C)C)CCCCS(=O)(=O)O)c4ccc(cc4)CNCCCOCCOCCOCCOCCOCCOCCNc5c(ccc(n6nc(c7c6CC(CC7=O)(C)C)C)c5)C(=O)N)C(c8c1cccc8)(C)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-006-036A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.660	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	500 mg sent for MTD etc.	
LCMS datafile				
yes				

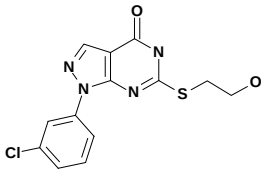
151. **HS-100132-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100132-01	1332.675	S2O14N7C71H93	2013-12-04	S(=O)(=O)([O-])CCCC[N+]1=C(C=CC(=CC=C2N(c3c(cccc3)C2(C)C)CCCCS(=O)(=O)O)c4ccc(cc4)C(=O)NCCCOCCOCCOCCOCCOCCOCCNc5c(ccc(n6nc(c7c6CC(CC7=O)(C)C)C)c5)C(=O)N)C(c8c1cccc8)(C)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-005-038A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.061	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	See PFH for sample; impure; may be resubmitted after purific	
LCMS datafile				
yes				

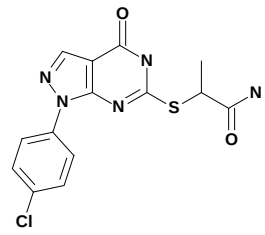
152. **HS-100133-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100133-01	322.772	Cl1S1O2N4C13H11	2013-12-18	Clc1cc(n2ncc3c(=O)[nH]c(nc23)SCCO)ccc1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC006_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
1.75	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38. ZIPK inhibitor.	
LCMS datafile				

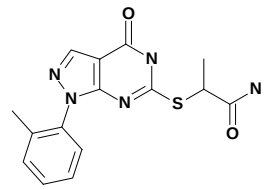
153. **HS-100134-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100134-01	349.797	Cl1S1O2N5C14H12	2014-01-08	Clc1ccc(n2ncc3c(=O)[nH]c(nc23)SC(C(=O)N)C)cc1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC008_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

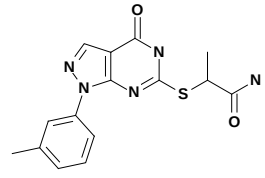
154. **HS-100135-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100135-01	329.379	S1O2N5C15H15	2014-01-08	S(c1[nH]c(=O)c2c(n(nc2)c3c(cccc3)C)n1)C(C(=O)N)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC008_2	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

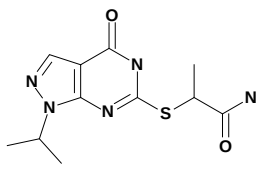
155. **HS-100136-01**



chemical registry

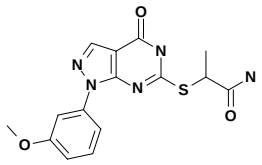
registry id	mol wt	formula	date	SMILES
HS-100136-01	329.379	S1O2N5C15H15	2014-01-08	S(c1[nH]c(=O)c2c(n(nc2)c3cc(ccc3)C)n1)C(C(=O)N)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC008_3	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

156. **HS-100137-01**



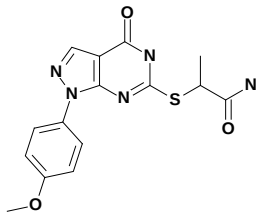
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100137-01	281.336	S1O2N5C11H15	2014-01-08	S(c1[nH]c(=O)c2c(n(nc2)C(C)C)n1)C(C(=O)N)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC009_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

157. **HS-100138-01**



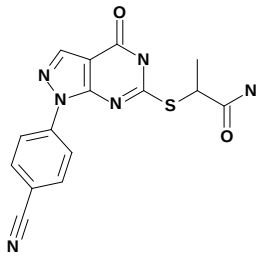
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100138-01	345.378	S1O3N5C15H15	2014-01-08	S(c1[nH]c(=O)c2c(n(nc2)c3cc(ccc3)OC)n1)C(C(=O)N)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC009_2	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

158. **HS-100139-01**



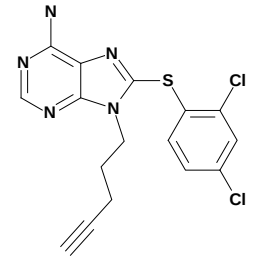
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100139-01	345.378	S1O3N5C15H15	2014-01-08	S(c1[nH]c(=O)c2c(n(nc2)c3ccc(cc3)OC)n1)C(C(=O)N)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC009_3	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

159. **HS-100140-01**



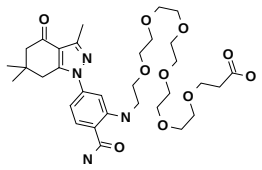
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100140-01	340.362	S1O2N6C15H12	2014-01-08	S(c1[nH]c(=O)c2c(n(nc2)c3ccc(cc3)C#N)n1)C(C(=O)N)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC009_4	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

160. **HS-100141-01**



chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100141-01	378.281	Cl2S1N5C16H13	2014-01-16	Clc1c(ccc(c1)Cl)Sc2n(c3ncnc(c3n2)N)CCCC#C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-005-044A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.016	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Grp94 selective inhibitor PU-H39 Nat. Chem. Biol. 2014; 9; 677-684.	
LCMS datafile				
yes				

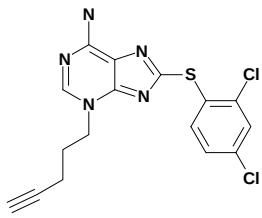
161. **HS-100142-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100142-01	648.748	O10N4C32H48	2014-02-04	O=C(O)CCOCCOCCOCCOCCOCCOCCNc1c(ccc(n2nc(c3c2CC(CC3=O)(C)C)C)c1)C(=O)N
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-005-048C	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.470	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Entire sample given to Chris Lascola	
LCMS datafile				
yes				

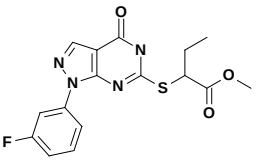
162. **HS-100143-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100143-01	378.281	Cl2S1N5C16H13	2014-03-13	Clc1c(ccc(c1)Cl)Sc2nc3n(cnc(c3n2)N)CCCC#C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-005-058B	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.028	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
			Isomer of HS-100141.	
LCMS datafile				

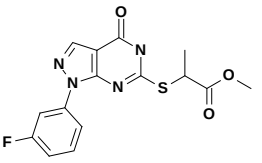
163. **HS-100144-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100144-01	362.381	S1F1O3N4C16H15	2014-03-21	S(c1[nH]c(=O)c2c(n(nc2)c3cc(ccc3)F)n1)C(C(=O)OC)CC
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC024_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

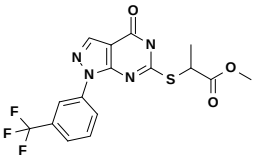
164. **HS-100145-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100145-01	348.354	S1F1O3N4C15H13	2014-03-21	S(c1[nH]c(=O)c2c(n(nc2)c3cc(ccc3)F)n1)C(C(=O)OC)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC024_2	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

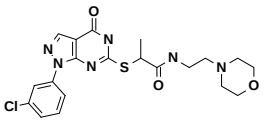
165. **HS-100146-01**



chemical registry

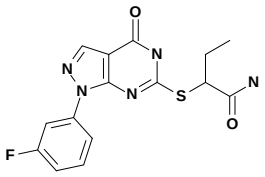
registry id	mol wt	formula	date	SMILES
HS-100146-01	398.362	S1F3O3N4C16H13	2014-03-27	S(c1[nH]c(=O)c2c(n(nc2)c3cc(ccc3)C(F)(F)F)n1)C(C(=O)OC)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC025_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

166. **HS-100147-01**



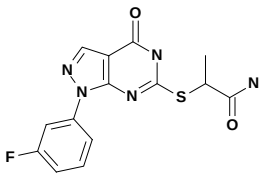
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100147-01	462.956	Cl1S1O3N6C20H23	2014-04-02	Clc1cc(n2ncc3c(=O)[nH]c(nc23)SC(C(=O)NCCN4CCOCC4)C)ccc1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC028_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.080	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

167. **HS-100148-01**



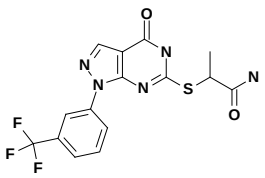
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100148-01	347.369	S1F1O2N5C15H14	2014-04-04	S(c1[nH]c(=O)c2c(n(nc2)c3cc(ccc3)F)n1)C(C(=O)N)CC
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC029_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.060	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

168. **HS-100149-01**



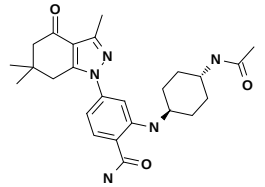
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100149-01	333.343	S1F1O2N5C14H12	2014-04-04	S(c1[nH]c(=O)c2c(n(nc2)c3cc(ccc3)F)n1)C(C(=O)N)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC029_2	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.060	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

169. **HS-100150-01**



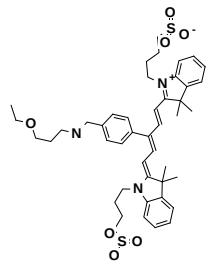
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100150-01	383.350	S1F3O2N5C15H12	2014-04-04	S(c1[nH]c(=O)c2c(n(nc2)c3cc(ccc3)C(F)(F)F)n1)C(C(=O)N)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC029_3	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.060	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

