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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 breas	st magnetic resonance in	haging (MRI), followe	d by biopsy a	nd 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					
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# 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 <sup>18</sup>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.** 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 1<sup>131</sup>. 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.



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 <u>wavelength</u> of 689 nm<sup>[1]</sup> in the presence of <u>oxygen</u>, produces highly reactive short-lived singlet oxygen and other reactive <u>oxygen radicals</u>. 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.



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





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.



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 unterhered 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.





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 p110tHER2 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  $\sim 20\%$ ), 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  $\mu$ M level (8-15 $\mu$ M) 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  $\mu$ M 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 1<sup>st</sup> 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



**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. 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 umol 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



FITC Signals from Organs: 6 h after FITC-HSP90i Administration

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



FITC Signals from Organs: 24 h after FITC-HSP90i Administration

**Figure 13A. Tissue Distribution of FITC-HSP90 inhibitors: 24 hours after administration.** Twentyfour 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.
- 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.

In vivo imaging with near infrared probes

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.
а	HS-100117-03	PFH-005-022A	1384.8	780 amine
b	HS-100118-01	PFH-005-007B	1484.9	820 amine
С	HS-100119-01	PFH-005-009C	1398.8	780 amide
d	HS-100120-01	PFH-005-010A	1498.9	820 amide
е	HS-100131-02	PFH-005-037B	1318.7	640 amine
f	HS-100132-01	PFH-005-038A	1332.7	640 amide

<u>1) In vitro and in vivo Imaging with NIR-tethered HSP90 inhibitor compound : HS-117</u> 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  $\mu$ M) with/without escin treatment. After 30 min incubation, cells were washed with PBS and acquired by LSRII machine. Red: unstained, Blue: 0.1  $\mu$ M, Green: 1  $\mu$ M, Black: 10  $\mu$ M.

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  $\mu$ M) 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

BT474M1 tumor imaging with HS117 (10 nmol) on day 5



Figure 18. Detection of metastatic breast tumor 5 days after HS117 injection. Two BT474M1 tumorbearing 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  $\mu$ M ~100  $\mu$ M), 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  $\mu$ M to 0.1  $\mu$ M (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  $\mu$ M to 0.1  $\mu$ M (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.** 





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. 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. 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.

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.









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<sup>8</sup> 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

#### NIR Signals from MDA-MB-468 Tumors: Over Time Change (3h-24h) background subtracted

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



#### NIR Signals from MDA-MB-468 Tumors: Over Time Change (3h-24h) background subtracted

**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



#### NIR Signals from MDA-MB-468 Tumors: Over Time Change (3h-24h) Ratio of Radiant Efficiency (tumor / background)

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

NIR Signals from Organs: 24 h after NIR-HSP90i Administration

**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.

<u>Project 1-Aim 2. Task 2:</u> 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).

<u>Project 1-Aim 2. Task 3:</u> 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.

<u>Project 1-Aim 2. Task 4:</u> 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.

<u>Project 1-Aim 2. Task 5:</u> 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.

# <u>Project 1-Aim 3. Task 1:</u> 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.

# <u>Project 1-Aim 3. Task 2:</u> 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.

# <u>Project 1-Aim 3. Task 3:</u> 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. 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

Project status: Production	Event Name: Baseline			
Data Collection	Lab ID		111	
	DEMOGRAPHICS			
Scheduling Record Status Dashboard Add / Edit Records	Patient Study Number * must provide value			
	Test Patient			
E Lab ID 111 Belect other record Event: Baseline Data Collection Instruments:	Year Consent Signed * must provide value			
Demographics	2014			
Prior History Current Medical	Year of Birth * must provide value			
Pathology	1936			
Systemic Treatment Primary Surgery Radiation Therapy	Gender * must provide value Female (\$			
Applications	Racial Background * must provide value			
Calendar Calendar Data Export Tool Data Comparison Tool Cogging	✓ Caucasian African American Asian or Pacific Islander American Indian,Aleutlan,Eskimo		Incomplete ¢	
Field Comment Log         File Repository         & Record Locking Customization         & E-signature and Locking Mgmt         Oraphical Data View & Stats	Spanish/Hispanic Other	on this form until someone with	<ul> <li>Lock</li> <li>V E-signature (<u>What is this?</u>)</li> </ul>	
			Save Record Save and Continue	

#### Figure 37



Figure 38

# **Racial Analysis**



#### Figure 39

# **Database Statistical Analysis Options**



<u>Project 1-Aim 3. Task 4:</u> 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.

<u>Project 1-Aim 4. Task 2:</u> 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.

<u>Project 1-Aim 4. Task 2:</u> 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

<u>Project 1-Aim 5. Task 1:</u> 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. <u>Project 1-Aim 5. Task 2:</u> 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.

<u>Project 1-Aim 6. Task 2:</u> 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.

<u>Project 1-Aim 6. Task 3:</u> 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



#### PHASE I STUDY OF NEAR INFRARED HSP90 INHIBITOR PROBE: Schema

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).

<u>Project 1-Aim 7. Task 2:</u> 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.

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

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

<u>Project 1-Aim 7. Task 5:</u> 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.

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

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

<u>Project 1-Aim 8. Task 6:</u> 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 responsibile for facilitating interactions between QIBA and many external organizations. These 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 tumorbearing 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.







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. 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.

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
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#### 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. 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. 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. Over time change of nIR signals from T-47D Tumors: HS118 vs. HS165.** NIR signals (800 pm change)) and in average (right

(800 nm channel) from tumor areas are shown for each mice (left, middle panel) and in average (right panel). Error Bar: SD.

#### Figure 43B

# Figure 43A

#### Figure 43C



**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. 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. 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. 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. 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. 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. 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 MMTVneu mice developed spontaneous breast tumors in 2<sup>nd</sup>~4<sup>th</sup> 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

Green: HS118 Red: HS152

**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

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. 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.

#### Figure 49B

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.
- 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 relationshippublished.
- 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.

#### 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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## 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.

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		registry id		mol w	t	fo	ormula		date		SMILES	
		HS-100001-01 360.207		)7	В	r1O2N3C16	H14	2010-07-09		Brc1ccc(	cc1)Nc2ncnc3cc(c(cc23)OC)OC	
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		HS-100005-01	323.778		CI101N3C18H14	201	10-08-27					Clc1ccc2NC(C3(c2c1)NCCc4c3InHlc5ccccc45)=0
		chirality	origin		chemist	not	ebook					salt form
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6.	HS-100006-01	chemical regis	chemical registry							
		registry id	mol wt	formula	date	SMILES				
		HS-100006-01	381.814	CI1O3N3C20H16	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				
	N O	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				
	N	LCMS datafile								
L 7										
7.	HS-100007-01	chemical regi	stry							

#### 7



chemical registry	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)=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 regi	chemical registry									
registry id	mol wt	formula	date	SMILES						
HS-100008-01	422.910	CI1O2N4C23H23	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										

#### HS-100009-01 9.



chemical reg	chemical registry									
registry id	mol wt	formula	date	SMILES						
HS-100009-01	456.926	CI1O2N4C26H21	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										

HS-100010-01 10.



chemical registr	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 regist	у						
		registry id	mol wt	formula	d	date	SMILES		
	0	HS-100010-02	410.512	O3N4C23	3H30 2	2011-02-15	5 O=C(c1ccc(cc1NC2CCC(CC2)O)n3nc(C)c4c3CC(CC4=O)(C)C)N		
	Ŭ /	chirality	origin	chemist	n	notebook	salt form		
	N O	{10-13T;}	Internal synthes	is Dave Car	lson 1	1dac046-1	None: Free base		
		amount available	program	primary ta	arget p	percent puri	rity elemental analysis		
		10.5	Purine_inhib		9	95-100			
	N	melting point	NMR data	LCMS da	ta c	comment	NMR datafile		
	)=o						yes		
	N	LCMS datafile							
12.	HS-100011-01	chemical regist	у		_				
		registry id I	nol wt	formula	date	SM	MILES		



chemical regi	chemical registry							
registry id	mol wt	formula	date	SMILES				
HS-100011-01	567.766	O4N5C32H49	2010-11-11	O=C(NCCCCCCCCCCccc1c(N)=O)n2nc(C)c3c2CC(CC3=O)(C)C)OC(C)(C)C)C(C)C(C)C(C)C(C)C(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 regis	hemical registry								
registry id	mol wt	formula	date	SMILES					
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 regist	ry			
registry id	mol wt	formula	date	SMILES
HS-100013-01	366.866	CI1S1O1N2C20H15	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** 

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chemical registry							
registry id	mol wt	formula	date	SMILES			
HS-100014-01	297.328	F1O1N3C17H16	2011-01-20	Fc1cc(ccc1C#N)n2nc(C)c3c2CC(CC3=O)(C)C			
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							

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									Page 4/45	
16	HS-100015-01	chemical regist	ry							
10.		registry id	mol wt		formul	a	date		SMILES	
	<b>o</b> /	HS-100015-01	356.421		O3N40	C19H24	2011-02-08	3	O=C(c1ccc(cc1NCCO)n2nc(C)c3c2CC(CC3=O)(C)C)N	
		chirality	origin		chemis	st	notebook		salt form	
	Ń	-	Internal syr	nthesis	Philip I	Hughes PFH-001-0		71A	None: Free base	
	N O	amount availabl	e program		primar	ry target	percent pu	rity	elemental analysis	
		0.233	Purine_inh	ib			95-100		-	
		melting point	NMR data		LCMS	data	comment		NMR datafile	
			on						yes	
	)o	LCMS datafile								
	N									
17.	HS-100016-01	chemical regist	ry							
		registry id	mol wt		formula	a	date		SMILES	
	<b>O</b> /	HS-100016-01	370.447		O3N4C	C20H26	2011-02-14		O=C(c1ccc(cc1NCCOC)n2nc(C)c3c2CC(CC3=O)(C)C)N	
		chirality	origin		chemis	st	notebook		salt form	
			Internal syr	nthesis	esis Philip Hu		PFH-001-07	72A	None: Free base	
	N 0-	amount availabl	e program		primary target		percent purity		elemental analysis	
		0.226	Purine_inhi	ib			95-100			
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18.	HS-100017-01	rogistry id	.ry		formula		data		SWII ES	
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		Crinality	Internal syn	thosis	Philip H	luabes	DEH-001-07	30	None: Free hase	
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19.	HS-100018-01	chemical regist	ry							
		registry id	mol wt		formula	d	late	SMI	LES	
	0	HS-100018-01	443.542		O4N5C23	H33 2	2011-02-15	0=0	C(c1ccc(cc1NCCOCCOCCN)n2nc(C)c3c2CC(CC3=O)(C)C)N	
		chirality	origin		chemist	n	otebook	salt	t form	
			Internal synthe	esis	Dave Carl	lson 1	DAC048-1	Non	e: Free base	
	N O	amount available	program		primary ta	irget p	ercent purity	elen	nental analysis	
	N	.200	Purine_inhib			9	95-100			
	N N	melting point	NMR data		LCMS dat	ta c	comment	NM	R datafile	
	o							yes		
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		yes								
	HS_100010_01	chemical regist	rv							
20.	10-100013-01	registry id	mol wt	formula	da	ate			SMILES	
		HS-100019-01	515.648	O5N5C2	27H41 20	011-02-15			0=C(c1ccc(cc1NCCCOCCOCCCN)n2nc(C)c3c2CC(CC3=O)(C)C)N	
	<b>o</b> ,	chirality	origin	chemist	n	otebook			salt form	
			nternal synthesis	Dave Ca	arlson 11	DAC049-1			None: Free base	
	$ \downarrow \downarrow N \rightarrow 0 $	amount available	program	primary	target De	ercent purity	/		elemental analysis	
	$\langle \rangle_{N}$	0	- Purine_inhib		95	5-100				
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LCMS datafile yes