170. **HS-100151-01**



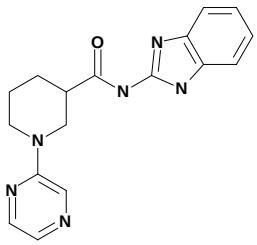
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100151-01	451.564	O3N5C25H33	2014-04-09	O=C(N)c1c(cc(n2nc(c3c2CC(CC3=O)(C)C)C)cc1)NC4CCC(NC(=O)C)CC4
chirality	origin	chemist	notebook	salt form
{24-27T;}	Internal synthesis	Philip Hughes	PFH-005-084A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.102	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
LCMS datafile				

171. **HS-100152-01**



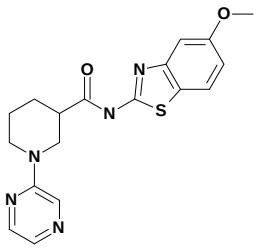
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100152-01	818.101	S2O7N3C45H59	2014-04-17	S(=O)(=O)([O-])CCCC[N+]1=C(C=CC(=CC=C2N(c3c(cccc3)C2(C)C)CCCCS(=O)(=O)O)c4ccc(cc4)CNCCCOCC)C(c5c1cccc5)(C)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-005-085A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.015	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	See PFH for sample	yes
LCMS datafile				
yes				

172. **HS-100153-01**



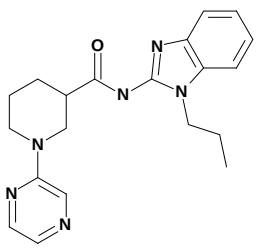
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100153-01	322.366	O1N6C17H18	2014-04-30	O=C(Nc1[nH]c2c(n1)cccc2)C3CN(c4nccnc4)CCC3
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC034_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
1.5	Purine_inhib	HSP70	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Racemic Mixture	
LCMS datafile				

173. **HS-100154-01**



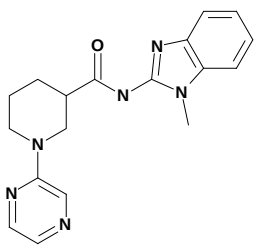
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100154-01	369.443	S1O2N5C18H19	2014-05-02	s1c(nc2cc(ccc12)OC)NC(=O)C3CN(c4nccnc4)CCC3
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC034_5	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	HSP70	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Racemic Mixture	
LCMS datafile				

174. **HS-100155-01**



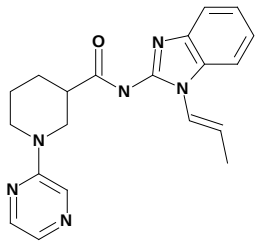
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100155-01	364.446	O1N6C20H24	2014-05-05	O=C(Nc1n(c2c(n1)cccc2)CCC)C3CN(c4nccnc4)CCC3
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC037_01	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	HSP70	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Racemic	
LCMS datafile				

175. **HS-100156-01**



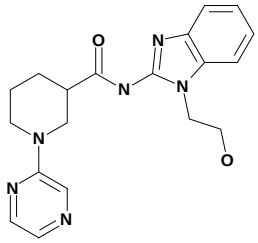
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100156-01	336.393	O1N6C18H20	2014-05-05	O=C(Nc1n(c2c(n1)cccc2)C)C3CN(c4nccnc4)CCC3
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC038_01	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.040	Purine_inhib	HSP70	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Racemic	
LCMS datafile				

176. **HS-100157-01**



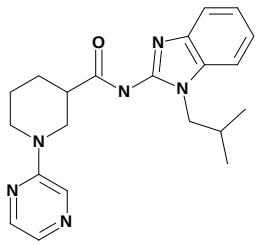
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100157-01	362.430	O1N6C20H22	2014-05-08	O=C(Nc1n(c2c(n1)cccc2)C=CC)C3CN(c4nccnc4)CCC3
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC039_2	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	HSP70	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Racemic	
LCMS datafile				

177. **HS-100158-01**



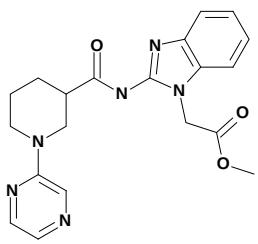
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100158-01	366.419	O2N6C19H22	2014-05-08	O=C(Nc1n(c2c(n1)cccc2)CCO)C3CN(c4nccnc4)CCC3
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC039_3	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	HSP70	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Racemic	
LCMS datafile				

178. **HS-100159-01**



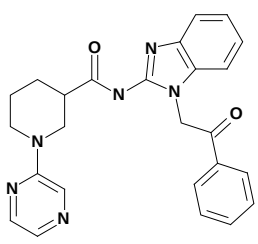
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100159-01	378.473	O1N6C21H26	2014-05-08	O=C(Nc1n(c2c(n1)cccc2)CC(C)C)C3CN(c4nccnc4)CCC3
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC039_4	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	HSP70	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Racemic	
LCMS datafile				

179. **HS-100160-01**



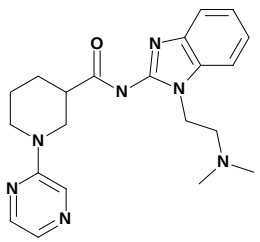
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100160-01	394.429	O3N6C20H22	2014-05-08	O=C(OC)Cn1c(nc2c1cccc2)NC(=O)C3CN(c4nccnc4)CCC3
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC039_5	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	HSP70	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Racemic	
LCMS datafile				

180. **HS-100161-01**



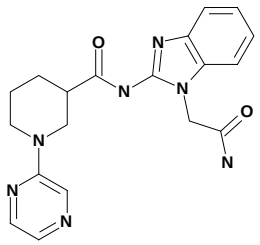
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100161-01	440.499	O2N6C25H24	2014-05-08	O=C(Nc1n(c2c(n1)cccc2)CC(=O)c3ccccc3)C4CN(c5nccnc5)CCC4
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC039_6	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	HSP70	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Racemic	
LCMS datafile				

181. **HS-100162-01**



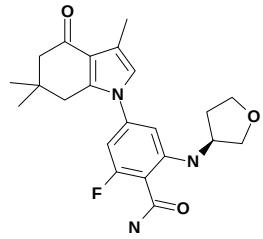
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100162-01	393.487	O1N7C21H27	2014-05-08	O=C(Nc1n(c2c(n1)cccc2)CCN(C)C)C3CN(c4nccnc4)CCC3
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC039_7	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	HSP70	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Racemic	
LCMS datafile				

182. **HS-100163-01**



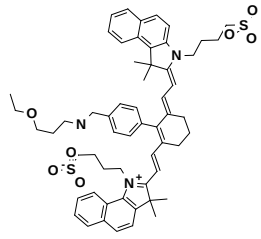
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100163-01	379.418	O2N7C19H21	2014-05-30	O=C(N)Cn1c(nc2c1cccc2)NC(=O)C3CN(c4nccnc4)CCC3
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC043_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.010	Purine_inhib	HSP70	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Racemic	
LCMS datafile				

183. **HS-100164-01**



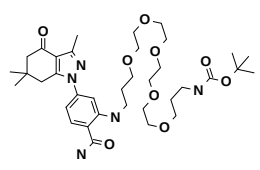
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100164-01	399.461	F1O3N3C22H26	2014-06-09	Fc1c(c(cc(n2c3c(c(c2)C)C(=O)CC(C)(C3)C)c1)NC4COCC4)C(=O)N
chirality	origin	chemist	notebook	salt form
{22S;}	Internal synthesis	Philip Hughes	PFH-006-001A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.108	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				
yes				

184. **HS-100165-01**



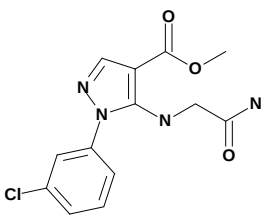
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100165-01	984.321	S2O7N3C58H69	2014-07-17	S(=O)(=O)([O-])CCCC[N+]1=C(C=CC2=C(C(=CC=C3N(c4c(c5c(cccc5)cc4)C3(C)C)CCCCS(=O)(=O)O)CCC2)c6ccc(cc6)CNCCCOCC)C(c7c1c8c(cccc8)cc7)(C)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-006-028A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.077	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				
yes				

185. **HS-100166-01**



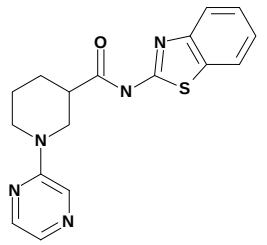
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100166-01	703.870	O9N5C36H57	2014-09-04	O=C(OC(C)(C)C)NCCCOCCOCCOCCOCCOCCOCCNc1c(ccc(n2nc(c3c2CC(CC3=O)(C)C)C)c1)C(=O)N
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-006-042A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.156	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Sample given to Melanie O´sullivan in Mike Therien group (Duke Chemistry)	
LCMS datafile				
yes				

186. **HS-100167-01**



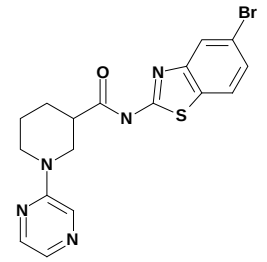
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100167-01	308.722	Cl1O3N4C13H13	2014-09-12	Clc1cc(n2ncc(c2NCC(=O)N)C(=O)OC)ccc1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC049_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.030	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

187. **HS-100168-01**



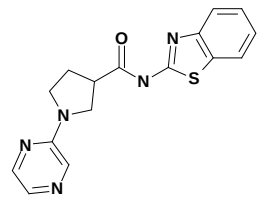
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100168-01	339.417	S1O1N5C17H17	2014-10-15	s1c(nc2c1cccc2)NC(=O)C3CN(c4nccnc4)CCC3
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC063_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.080	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Racemic HSP70 inhibitor analog	
LCMS datafile				