See Dave Carlson for compound

yes

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21.	HS-100020-01	chemical reg	jistry									
		registry id		mol wt			formula		date		SMILES	
	o	HS-100020-0	1	370.44	17		O3N4C20	DH26	2011-02-	-24	O=C(c1ccc(cc1NCCCO)n2nc(C)c3c2CC(CC3=O)(C)C)N	
		chirality		origin			chemist		notebool	<	salt form	
				Interna	al svn	thesis	Philip Hu	ahes	PFH-001	-075A	None: Free base	
		amount avail	ahle	progra	m		nrimary ta	arget	percent r	ourity	elemental analysis	
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		0.230		NMP data		LONG da	10	90-100		NMD dotofile		
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			chemical registry									
22.	HS-100021-01	chemical reg	JISUY				<u> </u>		1.4		01411 50	
		registry id		moi wt					date	~ /	SMILES	
	o, ,	HS-100021-01		384.47	4		O3N4C21	H28	2011-02-2	24	O=C(c1ccc(cc1NCCCOC)n2nc(C)c3c2CC(CC3=O)(C)C)N	
		chirality		origin			chemist		notebook		salt form	
				Internal synthesis		thesis	Philip Hug	ghes	PFH-001	-075B	None: Free base	
	~~~NO^	amount avail	able	program	m		primary ta	rget	percent p	urity	elemental analysis	
		0.260		Purine_	_inhit	C			95-100			
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23.	HS-100022-01	chemical reg	jistry									
		registry id		mol wt			formula		date		SMILES	
	0	HS-100022-01		398.501			O3N4C22H30		2011-02-24		O=C(c1ccc(cc1NCCCOCC)n2nc(C)c3c2CC(CC3=O)(C)C)N	
	ы Ш. /	chirality c		origin		chemist		notebook		salt form		
	N CO			Internal synthesis		thesis	is Philip Hughes		PFH-001-0	075C	None: Free base	
		amount available		program			primary tai	rget	percent purity		elemental analysis	
		0.234		Purine_inhib		)	. ,		95-100		,	
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l												
24	HS-100023-01	chemical registry										
2		registry id	mol	wt	formula		date		SMILES			
		HS-100023-01	603	.753	07N5C31		1H49 2011-02-25		O=C(c1c		ccc(cc1NCCCOCCOCCOCCOCCOCCN)n2nc(C)c3c2CC(CC3=O)(C)C)N	
	, o _	chirality	orig	in		chemist	noteb	notebook		salt form	1	
			Inte	rnal synthe	sis	Philip Hu	hes PEH-001-063A		A None: Fr		ree base	
		amount available	prog	ram		primary ta	rget percent purity		element		al analysis	
		0.01	Pur	ine inhib		1	95-10	0				
	( LN ( S	melting point	NM	R data		I CMS da	ta comm	nent	NMP da		tafile	
	, i co		-		_		See o	chemist f	or sample	ves		
	N N	LCMS datafile								,		
			-									
25	HS-100024-01	chemical rec	istrv									
25.		registry id	nol wt	1	formula		date		SMILES			
		HS-100024-01	301.797		Fe107N	5C42H59	2011-03-22		O=C(c1ccc)	cc1NCCCC	CCOCCOCCOCCCNCC2C=CC/(Fe)C3C=CC=C3)=C2)n4ncr(C)c5c4CC(CC5=O)(C)C)N	
		chirality	oriain		chemist		notebook		salt form			
			nternal s	nthesis	Philip Hu	idhes	PEH-001-080A		None: Free	base		
		amount available	rogram		primary t	arget	percent purity		elemental a	nalveie		
		0.046	Durine i-	hih	iaty t	9-1	95-100		Significant a	elemental analysis		
	N o	melting point	MD date		I CMP de	ata	comment		NMD dat-fil	0		
	N=0	moning point	wint data		Lowo da	440	Son Dilleri		www.catafil	~		
	IN .						See P Hughes fo	n Sample	yes			
		LUMS datafile										
		yes										

26	HS-100024-02	chemical r	egistry									
20.		registry id	mol wt	formula		date		9	SMILES			
		HS-100024-02	801 707	Ectore	CADHEO	2011-11-04			0=C(ctoss/octNCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC			
		H3-100024-02	001.797	Felonis	642039	2011-11-04						
		chirality	origin	chemist		notebook		5	salt form			
	<b>0</b>		Internal synth	esis Philip Hu	ghes	PFH-002-01	8C	1	None: Free base			
		amount available	program	primary t	irget	percent purit	у	6	eleme	antal analysis		
		490	Purine inhib			95-100						
	N Q									1. 6		
		meiting point	NMR data	LCMS da	ta	comment		r	NMR	datatile		
	NŬ					See P Hughe	es for S	Sample				
		LCMS datafile										
		yes										
27	HS-100025-01	chemical r	egistry									
21.		registry id	mol	Nt	form	nula	date			SMILES		
				200	05		200	11 04 07				
		HS-100025-0	01 048	030	051	10029030	20	11-04-07	_	0=C(c1chccc1)NCCOCCOCCNc2cc(ccc2C(N)=O)h3hc(C)c4c3CC(CC4=O)(C)C		
	<b>O</b> /	chirality	orig	า	che	mist	not	tebook		salt form		
			Inte	nal synthesis	a Dav	e Carlson	1D.	AC056-1		None: Free base		
		amount avail	able prog	ram	prin	nary target	per	rcent puri	ty	elemental analysis		
		.101	Puri	Purine inhib				95-100				
	(N' )	melting point	NM	data	1.0	CMS data		comment		NMR datafile		
	N C N					_ 5 30.00						
		10110										
		LCMS datafil	e									
		yes										
28.	HS-100026-01	chemical r	egistry									
		registry id	mol w	mol wt f		a c	date		S№	ЛILES		
		HS-100026-01	620.7	2	O6N6	C33H44 2	2011-0	04-07	O=	=C(c1cnccc1)NCCCOCCOCCOCCCNc2cc(ccc2C(N)=O)n3nc(C)c4c3CC(CC4=O)(C)C		
		chirality	origin		chemi	st r	notebo	ook	sal	It form		
			Intern	l synthesis	Dave	Carlson 1		057-1	No	nne: Free hase		
					Duro .				-10			
	$\rightarrow$ N $\langle V \rangle$	amount availab	e progra	m	primar	y target p	bercer	nt punty	eie	imentai anarysis		
		0.080	Purine	_inhib		ę	95-100	0				
		melting point	NMR	NMR data L		data d	comm	ent	NMR datafile			
	N <sup>20</sup>											
		LCMS datafile										
		yes										
								!				
20	HS-100027-01	chemical r	egistry									
23.		registry id	mol wt	formula	da	te		SMILES				
		HS-100027-01	993 137			2011-04-10		S=CINCCC0CC0CC0CC0CC0CC0cc0cc0cc0cc0cc0cc0cc0				
		10-100027-01		01012100002	Jozmbu 2011-04-10		3=Umutuutuutuutuutuutuutuutuutuutuutuutuutu					
	_ <b>o</b>	chirality	origin	cherhist	no	LEDOOK	book salt form		salt form			
	o, o, o		Internal synthe	s Philip Hughes	s PFH-001-091A			None: Free base				
		amount available	program	primary targe	pe	rcent purity		elemental ana	amental analysis			
		0.010	Purine_inhib		95	-100						
		melting point	NMR data	LCMS data	co	mment		NMR datafile				
					Se	e chemist for sar	nple	yes				
	N	LCMS datafile										
							-					
		700										
	HS-100027-02	chemical r	eaistry									
30.	n3-100027-02	registre / d	molut	formula		doto	0141	ES	_			
		registry id	THOI WE	Iormula		ualt	SMIL					
		HS-100027-02	993.137	S1O12N6C	2H60	2012-02-10	S=C(	S=C(NCCCOCCOCCOCCOCCCCCCc1c(N)=O)n2nc(C)c3c2CC(CC3=O)(C)C)Nc4ccc5c(C(OC56c7ccc(cc7Oc8cc(ccc68)O)O)=O)c4				
	,o	chirality	origin	chemist		notebook	salt fo	orm				
			Internal synthe	sis Philip Hughe	s	PFH-002-094C	None	e: Free base				
	° ° ° ° ° ° ° ° ° ° ° ° ° ° ° ° ° ° °	amount available	program	primary targ	ət	percent purity	elem	ental analysis				
		0.084	Purine_inhib			95-100						
		melting point	NMR data	LCMS data		comment	NMR	t datafile				
	∠⊂ <sup>N</sup> ∠o'			c-								
	N <sup>°</sup>			on								

LCMS datafile yes

		· •••••										
31.	HS-100027-03	chemical	registry									
		registry id	mol wt	1	formula	date		SMILES				
		HS-100027-03	993.137	:	S1O12N6C52H	50 2012	2-02-10	S=C(NCCCOCCOCCOCCOCC	COCCCNc1cc(ccc1C(N)=O)n2nc(C)c3c2CC(CC3=O)(C)C)Nc4ccc5c(C(OC56c7ccc(cc7Oc8cc(ccc68)O)O)=O)c4			
	,o	chirality	origin		chemist	notet	book	salt form				
			Internal syn	hesis	Philip Hughes	PFH	-002-094D	None: Free base				
		amount available	program	1	primary target	perce	ent purity	elemental analysis				
		0.180	Purine_inhit	)		95-10	00					
		melting point	NMR data	1	LCMS data	comment		NMR datafile				
	N=0				on							
		LCMS datafile										
		yes										
			·									
32.	HS-100028-01	chemical	registry									
		registry id mol wt		fe	formula da			SMILES				
		HS-100028-01	971.154	c	D11N8C51H70	2011-04-	-12	O=C(NCCc1ccc(c(c1)N=Nc	:2ccc(C(NCCCOCCOCCOCCOCCOCCNc3cc(ccc3C(N)=O)n4nc(C)c5c4CC(CC5=O)(C)C)=O)cc2)O)OC(C)(C)C			
	0	chirality	origin	c	chemist	notebook	k	salt form				
			Internal synt	hesis F	hilip Hughes	PFH-001	1-090B	None: Free base				
		amount available	program	P	orimary target	percent p	purity	elemental analysis				
		0.184	Purine_inhib			95-100						
	N <sup>EO</sup> _O, N	melting point	NMR data	L	CMS data	commen	it	NMR datafile				
	7 0					See cher	mist for sampl	e yes				
		LCMS datafile										
		yes										
33.	HS-100029-01	chemical	registry									
		registry id	mol wt		formula	date						
		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			
	μ so yno		Internal syn	Internal synthesis Philip Hu		PFH-001	-093A		None: Free base			
		amount available	program	1	primary target	t percent purity			elemental analysis			
		0.025	Purine_inhit	,		95-100						
		melting point	NMR data	1	LCMS data	comment	t	NMR datafile				
	N		on			In the ref	fridgerator; -O	radical; not -OH; MW 1 high	yes			
		LCMS datafile										
		yes										
	110 400000 04	chemical	rogistry									
34.	HS-100030-01			formula	data		SMILES					
		HS-100030-01 1	366 5 3 7	GHIO20N9	C57H78 2011-0	-22	0+010(64)2345	2700/0N2/01000-8(8\NC/0000N				
		chirality	inin	chamiet	control 2011-0	4	ealt form	34987/UU(UK2(C1CUC/38026(008)/C)CCC)CCCCCCCCCCCCCCCCCCCCCCCCCCCCC				
		ciniany c	igini	Daw Order	101600	••••••••••••••••••••••••••••••••••••••	Sat Iom					
		amount available	ternai synthesis	Dave Caliso		er 1	elementel enebrei					
		amount available p	ogram	primary targ	percent	punty	elemental analysi	5				
		U.100 F	unne_innib	1.0110.000	95-100		110 4-07-					
	N°O	menting point P	MR data	LUMS data	comme	n	NMR datarile					
				on	Diamm	onium salt						
		LCMS datafile										
	y	yes										
05	HS-100031-01	chemical registry										

N N

	chemical registry											
	registry id	mol wt	formula date		SMILES							
Γ	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							
Γ	chirality	origin	chemist	notebook	salt form							
Γ	{25-28T;}	Internal synthesis	Philip Hughes	PFH-002-011A	None: Free base							
	amount available	program	primary target	percent purity	elemental analysis							
Γ	0.089	Purine_inhib		95-100								
	melting point	NMR data	LCMS data	comment	NMR datafile							
Γ												
	LCMS datafile											
ſ												

36.	HS-100031-02	chemical regis	chemical registry										
	F F	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							
	O ↓ 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							
	N N	LCMS datafile											
	110 400000 04	chomical rogic	tru										

#### 37. HS-100032-01

N O NO
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chemical registry										
registry id	mol wt	formula	date	SMILES						
HS-100032-01	999.840	Fe2O7N5C53H69	2011-07-11	0+C(c1ccc(cc1NCC00CC0CC0CC0CCCN(CC2C+CC([Fe]C3C+CC=C3)=C2)CC4C=CC([Fe]C5C=CC=C5)=C4)n6nc(C):c7c6CC(CC7=0)(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**

S-100033-01	chemical registry											
	registry id	mol wt	formula	date	SMILES							
	HS-100033-01	766.844	O10N8C37H50	2011-08-16	o1nc2c(c(ccc2NCCCOCCOCCOCCOCCOCCOCCCNc3cc(ccc3C(N)=O)n4nc(C)c5c4CC(CC5=O)(C)C)[N+](=O)=[O-])n1							
O. N. O.	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								
N O	melting point	NMR data	LCMS data	comment	NMR datafile							
, ⊱o ∽			on	See P Hughes for Sample								
	LCMS datafile											
	yes											

## 39. **HS-100034-01**

	registry id
	HS-100034-
	chirality
N.N.N ∧√N <sup>∪</sup> N	{3S;}
	amount avai
	0.020
	melting poin
0	
	LCMS dataf

chemica	l registry							
registry id	mol wt	formula	date	SMILES				
HS-100034-01	1040.179	O11N13C51H69	2011-08-23	OC(C(CCC(NCCCOCCOCCOCCCCCCCCCCccctC(N)=0)n2nc(C)e3e2CC(CC3=0)(C)C)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc8N(nc8)(nc5)C)=0)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc8N(nc5)C)=0)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc8N(nc5)C)=0)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc8N(nc5)C)=0)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc8N(nc5)C)=0)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc8N(nc5)C)=0)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc8N(nc5)C)=0)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc8N(nc5)C)=0)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc8N(nc5)C)=0)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc6N(nc5)C)=0)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc6N(nc5)C)=0)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc6N(nc5)C)=0)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc6N(nc5)C)=0)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc6N(nc5)C)=0)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc6N(nc5)C)=0)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc6N(nc5)C)=0)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc6N(nc5)C)=0)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc6N(nc5)C)=0)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc6N(nc5)C)=0)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc6N(nc5)C)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc6N(nc5)C)=0)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc6N(nc5)C)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc6N(nc5)C)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc6N(nc5)C)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc6N(nc5)C)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc6N(nc5)C)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc6N(nc5)C)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc6N(nc5)C)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc5N(nc5)C)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc5N(nc5)C)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc5N(nc5)C)=0)NC(e4exc(ee4)N(Ce5ne8e(nc(N)nc5N(nc5)C)=0)NC(e4exc(ee4)N(nc5N(nc5)C)=0)NC(e4exc(ee4)N(nc5N(nc5)C)=0)NC(e4exc(ee4)N(nc5N(nc5)C)=0)NC(e5ne8e(nc5)N(nc5N(nc5)C)NC(e5ne8e(nc5N(nc5N(nc5N(nc5N(nc5N(nc5N(nc5N(nc5N				
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**

00035-01	chemical registry	chemical registry								
	registry id	mol wt	formula	date	SMILES					
	HS-100035-01	276.297	N6C15H12	2011-09-08	n1n(c(C)c(c1)c2cccc2)c3ncnc4[nH]cnc34					
$\langle \rangle$	chirality	origin	chemist	notebook	salt form					
$=\langle$		Internal synthesis	Dave Carlson	2DAC008_1	None: Free base					
N N	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									
`N ∕ <sup>™</sup>	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(NCCCOCCOCCOCCOCCOCCCCCCCCCC				
		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				
	N <sup>°</sup> O O			on						
		LCMS datafile								
42.	HS-100037-01	chemical I	egistry							
		registry id	mol wt	formula	date	SMLES				



chemical I	chemical registry									
registry id	mol wt	formula	date	SMLES						
HS-100037-01	1144.385	Gd1O14N9C47H72	2011-10-03	[6d+3][0]C(N1CCN(CC)(CCC0CC0CC0CC0CCCCCCCCCCCCCCCCCC)=2cc(ccc2C(N)=0]n3nc](C)=dc3CC(CC4=0)(C)(C)=0)CCN(CC[[0-]]=0)CCN(CC[[0-]]=0)CCN(CC[[0-]]=0)CCN(CC[[0-]]=0)CCN(CC[[0-]]=0)CCN(CC[[0-]]=0)CCN(CC[[0-]]=0)CCN(CC[[0-]]=0)CCN(CC[[0-]]=0)CCN(CC[[0-]]=0)CCN(CC[[0-]]=0)CCN(CCN(CC)(CC)(CCN(CC)(CC)(CCN(CC)(CC)						
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						
		an								
LCMS datafile										

## 43. HS-100038-01



chemical reg	chemical registry											
registry id	mol wt	formula	date	SMILES								
HS-100038-01	349.797	CI1S1O2N5C14H12	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 regist	ry			
registry id	mol wt	formula	date	SMILES
HS-100038-02	349.797	CI1S1O2N5C14H12	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				

45. **HS-100038-03** 



chemical registry											
registry id mol wt		formula	date	SMILES							
HS-100038-03	S-100038-03 349.797 CI1S1O2N5C14H12		2011-12-06	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SC(C)C(N)=O)=O							
chirality	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											
ves											

											Appendix B
											Page 10/45
3.	HS-100039-01	chemical	l registr	У							
		registry ic	ł	mol wt		formu	ula	date			SMILES
		HS-10003	39-01	276.297		N6C1	15H12	2012	-01-26		n1n(cc(c1C)c2ccccc2)c3ncnc4[nH]cnc34
	< <u> </u>	chirality		origin		chem	nist	noteb	book		salt form
				Internal synt	hesis	Dave	Carlson	2DA0	C013_1		None: Free base
		amount a	vailable	program		prima	ary target	perce	ent purity		elemental analysis
	N N	0.5		Purine_inhib	)			80-90	)		
	L	melting p	oint	NMR data		LCMS	S data	comr	nent		NMR datafile
	N N							conta	ains 25% H	S-100035	
		LCMS da	tafile								
r.	HS-100040-01	chemical	l registr	у							
		registry id	r	nol wt	formula		date			SMILES	
	0	HS-100040	0-01 4	109.527	O2N5C2	3H31	2012-02-23	3		O=C(c1ccc(c	c1NC2CCC(CC2)N)n3nc(C)c4c3CC(CC4=O)(C)C)N
	, ĭ, ,	chirality	C	origin	chemist		notebook			salt form	
	N N	{10-13T;}	1	nternal synthesis	Philip Hu	ighes	PFH-002-0	97A		None: Free b	ase
	N (	amount ava	ailable p	orogram	primary t	arget	percent pur	rity		elemental an	alysis
		0.689	F	Purine_inhib			95-100				
	N <sup>♥</sup>	melting poi	nt I	NMR data	LCMS da	ata	comment			NMR datafile	
	Þ				on		contains a t	trace of	bis product	t	
	N	LCMS data	afile								
		yes									
, [	HS-100041-01	chemical	l registr	у							
		registry id		mol wt	formula	I	date		SMILES		
		HS-100041-01 4		452.615 O2N		O2N5C26H38 2012-03-12		12	O=C(c1ccc(	cc1NC2CCC(	CC2)[N+](C)(C)C)n3nc(C)c4c3CC(CC4=O)(C)C)N
	<b>0</b>    /	chirality o		origin chem		mist notebook			salt form		
		{10-13T;}		Internal synthesis Phi		Philip Hughes PFH-00		-002A	None: Free	base	
		amount ava	ailable	program	primary target		percent p	urity	elemental a	nalysis	
		0.027		Purine_inhib			95-100				
	N N	melting poi	nt	NMR data	LCMS of	data	comment		NMR datafil	e	
	⊳o				on						
	N	LCMS data	afile								
		yes									
э.	HS-100042-01	chemical	l registr	У							
		registry id	mol wt	formula	date	SMIL	ES				
		HS-100042-01	1318.924	CI1S2F1O14N7C67H73	2012-03-14	Clc1c	cc(ccc1OCc2cccc(c2)F)No	c3nonc4ccc(cc	34)c5oc(CN(CCCNCCCO	CCOCCOCCOCCOCCNC(	4e6ccc7e(C(OC78e9cce(cce9Oc10cc(ccc810)O)O)=O)e6)=S)CCS(C)(=O)=O)cc5
	٥	chirality	origin	chemist	notebook	salt fo	orm				
	၀လို		Internal synthes	is Philip Hughes	PFH-003-010/	A None	: Free base				
	S (C) (C) ∕ N°N O	amount available	program	primary target	percent purity	eleme	ental analysis				
		0.014	Purine_inhib		95-100						
		melting point	NMR data	LCMS data	comment	NMR	datafile				
	U UN				see chemist						
		LCMS datafile				_					
<u>م</u> [	HS-100043-01	chemical	l registr	y							
J.		registry id	0.01	mol wt	form	ula		date			SMILES
		HS-100043	3-01	322.772	CI1S	102N4	4C13H11	2012-	03-20		Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SCCO)=O
	ο	chirality		origin	chen	nist		noteb	ook		salt form
	ļ			Internal synthesis	s Dave	e Carls	on	002D/	AC023_2		None: Free base

CI

amount available

melting point

LCMS datafile yes

0.027

ο

s

program

Purine\_inhib

NMR data

primary target

LCMS data

on

percent purity

Analog of HS38. ZIPK inhibitor.

95-100

comment

elemental analysis

NMR datafile

									Page 11/45
51.	HS-100044-01	chemical regis	chemical registry						
		registry id	mol wt		formula		date		SMILES
		HS-100044-01	334.826		CI1S1O1N4C15H15		2012-03-20		Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SCC(C)C)=O
	<u>o</u>	chirality	origin		chemist		notebook		salt form
	$\sim$		Internal synthe	esis	Dave Carlson		002DAC023_3		None: Free base
	N I N	amount available	program		primary target		percent purity		elemental analysis
	N N S	0.010	Purine_inhib				95-100		
		melting point	NMR data		LCMS data		comment		NMR datafile
	CI				on		Analog of HS38. ZIP	K inhibitor.	
		LCMS datafile							
		yes							
52.	HS-100045-01	chemical regis							
		registry id	mol wt form		formula d			SMILES	
		HS-100045-01	514.986	CI1S1	IO3N4C27H19	2012-03-2	20	Clc1cc(ccc1)n2ncc3c(n(CC(c4ccccc4)=O)c(nc23)SCC(c5ccccc5)=O)=O	
		chirality	origin	chem	ist	notebook		salt form	
	o U		Internal synthesis	Dave	Carlson	002DAC0	23_5	None: Free base	
	N	amount available	program	prima	ry target	percent p	urity	elemental analys	is
	N N N N N	0.036	Purine_inhib			95-100			
		melting point	NMR data	LCMS	6 data	comment		NMR datafile	
				on		Analog of	HS38. ZIPK inhibitor.		
		LCMS datafile							
		yes							

## 53. **HS-100046-01**

chemical regist	chemical registry											
registry id	mol wt	formula	date	SMILES								
HS-100046-01	403.288	CI2S1O1N4C18H12	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												

#### HS-100047-01 54.



chemical reg	hemical 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 reg	istry									
registry id	mol wt	formula	date	SMILES						
HS-100048-01	422.845	CI1S1O5N4C17H15	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										

		ab and a start	- 4						
56.	HS-100048-02	chemical regi	stry						
		registry id	mol wt f	ormula	date				SMILES
		HS-100048-02	422.845 0	11S1O5N4C17H1	5 2012-03	-20			Clc1cc(ccc1)n2ncc3c(n(CC(OC)=O)c(nc23)SCC(OC)=O)=O
	0, 0,	chirality	origin c	hemist	notebool	k			salt form
	o v v		Internal synthesis	ave Carlson	002DAC	AC023 14B			None: Free base
		amount available		rimony torget	norcont				
	N I I A		program p	ninary larget	percent	punty			
	N <sup>-</sup> \N <sup>-</sup> \S <sup>-</sup>	0.021	Purine_inhib		95-100				
	, Ó	melting point	NMR data L	CMS data	IS data comment				NMR datafile
	CI		c	n	Analog o	of HS38	<ol> <li>ZIPK inhibitor. Regioiso</li> </ol>	omer of HS	48
	5	LCMS datafile							
		yes							
57	HS-100049-01	chemical regi	stry						
••••		registry id	mol wt	formula		date	e		SMILES
		HS-100049-01	392.862	CI1S1O3	V4C17H17	201	2-03-20		Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SCCCC(OCC)=O)=O
		chirality	origin	chemist		note	ebook		salt form
	o I		Internal synthes	is Davo Car	500	002	DAC023 15		None: Free base
	<i>∕</i> ∼ <sup>⊥</sup> N	emerint ericitekte			3011	002			
		amount available	program	primary ta	rgei	pen			elemental analysis
		0.016	Purine_inhib			95-	100		
		melting point	NMR data	LCMS dat	а	con	nment		NMR datafile
				on		Ana	alog of HS38. ZIPK ir	nhibitor.	
		LCMS datafile							
		yes							
			·						
58.	HS-100050-01	chemical regi	stry						
		registry id	mol wt	formula	formula		date		SMILES
		HS-100050-01 364.809		CI1S1O3	V4C15H13	2012-03-20			Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SC(C)(C)C(O)=O)=O
	0	chirality	origin	chemist		note	ebook		salt form
	Į.		Internal synthes	is Dave Car	Dave Carlson		2DAC023 16		None: Free base
		amount available	program	primary ta	raet	per	cent purity		elemental analysis
	N N S O	0.032	Purine inhib	F	.9	95-	100		
					-	33-	100		NMD detecto
		meiting point NMR data		LCIVIS UAI				1.11.14	
					on		alog of HS38. ZIPK in	hibitor.	
		LCMS datafile							
		ahamiaal ragi							
59.	HS-100051-01								N// 50
		registry id	mol wt	formula		date		S	MILES
		HS-100051-01	406.846	CI1S1O4N	4C17H15	2012-	-03-20	C	lc1cc(ccc1)n2ncc3c([nH]c(nc23)SCC(CC(OCC)=O)=O)=O
	0	chirality	origin	chemist		noteb	book	Si	alt form
	~ Ŭ \		Internal synthes	s Dave Carls	on	002D	AC023_17	N	one: Free base
	N N I	amount available	program	primary tar	get	perce	ent purity	e	emental analysis
		0.031	Purine_inhib			95-10	00		
	0 0	melting point	NMR data	LCMS data		comm	nent	N	MR datafile
	CI-			on		Analo	og of HS38. ZIPK inhi	ibitor.	
		LCMS datafile							
		yes							
		L							
60	HS-100051-02	chemical regi	stry						
		registry id	mol wt	formula	1		date	SMILES	
		HS-100051-02	406.846	CI1S10	04N4C17H	15	2012-08-15	Clc1cc(	ccc1)n2ncc3c([nH]c(nc23)SCC(CC(OCC)=0)=0)=0
		chirality	origin	chemis	t		notebook	salt form	
	<b>O</b>		Internal synthe	sis Dave C	arlson		002DAC057 1	None <sup>,</sup> F	ree base
	N N N	amount available	program	nrimon	( target		percept purity	elemont	al analysis
	N N S S		During inkit	Plillidly	anger		percent purity elemental and		ar anayolo
		0.114	Purine_inhib				90-100		
	ci 🔨 🖉	melting point	NMK data	LCMS	oata		comment	NMR da	tatile
	5			on			Analog of HS38.		
		LCMS datafile							
		yes							

61	HS-100052-01	chemical registry								
01.	10 10002 01	registry id	mol wt	formula	dat	e	SMILI	ES		
		HS-100052-01	398.825	CI1S1O3N4C18H11	20'	12-03-20	Clc1c	c(ccc1)n2ncc3c([nH]c(nc23)Sc4ccc5OCOc5c4)=O		
		chirality	origin	chemist	not	rehook	salt fo	rm		
		ormany	Internal synthesis	Dave Carlson	002	2DAC025_1	None	Free base		
	N N O	amount available	program	primary target	ner		eleme			
			Buring inhib	primary target	05	100	cicilie			
					90-	-100	NIME	- 1 - 1 - 1 -		
	ci 🗸 🖉	meiting point	NIVIR data	LUMS data	cor		NIVIR	datanie		
				on	Ana	alog of HS38. ZIPK inhibitor.	_			
		LCMS datafile					_			
		yes								
	110 400050 04	chomical regist	r\/							
62.	HS-100053-01	registry id	molut	formula		data		SMILES		
			1101 WL		40					
	0	HS-100053-01	330.799	chamiet	13	2012-03-20				
	Ű	chirality	origin	cnemist						
	N		Internal synthesis	Dave Carlson		002DAC026_1		None: Free base		
		amount available	program	primary target		percent purity		elemental analysis		
		0.044	Purine_inhib			95-100				
	o o	melting point	NMR data	LCMS data		comment		NMR datafile		
	CI			on		Analog of HS38. ZIPK inhit	oitor.			
		LCMS datafile								
		yes								
60	HS-100054-01	chemical regist	rv							
63.	113-100034-01	registry id	mol wt	formula	dat	e	SMILE	-S		
		HS-100054-01	396.853	CI1S1O2N4C19H13	201	12-03-20	Clc1c	c(ccc1)n2ncc3c(InHlc(nc23)SCC(c4ccccc4)=O)=O		
	o	chirality	origin	chemist	notebook		salt form			
	, Å	ormany	Internal synthesis	Dave Carlson	002	2DAC026_2	None	None: Free base		
	N N	amount available	program	primary target	ner	cent purity	eleme	ntal analysis		
	N N S	0.046	Purine inhib	P	95-	100				
		melting point	NMR data	LCMS data	cor	nment	NMR	datafile		
	CI			on	Analog of HS38. ZIPK inhibitor.					
	~	LCMS datafile				5				
		yes								
64.	HS-100055-01	chemical registry								
		registry id	mol wt	formula	date		SMILES			
	o	HS-100055-01	431.298	Cl2S1O2N4C19H12	2012	2-03-20	Clc1cc(	ccc1)n2ncc3c([nH]c(nc23)SCC(c4ccc(cc4)Cl)=O)=O		
		chirality	origin	chemist	note	book	salt form	1		
	N N		Internal synthesis	Dave Carlson	0020	DAC026_3	None: F	ree base		
		amount available	program	primary target	perc	ent purity	element	al analysis		
		0.055	Purine_inhib		95-1	00				
	CI	melting point	NMR data	LCMS data	com	ment	NMR da	tafile		
	Ý			on	Anal	og of HS38. ZIPK inhibitor.				
	Сі	LCMS datafile								
		yes								
05	HS-100056-01	chemical regist	rv							
65.	13-100030-01	registry id	mol wt	formula		date		SMILES		
		HS-100056-01	317.755	CI1S101N5C13H	18	2012-03-20		Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SCC#N)=O		
	0	chirality	origin	chemist		notebook		salt form		
	Ŭ		Internal synthesis	Dave Carlson		002DAC026 4		None: Free base		
	N N	amount available	program	primary target		percent purity		elemental analysis		
	N <sup>N</sup> N <sup>S</sup> S	0.022	Purine_inhib			95-100				
	×N	melting point	NMR data	LCMS data		comment		NMR datafile		
	CI			on		Analog of HS38. ZIPK inhib	itor.			
	~	LCMS datafile								
		yes								
		L	1							

66	HS-100057-01	chemical registry								
50.		registry id	mol wt		formula		date		SMILES	
		HS-100057-01	332.810		CI1S1O1N4	4C15H13	2012-03-20		Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SCC=CC)=O	
	0	chirality	origin		chemist		notebook		salt form	
	U U		Internal synth	nesis	Dave Carls	on	002DAC026_5		None: Free base	
	N N	amount available	program		primary targ	get	percent purity		elemental analysis	
	N N S	0.034	Purine_inhib				95-100			
	$\square$	melting point	NMR data		LCMS data		comment		NMR datafile	
	CI				on		Analog of HS38.	ZIPK inhibito	r.	
		LCMS datafile								
		yes								
l ,					1				I	
67.	HS-100058-01	chemical regi	stry						1	
		registry id	mol wt		formula		date		SMILES	
		HS-100058-01	404.276		CI2S101N5C	17H11	2012-03-20		Clc1ncc(CSc2nc3n(c4cccc(c4)Cl)ncc3c([nH]2)=O)cc1	
	0	chirality	origin		chemist		notebook		salt form	
	$\sim$ $\overset{\parallel}{\sim}$ .		Internal synthe	esis	Dave Carlson	ı	002DAC026_6		None: Free base	
		amount available	program		primary target		percent purity		elemental analysis	
	N N S	0.026 Purine_inh					95-100			
	CI CI	melting point NMR data			LCMS data		comment		NMR datafile	
					on		Analog of HS38. ZIPK inhibitor.			
		LCMS datafile								
		yes								
69	HS-100059-01	chemical registry								
00.		registry id	mol wt	formul	а	date		SMILES		
		HS-100059-01	569.449	CI2S2	O2N8C23H14	2012-03-2	20	Clc1cc(ccc1)n	2ncc3c([nH]c(nc23)SCSc4nc5n(c6cccc(c6)Cl)ncc5c([nH]4)=O)=O	
		chirality	origin	chemi	mist notebook		salt form			
	o o		Internal synthesis	Dave	e Carlson 002DAC02		26_7 None: Free base		Se	
		amount available	program	primar	y target	percent p	urity elemental analysis		ysis	
	N <sup>™</sup> N <sup>™</sup> S <sup>^</sup> S <sup>™</sup> N <sup>™</sup> N	0.040	Purine_inhib		95-100					
	ci 🖉 🚺 Ci	melting point	NMR data	LCMS	data	comment		NMR datafile	9	
				on		Analog of	HS38. ZIPK inhibitor.			
		LCMS datafile								
		yes								
1		ah ang ing bagai	- 4							
69.	HS-100060-01	chemical regi	stry	6			1	I	244 50	
		registry id	moi wt	TO		01140	date		SMILES	
	<b>o</b>	HS-100060-01	4/5./49	Br	10115102N4C1	9H12	2012-03-20		src1ccc(U(CSc2nc3n(c4cccc(c4)Cl)ncc3c([nHj2)=O)=O)cc1	
		Ginany	Internal synthesis	cr						
	N I A A	amount evolable	program		imany target					
	N <sup>-</sup> N <sup>-</sup> S <sup>-</sup>		Purino inhih	pr	imary target		95-100		elemental analysis	
		molting point	NMR data		MS data		commont			
	CI	mening point	NIVIT Udla					nhibitor	www.uataine	
	Ý.			or	on		Analog of HS38. ZIPK Inhibitor.			

70. **HS-100061-01** 

|--|

LCMS datafile yes

	melting point	NMR data	LCMS data	comment	NMR datafile
$\searrow$			on	Analog of HS38. ZIPK inhibitor.	
Br	LCMS datafile				
	yes				
	chemical regis	try			
	registry id	mol wt	formula	date	SMILES
	HS-100061-01	350.782	CI1S1O3N4C14H11	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
~ <b>`</b> \	0.028	Purine_inhib		95-100	
	melting point	NMR data	LCMS data	comment	NMR datafile
			on	Analog of HS38, ZIPK inhibitor.	

71.	HS-100062-01	chemical reg	stry								
		registry id	mol wt		formula	d	late		SMI	LES	
		HS-100062-01	397.841		CI1S1O2N5C18	H12 2	2012-03-20	)	Clc1	cc(ccc1)n2ncc3c([nH]c(nc23)SCC(c4ncccc4)=O)=O	
	o	chirality	origin		chemist	n	otebook		salt	form	
			Internal s	ynthesis	Dave Carlson	0	002DAC026_10		Non	None: Free base	
	N <sup>n</sup> L , A , A	amount available	program		primary target	p	percent purity		elen	nental analysis	
		0.024	Purine_in	hib		9	95-100				
	ci -	melting point	NMR data	a	LCMS data	c	omment		NM	R datafile	
					on	Α	nalog of H	IS38. ZIPK inhibitor.			
		LCMS datafile									
		yes									
72.	HS-100063-01	chemical reg	stry				1				
		registry id mol			formula		date			SMILES	
		HS-100063-01	366.825		CI1S1O3N4C	15H15	2012-03	3-20		Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SCCOCCO)=O	
	O O	chirality	origin		chemist		noteboo	ik		salt form	
	N N		Internal	synthesis	Dave Carlson		002DA0	2028_1		None: Free base	
		amount available	program		primary target		percent	purity		elemental analysis	
	. N S 🌣	0.010	Purine_i	nhib			95-100				
		melting point	NMR da	ta	LCMS data		comme			NMK datafile	
					on		Analog	ot HS38. ZIPK inhibito	r.		
		LCMS datafile									
		yes									
70	HS-100064-01	chemical reg	strv								
13.		registry id mol wt			formula		date		_	SMILES	
		HS-100064-01 335.771			CI1S1O2N5C	13H10	2012-03-20			Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SCC(N)=O)=O	
	0	chirality or			chemist		notebook			salt form	
	. ľ	Internal synthe		synthesis	Dave Carlson		002DA	029_1		None: Free base	
	N N	amount available program		-	primary target		percent	purity		elemental analysis	
		0.008	Purine_inhib				95-100		_	-	
	, Ö	melting point	NMR data		LCMS data		comment			NMR datafile	
	CI				on		Analog	of HS38. ZIPK inhibito	or.		
	_	LCMS datafile									
		yes									
74.	HS-100065-01	chemical registry									
		registry id	mol wt		formula	date	e SMILES				
	, <b>o</b>	HS-100065-01	546.659		O7N4C28H42	2012-0	03-20	O=C(c1ccc(cc1NCC0	coco	COCCOCCOCCO)n2nc(C)c3c2CC(CC3=O)(C)C)N	
	$\mathbf{P}$ / $\langle \rangle$	chirality	origin		chemist	notebo	ok	salt form			
			Internal s	ynthesis	Philip Hughes	PFH-0	03-013A	None: Free base			
		amount available	program		primary target	percen	t purity	elemental analysis			
	, o	0.041	Purine_ir	ihib		95-100	)				
	N	melting point	NMR dat	a	LCMS data	comme	ent	NMR datafile			
					on	glass					
	N	LCMS datafile									
		yes									
75	HS-100066-01	chemical reg	stry								
75.		registry id m	ol wt	formula	date	SMILES					
		HS-100066-01 8	9.091	O9N8C48H6	6 2012-03-20	O=C(c1ccc	c(cc1NCCCOC	COCCOCCOCCOCCNc2cc(ccc	:2C(N)=	D)n3nc(C)c4c3CC(CC4=O)(C)C)n5nc(C)c6c5CC(CC6=O)(C)C)N	
		chirality or	gin	chemist	notebook	salt form					
	ంౖ∽ంౖంౢ	In	ernal synthesis	Philip Hughe	s PFH-003-013B	None: Free	e base				
		amount available pr	ogram	primary targe	t percent purity	elemental a	analysis				
	Ý Ý	0.026 P	rine_inhib		95-100						
		melting point N	/IR data	LCMS data	comment	NMR dataf	ile				
	Õ Ő			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	0=C(c1ccc(cc1NCCCOCCOCCOCCOCCOCCORc2cc(ccc2C(N)=O)n3nc(C)c4c3CC(CC4=O)(C)C)n5nc(C)c8c5CC(CC8=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				
	0 Ő			on	glass sample dissolved in DMSO at 10mM					
		LCMS datafile								
		yes								

## 77. HS-100067-01

chemical	registry			
registry id	mol wt	formula	date	SMLES
HS-100067-01	1035.217	S1012N6C55H66	2012-04-02	S=C(N(C(C)C)CCCCCCCCCCCCCCCCCCCCCCCCCCCCC
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 datafie
		on	3 mg in DMSO (10 mM) put in Khaldon box.	yes
LCMS datafile				
yes				

## 78. HS-100068-01



chemical r	chemical registry									
registry id	mol wt	formula	date	SMILES						
HS-100068-01	1151.059	I1S2O12N8C50H55	2012-04-23	lc1cc2OCOc2cc1Sc3nc4c(N)ncnc4n3CCCNCCCOCCOCCOCCOCCOCCNC(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 re	hemical registry										
registry id	mol wt	formula	date	SMILES							
HS-100069-01	602.745	O7N5C31H48X1	2012-05-18	O=C(c1ccc(cc1NCCCOCCOCCOCCOCCOCCOCCOC(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 re	chemical registry											
registry id	mol wt	formula	date	SMILES								
HS-100070-01	602.745	O7N5C31H48X1	2012-05-18	O=C(c1ccc(cc1NCCCOCCOCCOCCOCCOCCOCCO[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												

31.	HS-100071-01	chemical registry	/						
		registry id	mol wt	formula		date		SMILES	
		HS-100071-01	364.446	O1N6C2	20H24	2012-05-22		O=C(C1CN(CCC1)c2nccnc2)Nc3nc4ccccc4n3CCC	
	9 N (	chirality	origin	chemist	t	notebook		salt form	
		{3R;}	Internal synthesis	Philip H	lughes	PFH-003-044A		None: Free base	
	Ň N	amount available	program	primary	target	percent purity		elemental analysis	
	$\sim$	0.031	Purine_inhib			95-100			
	Ï \	melting point	NMR data	LCMS d	data	comment		NMR datafile	
	N			on		Derived from (R	) enantiomer		
	Ń	LCMS datafile							
	*	yes							
ſ									
32.	HS-100072-01	rogistry id	mol wt	formula		data		SWILES	
		HS-100072-01	364.446	OINEC	201124	2012-05-22			
		chirality	origin	chemict	201124	notebook		salt form	
		(3S·)	Internal synthesis	Philin H	luahes	PEH-003-0504		None: Free base	
	Countil N N	amount available	program	primary	target	percent purity		elemental analysis	
		0.0092	Purine inhib	printary	larget	95-100			
	Ň Ń	melting point	NMR data	LCMS d	data			NMR datafile	
	N			on	Derived from (		)-enantiomer		
		LCMS datafile							
		yes							
				L					
83.	HS-100072-02	chemical registry	1						
83.	HS-100072-02	chemical registry registry id	mol wt	formula		date		SMILES	
83.	HS-100072-02	chemical registry registry id HS-100072-02	Mol wt 364.446	formula O1N6C2	20H24	date 2012-07-31		SMILES O=C(C1CN(CCC1)c2nccnc2)Nc3nc4ccccc4n3CCC	
83.	HS-100072-02	chemical registry registry id HS-100072-02 chirality	mol wt 364.446 origin	formula O1N6C2 chemist	20H24	date 2012-07-31 notebook		SMILES O=C(C1CN(CCC1)c2nccnc2)Nc3nc4ccccc4n3CCC salt form	
33.	HS-100072-02	chemical registry registry id HS-100072-02 chirality (3S;)	mol wt 364.446 origin Internal synthesis	formula O1N6C2 chemist Philip H	20H24 i lughes	date 2012-07-31 notebook PFH-003-050B		SMILES O=C(C1CN(CCC1)c2nccnc2)Nc3nc4ccccc4n3CCC salt form None: Free base	
33.	HS-100072-02	chemical registry         registry id         HS-100072-02         chirality         {3S;}         amount available	mol wt 364.446 origin Internal synthesis program	formula O1N6C2 chemist Philip Hi primary	20H24 i lughes target	date 2012-07-31 notebook PFH-003-050B percent purity		SMILES O=C(C1CN(CCC1)c2nccnc2)Nc3nc4ccccc4n3CCC salt form None: Free base elemental analysis	
83.	HS-100072-02	chemical registry         registry id         HS-100072-02         chirality         {3S;}         amount available         0.021	/ mol wt 364.446 origin Internal synthesis program Purine_inhib	formula O1N6C2 chemist Philip H primary	20H24 i lughes target	date 2012-07-31 notebook PFH-003-050B percent purity 95-100		SMILES O=C(C1CN(CCC1)c2nccnc2)Nc3nc4ccccc4n3CCC salt form None: Free base elemental analysis	
83.	HS-100072-02	chemical registry         registry id         HS-100072-02         chirality         (3S;)         amount available         0.021         melting point	mol wt 364.446 origin Internal synthesis program Purine_inhib NMR data	formula O1N6C2 chemist Philip Hi primary LCMS d	20H24 tughes target	date 2012-07-31 notebook PFH-003-050B percent purity 95-100 comment		SMILES O=C(C1CN(CCC1)c2nccnc2)Nc3nc4ccccc4n3CCC salt form None: Free base elemental analysis NMR datafile	
33.	HS-100072-02	chemical registry registry id HS-100072-02 chirality {3S;} amount available 0.021 melting point	/ mol wt 364.446 origin Internal synthesis program Purine_inhib NMR data	formula O1N6C2 chemist Philip Hi primary LCMS d	20H24 t lughes target data	date 2012-07-31 notebook PFH-003-050B percent purity 95-100 comment Derived from (S	)-enantiomer	SMILES O=C(C1CN(CCC1)c2nccnc2)Nc3nc4ccccc4n3CCC salt form None: Free base elemental analysis NMR datafile	
333.	HS-100072-02	chemical registry         registry id         HS-100072-02         chirality         {3S;}         amount available         0.021         melting point         LCMS datafile	/ mol wt 364.446 origin Internal synthesis program Purine_inhib NMR data	formula O1N6C2 chemist Philip Hi primary LCMS d	20H24 t lughes target data	date 2012-07-31 notebook PFH-003-050B percent purity 95-100 comment Derived from (S	)-enantiomer	SMILES O=C(C1CN(CCC1)c2nccnc2)Nc3nc4ccccc4n3CCC salt form None: Free base elemental analysis NMR datafile	
333.	HS-100072-02	chemical registry registry id HS-100072-02 chirality (3S;) amount available 0.021 melting point LCMS datafile	mol wt 364.446 origin Internal synthesis program Purine_inhib NMR data	formula O1N6C2 Chemist Philip Hi primary LCMS d	20H24 lughes target data	date 2012-07-31 notebook PFH-003-050B percent purity 95-100 comment Derived from (S	)-enantiomer	SMILES O=C(C1CN(CCC1)c2nccnc2)Nc3nc4ccccc4n3CCC salt form None: Free base elemental analysis NMR datafile	
33.	HS-100072-02	chemical registry registry id HS-100072-02 chirality (3S;) amount available 0.021 melting point LCMS datafile	mol wt 364.446 origin Internal synthesis program Purine_inhib NMR data	formula O1N6C2 chemist Philip Hi primary LCMS d	20H24 tellughes target Jata	date 2012-07-31 notebook PFH-003-050B percent purity 95-100 comment Derived from (S	)-enantiomer	SMILES O=C(C1CN(CCC1)c2nccnc2)Nc3nc4ccccc4n3CCC salt form None: Free base elemental analysis NMR datafile	
833. [ [ 84. ]	HS-100072-02	chemical registry         registry id         HS-100072-02         chirality         (3S:)         amount available         0.021         melting point         LCMS datafile         .         chemical registry         registry id	/ mol wt 364.446 origin Internal synthesis program Purine_inhib NMR data	formula O1N6C2 chemist Philip Hi primary LCMS d	20H24 target data	date 2012-07-31 notebook PFH-003-050B percent purity 95-100 comment Derived from (S	)-enantiomer	SMILES O=C(C1CN(CCC1)c2nccnc2)Nc3nc4ccccc4n3CCC salt form None: Free base elemental analysis NMR datafile SMILES	
83. [ [ 84. [	HS-100072-02	chemical registry         registry id         HS-100072-02         chirality         (3S:)         amount available         0.021         melting point         LCMS datafile         chemical registry         registry id         HS-100073-01	/ mol wt 364.446 origin Internal synthesis program Purine_inhib NMR data / / mol wt 292.746	formula O1N6C2 chemist Philip H primary LCMS d	20H24 i lughes target data formula CI1S1O <sup>-</sup>	date 2012-07-31 notebook PFH-003-050B percent purity 95-100 comment Derived from (S	)-enantiomer date 2012-06-13	SMILES O=C(C1CN(CCC1)c2nccnc2)Nc3nc4ccccc4n3CCC salt form None: Free base elemental analysis NMR datafile SMILES Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SC)=O	
83. [ [ 84. [	HS-100072-02	chemical registry registry id HS-100072-02 chirality {3S;} amount available 0.021 melting point LCMS datafile Chemical registry registry id HS-100073-01 chirality	/ mol wt 364.446 origin Internal synthesis program Purine_inhib NMR data / / mol wt 292.746 origin	formula O1N6C2 chemist Philip Hi primary LCMS d	20H24 lughes target data formula CI1S1O <sup>7</sup> chemist	date 2012-07-31 notebook PFH-003-050B percent purity 95-100 comment Derived from (S	date 2012-06-13 notebook	SMILES O=C(C1CN(CCC1)c2nccnc2)Nc3nc4ccccc4n3CCC salt form None: Free base elemental analysis NMR datafile SMILES Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SC)=O salt form	
83. [ 84. [	HS-100072-02	chemical registry registry id HS-100072-02 chirality (3S;) amount available 0.021 metting point LCMS datafile 	/ mol wt 364.446 origin Internal synthesis program Purine_inhib NMR data / 292.746 origin Internal synthe	formula O1N6C2 chemist Philip H primary LCMS d LCMS d Siss 1	20H24 target data formula CI1S1O <sup>2</sup> chemist Dave Ca	date 2012-07-31 notebook PFH-003-050B percent purity 95-100 comment Derived from (S Derived from (S 100 200 200 200 200 200 200 200 200 200	date 2012-06-13 notebook 2DAC033_1	SMILES O=C(C1CN(CCC1)c2nccnc2)Nc3nc4ccccc4n3CCC salt form None: Free base elemental analysis NMR datafile SMILES Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SC)=O salt form None: Free base	
33.	HS-100072-02	chemical registry         registry id         HS-100072-02         chirality         (3S;)         amount available         0.021         melting point         LCMS datafile         registry id         HS-100073-01         chirality         amount available	/ mol wt 364.446 origin Internal synthesis program Purine_inhib NMR data // // // // // // // // // /	formula O1N6C2 chemist Philip H primary LCMS d LCMS d Siss 1	20H24 target data formula CI1S1O chemist Dave Ca primary f	date 2012-07-31 notebook PFH-003-050B percent purity 95-100 comment Derived from (S Derived from (S 100 comment Derived from (S 100 comment De	date 2012-06-13 notebook 2DAC033_1 percent purity	SMILES O=C(C1CN(CCC1)c2nccnc2)Nc3nc4ccccc4n3CCC salt form None: Free base elemental analysis NMR datafile SMILES Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SC)=O salt form None: Free base elemental analysis	