188. **HS-100169-01**



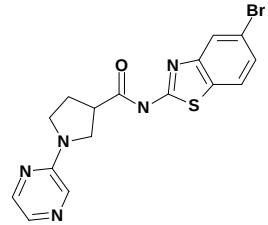
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100169-01	418.313	Br1S1O1N5C17H16	2014-10-15	Brc1cc2nc(sc2cc1)NC(=O)C3CN(c4nccnc4)CCC3
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC063_2	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.080	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Racemic HSP70 inhibitor analog	
LCMS datafile				

189. **HS-100170-01**



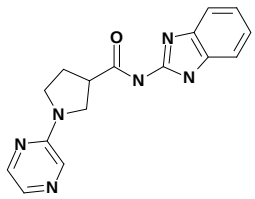
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100170-01	325.390	S1O1N5C16H15	2014-10-15	s1c(nc2c1cccc2)NC(=O)C3CN(c4nccnc4)CC3
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC064_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.080	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Racemic HSP70 inhibitor analog	
LCMS datafile				

190. **HS-100171-01**



chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100171-01	404.286	Br1S1O1N5C16H14	2014-10-15	Brc1cc2nc(sc2cc1)NC(=O)C3CN(c4nccnc4)CC3
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC064_2	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.080	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Racemic HSP70 inhibitor analog	
LCMS datafile				

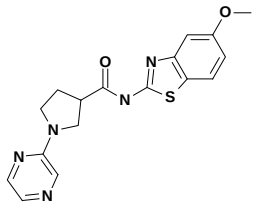
191. **HS-100172-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100172-01	308.339	O1N6C16H16	2014-10-21	O=C(Nc1[nH]c2c(n1)cccc2)C3CN(c4nccnc4)CC3
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC065_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Racemic HSP70 inhibitor analog	
LCMS datafile				

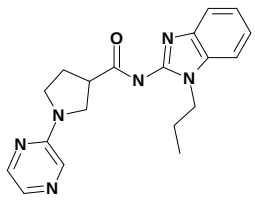
192. **HS-100173-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100173-01	355.416	S1O2N5C17H17	2014-10-21	s1c(nc2cc(ccc12)OC)NC(=O)C3CN(c4nccnc4)CC3
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC065_2	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Racemic HSP70 inhibitor analog	
LCMS datafile				

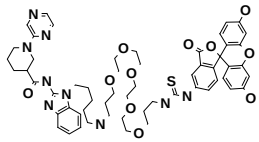
193. **HS-100174-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100174-01	350.419	O1N6C19H22	2014-10-23	O=C(Nc1n(c2c(n1)cccc2)CCC)C3CN(c4nccnc4)CC3
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC066_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.025	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Racemic HSP70 inhibitor analog	
LCMS datafile				

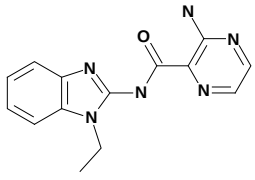
194. **HS-100175-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100175-01	1088.283	S1O11N9C57H69	2014-11-21	S=C(Nc1cc2c(cc1)C3(OC2=O)c4c(cc(cc4)O)Oc5cc(ccc35)O)NCCCOCCOCCOCCOCCOCCCNCCCCCn6c(nc7c6cccc7)NC(=O)C8CN(c9nccnc9)CCC8
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-006-069B	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.097	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Not as clean as the driven snow	
LCMS datafile				

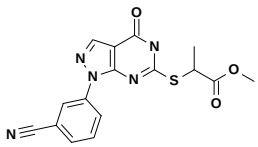
195. **HS-100176-01**



chemical registry

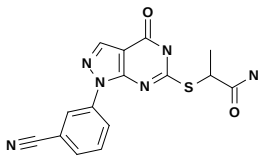
registry id	mol wt	formula	date	SMILES
HS-100176-01	282.302	O1N6C14H14	2015-01-16	O=C(Nc1n(c2c(n1)cccc2)CC)c3nccnc3N
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-006-071A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.804	Purine_inhib	NS-5 Dengue	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	ENAMINE T5843566	
LCMS datafile				
yes				

196. **HS-100177-01**



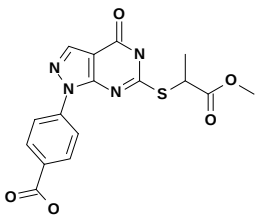
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100177-01	355.373	S1O3N5C16H13	2015-02-04	S(c1[nH]c(=O)c2c(n(nc2)c3cc(ccc3)C#N)n1)C(C(=O)OC)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC079_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.025	Purine_inhib	DAPK/PIM2	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

197. **HS-100178-01**



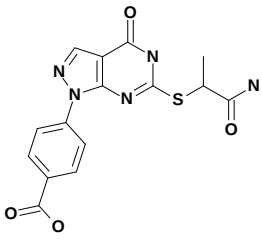
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100178-01	340.362	S1O2N6C15H12	2015-02-04	S(c1[nH]c(=O)c2c(n(nc2)c3cc(ccc3)C#N)n1)C(C(=O)N)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC079_2	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.025	Purine_inhib	DAPK/PIM2	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

198. **HS-100179-01**



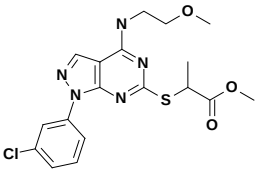
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100179-01	374.373	S1O5N4C16H14	2015-02-12	S(c1[nH]c(=O)c2c(n(nc2)c3ccc(cc3)C(=O)O)n1)C(C(=O)OC)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC080_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.030	Purine_inhib	DAPK/PIM2	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

199. **HS-100180-01**



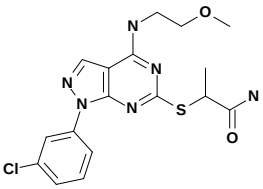
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100180-01	359.362	S1O4N5C15H13	2015-02-12	S(c1[nH]c(=O)c2c(n(nc2)c3ccc(cc3)C(=O)O)n1)C(C(=O)N)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC080_2	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.030	Purine_inhib	DAPK/PIM2	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

200. **HS-100181-01**



chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100181-01	421.904	Cl1S1O3N5C18H20	2015-03-16	Clc1cc(n2ncc3c(nc(nc23)SC(C(=O)OC)C)NCCOC)ccc1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC084_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	DAPK/PIM2	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

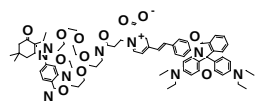
201. **HS-100182-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100182-01	406.892	Cl1S1O2N6C17H19	2015-03-17	Clc1cc(n2ncc3c(nc(nc23)SC(C(=O)N)C)NCCOC)ccc1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC085_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	DAPK/PIM2	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

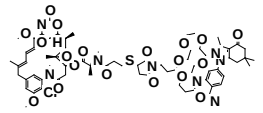
202. **HS-100183-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100183-01	1324.612	O12N9C76H93	2015-03-23	O=C[O-].O=C1N(c2ccc(cc2)C=Cc3cc[n+](cc3)CCC(=O)NCCCOCCOCCOCCOCCCNc4c(ccc(n5nc(c6c5CC(CC6=O)(C)C)C)c4)C(=O)N)C7(c8c(cc(cc8)N(CC)CC)Oc9cc(ccc79)N(CC)CC)c1c1cccc1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-007-001B	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.120	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	See chemist for sample	
LCMS datafile				
yes				

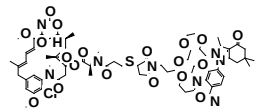
203. **HS-100184-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100184-01	1422.087	Cl1S1O19N8C70H97	2015-03-24	Clc1c(cc2cc1N(C(=O)CC(OC(=O)C(N(C(=O)CCSC3C(=O)N(C(=O)C3)CCCOCCOCCOCCOCCCNc4c(ccc(n5nc(c6c5CC(CC6=O)(C)C)C)c4)C(=O)N)C)C)C7(OC7C(C8OC(=O)NC(O)(C(OC)C=CC=C(C2)C)C8)C)C)OC
chirality	origin	chemist	notebook	salt form
{12S;16S;74R;76S;77S;78S;83S;85R	Internal synthesis	Philip Hughes	PFH-007-004A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.017	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	See chemist for sample	
LCMS datafile				
yes				

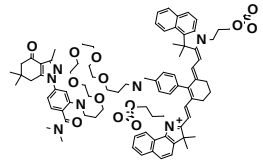
204. **HS-100184-02**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100184-02	1422.087	Cl1S1O19N8C70H97	2015-06-25	Clc1c(cc2cc1N(C(=O)CC(OC(=O)C(N(C(=O)CCSC3C(=O)N(C(=O)C3)CCCOCCOCCOCCOCCCNc4c(ccc(n5nc(c6c5CC(CC6=O)(C)C)C)c4)C(=O)N)C)C)C7(OC7C(C8OC(=O)NC(O)(C(OC)C=CC=C(C2)C)C8)C)C)OC
chirality	origin	chemist	notebook	salt form
{12S;16S;74R;76S;77S;78S;83S;85R	Internal synthesis	Philip Hughes	PFH-007-035A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.144	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Sent to UNC	
LCMS datafile				
yes				