33.	HS-100072-02	chemical registry registry id HS-100072-02 chirality (3S;) amount available 0.021 melting point LCMS datafile chemical registry registry id HS-100073-01 chirality amount available 0.035	/ mol wt 364.446 origin Internal synthesis program Purine_inhib NMR data ///////////////////////////////////	formula O1N6C2 chemist Philip Hi primary LCMS d LCMS d Siss 1	20H24 tughes target data formula CI1S1O <sup>2</sup> chemist Dave Ca primary t	date 2012-07-31 notebook PFH-003-050B percent purity 95-100 comment Derived from (S Derived from (S 100 100 100 100 100 100 100 100 100 10	date 2012-06-13 notebook 2DAC033_1 percent purity 95-100	SMILES O=C(C1CN(CCC1)c2nccnc2)Nc3nc4ccccc4n3CCC salt form None: Free base elemental analysis NMR datafile SMILES Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SC)=O salt form None: Free base elemental analysis	
33.	HS-100072-02	chemical registry registry id HS-100072-02 chirality (3S;) amount available 0.021 melting point LCMS datafile chemical registry registry id HS-100073-01 chirality amount available 0.035 melting point	/ mol wt a64.446 origin Internal synthesis program Purine_inhib NMR data ///////////////////////////////////	formula O1N6C2 chemist Philip H primary LCMS d LCMS d sis f sis f sis f	20H24 target target data formula CI1S1O chemist Dave Ca primary f	date 2012-07-31 notebook PFH-003-050B percent purity 95-100 comment Derived from (S Derived from (S notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebook notebo notebo notebo notebook	date 2012-06-13 notebook 2DAC033_1 percent purity 95-100 comment	SMILES O=C(C1CN(CCC1)c2nccnc2)Nc3nc4ccccc4n3CCC salt form None: Free base elemental analysis NMR datafile SMILES Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SC)=O salt form None: Free base elemental analysis INMR datafile NMR datafile NMR datafile	
333.	HS-100072-02 O N N N N N N N N N N N N N N N N N N N	chemical registry registry id HS-100072-02 chirality (3S;) amount available 0.021 melting point LCMS datafile chemical registry registry id HS-100073-01 chirality amount available 0.035 melting point	/ mol wt 364.446 origin Internal synthesis program Purine_inhib NMR data / 292.746 origin Internal synthe program Purine_inhib NMR data	formula O1N6C2 chemist Philip H primary LCMS d LCMS d sis f sis f sis f sis f	20H24 target target data formula CI1S1O chemist Dave Ca primary formula LCMS da on	date 2012-07-31 notebook PFH-003-050B percent purity 95-100 comment Derived from (S Derived from (S International IN4C12H9 arlson target	date 2012-06-13 notebook 2DAC033_1 percent purity 95-100 comment	SMILES O=C(C1CN(CCC1)c2nccnc2)Nc3nc4ccccc4n3CCC salt form None: Free base elemental analysis NMR datafile SMILES Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SC)=O salt form None: Free base elemental analysis INMR datafile NMR datafile NMR datafile	
33.	HS-100072-02 $\downarrow$ $\downarrow$ $\downarrow$ $\downarrow$ $\downarrow$ $\downarrow$ $\downarrow$ $\downarrow$ $\downarrow$ $\downarrow$	chemical registry registry id HS-100072-02 chirality (3S;) amount available 0.021 melting point LCMS datafile chemical registry registry id HS-100073-01 chirality amount available 0.035 melting point	/ mol wt 364.446 origin Internal synthesis program Purine_inhib NMR data / 292.746 origin Internal synthe program Purine_inhib NMR data	formula O1N6C2 chemist Philip H primary LCMS d LCMS d Sis 1	20H24 is lughes target data formula CI1S1O <sup>2</sup> chemist Dave Ca primary formula LCMS da on	date 2012-07-31 notebook PFH-003-050B percent purity 95-100 comment Derived from (S Derived from (S 100 comment Derived from (S 100 comment De	date 2012-06-13 notebook 2DAC033_1 percent purity 95-100 comment	SMILES O=C(C1CN(CCC1)c2nccnc2)Nc3nc4ccccc4n3CCC salt form None: Free base elemental analysis NMR datafile SMILES Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SC)=O salt form None: Free base elemental analysis elemental analysis NMR datafile NMR datafile	
333.	HS-100072-02 $\downarrow \qquad \qquad$	chemical registry registry id HS-100072-02 chirality {3S;} amount available 0.021 melting point LCMS datafile chemical registry registry id HS-100073-01 chirality amount available 0.035 melting point LCMS datafile yes	/ mol wt 364.446 origin Internal synthesis program Purine_inhib NMR data / 292.746 0 origin Internal synthe program Purine_inhib NMR data 1 00 wt	formula O1N6C2 chemist Philip H primary LCMS d LCMS d LCMS d Sis 1 Sis 1 Sis 1 C Sis 1 Sis 1 Sis 1 C Sis 1 C S	20H24 i lughes target data formula CI1S1O <sup>-</sup> chemist Dave Ca primary t LCMS da on	date 2012-07-31 notebook PFH-003-050B percent purity 95-100 comment Derived from (S Derived from (S 100 comment Derived from (S 100 comment De	date 2012-06-13 notebook 2DAC033_1 percent purity 95-100 comment	SMILES O=C(C1CN(CCC1)c2nccnc2)Nc3nc4ccccc4n3CCC salt form None: Free base elemental analysis    SMILES Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SC)=O salt form None: Free base elemental analysis elemental analysis NMR datafile NMR datafile NMR datafile NMR datafile	

85. **HS-100074-01** 



yes						
J						
chemical registry						
registry id	mol wt	formula	date	SMILES		
HS-100074-01	378.836	CI1S1O3N4C16H15	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	NMR data LCMS data		NMR datafile		
		on				
LCMS datafile						
yes						

86.	HS-100075-01	chemical registry	У							
		registry id	mol wt	for	rmula		date		SMILES	
		HS-100075-01	378.836	Cl	CI1S1O3N4C16H1		2012-06	5-13	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SC(CC)C(OC)=O)=O	
		chirality	origin	ch	chemist notebor		noteboo	ok	salt form	
	CI		Internal synthes	sis Da	ave Carlson		2DAC0	33 3	None <sup>,</sup> Free base	
	o o	amount available	program	nri	imary tara	ot	porcont purity			
			During inhib	- Pil	inary larg	01				
	N T U	0.023	Punne_innib				95-100			
		melting point	NMR data	LC	CMS data		comme	nt	NMR datafile	
	ö			on	1					
		LCMS datafile								
		yes								
87.	HS-100076-01	chemical registry	У							
		registry id	mol wt	fo	rmula		date		SMILES	
		HS-100076-01	363.824	CI	11S1O2N5	C15H14	2012-0	6-13	Clc1cc(ccc1)n2ncc3c([nH]c(nc23)SC(CC)C(N)=O)=O	
	$\sim$	chirality	origin	ch	nemist		notebo	ok	salt form	
	CI		Internal synthe	sis Da	ave Carlso	on	2DAC0	)42 2	None: Free base	
	м С	amount available	program	pr	imary tar	1et	percen	t purity	elemental analysis	
	N N S	0.012	Purine inhih			,	95-100	)		
	N T N	melting point		1.0	MS data		00-100	, ant	NMR datafile	
			NIVIT Uata				comme	5111		
	ö			or	1					
		LCMS datafile								
		yes								
88.	HS-100077-01	chemical registry	у							
		registry id	stry id mol wt		a	date		SMILES	ذ	
	0	HS-100077-01	536.408	1103N4	4C23H29	2012-06-1	2012-06-13 lc1c(cc		(c(C(N)=O)c1)NC2CCC(CC2)O)n3nc(C)c4c3CC(CC4=O)(C)C	
	, ⊥ į	chirality	origin	chemist		notebook	notebook salt for		1	
	N O	{12-15T;}	Internal synthesis	Dave Carlson		2DAC043	DAC043_MONO None:		ree base	
	N	amount available	program	primary target		percent pu	ercent purity elemen		al analysis	
		0.048	Purine_inhib	95-		95-100	-100			
		melting point	NMR data	LCMS data comment		comment	NMR da		tafile	
	$\leq$			on	วท					
	N N	LCMS datafile								
		ves								
00	HS-100078-01	chemical registr	v							
09.		registry id	mol wt	formula	formula date		s	MILES		
		HS-100078-01	662 305	12O3N4C23H28		2012-06-13 lc1c(cc(c(			(N)=0)c1)NC2CCC(CC2)0)p3pc(C)c4c3CC(C(C4=0)I)(C)C	
	<b>O</b>	chirolity	origin	chomic	203N4C23H28 2		notebook salt form			
		(12-15T-)	Internal ounth sair	Dove	Carlson	ADACO42 DIC Nor			ne: Free hase	
	, ⊥ ⊥ N NO	{12-151;}	internal synthesis	Dave C	ave carison 2DAC04				uase	
		amount available	program	primary	y target	percent purity ele		ienieniai analysis		
		0.074	Purine_inhib				95-100			
	N.	melting point	NMR data	LCMS	data	comment	N	MR datafile		
	, <b>⊳o</b>			on						
	N	LCMS datafile								
		yes								
90.	HS-100079-01	chemical registry	У							
		registry id	mol wt		formula		date		SMILES	
	<u></u>	HS-100079-01	338.472		S1N4C	19H22	2012-06	6-13	s1c2ncnc(c2c(C)c1C)NC3CN(CC3)Cc4ccccc4	
	N S	chirality	origin		chemist		noteboo	ok	salt form	
	N_	{13R;}	Internal synth	nesis	Philip H	ughes	PFH-00	3-058A	None: Free base	
	Ť /	amount available	program		primary	target	percent	purity	elemental analysis	
	∧ ∧ N	0.134	Purine inhib				95-100			
	_ N_	melting point	NMR data		LCMS	lata	comme	nt	NMR datafile	
		in in the second second			on				ves	
		I CMS datafile							,	
		yes			1					

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								

#### 92



chemical registry										
mol wt	formula	date	SMILES							
550.516	O10N2C28H26	2012-06-14	OC(c1cccc(c1C(c2c(cc(C(OC3CCCNCC3NC(c4ccc(cc4)O)=O)=O)cc2O)O)=O)O)=O							
origin	chemist	notebook	salt form							
{16R;22R;} Internal synthesis Philip Hughes		PFH-003-039A	None: Free base							
program	primary target	percent purity	elemental analysis							
Purine_inhib		95-100								
NMR data	LCMS data	comment	NMR datafile							
	on	Gift of Sphinx Pharmaceuticals; LC impurity from previous injection								
	egistry mol wt 550.516 origin Internal synthesis program Purino_inhib NMR data	rol wt     formula       550.516     010N2C28H26       origin     chemist       Internal synthesis     Philip Hughes       program     primary target       Purine_inhib     LCMS data       NMR data     LCMS data       Internal synthesis     pinary target	projection         formula         date           mol wt         formula         date           550.516         O10N2C28H26         2012-06-14           origin         chemist         notebook           origin         chemist         notebook           Internal synthesis         Philip Hughes         PFH-003-039A           program         primary target         percent purity           Purine_inhib         0         95-100           NMR data         LCMS data         comment           Internal synthesis         on         Gift of Sphinx Pharmaceuticals; LC impurity from previous injection           Internal         Internal         Internal         Internal							

## 93. **HS-100082-01**

s

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							

#### HS-100083-01 94.

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l	chemical registry	hemical registry									
	registry id	registry id mol wt		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	t 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	0.045	Purine_inhib		95-100					
	melting point	NMR data	LCMS data	comment	NMR datafile				
			on	Analog of HS38. ZIPK inhibitor.					
	LCMS datafile								
	yes								

							1 age 20/40	
96	HS-100085-01	chemical registr	у					
00.		registry id mol wt formu		formula	date		SMILES	
		HS-100085-01	283.310	S101N5C13H	19 2012-08-15		S(CC#N)c1nc2n(c3ccccc3)ncc2c([nH]1)=O	
	Q	chirality	origin	chemist	notebook		salt form	
			Internal synthesis	s Dave Carlson	002DAC054_4		None: Free base	
		amount available	program					
				primary target				
		0.060	Purine_innib		95-100			
	$\left  \right  = \left  \right $	melting point	NMR data	LCMS data	comment		NMR datafile	
				on	Analog of HS38. ZIPK inhi	bitor.		
	-	LCMS datafile						
					•		·	
97.	HS-100086-01	chemical registr	у					
		registry id	mol wt	formula	date	SMIL	.ES	
		HS-100086-01	330.364	S1O3N4C15H14	2012-08-15	S(C(	C)(C)C(=O)O)c1nc2n(c3ccccc3)ncc2c([nH]1)=O	
	<b>o</b>	chirality	origin	chemist	notebook	salt f	orm	
	$\sim$		Internal synthesis	Dave Carlson	002DAC054 5	None	e: Free base	
		amount available	program	primary target	percent purity	elem	ental analysis	
	N N S V O	0.044	Purine inhib		95-100			
		melting point	NMR data	I CMS data	comment	NMR	datafile	
		moning point	i initia dala			NIVIP		
				on	Analog of H538. ZIPK Inhibitor.			
		LCMS datafile						
		yes						
98.	HS-100087-01	chemical registr	<b>y</b>					
		registry id	mol wt	formula	date	SMI	LES	
		HS-100087-01	330.364	S1O3N4C15H14	2012-08-15	S(C	(C)C(OC)=O)c1nc2n(c3ccccc3)ncc2c([nH]1)=O	
	Q	chirality	origin	chemist	notebook	salt	form	
			Internal synthesis	Dave Carlson	002DAC054_6	Non	e: Free base	
	NÍ L	amount available	program	primary target	percent purity	elen	nental analysis	
	N N S	0.038	Purine_inhib		95-100			
	Ö	melting point	NMR data	LCMS data	comment	NM	R datafile	
				on	Analog of HS38. ZIPK inhibitor.			
	~	LCMS datafile						
		yes						
99	HS-100088-01	chemical registr	у					
00.		registry id	mol wt	formula	date	S	MILES	
		HS-100088-01	316.337	S1O3N4C14H12	2012-08-15	S	(CC(OC)=O)c1nc2n(c3ccccc3)ncc2c([nH]1)=O	
	0	chirality	origin	chemist	notebook	s	alt form	
	Ĭ		Internal synthesis	Dave Carlson	002DAC054_7	N	one: Free base	
	N	amount available	program	primary target	percent purity	 ام		
			Buring inhih	printary target				
		0.003			95-100	N	MD detefile	
		menung point	NIVIR Cala	LCIVIS data				
				on	Analog of HS38. ZIPK Inhibitor.			
		LCMS datafile						
		yes						
		chomical registr						
100.	HS-100089-01	to gista vid	y .	io mula	data	Chail P		
		registry id	mol wt	ormula	date	SMILE	-5	
		HS-100089-01	344.390	5103N4C16H16	2012-08-15	S(C(C	.)(U)U(UU)=U)c1nc2n(c3ccccc3)ncc2c([nH]1)=0	
	<b>O</b>	chirality	origin	chemist	notebook	salt fo	rm	
	N		Internal synthesis	Dave Carlson	002DAC054_8	None:	Free base	
	NIIIVO	amount available	program	orimary target	percent purity	eleme	ntal analysis	
	N <sup>-</sup> `N <sup>-</sup> `S <sup>-</sup> ↓ <sup>-</sup>	0.048	Purine_inhib		95-100			
	Ö	melting point	NMR data	LCMS data	comment	NMR	datafile	
				on	Analog of HS38. ZIPK inhibitor.			
	-	LCMS datafile						
		yes						
	· · · · · · · · · · · · · · · · · · ·	1						

101	HS-100090-01	chemical registry								
101.		registry id	mol wt	formula	date	e		SMILES		
		HS-100090-01	344.390	S1O3N4C16H16	201	2-08-15		S(C(CC)C(OC)=O)c1nc2n(c3ccccc3)ncc2c([nH]1)=O		
	0	chirality	origin	chemist	note	ebook		salt form		
			Internal synthesis	Dave Carlson	002	002DAC054_9		None: Free base		
	N	amount available	program	primary target	ner			elemental analysis		
			Purine inhih	printary target	95.	05 100				
		melting point	NMR data	LCMS data	com	nment		NMR datafile		
			Nini Cata		Ang	alog of US28_ZIPK in	hihitor			
		LCMS datafilo		011						
		yes								
100	HS-100091-01	chemical registr	v							
102.		registry id	mol wt	formula		date	SMILES			
		HS-100091-01	372.401	S104N4C17H	16	2012-08-15	SICCICO	C(OCC)=O)=O)c1nc2n(c3ccccc3)ncc2c([nH]1)=O		
		chirality	origin	chemist		notebook	salt form			
	Ŭ		Internal synthesis	B Dave Carlson		002DAC054_10	None: Fr	ee base		
	N N	amount available	program	primary target		percent purity	elementa	al analysis		
	Ŋ <sup>™</sup> N <sup>™</sup> S <sup>™</sup> O	0.075	Purine inhib			95-100				
	, ÖÖ	melting point	NMR data	LCMS data		comment	NMR dat	afile		
				on		Analog of HS38.				
		LCMS datafile								
		yes								
		-	1							
103.	HS-100092-01	chemical registr	у							
		registry id	mol wt	formula	da	date		SMILES		
		HS-100092-01	315.352	S1O2N5C14H13	20	2012-08-15		S(C(C)C(N)=O)c1nc2n(c3ccccc3)ncc2c([nH]1)=O		
	O 	chirality	origin	chemist	nc	otebook		salt form		
			Internal synthesis	Dave Carlson	00	02DAC056_2		None: Free base		
		amount available	program	primary target	pe	ercent purity		elemental analysis		
		0.017	Purine_inhib		95	5-100				
	ö	melting point	NMR data	LCMS data	со	comment		NMR datafile		
				on	Ar	Analog of HS38. ZIPK inhibitor.				
	_	LCMS datafile								
		yes								
	UE 400002 04	obamical registry								
104.	H3-100093-01	registry id	molwt	formula		date		SMILES		
		HS-100093-01	301 326	S102N5C13H11		2012-08-15		S(CC(N)=0)c1nc2n(c3ccccc3)ncc2c([nH]1)=0		
	Q	chirality	origin	chemist	r	notebook		salt form		
	~		Internal synthesis	Dave Carlson	0	002DAC056 3		None: Free base		
		amount available	program	primary target	r	percent purity		elemental analysis		
	N N S N	0.017	Purine inhib			95-100				
	o o	melting point	NMR data	LCMS data	6	comment		NMR datafile		
				on	Ā	Analog of HS38. ZIPK	inhibitor.			
		LCMS datafile								
		yes								
								•		
105.	HS-100094-01	chemical registr	У							
		registry id	mol wt	formula	date	e		SMILES		
	0	HS-100094-01	329.379	S1O2N5C15H15	201	12-08-15		S(C(C)(C)C(N)=O)c1nc2n(c3ccccc3)ncc2c([nH]1)=O		
	Ĭ	chirality	origin	chemist	note	ebook		salt form		
	N N		Internal synthesis	Dave Carlson	002	2DAC056_4		None: Free base		
		amount available	program	primary target	per	cent purity		elemental analysis		
		U.U16	Purine_inhib	LONG data	95-	TUU		NMD detectio		
		meiung point			con		hihitor			
		LCMS dotafile			Ana	aioy ul 11338. ZIPK IN	monor.			
		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			
	O II	chirality	origin	chemist	notebook	salt form			
			Internal synthesis	Dave Carlson	002DAC056_5	None: Free base			
	N I I N	amount available	program	primary target	percent purity	elemental analysis			
	N N S	0.016	Purine_inhib		95-100				
	, Ö	melting point	NMR data	LCMS data	comment	NMR datafile			
				on	Analog of HS38. ZIPK inhibitor.				
		LCMS datafile							
		yes							
		-							

## 107. **HS-100096-01**



ch	chemical registry							
registry	registry id mol wt formula date :		date	SMILES				
HS-10	10096-01	1077.340	S1O14N8C52H84	2012-09-27	S1C(C2NC(=0)NC2C1)CCCCC(=0)NCCCCCCCCCC(=0)NCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC			
chiralit	ty	origin	chemist	notebook	salt form			
(2S;3S	S;8R;}	Internal synthesis	Philip Hughes	PFH-003-074A	None: Free base			
amoun	nt available	program	primary target	percent purity	elemental analysis			
0.011		Purine_inhib		95-100				
melting	g point	NMR data	LCMS data	comment	NMR datafie			
			an	See chemist for sample				
LCMS	i datafile							
yes								

## 108. **HS-100096-02**



	chemical	chemical registry							
	registry id	mol wt	formula	date	SMILES				
	HS-100096-02	1077.340	S1014N8C52H84	2014-06-11	S1C(C2NC(=0)NC2C1)CCCCC(=0)NCC00CC0CC0CCCC(=0)NCCC00CC0CC0CC0CCCCAc3c(ccc(n4nc(c5c4CC)(CC5=0)(C)C)C)C(=3)C(=0)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 datafie				
			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									
ves									

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									

11.	HS-100099-01	chemical registry					
		registry id	mol wt	formula	date	SMILES	
		HS-100099-01	941.852	11O10N5C44H56	2012-12-03	lc1c(n2nc(c3e2CC(CC3=0)(C)C)C)cc(c(c1)C(=0)N)NCCCOCCOCCOCCOCCOCCOCCOCCOCCOCCOCCOCCOCC	
		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	
	I A COCN DO	0.013	Purine_inhib		95-100		
		melting point	NMR data	LCMS data	comment	NMR datafile	
	N O			on	lodine position is speculative; based on lack of eluting power		
		LCMS datafile					
		yes					
			•	•		•	

# 112. **HS-100100-01**

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chemical	registry			
registry id	mol wt	formula	date	SMILES
HS-100100-01	1067.748	12O10N5C44H55	2012-12-03	lc1c(n2nc(c3c2CC(C(l)C3=0)(C)C)C)cc(c(c1)C(=0)N)NCCCOCCOCCOCCOCCOCCOCCOCCOCCOCC(=0)c4ccc(cc4)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5cccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5ccc(cc5)Oc5cccc(cc5)Oc5cccccccccc
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	lodine positions are speculative; based on lack of Hsp90 eluting power	
LCMS datafile				
yes				

## 113. **HS-100101-01**

chemical regis	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)C)C)C)C)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**

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	cnemical	registry			
	registry id	mal wt	formula	date	SMILES
	HS-100103-01	941.852	11O10N5C44H56	2012-12-20	lc1c(ccc(c1)Oc2ccc(cc2)C(=O)NCCCOCCOCCOCCOCCCCNc3c(ccc(n4nc(c5c4CC(CC5=0)(C)C)C)C)C)C)C(=O)N)O
	chirality	origin	chemist	notebook	salt form
		Internal synthesis	Philip Hughes	PFH-004-016A	None: Free base
0	amount available	program	primary target	percent purity	elemental analysis
1 Vo	0.046	Purine_inhib		95-100	
$\square$	melting point	NMR data	LCMS data	comment	NMR datafie
. 0				lodine position is speculative; made under basic conditions and different from 100099.	
	LCMS datafile				

116	HS-100104-01	chemical r	egistry	1						
110.		registry id	mol wt	formula	date				SMILES	
		HS-100104-01	1067 748	120100504485	5 2012-12-20				InteleterintiOn2ee	
		10-100104-01	1007.140	Lonatoria	2012-12-20				in releterer journe	
		chirality	origin	chemist	notebook				salt form	
	o, (°)		Internal synthes	is Philip Hughes	PFH-004-0	16B			None: Free base	
		amount available	program	primary target	percent put	ity			elemental analysis	
		0.023	Purine_inhib		95-100					
		melting point	NMR data	LCMS data	comment				NMR datafile	
	N <sup>EO</sup> I O									
			an	an	lodine posr	ion are speculat	ive; made under basic condit	ions.	yes	
		LCMS datafile								
		yes								
117.	HS-100105-01	chemical r	egistry	1						
		registry id	mo	wt	formula		date		SM	ILES
	, O	HS-100105-01	492	2.547	S106N2C	26H24	2013-01-17		S=0	C(Nc1cc2c(cc1)C3(OC2=O)c4c(cc(cc4)O)Oc5cc(ccc35)O)NCCCOCC
		chirality	orio	in	chemist		notebook		salt	form
			Inte	rnal synthesis	Philip Hug	has	PEH-004-0224		Nor	ne: Free hase