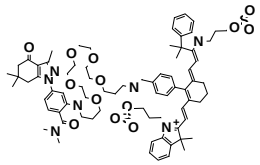
205. **HS-100185-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100185-01	1512.964	S2O13N7C86H109	2015-04-02	S(=O)(=O)([O-])CCCC[N+]1=C(C=CC2=C(C(=CC=C3N(c4c(c5c(cccc5)cc4)C3(C)C)CCCCS(=O)(=O)O)CCC2)c6ccc(cc6)CNCCCOCCOCCOCCOCCCNc7c(ccc(n8nc(c9c8CC(CC9=O)(C)C)C)c7)C(=O)N(C)C)C(c1c1c1c(ccc1)cc1)(C)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-007-006A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.044	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	control for HS-118	
LCMS datafile				
yes				

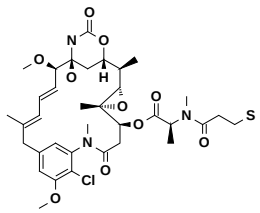
206. **HS-100186-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100186-01	1412.846	S2O13N7C78H105	2015-04-02	S(=O)(=O)([O-])CCCC[N+]1=C(C=CC2=C(C(=CC=C3N(c4c(cccc4)C3(C)C)CCCCS(=O)(=O)O)CCC2)c5ccc(cc5)CNCCCOCCOCCOCCOCCOCCOCCNc6c(ccc(n7nc(c8c7CC(CC8=O)(C)C)C)c6)C(=O)N(C)C)C(c9c1cccc9)(C)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-007-007A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.060	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
			HS-117 control	
LCMS datafile				
yes				

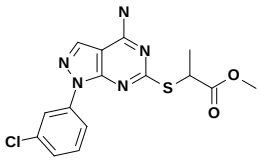
207. **HS-100187-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100187-01	738.292	Cl1S1O10N3C35H48	2015-04-07	Clc1c(cc2cc1N(C(=O)CC(OC(=O)C(N(C(=O)CCS)C)C)C3(OC3C(C4OC(=O)NC(O)(C(OC)C=CC=C(C2)C)C4)C)C)OC
chirality	origin	chemist	notebook	salt form
{12S;16S;25R;27S;28S;29S;34S;36R:}	Internal synthesis	Philip Hughes	PFH-007-004SIM_DM-1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.300	_____		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	DM-1; Mertansine; Tubulin inhibitor; gift of Genentech	
LCMS datafile				
yes				

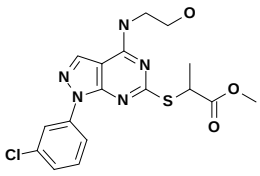
208. **HS-100188-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100188-01	363.824	Cl1S1O2N5C15H14	2015-04-09	Clc1cc(n2ncc3c(nc(nc23)SC(C(=O)OC)C)N)ccc1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC088_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.040	Purine_inhib	DAPK/PIMK	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

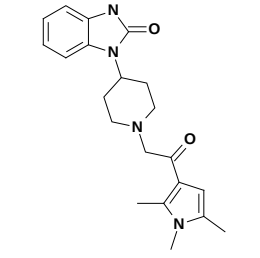
209. **HS-100189-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100189-01	407.877	Cl1S1O3N5C17H18	2015-04-09	Clc1cc(n2ncc3c(nc(nc23)SC(C(=O)OC)C)NCCO)ccc1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	3DAC089_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.040	Purine_inhib	DAPK/PIMK	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

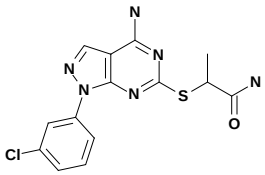
210. **HS-100190-01**



chemical registry

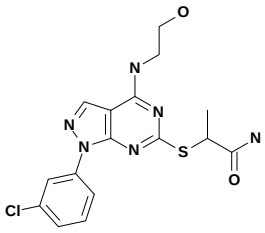
registry id	mol wt	formula	date	SMILES
HS-100190-01	366.459	O2N4C21H26	2015-04-23	O=c1n(c2c([nH]1)cccc2)C3CCN(CC(=O)c4c(n(c(c4)C)C)C)CC3
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	4DAC005_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.5	Purine_inhib	NLRP3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Synthesis for Justin Macdonald	
LCMS datafile				

211. **HS-100191-01**



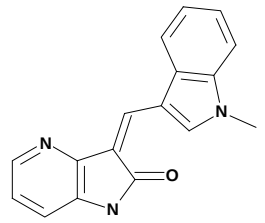
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100191-01	348.813	Cl1S1O1N6C14H13	2015-04-30	Clc1cc(n2ncc3c(nc(nc23)SC(C(=O)N)C)N)ccc1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	4DAC001_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.035	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

212. **HS-100192-01**



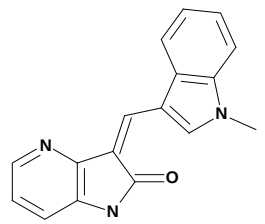
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100192-01	392.866	Cl1S1O2N6C16H17	2015-04-30	Clc1cc(n2ncc3c(nc(nc23)SC(C(=O)N)C)NCCO)ccc1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	4DAC002_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.035	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

213. **HS-100193-01**



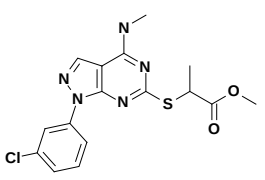
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100193-01	275.306	O1N3C17H13	2015-05-12	O=c1[nH]c2c(nccc2)c1=Cc3cn(c4c3cccc4)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	2DAC080_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	ACC	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	GW441756	
LCMS datafile				

214. **HS-100193-02**



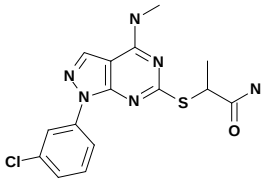
chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100193-02	275.306	O1N3C17H13	2015-06-25	O=c1[nH]c2c(nccc2)c1=Cc3cn(c4c3cccc4)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	4DAC012_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.450	Purine_inhib	ACC	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	GW441756	
LCMS datafile				

215. **HS-100194-01**



chemical registry				
registry id	mol wt	formula	date	SMILES
HS-100194-01	377.851	Cl1S1O2N5C16H16	2015-05-20	Clc1cc(n2ncc3c(nc(nc23)SC(C(=O)OC)C)NC)ccc1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	4DAC006_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

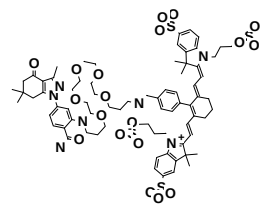
216. **HS-100195-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100195-01	362.839	Cl1S1O1N6C15H15	2015-05-20	Clc1cc(n2ncc3c(nc(nc23)SC(C(=O)N)C)NC)ccc1
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	4DAC008_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.050	Purine_inhib	DAPK/PIM3	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Analog of HS38	
LCMS datafile				

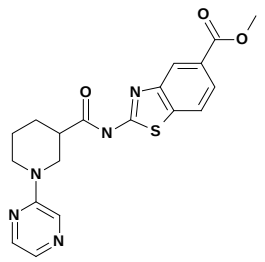
217. **HS-100196-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100196-01	1544.920	S4O19N7C76H101	2015-06-03	S(=O)(=O)(O)c1cc2c(cc1)N(C(=CC=C3C(=C(C=CC4=[N+](c5c(cc(cc5)S(=O)(=O)O)C4(C)C)CCCCS(=O)(=O)[O-])CCC3)c6ccc(cc6)CNCCCOCCOCCOCCOCCOCCOCCNc7c(ccc(n8nc(c9c8CC(CC9=O)(C)C)C)c7)C(=O)N)C2(C)C)CCCCS(=O)(=O)O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-007-015D	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.043	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
	on	on	See Chemist for sample	yes
LCMS datafile				
yes				

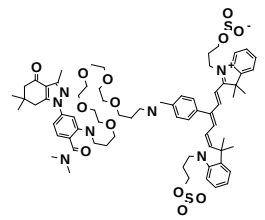
218. **HS-100197-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100197-01	397.453	S1O3N5C19H19	2015-06-10	s1c(nc2cc(ccc12)C(=O)OC)NC(=O)C3CN(c4nccnc4)CCC3
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Dave Carlson	4DAC009_1	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.250	Purine_inhib	Hsp70	95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on		
LCMS datafile				

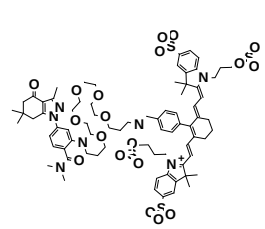
219. **HS-100198-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100198-01	1346.745	S2O13N7C73H99	2015-06-11	S(=O)(=O)([O-])CCCC[N+]1=C(C=CC(=CC=C2N(c3c(cccc3)C2(C)C)CCCCS(=O)(=O)O)c4ccc(cc4)CNCCCOCCOCCOCCOCCOCCNc5c(ccc(n6nc(c7c6CC(CC7=O)(C)C)C)c5)C(=O)N(C)C)C(c8c1cccc8)(C)C
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-007-030A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.049	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	500 mg sent for MTD etc.	
LCMS datafile				
yes				

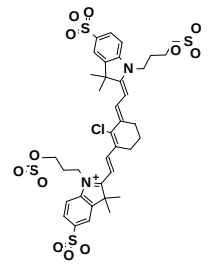
220. **HS-100199-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100199-01	1572.974	S4O19N7C78H105	2015-06-23	S(=O)(=O)(O)c1cc2c(cc1)N(C(=CC=C3C(=C(C=CC4=[N+](c5c(cc(cc5)S(=O)(=O)O)C4(C)C)CCCCS(=O)(=O)[O-])CCC3)c6ccc(cc6)CNCCCOCCOCCOCCOCCOCCOCCNc7c(ccc(n8nc(c9c8CC(CC9=O)(C)C)C)c7)C(=O)N(C)C)C2(C)C)CCCCS(=O)(=O)O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-007-032B	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.017	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	See Chemist for sample	
LCMS datafile				
yes				

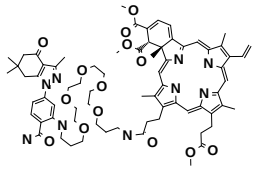
221. **HS-100200-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100200-01	887.505	Cl1S4O12N2C38H47	2015-06-29	ClC1=C(C=CC2=[N+](c3c(cc(cc3)S(=O)(=O)O)C2(C)C)CCCCS(=O)(=O)[O-])CCCC1=CC=C4N(c5c(cc(cc5)S(=O)(=O)O)C4(C)C)CCCCS(=O)(=O)O
chirality	origin	chemist	notebook	salt form
	Internal synthesis	Philip Hughes	PFH-007-027A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.409	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
			See Chemist for sample	
LCMS datafile				

222. **HS-100201-01**



chemical registry

registry id	mol wt	formula	date	SMILES
HS-100201-01	1304.536	O14N9C72H89	2015-07-17	O=C(OC)C1C2(C3=Cc4[nH]c(c(c4C)CCC(=O)NCCCOCCOCCOCCOCCOCCOCCNc5c(ccc(n6nc(c7c6CC(CC7=O)(C)C)C)c5)C(=O)N)C=c8nc(c(c8CCC(=O)OC)C)C=c9[nH]c(=CC(=N3)C2=CC=C1C(=O)OC)c(c9C=C)C)C
chirality	origin	chemist	notebook	salt form
(5S,6R:)	Internal synthesis	Philip Hughes	PFH-007-046A	None: Free base
amount available	program	primary target	percent purity	elemental analysis
0.036	Purine_inhib		95-100	
melting point	NMR data	LCMS data	comment	NMR datafile
		on	Mixture of isomers from verteporfin	
LCMS datafile				
yes				

2016 MILESTONE REPORT

Name	Resource Names	Start	Finish
Aim 1 - Lead Optimization Studies on Existing NIR Hsp90 Inhibitors	Dr. Philip Hughes,Dr. Timothy Haystead	Fri 1/2/15	Fri 7/31/15
Aim 4 - Phase I Clinical trial of Ad5 [E1-, E2b-]-HER3	Duke University	Mon 11/23/15	Fri 12/16/16
Patient accrual goal per quarter at Duke	Duke University	**Mon 11/23/15**	**Fri 12/16/16**
Aim 7 - Begin Phase I Study with Lead NIR HSP90 Inhibitor	Duke University	**Thu 10/1/15**	**Fri 12/30/16**
Aim 8 - Optimize lead NIR contrast agent	Duke University	**Thu 10/1/15**	**Wed 9/28/16**
Aim 9 - Develop alternative small molecule NIR contrast ligands	Duke University	**Thu 10/1/15**	**Thu 9/28/17**
Aim 10 - Determine optimal strategies for in vivo NIR or RF thermal therapy	Duke University	**Thu 10/1/15**	**Wed 12/28/16**
Aim 11 - Optimize NIR imaging sequences for contrast detection, thermography, and therapeutic assessment in vivo	Duke University	**Thu 10/1/15**	**Thu 9/27/18**
Aim 12 - Phase I Study: Begin Phase I Study of NIR-Hsp90i with NIR or RF mediated thermal therapy	Duke University	**Mon 10/3/16**	**Fri 12/29/17**

Future Statement of Work

Aim 7. Begin Phase I Study with Lead NIR HSP90 Inhibitor

Aim 7. Task 1: Begin the Phase I study

Aim 7. Task 2: Define the safety and PK profiles of the clinical NIR lead compound in the phase I study.

Aim 7. Task 3: Identify a dose and schedule (single or daily x 3) for Phase II trials

Aim 7. Task 4: Perform PK and imaging studies to measure NIR-Hsp90i accumulation in tumors

Aim 7. Task 5: Perform PD analysis of tumor biopsies to verify the effects of the NIR inhibitor on the Hsp90 signaling node

Future Statement of Work

Aim 8: Optimize lead NIR contrast agent.

Aim 8. Task 2: Synthesize a first generation library of NIR Hsp90i derivatives with potential for NIR or RF thermal enhancement

Aim 9 Develop alternative small molecule NIR contrast ligands.

Aim 9. Task 1: Design and synthesize additional NIR Hsp90i moieties for NIR or RF thermal enhancement

Aim 10 Determine optimal strategies for *in vivo* NIR or RF thermal therapy.

Aim 10. Task 1: Build or collaborate with other investigators with NIR compatible NIR or RF systems for delivery of NIR or RF thermal therapy for pre-clinical studies.

Aim 3. Task 2: Build or collaborate with other investigators with NIR compatible NIR or RF systems for use in clinical systems

Aim 11 Optimize NIR imaging sequences for contrast detection, thermography, and therapeutic assessment *in vivo*

Aim 11. Task 1: Establish conventional and novel quantitative NIR imaging for tumor detection, thermography, and response to therapy

Aim 11. Task 2:Incorporate rapid functional methods for assessing tumor response to therapy

Future Statement of Work

Appendix C

Aim 12. Phase I Study: Begin Phase I Study of NIR-Hsp90i with NIR or RF mediated thermal therapy

Aim 12. Task 1: Obtain regulatory approval of a Phase I study

Aim 12. Task 2: Begin Phase I study

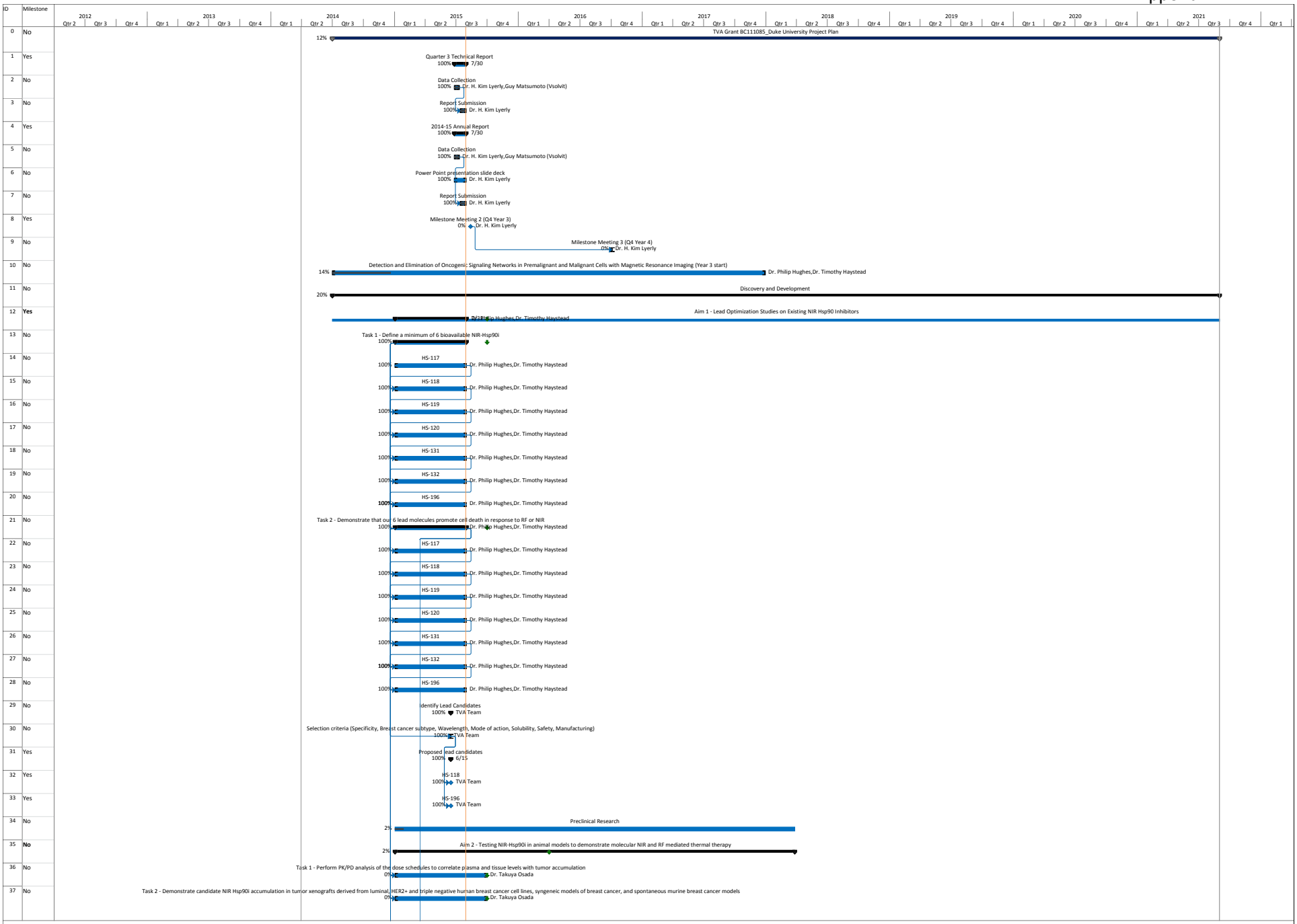
Aim 12. Task 3: Define MTD of combination of P2D from Phase I study with NIR or RF mediated thermal therapy

Aim 12. Task 4: Define therapy related toxicities

Aim 12. Task 5: Perform imaging studies to measure NIR-Hsp90i accumulation and indicators of temperature change

Aim 12. Task 6: Perform analysis of cell viability and Hsp90 expression in samples obtained pre and post therapy.