	u ≥o ∕o			anidi synulesis	r niip riug		FTTF-004-022A			
		amount availabl	e pro	gram	primary ta	gei	percent punty		eler	nentai anaiysis
	s 🚺	0.062	Pu	ine_inhib			95-100			
	N O	melting point	NN	R data	LCMS dat	a	comment		NM	R datafile
	∕_N				on		non targeted flu	orescein ana	log	
	$\langle \rangle$	LCMS datafile								
	<u> </u>	yes								
118	HS-100106-01	chemical r	egistry	1						
110.		registry id		mol wt		form	ula	date		SMILES
		HS-100106	-01	338 472		S1N	4C19H22	2013-02-	08	s1c2pcpc(c2c(c1C)C)NC3CN(Cc4ccccc4)CC3
	_NS	HS-100106-01		origin		S1N4C19H22 2		2013-02-00		
		chirality				Chemist r				
	N			Internal synthesi		Philip Hughes		PFH-004-033B		C: IsOH
	~ .N	amount available		program		prim	primary target p		ourity	elemental analysis
	$\langle \gamma$	3.51		Purine_inhib		9		95-100		
	N N	melting poir	nt	NMR data		LCMS data d		comment		NMR datafile
								Racemic	; TsOH sa	lt
		LCMS data	file							
110	HS-100106-02	chemical r	egistry	1						
115.		registry id		mol wt		form	ula	date		SMILES
		HS-100106	-02	338 /72		S1N	/∩10H22	2015-06-	25	
	N S	abiaslity	02	000.472				2010 00	20	
		chirality		ongin		chen	nist	notebook		
	N			Internal s	yntnesis	Philip	p Hugnes	PFH-007	-034A	C: ISOH
	~ . <sup> </sup> \	amount ava	ailable	program		prim	ary target	percent p	ourity	elemental analysis
	$\langle \uparrow$	3.7		Purine_ir	hib			95-100		
	N N	melting poir	nt	NMR dat	a	LCM	IS data	comment		NMR datafile
	$\langle \rangle$					on		Racemic	; TsOH sa	alt
		LCMS data	file							
		yes								
				_		_				
120	HS-100107-01	chemical r	egistry	1						
120.		registry id		mol wt	1	ormula	1	date		SMILES
		HS-100107	·-01	364.809		CI1S1C	3N4C15H13	3 2013-0	2-18	C c1c(n2ncc3c(=O)[nH]c(nc23)SC(C(=O)OC)C)cccc1
	-	chirality		origin		hemist	+	notebo	lok	salt form
	0 	ormanty		Internal cy	athonic I		arlson		C070_1	None: Free base
	N <sup>H</sup>			internal sy		Jave C		00204		
	N L O	amount ava	allable	program		orimary	larget	percen	it purity	
		0.050		Purine_inh	d			95-100	)	
	o o	melting poir	nt	NMR data	I	_CMS o	data	comme	ent	NMR datafile
					(	on		Analog	of HS38	
		LCMS data	file							

July 17, 2015, 3:46 pm

									Ŭ
121.	HS-100108-01	chemical reg	listry					1.	
		registry id	m	iol wt		formula		date	SMILES
	o	HS-100108-0	1 32	22.772	2	CI1S102N40	13H11	2013-02-19	Clc1c(n2ncc3c(=O)[nH]c(nc23)SCCO)cccc1
	Ĵн	chirality	or	rigin		chemist		notebook	salt form
	N <sup>-</sup>		In	iternal	synthesis	Dave Carlson		002DAC071_1	None: Free base
		amount availa	able pr	rogram	1	primary targe	t	percent purity	elemental analysis
		0.020	Pi	urine_	inhib			95-100	
	H <sup>O</sup>	melting point	N	MR da	ata	LCMS data		comment	NMR datafile
						on			
		LCMS datafile	e						
		chemical rec	lietry						
122.	HS-100109-01	registry id	jisti y	ol wt		formula		date	SMILES
		HS-100100-0	1 33	36 700	1		1/113	2013-02-19	
	<b>O</b>	chirality		igin	·	chemist	141113	notebook	salt form
	~ H	Crintanty	Int	ternal	synthesis	Dave Carlson			None: Free base
	N N	amount avails		oaram	Synthesis	primary target		percent purity	
		0.020		urine i	' inhih			95-100	
		melting point		MR da	ita	LCMS data		comment	NMR datafile
	/~``o				ita			Comment	
		LCMS datafile	<u></u>						
			-						
123.	HS-100110-01	chemical reg	jistry						
		registry id	mc	ol wt		formula		date	SMILES
	-	HS-100110-0	1 36	6.825		CI1S1O3N4C1	5H15	2013-02-19	Clc1c(n2ncc3c(=O)[nH]c(nc23)SCCOCCO)cccc1
	<b>O</b>	chirality	ori	igin		chemist	1	notebook	salt form
	N H		Inte	ernal s	synthesis	Dave Carlson	(	002DAC071_3	None: Free base
	N I I	amount availa	able pro	ogram		primary target	1	percent purity	elemental analysis
	CĮ N <sup>×</sup> N <sup>×</sup> S <sup>×</sup>	0.020	Pu	ırine_ir	nhib		9	95-100	
	H O	melting point	NN	VIR dat	ta	LCMS data		comment	NMR datafile
						on			
		LCMS datafile	e						
124.	HS-100111-01	cnemical reg	listry					0.00	
		registry id	moi wt	torn				SMILES	
		HS-100111-01	833./5/	aho	mint	2013-02-22		acit form	CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
	o (° )	crimanty	Internal synthesi	is Phil	lin Hughes	PEH-004-027A		None: Free base	
		amount available	program	no rin	non/tores	percent purity		elemental analysis	
		0.0103	Purine inhib	pin	naly talget	25-100		elemental analysis	
		melting point	NMR data	10	MS data	comment		NMR datafile	
	)⊨o	notang point	data a	00	ino dutu	Made up as 10 mM and give	n to Jared	Thirt datance	
		LCMS datafile							
		ves							
125.	HS-100111-02	chemical reg	jistry						
		registry id	mol wt		formula	date	SMILES		
		HS-100111-02	833.757		1108N5C38H	52 2013-06-18	lc1cc(ccc1	1)C(=O)NCCCOCCOCC	COCCOCCOCCCNc2c(ccc(n3nc(c4c3CC(CC4=O)(C)C)C)c2)C(=O)N
		chirality	origin		chemist	notebook	salt form		
	o ()		Internal syr	nthesis	Philip Hughes	PFH-004-069A	None: Free	e base	
		amount available	program		primary target	percent purity	elemental	analysis	
	jo n l	0.0198	Purine_inhi	ib		95-100			
		melting point	NMR data		LCMS data	comment	NMR data	file	
	N~U				on				

LCMS datafile

6.	HS-100112-01	chemical	registry									
		registry id		mol wt		formula		date		SMILES		
		HS-10011	2-01	349.797		CI1S10	2N5C14H12	2013-0	2-26	Clc1c(n2	ncc3c(=O)[nH]c(nc23)SC(C(=O)N)C)cccc1	
	0	chirality		origin d		chemist		notebo	ok	salt form		
	N <sup>H</sup>			Internal synthesis		Dave Carlson		002DA	C070_2	0_2 None: Free base		
		amount av	/ailable	program		primary	target	percent	t purity	y elemental analysis		
		0.048		Purine_inhib				95-100				
	) –  Ö	melting point		NMR data		LCMS d	lata	comme	ent	NMR datafile		
						on		Analog	of HS38			
		LCMS datafile										
7.	HS-100113-01	chemical	registry									
		registry id	mol wt	formula	date		SMILES					
		HS-100113-01	1209.156	I1S1O12N6C59H65	2013-03-2	17	lc1cc(ccc1)CN(C(=S)Nc2o	c3c(cc2)C4(OC3=C	0)c5c(cc(cc5)O)Oc6cc(c	cc46)O)CCCOCCOCC	COCCOCCCNc7c(ccc(n8nc(c9c8CC(CC9=O)(C)C)C)c7)C(=O)N	
	O	chirality	origin	chemist	notebook		salt form					
			Internal synthesis	Philip Hughes	PFH-004-	038A	None: Free base					
		amount available	program	primary target	percent pr	arity	elemental analysis					
		0.028	Purine_inhib		95-100							
	VN' CO V	melting point	NMR data	LCMS data	comment		NMR datafile	MR datafile				
	N <sub>⊭O</sub> I			on	See chem	ist for sample						
		LCMS datafile										
		yes										
_	US 400144.04	chemical	rogistry									
8.	HS-100114-01	registry id mol wt	formula	date		SMILES						
		HS-100114-01 1846 F	43 CI185E10	22N8C88 2013-03-27		Cictorea	(c1)Nc2ncnc3ccc(c4oc(cc4)CN(	CCS(=0)(=0)C)CC	CNCCCOCCOCCOCC	OCCOCCCNC(=O)CCC		
		chirality origin	chemist	notebook		salt form	salt form					
	8, 0	Interna	I synthe Philip Hug	hes PFH-004-047A	-047A Nor		one: Fire base					
		amount availal progra	m primary ta	get percent purity	elemr		mental analysis					
		0.002 Purine	inhib Her2	95-100								
		melting point NMR of	iata LCMS dat	95-100		NMR data	afile					
			on	Maybe a Hunig's bas	e salt. See ch	iemist						
		LCMS datafile										
		yes										
			I									
9.	HS-100115-01	chemical	registry									
		registry id		mol wt		fo	ormula	d	ate		SMILES	
		HS-10011	5-01	333.167		ľ	1O2N1C12H1	6 2	013-06-11		Ic1cc(ccc1)C(=O)NCCCOCC	
	0	chirality		origin		c	chemist	n	otebook		salt form	
	Ĩ Î			Internal sy	nthesi	s F	Philip Hughes	P	PFH-004-0	65A	None: Free base	
		amount av	/ailable	program		р	primary target	р	ercent pur	ity	elemental analysis	
		0.114		Purine_inh	ib			9	5-100			
		melting po	pint	NMR data		L	CMS data	C	omment		NMR datafile	
	<b>o</b>					0	on	g	ave 4 mg	to Ganesa	an	
		LCMS dat	afile									
		yes										
0.	HS-100116-01	chemical	registry	and suit								
		registry id	0.04			Tormula	a	date	C 44		SMILES	
		HS-10011	b-01	310.011		Sn102	ZIN1C15H25	2013-0	<b>1</b> 7-0			

N Sn
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yes								
chemical registry								
registry id	egistry id mol wt		ula	date		SMILES		
HS-100116-01	370.077	Sn10	O2N1C15H25	2013	-06-11	Sn(c1c	c(ccc1)C(=O)NCCCOCC)(C)(C)C	
chirality	origin	chen	nist	note	book	salt form		
	Internal synthesis	Phili	p Hughes	PFH	-004-066A	None: Free base		
amount available	program	prim	ary target	perc	ent purity	elemer	ntal analysis	
0.174	Purine_inhib			95-100				
melting point	NMR data	LCM	IS data	com	ment	NMR d	atafile	
				gave 21 mg to Ganesan				
LCMS datafile	LCMS datafile							
yes								

131.	HS-100117-01	chemica	al registr	у		
		registry id	mol wt	formula	date	SMILES
		HS-100117-01	1384.793	S2O13N7C76H101	2013-09-04	S(=0)(=0)([0-](CCCC(N+1)=C(C-CC2+C(C(=CC=C2N(cdc(cccc4)C3(C)C)CCCCS(=0)(=0)(0)(C)CC2)cfacct(cc5)CNCCC0CC0CC0CC0CC0CC0CC0CC0CCC0CCC0+0)(C)(C)(C)(C)(C)(C)(C)(C)(C)(C)(C)(C)(C)
	S S	chirality	ongin	chemist	notebook	satiom
			Internal synthesis	Philip Hughes	PFH-005-003B	None: Free base
		amount available	program	primary target	percent purity	elemental analysis
	MO NON	0.031	Purine_inhib		95-100	
	N <sup>EO</sup> O N <sup>†</sup>	melting point	NMR data	LCMS data	comment	NMR datatie
		LCMS datafile				
l						
100	HS-100117-02	chemic	al registr	v		
132.	113-100117-02			, 		
		registry id	moiwt	tormula	date	SMILES
		HS-100117-02	1384.793	S2O13N7C76H101	2013-09-13	S(=0)(=0)([0-])CCCC(N+]1=C(C=CC2=C(C(=CC=C3N(cdc(cccc4)C3(C)C)CCCCS(=0)(=0)0)CCC2)cfccc(cc5)CNCCC0CC0CC0CC0CCCCCdcfcccc(n7nc(cdc7CC(CC8=0)(C)C)C)C)c5)C(=0)N)C(cdc1cccc4)C3(C)CCC2)cfccc(cc5)CNCCC0CC0CC0CC0CC0CC0CC0CCCCdcfcccc(n7nc(cdc7CC(CC8=0)(C)C)C)C)C)C2)cfccc(cc5)CNCCC0CC0CC0CC0CC0CC0CC0CC0CC0CCCCCCC0CC0
	0	chirality	origin	chemist	notebook	salt form
	©o°o		Internal synthesis	Philip Hughes	PFH-005-003C	None: Free base
		amount available	program	nrimany target	percent purity	alamanhi anabair
	KINO O NAL		program	printing target	percent party	Sourcement week and
		0.050	Purine_inhib		95-100	
		melting point	NMR data	LCMS data	comment	NMR datafie
	0+			on		yes
		LCMS datafile				
		yes				
133.	HS-100117-03	chemic	al registr	у		
		registry id	mol wt	formula	date	SMILES
		HS-100117-03	1384.793	S2O13N7C76H101	2014-03-12	S(=0)(=0)([0-])CCCC(N+]1=C(C=CC2=C(C(=CC=C3N(c4c(cccc4)C3(C)C)CCCCS(=0)(=0)0)CCC2)cdccc(ccb)CNCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
		chirality	origin	chemist	notebook	salt form
	0 <sub>0</sub> 0					
	° , o → ↓N / → 0		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 dutafile
	N CH				See Chemist for s	male
	N OH				See Chemist for s	mple
	N OH	LCMS datafile			See Chemist for s	npe
	N OH	LCMS datafile			See Chemist for s	mpb            Image: Image
	N GA	LCMS datafile			See Chemist for s	npe
134.	N GH HS-100118-01	LCMS datafile	al registr	y	See Chemist for s	mpie
134.	N GH HS-100118-01	LCMS datafile	al registr	<b>y</b> formula	date	mpia
134.	N GH HS-100118-01	LCMS datafile Chemics registry id HS-100118-01	al registr	y formula S2013N/CR4H105	date :	Imple         Imple
134.	N GH HS-100118-01	LCMS datafile Chemica registry id HS-100118-01	al registr mol wt 1484.911	formula S2013N7C84H105	date 2 2013-10-01	npie
134.	HS-100118-01	LCMS datafile Chemics registry id HS-100118-01 chirality	mol wt 1484.911 origin	formula S2013N7C84H105 chemist	See Chemist for a date : 2013-10-01 : notebook :	npie
134.	HS-100118-01	LCMS datafile Chemics registry id HS-100118-01 chirality	mol wt 1484.911 origin Internal synthesis	formula S2013N7C84H106 chemist Philip Hughes (	See Chemist for a           date         3           2013-10-01         2           notebook         1           PFH-005-007B         1	mpie
134.	HS-100118-01	LCMS datafile Chemics registry id HS-100118-01 chirality amount available	mol wt 1484.911 origin Internal synthesis program	formula S2013N7C84H106 chemist Philip Hughes primary target	See Chemist for at date date 2013-10-01 2 PFH-005-007B 2 percent purity 4	mpbe
134.	HS-100118-01 (1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0	LCMS datafile  Chemics registry id HS-100118-01 chirality amount available 0.074	al registr mol wt 1484911 origin internal synthesis program Purire_inhib	y formula S2O13N7C84H106 chemist Philip Hughes primary target	See Chemist for 1           date         2           2013-10-01         2           notebook         2           PFH-005-007B         1           percent purify         4           95-100         2	mpie
134.	HS-100118-01 $\begin{array}{c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & $	LCMS detaile	Internal synthesis Portre_invibil	y tomula S2013N/C64H06 chamist 4 phisp hughes p	See Chemistor of date 2 2013-10-01 2 2013-00-01 2 2013-00-01 2013-00-01 2013-00-01 2013-00-01 2013-00-01 2013-00-01 2013-00-01 2013-00-01 2013-00-01 2013-00-01 2013-00-01 2013-00-01 2013-00-01 2013-00-01 2013-00-01 2013-00-00-00-00-00-00-00-00-00-00-00-00-00	mpie
134.	HS-100118-01	LCMS statile  Chemic: registry id INS-100118-01 chratity  amount available 0.074 metting pont	Internal synthesis program Purine_inhib NMR data	Iomida 8 S2013h7C84H06 dhemist 6 phiap Hughes 1 phiap Hughes 1 LCMS dela 1	See Chemistor of anti- comment         2           James of anti- percent purity         2           PPH-055-007B         1           percent purity         2           95-100         2           comment         1	mpie
134.	HS-100118-01	LCMS statile  Chemic: registry id RS-100118-01 dviratity  amount available 0.074 metting point	Internal synthesis program Purineinhbit NMR data	formala S2013H7C84H105 dramitat phinay hangeta phinay hangeta LCMS data on	date Chemistor of date date data 2013-10-01 di notebook di PPH-005-00 di percent purity di 66-100 di comment di	mpie
134.	HS-100118-01	LCMS datalie  Chemic: regatry d HS-100116-01 chirally amount available 0.074 meting point LCMS datalie	nol vit 1484.911 origin program Purine_,nhb NMR data	binnan same S2013H7CB4H05 chamiat appinany target pinany target LCMS data appinany target con appinany target	See Chemistor it date i 2013-10-01 i 2013-10-01 i 2013-10-01 i 2013-10-01 i 30-00 96-100 i 96-100 i 96-1000 i 96-100 i 96-100 i 96-100 i 9	mpie
134.	HS-100118-01 $\begin{array}{c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & & \\ & & & & $	LCMS datalie  Chemic: registry id HS-100116-01 ditrally amount available 0.074 meting point LCMS datalie yes	nci vt 1484911 origin aprilational program Purine_,nhba Purine_,nhba I NMR data	formufa  S2013H7C84H105 chamita  Philp Hughes  primary target LCMS data  on	See Chemistor of antipage         I           date         I           2013-10-01         I           percent purtly         I           percent purtly         I           95-100         I           95	mpie
134.	HS-100118-01 $P_{N,0}^{(0)} = P_{N,0}^{(0)} =$	LCMS datafie  registry id  HS-100118-01  divially  amount available  0.074  meting point  LCMS datafie  yes	nol vt 1484.911 1484.911 Iridenal synthesis program Purine_inhib NMR data	formufa s S2013AVC84H105 chamiet of primary target LCMS data on on called a start of the start o	See Chemistor of date data and and and and and and and and and an	mpie Carlow Constraints of the Constraint of the
134.	HS-100118-01 $f_{N,0}^{0,0} = f_{N,0}^{0,0} $	LCMS datafie  Chemic: registry id HS-100116-01 divially amount available 0.074 metting point LCMS datafile yes Chemic;	nol vt 1484.911 orójn o program Purine_inhb NMR data	V form/a S2013AVC64H105 chanicit chanicit primary target primary target on construction on con	See Chemistor of date and 2013-10-01 [2] 2013-10-01 [2] 2013-10-01 [2] PF7+-005-070 [2] 965-100 [2]	mpie
134.	HS-100118-01 $f_{N,0}^{0,0} f_{N,0}^{0,0} f$	LCMS datafie	al registr nol ut 1484.911 internal synthesis program Purice_inhib NMR data	y formaa s S2013AVC&H106 chemiat c primary target LCMS data o on 1 LCMS data o on 1 LCMS data o on 1 LCMS data o to 1	See Chemistor of date i 2013-10-01 i 2013-10-01 i 2013-10-01 i PF7H-005-070 i 95-100 i 95-100 i 95-100 i 0 i 0 i 0 i 0 i 0 i 0 i 0 i	mpm         Image: Control (Control (Contro) (Contro) (Control (Contro) (Control (Contro) (Control (Contro
134.	HS-100118-01 $\varphi_{N} \circ \varphi_{N} \circ$	LCMS datafie  Chemic: registry id HS-100116-01 datafiy amount available 0.074 meting point LCMS datafie yes  Chemic: registry id	al registr mol ut 1484911 1484911 0 ningin 112 program 112 progra	y temula 2 S2013N7C84H06 chemat 2 Philip Hughes 2 primary target 2 LCMS data 2 on 2 CMS data 2 chemat	See Chemistor of University         I           Image: I	mpei
134.	HS-100118-01 $f_{N}^{0} \circ f_{0}^{0} \circ f_{$	LCMS datafile	Al registreament of the second		Bee Chemistor of a construction         I           Image: Image of a construction of a constructi	mpei
134.	HS-100118-01 $f_{N}^{0} \circ f_{0}^{0} = f_{N}^{0} \circ f_{0}^{0}$ $f_{N}^{0} \circ f_{0}^{0} = f_{N}^{0} \circ f_{0}^{0}$ $h_{0}^{0} \circ f_{0}^{0} = f_{0}^{0}$ HS-100118-02	LCMS datafile  registry id  iKS-10011B-01  divitality  amount available  0.074  metting point  LCMS datafile  yes  chemic: registry id  HS-10011B-02  divitality	Al registreament of the second		Bee Chemistor et         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I	mpei
134.	HS-100118-01 $HS-100118-01$ $HS-100118-02$ $HS-100118-02$	LCMS datafile  registry id  rs5100118-01  ditratity  amount available  0.074  metting point  LCMS datafile  yes  Chemic:  registry id  HS-100118-02  dituality	Interception           notation           1484.911           origin           Internal synthesis           program           Purina_sinhib           NMR data           Internal synthesis           Internal synthesis           Internal synthesis           Internal synthesis           Internal synthesis           Internal synthesis		Bee Chemistor et         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I	mpei
134.	HS-100118-01 HS-100118-01 HS-100118-02 HS-100118-02 $\varphi_{1} \varphi_{0}$	LCMS datafile  registry id  registry id	Al registre de la constant de la con		Bee Chemistor et         I           I         I           date         I           2013-10-01         I           notebook         I           PPFH-005-007B         I           26-100         I           Comment         I           Comment         I           2013-04-01         I           2015-04-01         I           PPFH-005-020A         I           PPFH-005-020A         I	mpine
134.	HS-100118-01 $HS-100118-02$ $HS-100118-02$	LCMS datalie  Chemic: regatry id R5-00116-01 chralby amount available 0.074 meting point LCMS datalie yes  Chemic: regatry id IS-100116-02 chralby amount available	Al registreament of the second	Inmaine State Stat	Bee Chemistor at         I           I         I           data         I           2013-10-01         I           notebook         I           9PH-005-021A         I           60-10         I           00-10         I           10-10         I	mpm         Image: Control (Control (Contro) (Control (Control (Contro) (Control (Control (Control (Contro
134.	HS-100118-01 $HS-100118-01$ $HS-100118-02$ $HS-100118-02$	LCMS datalie  Chemic: registry id HS-100116-01 ditrally amount available 0.074 meting point LCMS datalie yes  Chemic: registry id HS-100116-02 ditrally amount available 0.239	Al registreament of the second	Initial Salation of Control of Co	Bee Chemister is a fill of the second seco	mpm         Image: Control of Cont
134.	HS-100118-01 $HS-100118-01$ $HS-100118-02$ $HS-100118-02$ $HS-100118-02$	LCMS statile	Al registreament of the second	Initial States of States o	See Chemistor it         I           I         I           date         I           2013-10-01         I           notebook         I           percent purity         I           96-100         I           000000000000000000000000000000000000	member         Image: Control of C
134.	HS-100118-01 $HS-100118-01$ $HS-100118-02$ $HS-100118-02$ $HS-100118-02$	LCMS statile  Chemic: registry id I45-100118-01 divially amount available 0.074 meting point LCMS statile yes  Chemic: registry id I45-100118-02 divially amount available 0.229 meting point	Internitional       noi/wi       1484911       1484911       program       Purineinhib       NMR data       Internitional       noi/wi       Internitional       Purineinhib       Internitional       Internit		See Chemistor it         I           I         I           date         I           2013-10-01         I           notebook         I           percent purity         I           95-100         I           95-100         I           000000000000000000000000000000000000	memory
134.	HS-100118-01 $HS-100118-01$ $HS-100118-02$ $HS-100118-02$ $HS-100118-02$	LCMS datalie	al registre       mol wt       1484.911       origin       iderail synthess       program       Purice_inhib       NMR data       and       registre       internal synthess       program       internal synthess		See Chemistor it         I           I         I           I         I           2013-10-01         I           I         I           Instebook         I           PPT+005-002         I           I         I           Operant purity         I           I         I           Operant purity         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I <t< td=""><td>initial         initial           initial         &lt;</td></t<>	initial         initial           initial         <
134.	HS-100118-01 $HS-100118-01$ $HS-100118-02$ $HS-100118-02$	LCMS datafile registry id iNS-100118-01 distality amount available 0.074 metting point LCMS datafile yes chemotics registry id HS-100118-02 distality amount available 0.239 metting point LCMS datafile 0.239 metting point LCMS datafile 0.239 metting point	al registrest mol wit and		See Chemistor of U         I           I         I           I         I           2013-10-01         I           I         I           I         I           PPT-005-002         I           I         I           PERCENT purition         I           I         I           QUI-00-000         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I           I         I	menu

HS-100119-01	chemica										
	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(=	D)(=O)O)CCC2)e5ccc(cc5)C(=O)NCCCOCCOCCOCCOCCCCCRe8c(ccc(n7nc(c8c7CC(CC8=O)(C)C)C)c6)C(=O)N)C(c9c1cccc9)(C)C				
0	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						
TNO CON NO	0.036	Purine_inhib		95-100							
	melting point	NMR data	LCMS data	comment	NMR datafile						
N° CN		on	on	See PFH for sample	ves	yes					
ý.	LCMS datafile										
	June										
	,	L									
HS-100120-01	chemic	al regist	v								
	registry id	molwt	formula	date S	MILES						
	HS-100120-01	1498.894	S2O14N7C84H103	2013-10-10 S	(=0)(=0)([0-])CCCC[N+]1=C(C=CC2=C(C(=C	:C=C3N(c4c(c5c(cccc5)cc4)C3(C)C)CCC	25(=0)(=0)0)CCC2/e8ccc(cc8)C(=0)NCCC0CC0CC0CC0CC0CC0CC0c7c(ccc(n8nc(c9c8CC(CC9=0)(C)C)C)c7)C(=0)N)C(c1c1c1cross				
	chirality	origin	chemist	notebook si	alt form						
		Internal synthesis	Philip Hughes	PEH-005-010A N	nne: Free base						
$2/20$ $+$ $N^{-1}$	amount available	program	primary target	percent purity al	amantal analysis						
The of or the of	0.095	Projection	,	05 100							
	0.000		1010 100	30-100	10 400						
N°O O NT	menting point	NIMIR data	LCMS data	comment N	NIK Gatanie						
		on	on	See PEH for sample ye	85						
	LCMS datafile										
	yes										
HS-100121-01	chemic	al regist	v								
113-100121-01	registry	id	molwt		formula	date	SMILES				
	HS-100 <sup>-</sup>	121-01	364.80	9	CI1S1O3N4C15H1	13 2013-11-05	C[c1ccc(n2ncc3c(=0)[nH]c(nc23)SC(C(=0)OC)C)cc1				
<b>o</b>	chirality		origin	<u> </u>	chemist	notebook	salt form				
	chirality		Interna	Levnthesis	Dave Carlson		None: Free base				
N I N			nitemai synthesis		primary target	percent purity					
N N S	0.050	available	Purine inhib			95-100					
Ö	molting	point	NMR data			commont	NMP datafilo				
	menning			ala							
CI	LCMS d	latafilo									
	LONIO U	atame									
	<u>الــــــــــــــــــــــــــــــــــــ</u>										
110 400400 04	chomio	al registr	y								
HS-100122-01	chemica						SMILES				
HS-100122-01	registry	id	mol wt		formula	date	SMILES				
HS-100122-01	registry HS-100	id 122-01	mol wt 344.39	0	formula S1O3N4C16H16	date 2013-11-07	SMILES S(c1[nH]c(=O)c2c(n(nc2)c3c(cccc3)C)n1)C(C(=O)OC)C				
HS-100122-01	registry HS-100 <sup>2</sup> chirality	id 122-01	mol wt 344.39 origin	0	formula S1O3N4C16H16 chemist	date 2013-11-07 notebook	SMILES S(c1[nH]c(=O)c2c(n(nc2)c3c(cccc3)C)n1)C(C(=O)OC)C salt form				
O	registry HS-100 <sup>-</sup> chirality	id 122-01	mol wt 344.39 origin	0 I synthesis	formula S1O3N4C16H16 chemist Dave Carlson	date 2013-11-07 notebook 3DAC003_2	SMILES S(c1[nH]c(=O)c2c(n(nc2)c3c(cccc3)C)n1)C(C(=O)OC)C salt form None: Free base				
N N N	registry HS-100 <sup>-</sup> chirality	id 122-01	mol wt 344.39 origin Interna	0 I synthesis	formula S1O3N4C16H16 chemist Dave Carlson	date 2013-11-07 notebook 3DAC003_2 percent purity	SMILES S(c1[nH]c(=O)c2c(n(nc2)c3c(cccc3)C)n1)C(C(=O)OC)C salt form None: Free base elemental analysis				
	registry HS-100 <sup>-</sup> chirality amount 0.050	id 122-01 available	mol wt 344.39 origin Interna program	0 I synthesis m inhib	formula S1O3N4C16H16 chemist Dave Carlson primary target DAPK/PIM3	date 2013-11-07 notebook 3DAC003_2 percent purity 95-100	SMILES S(c1[nH]c(=O)c2c(n(nc2)c3c(cccc3)C)n1)C(C(=O)OC)C salt form None: Free base elemental analysis				
	registry HS-100 chirality amount 0.050	id 122-01 available	mol wt 344.39 origin Interna program Purine	0 Il synthesis m _inhib ata	formula S1O3N4C16H16 chemist Dave Carlson primary target DAPK/PIM3 LCMS data	date 2013-11-07 notebook 3DAC003_2 percent purity 95-100	SMILES S(c1[nH]c(=O)c2c(n(nc2)c3c(cccc3)C)n1)C(C(=O)OC)C salt form None: Free base elemental analysis				
	registry HS-100 chirality amount 0.050 melting	id 122-01 available point	mol wt 344.39 origin Interna progra Purine NMR d	0 I synthesis m _inhib lata	formula S1O3N4C16H16 chemist Dave Carlson primary target DAPK/PIM3 LCMS data on	date 2013-11-07 notebook 3DAC003_2 percent purity 95-100 comment Apalog of HS38	SMILES S(c1[nH]c(=O)c2c(n(nc2)c3c(cccc3)C)n1)C(C(=O)OC)C salt form None: Free base elemental analysis NMR datafile				
	registry HS-100 <sup>-</sup> chirality amount 0.050 melting	id 122-01 available point	mol wt 344.39 origin Interna prograu Purine NMR d	0 Il synthesis m _inhib lata	formula S1O3N4C16H16 chemist Dave Carlson primary target DAPK/PIM3 LCMS data on	date 2013-11-07 notebook 3DAC003_2 percent purity 95-100 comment Analog of HS38	SMILES S(c1[nH]c(=O)c2c(n(nc2)c3c(cccc3)C)n1)C(C(=O)OC)C salt form None: Free base elemental analysis NMR datafile				
	registry HS-100 chirality amount 0.050 melting LCMS d	available	mol wt 344.39 origin Interna Purine NMR d	0 I synthesis m _inhib lata	formula S1O3N4C16H16 chemist Dave Carlson primary target DAPK/PIM3 LCMS data on	date 2013-11-07 notebook 3DAC003_2 percent purity 95-100 comment Analog of HS38	SMILES S(c1[nH]c(=O)c2c(n(nc2)c3c(cccc3)C)n1)C(C(=O)OC)C salt form None: Free base elemental analysis NMR datafile				
	registry HS-100 chirality amount 0.050 melting	available point latafile	mol wt 344.39 origin Interna program Purine, NMR d	0 Il synthesis m _inhib ata	formula S1O3N4C16H16 Chemist Dave Carlson primary target DAPK/PIM3 LCMS data on	date 2013-11-07 notebook 3DAC003_2 percent purity 95-100 comment Analog of HS38	SMILES S(c1[nH]c(=O)c2c(n(nc2)c3c(cccc3)C)n1)C(C(=O)OC)C salt form None: Free base elemental analysis NMR datafile				
HS-100122-01	registry HS-100 chirality amount 0.050 melting p LCMS d	available point latafile al registr	mol wt 344.39 origin Interna progra Purine NMR d	0 Il synthesis m _inhib lata	formula S1O3N4C16H16 Chemist Dave Carlson primary target DAPK/PIM3 LCMS data on	date 2013-11-07 notebook 3DAC003_2 percent purity 95-100 comment Analog of HS38	SMILES S(c1[nH]c(=O)c2c(n(nc2)c3c(cccc3)C)n1)C(C(=O)OC)C salt form None: Free base elemental analysis NMR datafile				
HS-100122-01	registry HS-100 chirality amount 0.050 melting LCMS d	available point latafile al registr	mol wt 344.39 344.39 344.39 origin Interna program program Purine, NMR d	0 Il synthesis m _inhib lata	formula S1O3N4C16H16 chemist Dave Carlson primary target DAPK/PIM3 LCMS data on	date 2013-11-07 notebook 3DAC003_2 percent purity 95-100 comment Analog of HS38 Analog of HS38	SMILES S(c1[nH]c(=O)c2c(n(nc2)c3c(cccc3)C)n1)C(C(=O)OC)C salt form None: Free base elemental analysis NMR datafile SMILES				
HS-100122-01	chemic registry HS-100 chirality amount 0.050 melting LCMS d chemic registry HS-100 <sup>-</sup>	available point latafile al registr id 123-01	mol wt 344.39 344.39 344.39 origin Interna program Purine, NMR d	0 Il synthesis m inhib lata 0	formula S1O3N4C16H16 chemist Dave Carlson primary target DAPK/PIM3 LCMS data on 	date 2013-11-07 notebook 3DAC003_2 percent purity 95-100 comment Analog of HS38 Analog of HS38 date 2013-11-07	SMILES           S(c1[nH]c(=O)c2c(n(nc2)c3c(cccc3)C)n1)C(C(=O)OC)C           salt form           None: Free base           elemental analysis           NMR datafile           SMILES           SMILES           SC(1[nH]c(=O)c2c(n(nc2)c3cc(ccc3)C)n1)C(C(=O)OC)C				
HS-100122-01 N $N$ $N$ $N$ $S$ $OHS-100123-01$	chemic registry HS-100 chirality amount 0.050 melting LCMS d LCMS d chemic registry HS-100 chirality	available point latafile al registr id 122-01	mol wt 344.39 344.39 344.39 origin Interna Program Purine, NMR d NMR d 2 74 74 74 74 74 74 74 74 74 74 74 74 74	0 Il synthesis m inhib lata 0	formula S1O3N4C16H16 chemist Dave Carlson primary target DAPK/PIM3 LCMS data on 	date 2013-11-07 notebook 3DAC003_2 percent purity 95-100 comment Analog of HS38 Analog of HS38 date 2013-11-07 notebook	SMILES           S(c1[nH]c(=O)c2c(n(nc2)c3c(cccc3)C)n1)C(C(=O)OC)C           salt form           None: Free base           elemental analysis           Image: Simple state				
HS-100122-01 N $N$ $N$ $N$ $S$ $OHS-100123-01N$ $O$	chemica registry HS-100 chirality amount 0.050 melting LCMS d LCMS d chemica registry HS-100 chirality	available point latafile al registr id 122-01	mol wt 344.39 origin Interna NMR d NMR d States Sta	0 Il synthesis m _inhib lata 0 0	formula S1O3N4C16H16 chemist Dave Carlson primary target DAPK/PIM3 LCMS data on chemist formula S1O3N4C16H16 chemist Dave Carlson	date 2013-11-07 notebook 3DAC003_2 percent purity 95-100 comment Analog of HS38 Analog of HS38 date 2013-11-07 notebook 3DAC003_3	SMILES           S(c1[nH]c(=O)c2c(n(nc2)c3c(cccc3)C)n1)C(C(=O)OC)C           salt form           None: Free base           elemental analysis           NMR datafile           SMILES           S(c1[nH]c(=O)c2c(n(nc2)c3cc(ccc3)C)n1)C(C(=O)OC)C           salt form           None: Free base				
HS-100122-01 N N N N N N N N	chemica registry HS-100 chirality amount 0.050 melting LCMS d chemica registry HS-100 chirality amount	available point latafile al registr id 123-01 available	mol wt 344.39 344.39 origin Interna Program Purine, NMR d NMR d 344.39 77 77 77 77 77 77 77 77 77 77 77 77 77	0 Il synthesis m inhib lata 0 0 Il synthesis m	formula S1O3N4C16H16 chemist Dave Carlson primary target DAPK/PIM3 LCMS data on chemist S1O3N4C16H16 chemist Dave Carlson primary target	date 2013-11-07 notebook 3DAC003_2 percent purity 95-100 comment Analog of HS38 Analog of HS38 date 2013-11-07 notebook 3DAC003_3 percent purity	SMILES S(c1[nH]c(=O)c2c(n(nc2)c3c(cccc3)C)n1)C(C(=O)OC)C salt form None: Free base elemental analysis NMR datafile NMR datafile SMILES S(c1[nH]c(=O)c2c(n(nc2)c3cc(ccc3)C)n1)C(C(=O)OC)C salt form None: Free base elemental analysis				
HS-100122-01 N N N N N N N N	chemica registry HS-100 chirality amount 0.050 melting LCMS d chemica registry HS-100 chirality amount 0.050	available point atafile al registr id 122-01 available	mol wt       344.39       origin       Interna       program       Purine,       NMR d       Mol wt       344.39       origin       Interna       June       Write,       Interna       Interna       Interna       Interna       Interna       Interna       Program       Purine,       Purine,	0 Il synthesis m inhib lata 0 0 Il synthesis m inhib	formula S1O3N4C16H16 Chemist Dave Carlson primary target DAPK/PIM3 LCMS data on CMS data on S1O3N4C16H16 Chemist Dave Carlson primary target DAPK/PIM3	date 2013-11-07 notebook 3DAC003_2 percent purity 95-100 comment Analog of HS38 4 2013-11-07 notebook 3DAC003_3 percent purity 95-100	SMILES S(c1[nH]c(=O)c2c(n(nc2)c3c(cccc3)C)n1)C(C(=O)OC)C salt form None: Free base elemental analysis NMR datafile SMILES S(c1[nH]c(=O)c2c(n(nc2)c3cc(ccc3)C)n1)C(C(=O)OC)C salt form None: Free base elemental analysis				
HS-100122-01 N N N N N N N N	chemic registry HS-100 chirality amount 0.050 melting LCMS d chemica registry HS-100 chirality amount 0.050 melting	available point latafile al registr id 123-01 available point	mol wt       344.39       origin       Interna       program       Purine,       NMR d       Interna       mol wt       Mol wt       344.39       origin       Interna       program       Interna       Purine,       NMR d       NMR d       NMR d	0 I synthesis m _inhib ata 0 0 I synthesis m _inhib ata	formula S1O3N4C16H16 Chemist Dave Carlson primary target DAPK/PIM3 LCMS data on CMS data on S1O3N4C16H16 Chemist Dave Carlson primary target DAPK/PIM3 LCMS data	date 2013-11-07 notebook 3DAC003_2 percent purity 95-100 comment Analog of HS38 Analog of HS38 date 2013-11-07 notebook 3DAC003_3 percent purity 95-100 comment	SMILES S(c1[nH]c(=O)c2c(n(nc2)c3c(ccc3)C)n1)C(C(=O)OC)C salt form None: Free base elemental analysis NMR datafile SMILES S(c1[nH]c(=O)c2c(n(nc2)c3cc(ccc3)C)n1)C(C(=O)OC)C salt form None: Free base elemental analysis NMR datafile				
HS-100122-01 N N N N N N N N	chemic registry HS-100 chirality amount 0.050 melting LCMS d chemica registry HS-100 <sup>-</sup> chirality amount 0.050 melting	available point latafile al registr id 123-01 available point	mol wt 344.39 origin Interna Program Purine, NMR d Status V Status	0 I synthesis m _inhib lata 0 I synthesis m _inhib lata	formula S1O3N4C16H16 Chemist Dave Carlson primary target DAPK/PIM3 LCMS data on Con S1O3N4C16H16 Chemist Dave Carlson primary target DAPK/PIM3 LCMS data on	date 2013-11-07 notebook 3DAC003_2 percent purity 95-100 comment Analog of HS38 7 4 4 2013-11-07 date 2013-11-07 date 2013-11-07 someok 3DAC003_3 percent purity 95-100 comment Analog of HS38	SMILES S(c1[nH]c(=O)c2c(n(nc2)c3c(cccc3)C)n1)C(C(=O)OC)C salt form None: Free base elemental analysis NMR datafile SMILES S(c1[nH]c(=O)c2c(n(nc2)c3cc(ccc3)C)n1)C(C(=O)OC)C salt form None: Free base elemental analysis NMR datafile				
HS-100122-01 N $N$ $N$ $N$ $S$ $0HS-100123-01HS-100123-01N$ $N$ $N$ $S$ $00$	chemic registry HS-100 chirality amount 0.050 melting LCMS d chemica registry HS-100 <sup>-</sup> chirality amount 0.050 melting	available point latafile al registr id 123-01 available point latafile	mol wt 344.39 origin Interna Progra Purine NMR d S S S S S S S S S S S S S S S S S S S	0 I synthesis m _inhib lata 0 0 I synthesis m _inhib lata	formula S1O3N4C16H16 Chemist Dave Carlson primary target DAPK/PIM3 LCMS data on S1O3N4C16H16 Chemist Dave Carlson primary target DAPK/PIM3 LCMS data on	date 2013-11-07 notebook 3DAC003_2 percent purity 95-100 comment Analog of HS38 4 2013-11-07 date 2013-11-07 date 2013-11-07 somet 3DAC003_3 percent purity 95-100 comment Analog of HS38	SMILES S(c1[nH]c(=O)c2c(n(nc2)c3c(ccc3)C)n1)C(C(=O)OC)C salt form None: Free base elemental analysis NMR datafile SMILES S(c1[nH]c(=O)c2c(n(nc2)c3cc(ccc3)C)n1)C(C(=O)OC)C salt form None: Free base elemental analysis INMR datafile NMR datafile				
	HS-100113-01 $ \begin{array}{c} \downarrow \\ N \\ $	HS-100113-01 $f(x) = 0$ $f(x)$	$HS-100113-01$ $\int_{N}^{1} \int_{0}^{1} \int_{0}^{1}$	$HS-100119-01 \qquad \qquad$	$HS-100119-01$ $\int_{V} \left( \int_{V} \int_{V$	$HS-100119-01$ $= \int_{0}^{1} \int_{0}^{$	HS-1001 (S-0)       HS-100 (S-0)				

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141.	HS-100124-01	chemical r	egistry								
		registry id	mol wt	formula	date	SMILES					
	. 0	HS-100124-01	884.203	S2O7N3C50H65	2013-11-11	S(=O)(=O)([O-])	cccc[	N+]1=C(C=CC2=C(C(=C	C=C3N(c4c(cccc4)C3(	C)C)CCCCS(=O)(=O)O)CCC2)c5ccc(cc5)CNCCCOCC)C(c6c1cccc6)(C)C	
		chirality	origin	chemist	notebook	salt form					
	N_N_		Internal synthe	esis Philip Hughes	PFH-005-030A	None: Free base	•				
	、	amount available	program	primary target	percent purity	elemental analys	eie				
		0.021	Purine inhih		95-100	,,					
		0.021				NND data file					
		meiting point	NIVIR data	LCMS data	comment	NMR datanie					
				on							
		LCMS datafile									
		yes									
ſ		ah amiaal r	a allatar								
142.	HS-100125-01	chemicari	egistry	an al cost	6			data		<u></u>	
		registry id		mol wt	form	nula	~	date	SMILES		
		HS-100125	5-01	296.347	S10	D3N4C12H1	6	2013-11-12	S(c1[nF	IJc(=O)c2c(n(nc2)C(C)C)n1)C(C(=O)OC)C	
	o	chirality		origin	che	mist		notebook	salt forr	n	
				Internal synthes	is Dav	e Carlson		3DAC004_1	None: F	ree base	
	N N	amount ava	ailable	program	prin	nary target		percent purity	elemen	al analysis	
	N N S	0.100		Purine_inhib	DAF	PK/PIM3		95-100			
		melting poi	nt	NMR data	LCN	//S data		comment	NMR da	atafile	
	$\mathbf{i}$				on			Analog of HS	38		
		LCMS data	file								
l											
143.	HS-100126-01	chemical r	egistry								
		registry id		nol wt	formul	a	dat	te	SMILES		
		HS-100126-01 36		60.390	S1O4	N4C16H16	20	13-11-12	S(c1[nH]c(=O)c2c(n(nc2)c3cc(ccc3)OC)n1)C(C(=O)OC		
	0	chirality or		origin	chemi	st	no	tebook	salt form		
				nternal synthesis	Dave	Carlson	3D	AC004_2	None: Free I	base	
	N N	amount available		orogram	primar	ry target	pe	rcent purity	elemental ar	nalysis	
		0.050 F		Purine_inhib	DAPK	/PIM3	95	-100			
	, <b>O</b>	melting poi	nt N	MR data	LCMS	data	coi	mment	NMR datafile	3	
	0				on	on		alog of HS38			
		LCMS data	file					-			
l						۱I					
144.	HS-100127-01	chemical r	egistry								
		registry id	n	nol wt	formul	a	dat	te	SMILES		
		HS-100127	'-01 3	60.390	S104	N4C16H16	20	13-11-12	S(c1[nH]c(=O)c2c(n(nc2)c3ccc(cc3)OC)n1)C(C(=O)OC)C		
	<b>O</b>	chirality	c	origin	chemi	st	no	tebook	salt form		
			1	nternal synthesis	Dave	Carlson	3D	AC004_3	None: Free I	base	
		amount ava	ailable p	orogram	primar	ry target	pe	rcent purity	elemental ar	nalysis	
		0.050	F	Purine_inhib	DAPK	/PIM3	95	-100			
		melting poi	nt N	MR data	LCMS	data	coi	mment	NMR datafile	9	
	$\succ$				on		An	alog of HS38			
	0	LCMS data	file					5			
l											
145.	HS-100128-01	chemical r	egistry								
		registry id	n	nol wt	formula	ı	date	e	SMILES		
	0	HS-100128-0	)1 3	55.373	\$103N	5C16H13	201	3-11-12	S(c1[nH]c(=O)	c2c(n(nc2)c3ccc(cc3)C#N)n1)C(C(=O)OC)C	
	Ĭ.	chirality	0	rigin	chemis	t	note	ebook	salt form		
			lı	nternal synthesis	Dave C	arlson	3D/	AC004_4	None: Free ba	Se	
	N N S N	amount avail	able p	rogram	primarv	r target	per	cent purity	elemental anal	ysis	
		0.050	F	Purine inhib	DAPK/	PIM3	95-	100			
		melting point	N	IMR data	LCMS	data	con	nment	NMR datafile		
	<u>۲</u>				on		Ana	alog of HS38			
	///	LCMS datafil	e					3			
	N		-								
					1						

46.	HS-100129-01	chemi	cal reg	gistry									
		registry	/ id		mol wt		formula			date	SMILES		
		HS-100	0129-0	)1	349.79	17	CI1S1O2	N5C14	4H12	2013-11-25	Clc1cc(n2ncc3c(=O)[nH]c(nc23)SC(C(=O)N)C)ccc1		
		chirality	у		origin		chemist			notebook	salt form		
					Interna	al synthesis	Dave Car	lson		3DAC005_1	None: Free base		
		amoun	t availa	able	progra	m	primary ta	rimary target		percent purity	elemental analysis		
	N N S	2 g			Purine	_inhib				95-100			
		melting	g point		NMR c	lata	LCMS data			comment	NMR datafile		
							on						
	o	LCMS	datafil	е									
47.	HS-100130-01	chemie	hemical registry										
		registry id		mol wt		formula	date		SMI	ILES			
	0 So-	HS-100130-01		705.727		Br1S2O6N2C33H41	2013-12-0	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			
	N+			Internal synthesis		Philip Hughes	PFH-005-	036A	Non	e: Free base			
	~~~ (~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	amount available		program		primary target	percent p	urity	eler	nental analysis			
	Br	0.144	0.144 Purine		nhib		95-100						
	×1-	melting poin	ıt	NMR da	ta	LCMS data	comment		NM	R datafile			
						on	See PFH	ior sample					
	<b>0</b>	LCMS datafi	ile										
	- S:O O	yes											
8	HS-100131-01	chemical registry											
0.		registry id	mol wt	form	nula d	ate		SMILES					
		HS-100131-01	1318.691	S20	013N7C71H95 2	013-12-04		S(=0)(=0)([0-])CCCC[N+]1=C(C=CC)(=CC=C2N(c3x(cxcc3)C2(C)C)CCCCS(=0)(=0)(0-0)(0-4ccc(cx4)CNCCCOCCOCCOCCOCCOCCOCCCCccfeder(c7/e6CC(CC7=0)(C)C					
	0 20-	chirality	origin	che	mist n	otebook		salt form					
			Internal syr	nthesis Phil	ip Hughes P	FH-005-037A		None: Fire base					
		amount available	e program	prin	narv target p	ercent purity		elemental analysis					
	MOLON N	0.061	Purine inhi	ib	9	5-100							
		melting point	NMR data	LCI	AS data cr	omment		NMR datalle					
	N S SN			on	s	ee PFH for sample: impure: m	av be resubmitted after	NMR datafie					
	óso	LCMS datafile											
	Ū.			_									
٥	HS-100131-02	chemie	cal reg	gistry									
э.		registry id	mol wt	formula c		date		SMILES					
		HS-100131-02	1318.691	S2	O13N7C71H95	2013-12-05		S(=O)(=0	D)([0-])CCCC[M	N+]1=C(C=CC(=CC=C2N(c3c(cccc3)C	22(C)C)CCCS(=0)(=0)(0)c4ccc(cc4)CNCCCOCCOCCOCCOCCCNc5c(ccc(n6nc(c7c8CC(CC7=0)(C)C)C)c5)C(=0)N)C(c8c cc		
	0 - <sup>5</sup> 0	chirality	origin	chi	emist	notebook		salt form					
			Internal sys	nthesis Ph	ilip Hughes	PFH-005-037B		None: Fr	ee base				
		amount available	e program	prir	mary target	percent purity		elementa	al analysis				
	× NO OLON OL	0.045	Purine_inh	ib		95-100							
		melting point	NMR data	LC	MS data	comment		NMR dat	tafile				
	N ~ SN					See PFH for sample: This ram	ple is purified HS-1001	11-					
	0 <sub>so</sub>	LCMS datafile											
	č	ves											
		,											
0	HS-100131-03	chemi	cal red	gistrv									
υ.		registry id	mol wt		formula	date	SMILES						
		HS-100131-03	1318.69	1	S2013N7C71H9	5 2014-08-07	S(=O)(=O)([O-])	CCC[N+]1=C	C(C=CC(=CC=C	22N(c3c(cccc3)C2(C)C)CCCCS(=O)(=	0/0)o4ccc(cc4)CNCCCOCCOCCOCCOCCCCNc5c(ccc(n8nc(c7e8CC(CC7=0)(C)C)C)c5)C(=0)N)C(c8e1cccc6)(C)C		
	0 So-	chirality	origin		chemist	notebook	salt form						
			Internal	synthesis	Philip Huohes	PFH-006-0364	None: Free have						
	N S O	amount ourily h	e orcero-		nimary target	perpert surity	elemental and	is					
	/ / NNO VOVN () / /	0.690	- program	inhih	,ay unget	Q5-100	crementar analys	-					
		0.060	Punne_ii	****D	10115	90-100							
	N <sup>°O</sup>	melting point	NMR dar	ta	LCMS data	comment	NMR datafile						
	oso				on	500 mg sent for MTD et	c.						
	0	LCMS datafile											