Brian Pogue, Dartmouth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2019 Qtr 1 Qtr 2 Qtr 3 Qtr 4
2020 Qtr 1 Qtr 2 Qtr 3 Qtr 4
2021 Qtr 1 Qtr 2 Qtr 3 Qtr 4 Qtr 1
0 No TVA Grant BC111085_Duke University Project Plan 12%
1 Yes Quarter 3 Technical Report 100% 7/30
2 No Data Collection 100% Dr. H. Kim Lyerly,Guy Matsumoto (Vsolvit)
3 No Report Submission 100% Dr. H. Kim Lyerly
4 Yes 2014-15 Annual Report 100% 7/30
5 No Data Collection 100% Dr. H. Kim Lyerly,Guy Matsumoto (Vsolvit)
6 No Power Point presentation slide deck 100% Dr. H. Kim Lyerly
7 No Report Submission 100% Dr. H. Kim Lyerly
8 Yes Milestone Meeting 2 (Q4 Year 3) 0% Dr. H. Kim Lyerly
9 No Milestone Meeting 3 (Q4 Year 4) 0% Dr. H. Kim Lyerly
10 No Detection and Elimination of Oncogenic Signaling Networks in Premalignant and Malignant Cells with Magnetic Resonance Imaging (Year 3 start) 14% Dr. Philip Hughes,Dr. Timothy Haystead
11 No Discovery and Development 20%
12 Yes Aim 1 - Lead Optimization Studies on Existing NIR Hsp90 Inhibitors
13 No Task 1 - Define a minimum of 6 bioavailable NIR-Hsp90i 100%
14 No HS-117 100% Dr. Philip Hughes,Dr. Timothy Haystead
15 No HS-118 100% Dr. Philip Hughes,Dr. Timothy Haystead
16 No HS-119 100% Dr. Philip Hughes,Dr. Timothy Haystead
17 No HS-120 100% Dr. Philip Hughes,Dr. Timothy Haystead
18 No HS-131 100% Dr. Philip Hughes,Dr. Timothy Haystead
19 No HS-132 100% Dr. Philip Hughes,Dr. Timothy Haystead
20 No HS-196 100% Dr. Philip Hughes,Dr. Timothy Haystead
21 No Task 2 - Demonstrate that our 6 lead molecules promote cell death in response to RF or NIR 100% Dr. Philip Hughes,Dr. Timothy Haystead
22 No HS-117 100% Dr. Philip Hughes,Dr. Timothy Haystead
23 No HS-118 100% Dr. Philip Hughes,Dr. Timothy Haystead
24 No HS-119 100% Dr. Philip Hughes,Dr. Timothy Haystead
25 No HS-120 100% Dr. Philip Hughes,Dr. Timothy Haystead
26 No HS-131 100% Dr. Philip Hughes,Dr. Timothy Haystead
27 No HS-132 100% Dr. Philip Hughes,Dr. Timothy Haystead
28 No HS-196 100% Dr. Philip Hughes,Dr. Timothy Haystead
29 No Identify Lead Candidates 100% TVA Team
30 No Selection criteria (Specificity, Breast cancer subtype, Wavelength, Mode of action, Solubility, Safety, Manufacturing) 100% TVA Team
31 Yes Proposed lead candidates 100% 6/15
32 Yes HS-118 100% TVA Team
33 Yes HS-196 100% TVA Team
34 No Preclinical Research 2%
35 No Aim 2 - Testing NIR-Hsp90i in animal models to demonstrate molecular NIR and RF mediated thermal therapy 2%
36 No Task 1 - Perform PK/PD analysis of the dose schedules to correlate plasma and tissue levels with tumor accumulation 0% Dr. Takuya Osada
37 No Task 2 - Demonstrate candidate NIR Hsp90i accumulation in tumor xenografts derived from luminal, HER2+ and triple negative human breast cancer cell lines, syngeneic models of breast cancer, and spontaneous murine breast cancer models 0% Dr. Takuya Osada
Project: TVA Grant BC111085_Du
Date: Thu 7/30/15
Task
Split
Milestone
Summary
Project Summary
External Tasks
External Milestone
Inactive Task
Inactive Milestone
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Start-only
Finish-only
Deadline
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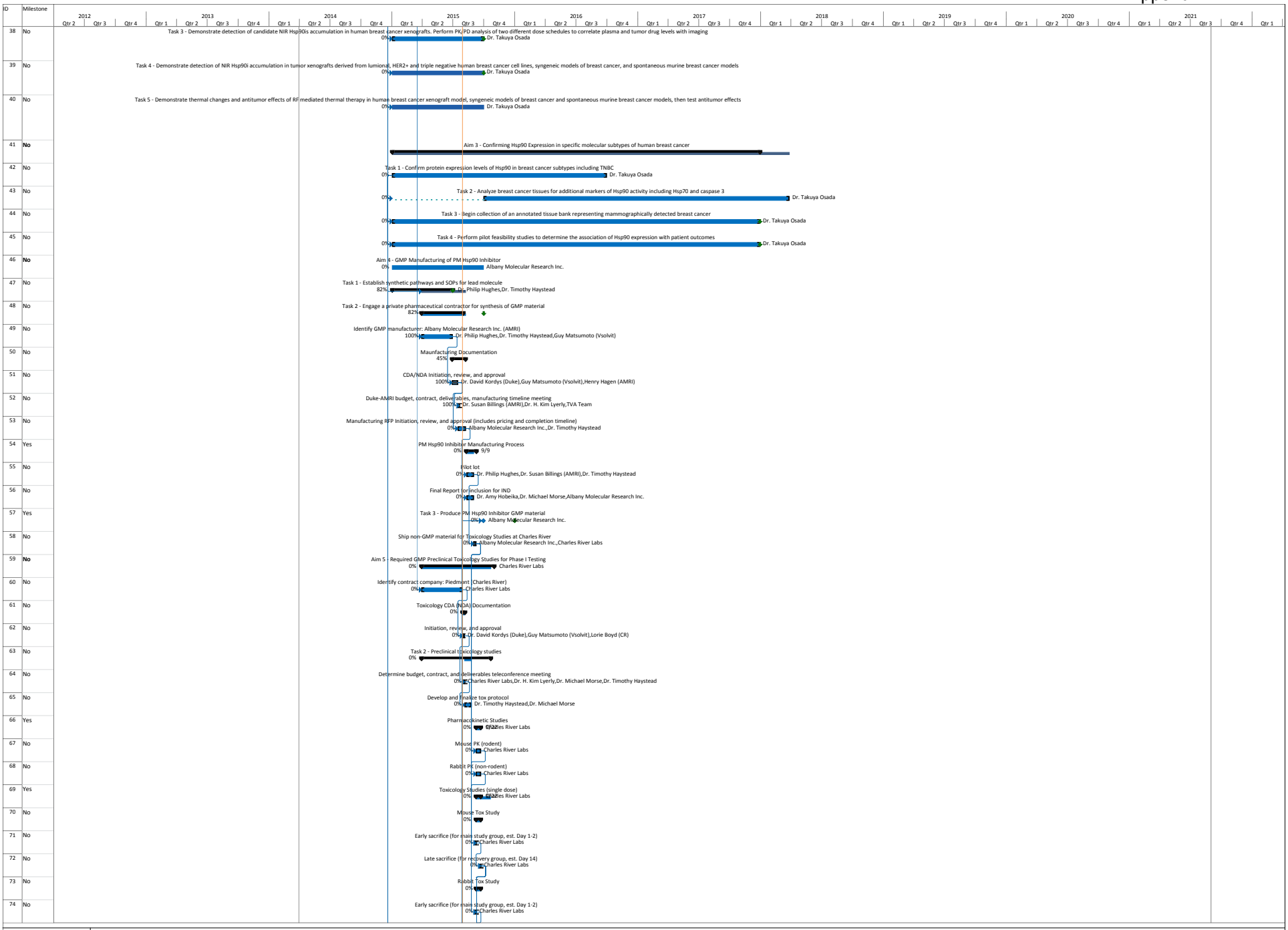
Page 1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2019 Qtr 1 Qtr 2 Qtr 3 Qtr 4
2020 Qtr 1 Qtr 2 Qtr 3 Qtr 4
2021 Qtr 1 Qtr 2 Qtr 3 Qtr 4 Qtr 1
38 No Task 3 - Demonstrate detection of candidate NIR Hsp90is accumulation in human breast cancer xenografts. Perform PK/PD analysis of two different dose schedules to correlate plasma and tumor drug levels with imaging 0% Dr. Takuya Osada
39 No Task 4 - Demonstrate detection of NIR Hsp90i accumulation in tumor xenografts derived from luminal, HER2+ and triple negative human breast cancer cell lines, syngeneic models of breast cancer, and spontaneous murine breast cancer models 0% Dr. Takuya Osada
40 No Task 5 - Demonstrate thermal changes and antitumor effects of RF-mediated thermal therapy in human breast cancer xenograft model, syngeneic models of breast cancer and spontaneous murine breast cancer models, then test antitumor effects 0% Dr. Takuya Osada
41 No Aim 3 - Confirming Hsp90 Expression in specific molecular subtypes of human breast cancer
42 No Task 1 - Confirm protein expression levels of Hsp90 in breast cancer subtypes including TNBC 0% Dr. Takuya Osada
43 No Task 2 - Analyze breast cancer tissues for additional markers of Hsp90 activity including Hsp70 and caspase 3 0% Dr. Takuya Osada
44 No Task 3 - Begin collection of an annotated tissue bank representing mammographically detected breast cancer 0% Dr. Takuya Osada
45 No Task 4 - Perform pilot feasibility studies to determine the association of Hsp90 expression with patient outcomes 0% Dr. Takuya Osada
46 No Aim 4 - GMP Manufacturing of PM Hsp90 Inhibitor 0% Albany Molecular Research Inc.
47 No Task 1 - Establish synthetic pathways and SOPs for lead molecule 82% Dr. Philip Hughes,Dr. Timothy Haystead