LCMS datafile yes

	HE 100122 01	chemi	cal regist	rv						-				
۱.	13-100132-01	registry id	mol wt	formula	date		SMILES							
		HS-100132-01	1332.675	S2O14N7C71H9	3 2013-12-04		S(=0)(=0)([0-])CCCC(N+]1=C(C=CC=C2N(c3c(cccc3)C2(C)(C)CCCCS(=0)(=0)0)c4ccc(cc4)C(=0)NCCCCCCCCCCCCCCCCCCCCCCCccccnefic(ccnefic(c7e8CC(CC7=0)(C)C)C)C)c5)C(=C)(C)(C)(C)(C)(C)(C)(C)(C)(C)(C)(C)(C)(C							
	0 \$0 <sup>-</sup>	chirality	origin	chemist	notebook		salt form							
			Internal synthesis	Philip Hughes	PFH-005-038A		None: Free base							
		amount availabl	le program	primary target	percent purity		elemental analysis							
		0.061	Purine_inhib		95-100									
	N <sup>O</sup> N	melting point	NMR data	LCMS data	comment		NMR datafile							
				on	See PFH for sample; impure	e; may be resubmitted after purifi	c							
	0	LCMS datafile												
		yes												
		chomi	chemical registry											
52.	H3-100133-01	registry	id	mol wt		formula		date		SMILES				
		HS-100	133-01	322.77	72	CI1S102N4C13	H11	2013-12-18		Clc1cc(n2ncc3c(=O)[nH]c(nc23)SCCO)ccc1				
	0	chirality		origin	_	chemist		notebook		salt form				
	) U			Interna	al synthesis	Dave Carlson		3DAC006 1		None: Free base				
	N N	amount	available	progra	m	primary target		percent purity		elemental analysis				
	N N S O	1.75		Purine	_inhib			95-100						
		melting	point	NMR o	data	LCMS data		comment		NMR datafile				
	CI					on		Analog of HS38. ZIF	K inhibitor.					
		LCMS d	latafile											
53.	HS-100134-01	rogistro	cal regist	ry	a/t	formula		data	SMILES					
		HS-10	0134-01	349	797	CI1S1O2N5	C14H1	12 2014-01-08		$p^{2}pcc^{3}c(-\Omega)[pH]c(pc^{2}3)SC(C(-\Omega)N)C)cc^{1}$				
	<b>o</b>	chiralit	v	origi	n	chemist		notebook	salt form					
	Ń N	chirality		Inter	nal synthesis	Dave Carlson		3DAC008 1	None: Fr	ee base				
		amoun	t available	e prog	ram	primary target		percent purity	elementa	I analysis				
		0.050		Purir	ne_inhib	DAPK/PIM3		95-100						
	<b>o</b>	melting	g point	NMF	R data	LCMS data		comment	NMR dat	afile				
						on		Analog of HS3	38					
	cı	LCMS	datafile											
54.	HS-100135-01	rogistro	cal regist	.ry		formula		data	SMILES					
		HS-10	0135-01	329	379	S1O2N5C1	5H15	2014-01-08	Skills					
	ο	chiralit	v	Origi	n	chemist	5115	notebook	salt form					
	, j		J	Inter	nal svnthesis	Dave Carlso	on	3DAC008 2	None: Free	base				
	N N	amoun	t available	e prog	ram	primary tarc	jet	percent purity	elemental a	nalysis				
		0.050		Puri	ne_inhib	DAPK/PIM3	3	95-100						
	) — d	melting	g point	NMF	R data	LCMS data		comment	NMR datafil	e				
						on		Analog of HS38						
		LCMS	datafile											
1														
55.	HS-100136-01	chemi	cal regist	ry	A. (†	formul-		data	SMILE C					
			y IU	1001	wl	S102NEC4	5415		SIVILES	0)020(n(no2)020(0002)(0)=4)(0(0) 0)***				
	-	chirolit	0130-01	329.	5/9 n	STU2IN5U1	5115	2014-01-08	S(CI[NH]C(=	Ojeze(n(nez)esee(eee3)C)n1)C(C(=O)N)C				
	o 	chiralit	у	Inter	nal synthesis	Dave Carley	n		None: Free	hase				
	N I	amoun	t availabl		ram	Dave CallSo	iet	percent purity	elemental a	nalvsis				
	N N S N	0.050	a available	Puri	ne inhih		3	95-100	Siciliental d	naryon				
		melting	a point	NMF	R data	LCMS data		comment	NMR datafil	e				
			, por			on		Analog of HS38	Catalin	-				
		LCMS	datafile											
						-								

	UE 400427.04	chemical registry											
156.	H3-100137-01	rogistry id	anemican registi y radistruid mel wit formula data CMILES										
		HS-100137-01		281.336		51	S102N5C11H15		2014-01-08		S(c1[nH]c(=O)c2c(n(nc2)C(C)C)n1)C(C(=O)N		
		chirality		origin		ch	chemist		notebook		salt form		
				Internal synthesis		Da	Dave Carlson		3DAC009_1		None: Free base		
		amount available		program		pri	primary target		percent purity		elemental analy	sis	
		0.050		Purine_inhib		DA	DAPK/PIM3		95-100				
		melting point		NMR data		LC	LCMS data		comment		NMR datafile		
						on		Ana	Analog of HS38				
		LCMS datafile											
۱ ,													
157.	HS-100138-01	chemical registry											
		registry id		mol wt fo		orm	rmula da		ate SN		LES		
		HS-100138-01	34	345.378		S10	3N5C15H15	2014-01-08		S(c1[nH]c(=O)c2c(n(nc2)c3cc(ccc3)OC)n1)C(C(=O)N)C			
		chirality	ori	origin d		chen	nist	notebo	notebook		salt form		
				Internal synthesis		Dave	ave Carlson		DAC009_2		None: Free base		
		amount available p		program p		orima	rimary target p		ercent purity e		elemental analysis		
		0.050		urine_inh	ib I	DAP	K/PIM3	95-100	5-100				
		melting point		MR data	1	CM	S data	comme	ent	NMF	R datafile		
				(		on		Analog	nalog of HS38				
		LCMS datafile											
۱													
158.	HS-100139-01 chemical registry												
		registry id	mo	mol wt		orm	ula	date		SMI	3MILES		
		HS-100139-01	34	345.378		31O3N5C15H15		2014-0	I4-01-08 S(c1[nH]c(=O)c2c(n		[nH]c(=O)c2c(n(	(nc2)c3ccc(cc3)OC)n1)C(C(=O)N)C	
		chirality	ori	origin		chen	nist	notebo	tebook salt form		form		
				Internal synthesis		Dave	e Carlson	3DAC0	AC009_3 None: Free base		e: Free base		
		amount availat	ole pro	program r		orima	ary target	percen	ent purity elemental analysis		nental analysis		
		0.050		Purine_inhib		DAPK/PIM3		95-100	-100				
		melting point	NN	NMR data		LCMS data		comme	mment NMR datafile		R datafile		
						on		Analog	nalog of HS38				
		LCMS datafile											
159.	HS-100140-01												
		registry id	mo	1101 WL				date	1.00	SMILES			
		HS-100140-01		340.302		STO2NOC ISH12		2014-0	1-08	S(c1[nH]c(=O)c2c(n)		hc2)c3ccc(cc3)C#N(h1)C(C(=O)N)C	
		chirality		origin		cnemist		noteboo	ОК	salt form			
				internal synthesis		Dave Carison		3DAC0	009_4	None: Free base			
		amount available p		program p				percent	t purity	ty elemental analysis			
		0.050 Pu				JAPI		95-100					
		melting point		INIVIR data		LCMS data		comme	nment NMR datafile		datatile		
					on			Analog	of HS38				
		LCMS datafile	LCMS datafile										
100	Lis 400444.04 chemical registry												
160.		registry id	mol wt	t formula			date					SMILES	
		HS-100141-01 378.281			CI2S1N5C16H		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 int	hib	plantary target		95-100						
		melting point	NMR data	<b>2</b>	LCMS data		comment					NMR datafile	
		moning point	uaid	-			Grp94 selective inhibitor PU-H39 Nat. Chem Biol				2014: 9: 677-684		
		LCMS datafile								5101.			
	11/	Ves											
		усъ											
161.	HS-100142-01	chemical regi	stry	у									
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		registry id n	ol wt	formula	date	:	SMILES						
		HS-100142-01 6	48.748	O10N4C32H48	2014-02-04		O=C(O)CCOC0	coccoc	COCCOCCOCCNc1c(ccc(n2nc(c3c2CC(CC3=O)(C)C)c1)C(=O)N				
	-	chirality 0	igin	chemist	notebook	1	salt form						
	° v v v	1	ternal synthesis	Philip Hughes	PFH-005-048C	1	None: Free bas	se					
		amount available p	rogram	primary target	percent purity		elemental analy	lysis					
		0.470 F	urine_inhib		95-100								
	$\langle \rangle_{N}$	melting point N	MR data	LCMS data	comment		NMR datafile						
	) = o			on	Entire sample given to Chris	s Lascola							
	N	LCMS datafile											
		ves											
		,											
162	HS-100143-01	chemical regi	stry										
102.		registry id	mol wt		formula	date			SMILES				
		HS-100143-01	378.28	1	CI2S1N5C16H13	2014-03-1	13		Clc1c(ccc(c1)Cl)Sc2nc3n(cnc(c3n2)N)CCCC#C				
	N	chirality	origin		chemist	notebook			salt form				
	N N		Internal	synthesis	Philip Hughes	PFH-005-	-058B		None: Free base				
	S CI	amount availat	le progran	n	primary target	percent p	urity		elemental analysis				
	N	0.028	Purine_	inhib		95-100	-						
		melting point	NMR da	ata	LCMS data	comment			NMR datafile				
	CI					Isomer of	HS-100'	141.					
		LCMS datafile											
163.	HS-100144-01	chemical regi	stry										
		registry id	mol wt		formula	date	5	SMILE	5				
		HS-100144-01	362.381		S1F1O3N4C16H15	2014-03-21	1 5	S(c1[nł	H]c(=O)c2c(n(nc2)c3cc(ccc3)F)n1)C(C(=O)OC)CC				
	o	chirality	origin		chemist	notebook	5	salt for	n				
			Internal s	ynthesis	Dave Carlson	3DAC024_	1 1	None: I	Free base				
		amount available	program		primary target	percent pur	rity e	elemen	tal analysis				
		0.050	Purine_in	hib	DAPK/PIM3	95-100							
	0	melting point	NMR data	a	LCMS data	comment	1	NMR d	atafile				
	r 🗾				on	Analog of H	-IS38						
		LCMS datafile											
	US 400445.04	chemical regi	strv										
164.	HS-100145-01	registry id	mol wt		formula	date		SMILES					
		HS-100145-01	348 354		S1F1O3N4C15H1	3 2014-03-	2014-03-21 S		S(c1[nH]c(-O)c2c(n(nc2)c3cc(ccc3)E)n1)C(C(-O)OC)C				
		chirality	origin		chemist	notebook	<u>_</u> .	salt form					
	<b>o</b> 	ormany	Internal	svnthesis	Dave Carlson	3DAC024	4 2	None	: Free base				
	N I	amount availat	le program	1	primary target	percent p	ourity	eleme	ental analysis				
	<sup>™</sup> N <sup>™</sup> N <sup>™</sup> S <sup>™</sup> O	0.050	Purine	inhib	DAPK/PIM3	95-100							
	, ö	melting point	NMR da	ita	LCMS data	comment	t	NMR	datafile				
	F				on	Analog of	f HS38						
		LCMS datafile											
			-										
165.	HS-100146-01	chemical regi	stry										
		registry id	mol wt	fo	ormula	date	SMI	ILES					
		HS-100146-01	398.362	S	1F3O3N4C16H13	2014-03-27	S(c1	1[nH]c(	=O)c2c(n(nc2)c3cc(ccc3)C(F)(F)F)n1)C(C(=O)OC)C				
	o	chirality	origin	c	hemist	notebook	salt	form					
	N I		Internal sy	nthesis D	Dave Carlson	3DAC025_1	Non	ne: Free	base				
	N N K C	amount available	program	p	rimary target	percent purity	elen	nental a	analysis				
		0.050	Purine_inh	nib C	APK/PIM3	95-100							
	F	melting point	NMR data	L	CMS data	comment	NMF	R dataf	ile				
	F			0	n	Analog of HS3	38						
		LCMS datafile											

166	HS-100147-01	chemical registry								
		registry id	mol wt	formula	c	date	SM	AILES		
		HS-100147-01	462.956	CI1S1O3N6C20	H23 2	2014-04-0	2 Clo	c1cc(n2ncc3c(=O)[nH]c(nc23)SC(C(=O)NCCN4CCOCC4)C)ccc1		
		chirality	origin	chemist	r	notebook	sal	It form		
	0		Internal synthesis	Dave Carlson	3		1 No	ne: Free hase		
	N.	amount available	program	primary target	-		rity ele			
			Buring, inhib		۲ د	5 100				
	ő Vo	0.080					NIN	AD datafila		
	CI-	mening point	INIVIR Udia							
				on		Analog of I	1536			
		LUNS datafile								
	110 400440 04	chemical registr	W							
167.	H3-100146-01	rogistry id	y mol wt	formulo		data		SMILES		
			247.260	0111101a		4 2014	04.04	Similes S(a1[nH]a(-0)a2a(n/na2)a2aa(aaa2)E)n1)C(C(-0)N)CC		
		H3-100140-01	347.309	STFTUZIN		4 2014	-04-04			
	<b>o</b> 	chirality	Ungin	Chemist				Sait form		
	N N		Internal synthesi	s Dave Caris	son	3DAG	C029_1	None: Free base		
		amount available	program	primary tar	get	perce	ent purity	elemental analysis		
		0.060	Purine_inhib	DAPK/PIM	3	95-10	00			
		melting point	NMR data	LCMS data	1	comr	ment	NMR datafile		
	F-			on		Anal	og of HS3	8		
		LCMS datafile								
168.	HS-100149-01	chemical registr	<b>y</b>	6 1				01411 50		
		registry id	moi wt	formula	504411	date	,			
		HS-100149-01	333.343	STFTUZN	5C14H	12 2014	4-04-04	S(C1[nH]C(=O)C2C(n(nC2)C3CC(CCC3)F)n1)C(C(=O)N)C		
	<b>o</b>	chirality	origin	cnemist		note				
	N I		Internal synthesi	s Dave Carl	son	3DA	C029_2	None: Free base		
		amount available	program	primary ta	rget	perc	cent purity	elemental analysis		
		0.060	Purine_inhib	DAPK/PIN	13	95-1	100			
		melting point	NMR data	LCMS dat	a	com	iment	NMR datafile		
	F=			on		Ana	log of HS3	38		
		LCMS datafile				_				
	HE 400450 04	chemical registr	v							
169.	H3-100150-01	registry id	<b>y</b> mol wt	formula		date		SMILES		
		HS-100150-01	383 350	S1E3O2N5C1	5H12	2014-04	-04	S(c1[nH]c(-O)c2c(n(nc2)c3cc(ccc3)C(E)(E)E)n1)C(C(-O)N)C		
	-	chirality	origin	chemist	01112	noteboo	ik l	salt form		
	8 II	onnunty	Internal synthesis	Dave Carlson		3DAC02	× 29 3	None: Free base		
	N I I	amount available	program	primary target		nercent	nurity	elemental analysis		
			Purino inhih			05-100	punty			
	F Ö	molting point	NMR data			commor	at .	NMP datafila		
	F		NIVITY Udita				n of US28	Nin uatanie		
	F	LCMS datafile		on		Analog	5111050			
170	HS-100151-01	chemical registr	у							
170.		registry id	mol wt 1	formula	date		SMILES			
		HS-100151-01	451.564	O3N5C25H33	2014-04	4-09	O=C(N)c1	c(cc(n2nc(c3c2CC(CC3=O)(C)C)C)cc1)NC4CCC(NC(=O)C)CC4		
	o, ,	chirality	origin	chemist	noteboo	ok	salt form			
		{24-27T;}	Internal synthesis	Philip Hughes	PFH-00	5-084A	None: Free	e base		
		amount available	program	primary target	percent	purity	elemental	analysis		
	· · · · · · · · · · · · · · · · · · ·	0.102	Purine inhib	,	95-100	. ,				
	N N	melting point	NMR data	LCMS data	comme	nt	NMR data	file		
	)o									
	N <sup>°</sup>	LCMS datafile								

171	HS-100152-01	chemical registry									
		registry id	mol wt	formula	date	8	SMILES				
	Q	HS-100152-01	818.101	S2O7N3C45H59	201	4-04-17	S(=O)(=O	)([O-])CCCC[N+]1=C(C=CC(	=CC=C	22N(c3c(cccc3)C2(C)C)CCCCS(=O)(=O)O)c4ccc(cc4)CNCCCOCC)C(c5c1cccc5)(C)C	
		chirality	origin	chemist	note	ebook	salt form				
	( <sub>N</sub> +C)		Internal synth	esis Philip Hughes	PF	1-005-085A	None: Fre	e base			
		amount available	program	primary target	per	cent purity	elemental	l analysis			
		0.015	Purine_inhib		95-	100					
	(L	melting point	NMR data	LCMS data	com	nment	NMR data	afile			
	$\langle N \rangle$			on	See	PFH for sample	yes				
	050	LCMS datafile									
	o	yes									
172.	HS-100153-01	cnemical r	egistry		( )						
		registry id	04			formula	140	date	_	SMILES	
		HS-100153	-01	322.300		UTIN6C17	H18	2014-04-30	_		
	O N	chirality			oio	Dava Carl	000		_	Salt IOIIII	
		amount available			515	Dave Call	son	SDAC034_1	_	elemental analysis	
		amount available					igei		_		
	<b>N</b>	1.0		NMR data		LCMS dat	<u>.</u>	comment	-	NMP datafile	
		meiting point		NIVILY UALA		on	u	Racemic Mivture		Hint Galanie	
		LCMS data	file						6		
		Lowe datame							_		
173. HS-100154-01 chemical registry											
		registry id	I	mol wt		formula		date		SMILES	
	, <b>o</b> —	HS-100154	-01 :	369.443		S1O2N5C1	8H19	2014-05-02		s1c(nc2cc(ccc12)OC)NC(=O)C3CN(c4nccnc4)CCC3	
		chirality	(	origin		chemist		notebook		salt form	
			1	Internal synthes	sis	Dave Carlso	on	3DAC034_5		None: Free base	
		amount ava	ailable p	program		primary targ	get	percent purity		elemental analysis	
		0.050	I	Purine_inhib		HSP70		95-100			
		melting poir	nt I	NMR data		LCMS data		comment		NMR datafile	
	N					on		Racemic Mixtu	re		
		LCMS datafile									
474	HC 100155 01	chemical r	eaistry								
174.	113-100133-01	registry id	- <u>-</u>	mol wt		formula	1	date	SM	ILES	
		HS-100155	-01	364.446		O1N6C20	H24	2014-05-05	0=	C(Nc1n(c2c(n1)cccc2)CCC)C3CN(c4nccnc4)CCC3	
	0 N (	chirality		origin		chemist		notebook	salt	t form	
				Internal synthe	sis	Dave Carl	son	3DAC037_01	Nor	ne: Free base	
		amount ava	ailable	program		primary ta	rget	percent purity	elei	mental analysis	
		0.050		Purine_inhib		HSP70		95-100			
	Ϊ \	melting poir	nt	NMR data		LCMS dat	a	comment	NM	R datafile	
	N					on		Racemic			
	l └Ń	LCMS data	file								
		chomical -	ogietar								
175.	no-100156-01	registry id	egistiy	mol wt		formula		date	9	MILES	
		HS-100156	-01	336 393		O1N6C1	BH20	2014-05-05	0	= C(Nc1n(c2c(n1)cccc2)C)C3CN(c4nccnc4)CCC3	
		chirality		origin		chemist	51 120	notebook	6	alt form	
	ĭ Ĩ ≫	Simulty		Internal synthe	esis	Dave Car	rlson	3DAC038_01	N	lone: Free base	
	N N	amount ava	ailable	program		primary ta	arget	percent purity	P	lemental analysis	
		0.040		Purine inhib		HSP70		95-100			
		meltina poir	nt	NMR data		LCMS da	ıta	comment	N	IMR datafile	
	N N	3 - 51				on		Racemic	-		
	U ∠N	LCMS data	file								