48 No Task 2 - Engage a private pharmaceutical contractor for synthesis of GMP material 82%
49 No Identify GMP manufacturer: Albany Molecular Research Inc. (AMRI) 100% Dr. Philip Hughes,Dr. Timothy Haystead,Guy Matsumoto (Vsolvit)
50 No Maunfacturing Documentation 45%
51 No CDA/NDA Initiation, review, and approval 100% Dr. David Kordys (Duke),Guy Matsumoto (Vsolvit),Henry Hagen (AMRI)
52 No Duke-AMRI budget, contract, deliverables, manufacturing timeline meeting 100% Dr. Susan Billings (AMRI),Dr. H. Kim Lyerly,TVA Team
53 No Manufacturing RFP Initiation, review, and approval (includes pricing and completion timeline) 0% Albany Molecular Research Inc.,Dr. Timothy Haystead
54 Yes PM Hsp90 Inhibitor Manufacturing Process 0% 9/9
55 No Pilot lot 0% Dr. Philip Hughes,Dr. Susan Billings (AMRI),Dr. Timothy Haystead
56 No Final Report for inclusion for IND 0% Dr. Amy Hobeika,Dr. Michael Morse,Albany Molecular Research Inc.
57 Yes Task 3 - Produce PM Hsp90 Inhibitor GMP material 0% Albany Molecular Research Inc.
58 No Ship non-GMP material for Toxicology Studies at Charles River 0% Albany Molecular Research Inc.,Charles River Labs
59 No Aim 5 - Required GMP Preclinical Toxicology Studies for Phase I Testing 0% Charles River Labs
60 No Identify contract company: Piedmont (Charles River) 0% Charles River Labs
61 No Toxicology CDA (NDA) Documentation 0%
62 No Initiation, review, and approval 0% Dr. David Kordys (Duke),Guy Matsumoto (Vsolvit),Lorie Boyd (CR)
63 No Task 2 - Preclinical toxicology studies 0%
64 No Determine budget, contract, and deliverables teleconference meeting 0% Charles River Labs,Dr. H. Kim Lyerly,Dr. Michael Morse,Dr. Timothy Haystead
65 No Develop and finalize tox protocol 0% Dr. Timothy Haystead,Dr. Michael Morse
66 Yes Pharmacokinetic Studies 0% 0/22 Charles River Labs
67 No Mouse PK (rodent) 0% Charles River Labs
68 No Rabbit PK (non-rodent) 0% Charles River Labs
69 Yes Toxicology Studies (single dose) 0% 0/22 Charles River Labs
70 No Mouse Tox Study 0%
71 No Early sacrifice (for main study group, est. Day 1-2) 0% Charles River Labs
72 No Late sacrifice (for recovery group, est. Day 14) 0% Charles River Labs
73 No Rabbit Tox Study 0%
74 No Early sacrifice (for main study group, est. Day 1-2) 0% Charles River Labs
Project: TVA Grant BC111085_Du
Date: Thu 7/30/15
Task
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Summary
Project Summary
External Tasks
External Milestone
Inactive Task
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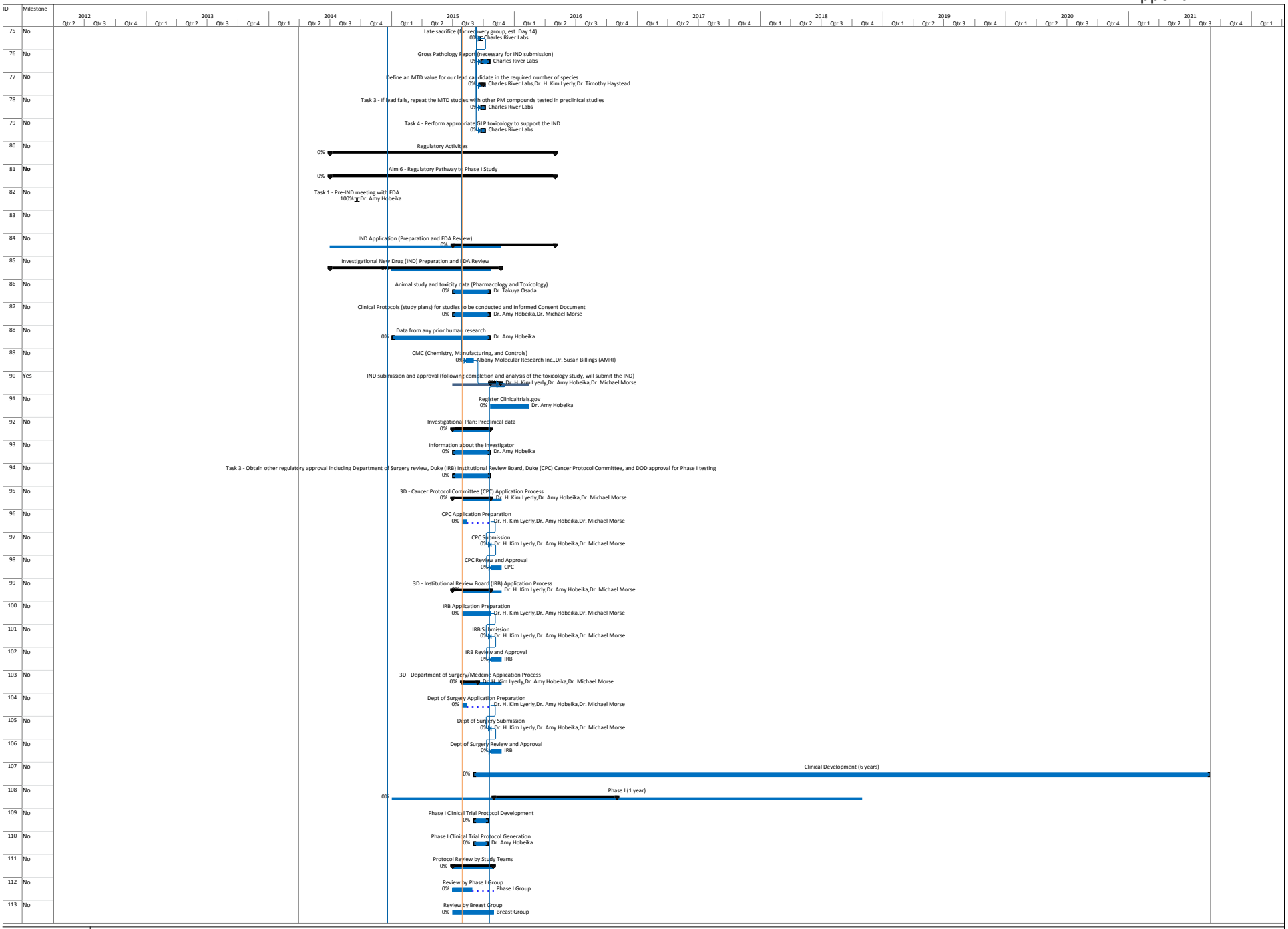
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2019 Qtr 1 Qtr 2 Qtr 3 Qtr 4
2020 Qtr 1 Qtr 2 Qtr 3 Qtr 4
2021 Qtr 1 Qtr 2 Qtr 3 Qtr 4 Qtr 1
75 No Late sacrifice (for recovery group, est. Day 14) 0% Charles River Labs
76 No Gross Pathology Report (necessary for IND submission) 0% Charles River Labs
77 No Define an MTD value for our lead candidate in the required number of species 0% Charles River Labs,Dr. H. Kim Lyerly,Dr. Timothy Haystead
78 No Task 3 - If lead fails, repeat the MTD studies with other PM compounds tested in preclinical studies 0% Charles River Labs
79 No Task 4 - Perform appropriate GLP toxicology to support the IND 0% Charles River Labs
80 No Regulatory Activities 0%
81 No Aim 6 - Regulatory Pathway to Phase I Study 0%
82 No Task 1 - Pre-IND meeting with FDA 100% Dr. Amy Hobeika
83 No
84 No IND Application (Preparation and FDA Review) 0%
85 No Investigational New Drug (IND) Preparation and FDA Review 0%
86 No Animal study and toxicity data (Pharmacology and Toxicology) 0% Dr. Takuya Osada
87 No Clinical Protocols (study plans) for studies to be conducted and Informed Consent Document 0% Dr. Amy Hobeika,Dr. Michael Morse
88 No Data from any prior human research 0% Dr. Amy Hobeika
89 No CMC (Chemistry, Manufacturing, and Controls) 0% Albany Molecular Research Inc.,Dr. Susan Billings (AMRI)
90 Yes IND submission and approval (following completion and analysis of the toxicology study, will submit the IND) Dr. H. Kim Lyerly,Dr. Amy Hobeika,Dr. Michael Morse
91 No Register Clinicaltrials.gov 0% Dr. Amy Hobeika
92 No Investigational Plan: Preclinical data 0%
93 No Information about the investigator 0% Dr. Amy Hobeika
94 No Task 3 - Obtain other regulatory approval including Department of Surgery review, Duke (IRB) Institutional Review Board, Duke (CPC) Cancer Protocol Committee, and DOD approval for Phase I testing 0%
95 No 3D - Cancer Protocol Committee (CPC) Application Process 0% Dr. H. Kim Lyerly,Dr. Amy Hobeika,Dr. Michael Morse
96 No CPC Application Preparation 0% Dr. H. Kim Lyerly,Dr. Amy Hobeika,Dr. Michael Morse
97 No CPC Submission 0% Dr. H. Kim Lyerly,Dr. Amy Hobeika,Dr. Michael Morse
98 No CPC Review and Approval 0% CPC
99 No 3D - Institutional Review Board (IRB) Application Process Dr. H. Kim Lyerly,Dr. Amy Hobeika,Dr. Michael Morse
100 No IRB Application Preparation 0% Dr. H. Kim Lyerly,Dr. Amy Hobeika,Dr. Michael Morse
101 No IRB Submission 0% Dr. H. Kim Lyerly,Dr. Amy Hobeika,Dr. Michael Morse
102 No IRB Review and Approval 0% IRB
103 No 3D - Department of Surgery/Medicine Application Process 0% Dr. H. Kim Lyerly,Dr. Amy Hobeika,Dr. Michael Morse
104 No Dept of Surgery Application Preparation 0% Dr. H. Kim Lyerly,Dr. Amy Hobeika,Dr. Michael Morse
105 No Dept of Surgery Submission 0% Dr. H. Kim Lyerly,Dr. Amy Hobeika,Dr. Michael Morse
106 No Dept of Surgery Review and Approval 0% IRB
107 No Clinical Development (6 years) 0%
108 No Phase I (1 year) 0%
109 No Phase I Clinical Trial Protocol Development 0%
110 No Phase I Clinical Trial Protocol Generation 0% Dr. Amy Hobeika
111 No Protocol Review by Study Teams 0%
112 No Review by Phase I Group 0% Phase I Group
113 No Review by Breast Group 0% Breast Group
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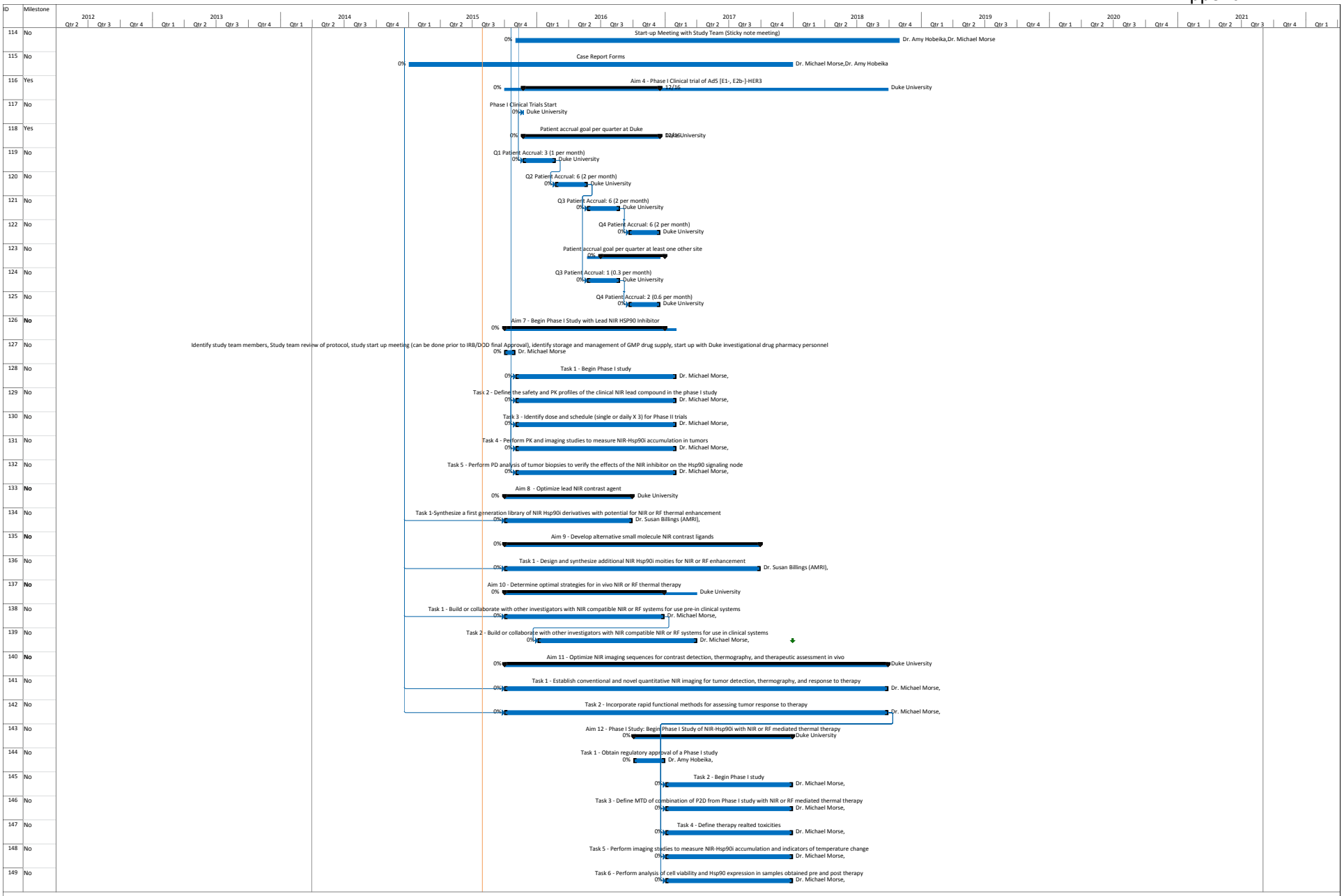
Page 3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2019 Qtr 1 Qtr 2 Qtr 3 Qtr 4
2020 Qtr 1 Qtr 2 Qtr 3 Qtr 4
2021 Qtr 1 Qtr 2 Qtr 3 Qtr 4 Qtr 1
114 No Start-up Meeting with Study Team (Sticky note meeting) 0% Dr. Amy Hobeika,Dr. Michael Morse
115 No Case Report Forms 0% Dr. Michael Morse,Dr. Amy Hobeika
116 Yes Aim 4 - Phase I Clinical trial of Ad5 [E1-, E2b-]-HER3 0% 12/16 Duke University
117 No Phase I Clinical Trials Start 0% Duke University
118 Yes Patient accrual goal per quarter at Duke 0% 12/16 University
119 No Q1 Patient Accrual: 3 (1 per month) 0% Duke University
120 No Q2 Patient Accrual: 6 (2 per month) 0% Duke University
121 No Q3 Patient Accrual: 6 (2 per month) 0% Duke University
122 No Q4 Patient Accrual: 6 (2 per month) 0% Duke University
123 No Patient accrual goal per quarter at least one other site 0%
124 No Q3 Patient Accrual: 1 (0.3 per month) 0% Duke University
125 No Q4 Patient Accrual: 2 (0.6 per month) 0% Duke University
126 No Aim 7 - Begin Phase I Study with Lead NIR HSP90 Inhibitor 0%
127 No Identify study team members, Study team review of protocol, study start up meeting (can be done prior to IRB/DOD final Approval), identify storage and management of GMP drug supply, start up with Duke investigational drug pharmacy personnel 0% Dr. Michael Morse
128 No Task 1 - Begin Phase I study 0% Dr. Michael Morse,
129 No Task 2 - Define the safety and PK profiles of the clinical NIR lead compound in the phase I study 0% Dr. Michael Morse,
130 No Task 3 - Identify dose and schedule (single or daily X 3) for Phase II trials 0% Dr. Michael Morse,
131 No Task 4 - Perform PK and imaging studies to measure NIR-Hsp90i accumulation in tumors 0% Dr. Michael Morse,
132 No Task 5 - Perform PD analysis of tumor biopsies to verify the effects of the NIR inhibitor on the Hsp90 signaling node 0% Dr. Michael Morse,
133 No Aim 8 - Optimize lead NIR contrast agent 0% Duke University
134 No Task 1-Synthesize a first generation library of NIR Hsp90i derivatives with potential for NIR or RF thermal enhancement 0% Dr. Susan Billings (AMRI),
135 No Aim 9 - Develop alternative small molecule NIR contrast ligands 0%
136 No Task 1 - Design and synthesize additional NIR Hsp90i moities for NIR or RF enhancement 0% Dr. Susan Billings (AMRI),
137 No Aim 10 - Determine optimal strategies for in vivo NIR or RF thermal therapy 0% Duke University
138 No Task 1 - Build or collaborate with other investigators with NIR compatible NIR or RF systems for use pre-in clinical systems 0% Dr. Michael Morse,
139 No Task 2 - Build or collaborate with other investigators with NIR compatible NIR or RF systems for use in clinical systems 0% Dr. Michael Morse,
140 No Aim 11 - Optimize NIR imaging sequences for contrast detection, thermography, and therapeutic assessment in vivo 0% Duke University
141 No Task 1 - Establish conventional and novel quantitative NIR imaging for tumor detection, thermography, and response to therapy 0% Dr. Michael Morse,
142 No Task 2 - Incorporate rapid functional methods for assessing tumor response to therapy 0% Dr. Michael Morse,
143 No Aim 12 - Phase I Study: Begin Phase I Study of NIR-Hsp90i with NIR or RF mediated thermal therapy 0% Duke University
144 No Task 1 - Obtain regulatory approval of a Phase I study 0% Dr. Amy Hobeika,
145 No Task 2 - Begin Phase I study 0% Dr. Michael Morse,
146 No Task 3 - Define MTD of combination of P2D from Phase I study with NIR or RF mediated thermal therapy 0% Dr. Michael Morse,
147 No Task 4 - Define therapy realted toxicities 0% Dr. Michael Morse,
148 No Task 5 - Perform imaging studies to measure NIR-Hsp90i accumulation and indicators of temperature change 0% Dr. Michael Morse,
149 No Task 6 - Perform analysis of cell viability and Hsp90 expression in samples obtained pre and post therapy 0% Dr. Michael Morse,
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Progress
Page 4