176	HS-100157-01	chemical registry											
110.		registry id	mol wt	formula	date		SMILES						
		HS-100157-01	362.430	O1N6C20H2	2 2014-05-0	08	O=C(Nc1n(c2c(n1)cccc2)C=CC)C3CN(c4nccnc4)CCC3						
		chirality	origin	chemist	notebook		salt form						
			Internal synthesis	Dave Carlso	n 3DAC039	) 2	None: Free base						
	N N	amount available	program	primary targe	et percent p	urity	elemental analysis						
		0.050	Purine inhib	HSP70	95-100								
	N \	melting point	NMR data	LCMS data	comment		NMR datafile						
	N			on	Racemic								
	ĺĺ _N	LCMS datafile											
177	HS-100158-01	chemical registry	,										
		registry id	mol wt	formula	date		SMILES						
		HS-100158-01	366.419	O2N6C19H2	22 2014-05-	-08	O=C(Nc1n(c2c(n1)cccc2)CCO)C3CN(c4nccnc4)CCC3						
	9 N (	chirality	origin	chemist	notebook	ĸ	salt form						
			Internal synthesis	Dave Carlso	on 3DAC039	9_3	None: Free base						
		amount available	program	primary targ	et percent p	ourity	elemental analysis						
		0.050	Purine_inhib	HSP70	95-100								
	j	melting point	NMR data	LCMS data	comment	t	NMR datafile						
	N			on	Racemic								
	└ _ Ń	LCMS datafile											
	$\sim$												
178.	HS-100159-01	chemical registry	1	-1									
		registry id	mol wt	formula	date		SMILES						
	o N	HS-100159-01	378.473	O1N6C21H2	6 2014-05-0	8	O=C(Nc1n(c2c(n1)cccc2)CC(C)C)C3CN(c4nccnc4)CCC3						
		chirality	origin	chemist	notebook		salt form						
			Internal synthesis	Dave Carlson	n 3DAC039_	_4	None: Free base						
	N N	amount available	program	primary targe	et percent pu	irity	elemental analysis						
		0.050	Purine_inhib	HSP70	95-100								
	```````````````````````````````````````	melting point	NMR data	LCMS data	comment		NMR datafile						
				on	Racemic								
	r N	LCMS datafile											
470	HS-100160-01	chemical registry	,										
179.	13-100100-01	registry id	mol wt	formula	date	5	SMILES						
		HS-100160-01	394.429	O3N6C20H22	2 2014-05-08	3 (	D=C(OC)Cn1c(nc2c1cccc2)NC(=O)C3CN(c4nccnc4)CCC3						
		chirality	origin	chemist	notebook	s	salt form						
	, ĭ ï >		Internal synthesis	Dave Carlson	3DAC039	5 N	None: Free base						
	N N	amount available	program	primary target	t percent pur	rity e	elemental analysis						
		0.050	Purine_inhib	HSP70	95-100		-						
	, v	melting point	NMR data	LCMS data	comment	Ν	NMR datafile						
	N			on	Racemic								
	Ų <b>N</b>	LCMS datafile											
	$\sim$												
			•	1									
180.	HS-100161-01	chemical registry	,										
		registry id	mol wt	formula	date	SMIL	ES						
		HS-100161-01	440.499	O2N6C25H24	2014-05-08	O=C	(Nc1n(c2c(n1)cccc2)CC(=O)c3ccccc3)C4CN(c5nccnc5)CCC4						
	0 N 🗸 🔪	chirality	origin	chemist	notebook	salt f	orm						
			Internal synthesis	Dave Carlson	3DAC039_6	None	a: Free base						
		amount available	program	primary target	percent purity	elem	ental analysis						
		0.050	Purine_inhib	HSP70	95-100								
		melting point	NMR data	LCMS data	comment	NMR	t datafile						
				on	Racemic								
		LCMS datafile											

181.	HS-100162-01	chemical	registry	1							
-		registry id		mol wt	f	formula	date	SMILES			
		HS-10016	2-01	393.487	(	O1N7C21H2	2014-05-08	O=C(Nc1n(c2c(n1)cccc2)CCN(C)C)C3CN(c4nccnc4)CCC3			
	9 N /	chirality		origin	(	chemist	notebook	salt form			
				Internal synthe	esis I	Dave Carlson	3DAC039_7	None: Free base			
	N <sup>×</sup> N	amount av	ailable	program	ł	primary targe	percent purity	elemental analysis			
	N	0.050		Purine_inhib	I	HSP70	95-100				
	, N	melting po	int	NMR data		LCMS data	comment	NMR datafile			
	N Ý				(	on	Racemic				
	Ň	LCMS data	afile								
192	HS-100163-01	chemical	registry	,							
102.		registry id		mol wt		formula	date	SMILES			
		HS-10016	3-01	379.418		O2N7C19H2	1 2014-05-30	O=C(N)Cn1c(nc2c1cccc2)NC(=O)C3CN(c4nccnc4)CCC3			
	o n (	chirality		origin		chemist	notebook	salt form			
				Internal synth	esis	Dave Carlson	a 3DAC043_1	None: Free base			
	N N	amount available		program		primary targe	t percent purit	y elemental analysis			
	N N	0.010		Purine_inhib		HSP70	95-100				
	) N	melting po	int	NMR data		LCMS data	comment	NMR datafile			
	N					on	Racemic				
	ЦŃ	LCMS data	afile								
183	HS-100164-01	chemical registry									
105.		registry id	r	mol wt	form	ormula date		SMILES			
	0	HS-100164-	01 3	399.461	F10	3N3C22H26	2014-06-09	Fc1c(c(cc(n2c3c(c(c2)C)C(=O)CC(C)(C3)C)c1)NC4COCC4)C(=O)N			
		chirality	(	origin	cher	mist	notebook	salt form			
		{22S;}	1	nternal synthesis	Phili	ip Hughes	PFH-006-001A	None: Free base			
	Ň	amount avai	lable p	orogram	prim	nary target	percent purity	elemental analysis			
	<b>o</b>	0.108	F	Purine_inhib			95-100				
	N	melting poin	t I	NMR data	LCM	/IS data	comment	NMR datafile			
	F				on						
	N -0	LCMS datafi	le								
		yes									
104	HS-100165-01	chemical	reaistrv	1							
104.	113-100103-01	registry id	mol wt	formula	date	SMILES					
		HS-100165-01	984.321	S207N3C58H69	2014-07-17	S(=O)(=O)([O-])C	CC[N+]1=C(C=CC2=C(C(=CC=C3N	e4c(c5c(cccc5)cc4)C3(C)C)CCCCS(=0)(=0)(=0)(0)CCC2)e8ccc(cc6)CNCCCOCC)C(c7c1e8c(cccc8)ec7)(C)C			
	,ō,s	chirality	origin	chemist notebook salt fo							
			Internal synthes	is Philip Hughes	PFH-006-02	28A None: Free base					



chemical	chemical registry										
registry id	mol wt	formula	date	SMILES							
HS-100165-01	984.321	S2O7N3C58H69	2014-07-17	S(=0)(=0)([0-])CCCC[N+]1=C(C=CC2=C(C =CC=C3N(odc(c5c(cxxc5)cc4)C3(C)C)CCCCS(=0)(=0)(0)(CCC2)c6ccc(cx6)(CNCCCCCCC)C(c7c1c8c(cxxc5)cc7)(C)CCC2)c6ccc(cx6)(CNCCCCCCC)C(c7c1c8c(cxxc5)cc7)(C)CCC2)c6ccc(cx6)(CNCCCCCCC)C(c7c1c8c(cxxc5)cc7)(C)CCC2)c6ccc(cx6)(CNCCCCCCC)C(c7c1c8c(cxxc5)cc7)(C)CCC2)c6ccc(cx6)(CNCCCCCCC)C(c7c1c8c(cxxc5)cc7)(C)CCC2)c6ccc(cx6)(CNCCCCCCC)C(c7c1c8c(cxxc5)cc7)(C)CCC2)c6ccc(cx6)(CNCCCCCCC)C(c7c1c8c(cxxc5)cc7)(C)CCC2)c6ccc(cx6)(CNCCCCCCC)C(c7c1c8c(cxxc5)cc7)(C)CCC2)c6ccc(cx6)(CNCCCCCCC)C(c7c1c8c(cxxc5)cc7)(C)CCC2)c6ccc(cx6)(CNCCCCCCC)C(c7c1c8c(cxxc5)cc7)(C)CCC2)c6ccc(cx6)(CNCCCCCCC)C(c7c1c8c(cxxc5)cc7)(C)CCC2)c6ccc(cx6)(CNCCCCCCC)C(c7c1c8c(cxx6)cc7)(C)CCC2)c6ccc(cx6)(CNCCCCCC)C(c7c1c8c(cxx6)cc7)(C)CCC2)c6ccc(cx6)(CNCCCCCC)C(c7c1c8c(cxx6)cc7)(C)CCC2)c6ccc(cx6)(CNCCCCCC)C(c7c1c8c(cxx6)cc7)(C)CCC2)c6ccc(cx6)(CNCCCCCC)(C)CCC2)c6ccc(cx6)(CNCCCCCC)(C)CCCCCCCC)(C)CCCC2)c6ccc(cx6)(CNCCCCCC)(C)CCC2)c6ccc(cx6)(CNCCCCCC)(C)CCC2)c6ccc(cx6)(CNCCCCCC)(C)CCC2)c6ccc(cx6)(CNCCCCCC)(C)CCC2)(C)CCC2)c6ccc(cx6)(CNCCCCCC)(C)CCC2)c6ccc(cx6)(CNCCCCCC)(C)CCC2)c6ccc(cx6)(CNCCCCCCC)(C)CCC2)c6ccc(cx6)(CNCCCCCC)(C)CCC2)c6ccc(cx6)(CNCCCCCC)(C)CCC2)c6ccc(cx6)(CNCCCCCC)(C)CCC2)c6ccc(cx6)(CNCCCCCCC)(C)CCC2)c6ccc(cx6)(CNCCCCCCC)(C)CCC2)c6ccc(cx6)(CNCCCCCC)(C)CCC2)c6ccc(cx6)(CNCCCCCCC)(C)CCC2)c6ccc(cx6)(CNCCCCCCC)(C)CCC2)c6ccc(cx6)(CNCCCCCCC)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6cccC2)c6cccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccc(cx6)(C)CCC2)c6ccCCCCCCCCCCCCCCCCCCCCCCCCCCCCC							
chirality	origin	chemist	notebook	salt form							
	Internal synthesis	Philip Hughes	PFH-006-028A	None: Firee 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)NCCCOCCOCCOCCOCCOCCOCCOCCNe1e(ccc(n2nc(c3e2CC(CC3=0)(C)C)C)c))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 registr	y l		( )		1.4	01411 50			
		registry id	moi wt		formula		date	SMILES			
	o	HS-100167-01	308.722		CI1O3N4C <sup>2</sup>	I3H13	2014-09-12	Clc1cc(n2ncc(c2NCC(=O)N)C(=O)OC)ccc1			
		chirality	origin		chemist		notebook	salt form			
	0		Internal synthe	esis	Dave Carls	on	3DAC049_1	None: Free base			
		amount available	program		primary targ	get	percent purity	elemental analysis			
	N <sup>-</sup> N <sup>-</sup> N <sup>-</sup>	0.030	Purine_inhib		DAPK/PIM3	3	95-100				
	, o	melting point	NMR data		LCMS data		comment	NMR datafile			
					on		Analog of HS38				
		LCMS datafile									
187.	HS-100168-01	chemical registr	у								
		registry id	mol wt	formula		date		SMILES			
		HS-100168-01	339.417	S101	N5C17H17	2014-10-1	5	s1c(nc2c1cccc2)NC(=O)C3CN(c4nccnc4)CCC3			
	0 N /	chirality	origin	chemi	st	notebook		salt form			
			Internal synthesis	Dave	Carlson	3DAC063	_1	None: Free base			
	∧ `N´ `S	amount available	program	prima	ry target	percent pu	ırity	elemental analysis			
	N	0.080	Purine_inhib			95-100					
	Ï	melting point	NMR data	LCMS	i data	comment		NMR datafile			
	N			on		Racemic H	ISP70 inhibitor analog				
	L N	LCMS datafile									
	~										
l											
188.	HS-100169-01	chemical registr									
	_	registry id	mol wt	formula	mula da			SMILES			
	Br	HS-100169-01	418.313	Br1S1O	1N5C17H16	2014-10-	15	Brc1cc2nc(sc2cc1)NC(=O)C3CN(c4nccnc4)CCC3			
		chirality	origin	chemist	:	notebook		salt form			
			Internal synthesis	Dave C	arlson	3DAC06	3_2	None: Free base			
	N S	amount available	program	primary	target	percent p	ourity	elemental analysis			
		0.080	Purine_inhib			95-100					
	N	melting point	NMR data	LCMS o	lata	comment	:	NMR datafile			
	Ň			on		Racemic	HSP70 inhibitor analog				
	L N	LCMS datafile									
	~										
189.	HS-100170-01	chemical registr	y					01/11/20			
		registry id	mol wt	formu	lla	date		SMILES			
		HS-100170-01	325.390	5101	N5C16H15	2014-10-	15	s1c(nc2c1cccc2)NC(=O)C3CN(c4nccnc4)CC3			
	0 N 🖌 🔪	chirality	origin	cnem	IST Oculaan	notebook	4	Salt form			
		amount quailable	internal synthesis	Dave	Carison	3DAC064	I				
	$\langle \gamma \gamma N \gamma S$		program During in hit	prima	iry largel	percent p	unity				
	N	0.080		1.014		95-100		NMD datafile			
	N	meiling point		LONG	5 dala	Desemis					
	-N	LONG datafile		on		Racemic	HSP70 Inhibitor analog				
		LCMS datalle									
100	HS-100171-01	chemical registr	у								
190.		registry id	mol wt	formula	1	date		SMILES			
	<b>D</b> -	HS-100171-01	404.286	Br1S1C	D1N5C16H14	2014-10	-15	Brc1cc2nc(sc2cc1)NC(=O)C3CN(c4nccnc4)CC3			
	Br	chirality	origin	chemis	t	noteboo	k	salt form			
			Internal synthesis	Dave C	arlson	3DAC06	4_2	None: Free base			
	j j 🎽 📜	amount available	program	primary	v target	percent		elemental analysis			
	✓ `N´ `S`	0.080	Purine inhib	,		95-100					
	N	melting point	NMR data	LCMS	data	commer	t	NMR datafile			
	N			on		Racemic	HSP70 inhibitor analog				
	(N	LCMS datafile									

									1 ugo 00/40
191.	HS-100172-01	chemical	registr	у					
		registry id		mol wt	form	ula	date		SMILES
		HS-100172	-01	308.339	01N	6C16H16	2014-10	-21	O=C(Nc1[nH]c2c(n1)cccc2)C3CN(c4nccnc4)CC3
		chirality		origin	chem	nist	noteboo	k	salt form
	O N			Internal synthes	is Dave	Carlson	3DAC06	5_1	None: Free base
	N N	amount ava	ilable	program	prima	ary target	percent	purity	elemental analysis
	N-	0.050		Purine_inhib			95-100		
	N	melting poir	nt	NMR data	LCM	S data	commer	nt	NMR datafile
	$\langle \rangle$				on		Racemic	HSP70 inhibitor analog	
	\ <b>⊆</b> N	LCMS data	file						
192.	HS-100173-01	chemical	registr	у					
				mol wt	formul	a	date		SMILES
	o—	HS-100173-01		355.416	S102	N5C17H17	2014-1	0-21	s1c(nc2cc(ccc12)OC)NC(=O)C3CN(c4nccnc4)CC3
	$\neg = \langle$	chirality		origin	chemi	st	noteboo	ok	salt form
	₽ N			Internal synthesi	s Dave (	Carlson	3DAC0	65_2	None: Free base
	N S	amount ava	ilable	program	primar	y target	percent	t purity	elemental analysis
		0.050		Purine_inhib	1.0140	1-4-	95-100	-4	NMD detecte
	N-	meiting poir	IT	NIVIR data	LCIVIS	data	comme	int	
	N N		CI		on		Racem	IC HSP70 Inhibitor analog	
		LCMS datafile							
103	HS-100174-01	chemical	registr	у					
155.	10 100174 01	registry id		mol wt	formu	la	date		SMILES
		HS-100174	-01	350.419	O1N6	C19H22	2014-10-2	23	O=C(Nc1n(c2c(n1)cccc2)CCC)C3CN(c4nccnc4)CC3
		chirality		origin	chemi	st	notebook		salt form
	₽ N			Internal synthesi	s Dave	Carlson	3DAC066	_1	None: Free base
	N N	amount available		program	prima	ry target	percent p	urity	elemental analysis
	N	0.025		Purine_inhib			95-100		
	N-	melting point		NMR data	LCMS	LCMS data			NMR datafile
					on	on F		HSP70 inhibitor analog	
	<u> </u>	LCMS data	file						
	110 400475 04	chemical	rogistr	<b>N</b>					
194.	HS-100175-01	registry id	molwt	y formula	date		SMILES		
		HS-100175-01	1088.283	S1011N9C57H69	2014-11-21		S=C(Nc1cc2c(c	cc1)C3(OC2=O)c4c(cc(cc4)O)Oc5cc(ccc35)O)NCCCOC	COCCOCCCCCCCCCCcn8c(nc7c8cccc7)NC(=0)C8CN(c9nccnc9)CCC8
		chirality	origin	chemist	notebook		salt form		
	N-5 _0		Internal synth	esis Philip Hughes	PFH-006-069B		None: Free bas	e	
		amount available	program	primary target	percent purity		elemental analy	rsis	
		0.097	Purine_inhib		95-100				
		melting point	NMR data	LCMS data	comment		NMR datafile		
	CICN Co'			on	Not as clean as t	he driven snow			
		LCMS datafile							
195.	HS-100176-01	chemical	registr	У					
		registry id		mol wt		tormula		date	SMILES
		HS-10017	6-01	282.302		O1N6C	14H14	2015-01-16	U=C(Nc1n(c2c(n1)cccc2)CC)c3nccnc3N
	N	chirality		origin		chemist		notebook	salt form
	• • • • • • • • • • • • • • • • • • •			Internal sy	nthesis	Philip H	ughes	PFH-006-071A	None: Free base
		amount av	/allable	program		primary	target	percent purity	elemental analysis
		0.804		I Purine inh	(D)	1 NS-5 De	enque	195-100	

melting point

LCMS datafile

yes

NMR data

LCMS data

on

comment

ENAMINE T5843566

NMR datafile

106	HS-100177-01	chemical registry									
196.		registry id	mol wt	formula	date	SM	ILES.				
		HS-100177-01	355 373	S1O3N5C16H13	2015-02-04	Sic	$\frac{1}{2} = \frac{1}{2}$				
		113-100177-01	outrinin	shamiat	2013-02-04	0(0					
	0	chirality	ongin	chemist	nolebook	san					
	N I		Internal synthesis	Dave Carlson	3DAC079_1	Nor	he: Free base				
		amount available	program	primary target	percent purity	elei	mental analysis				
		0.025	Purine_inhib	DAPK/PIM2	95-100						
		melting point	NMR data	LCMS data	comment	NM	R datafile				
	N=			on	Analog of HS38						
		LCMS datafile									
197.	HS-100178-01	chemical registry	/								
		registry id	mol wt	formula	date	SN	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				
	o	chirality	origin	chemist	notebook	sa	It form				
	~		Internal synthesis	Dave Carlson	3DAC079_2	No	one: Free base				
	N N N	amount available	program	primary target	percent purity	ele	emental analysis				
		0.025	Purine_inhib	DAPK/PIM2	95-100						
	0	melting point	NMR data	LCMS data	comment	N	MR datafile				
	N			on	Analog of HS38	В					
		LCMS datafile									
198.	HS-100179-01	chemical registry									
		registry id	mol wt	formula	date	SMIL	ES				
	0	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 fo	orm				
			Internal synthesis	Dave Carlson	3DAC080_1	None	: Free base				
		amount available	program	primary target	percent purity	eleme	ental analysis				
	, ü	0.030	Purine_inhib	DAPK/PIM2	95-100						
		melting point	NMR data	LCMS data	comment	NMR	datafile				
				on	Analog of HS38						
	0 <sup></sup> `0	LCMS datafile									
199.	HS-100180-01	chemical registry	/								
		registry id	mol wt	formula	date	SMI	LES				
	0	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				
	N I I N		Internal synthesis	Dave Carlson	3DAC080_2	None	e: Free base				
	N <sup>×</sup> N <sup>×</sup> S <sup>×</sup>	amount available	program	primary target	percent purity	elem	nental analysis				
	Ö	0.030	Purine_inhib	DAPK/PIM2	95-100						
		melting point	NMR data	LCMS data	comment	NMF	R datafile				
				on	Analog of HS38						
	00	LCMS datafile									
		obamical registra									
200.	HS-100181-01	chemical registry		fa mar da	data						
		registry la	moi wt	formula	date		SMILES				
		HS-100181-01	421.904	CITS103N5C18H20	2015-03-16	_	cicicc(n2ncc3c(nc(nc23)SC(C(=0)OC)C)NCCOC)ccc1				
	Ņ~~O~	chirality		chemist	notebook		sautorn				
			Internal synthesis	Dave Carlson	3DAC084_1		None: Free base				
	N″ I I o I	amount available	program	primary target	percent purity		elemental analysis				
	S´_N´`_S´`	0.050	Purine_inhib	DAPK/PIM2	95-100						
	0	melting point	NMR data	LCMS data	comment		NMR datafile				
				on	Analog of HS3	8					
		LCMS datafile									

	110 400400 04	chomic	al rogist	m/									
201.	HS-100182-01	registry	id	molw	+	form	ula	date	SMILES				
			192.01	106.90	י רי			2015 02 17					
	. 0	no-100	102-01	400.0	92	che		2013-03-17					
	N S	chirality		ongin	- 1	chei	nist . Oarlaar						
	N I			Interna	ai syntnes	is Dav	e Carison	3DAC085_1	None: Free base				
	N. I. I. N	amount	available	e progra	am	prim	ary target	percent purity	elemental analysis				
	N <sup>×</sup> N <sup>×</sup> S <sup>×</sup>	0.050		Purine	e_inhib	DAF	PK/PIM2	95-100					
	<b>o</b>	melting	point	NMR	data	LCN	IS data	comment	NMR datafile				
	CI							Analog of HS38					
		LCMS c	latafile										
	HS-100182-01	chemic	al regist	rv									
202.	13-100103-01	registry id	mol wt	formula	date	SN	ILES						
		HS-100183-01	1324.612	O12N9C76H	93 2015-03-23	0-	C[O-].O=C1N(c2ccc(cc2)C=Cc3cc[n+](c	e3)CCC(=0)NCCCOCCOCCOCCOCCO	CCCNs4c(cccr(n5nc(c8c5CC(CC8=O)(C)C)C)c4)C(=O)N)C7(c8c(cc2(cs8)N(CC)CC)Oc9cc(ccc79)N(CC)CC)c1c1ccccc1				
		chirality	origin	chemist	notebook	sal	form						
			Internal synthesi	is Philip Hughe	s PFH-007-001	3 No	None: Free base						
		amount available	program	primary targe	t percent purity	elemental analysis							
		0.120	Purine_inhib		95-100								
		melting point	NMR data	LCMS data	comment	NN	R datafile						
				on	See chemist fr	or sample	,						
		LCMS datafile											
		yes											
203.	HS-100184-01	chemic	al regist	ry									
		registry id		mol wt	formula	date	SMILES						
		HS-100184-01		1422.087	CI1S1O19N8C70H97	2015-03-24	Cic1c(cc2cc1N(C(=O)CC(OC(=	D)C(N(C(=O)CCSC3C(=O)N(C(=O)C3)C1	CCOCCOCCOCCOCCCNc4c(ccc(n5nc(c6c5CC(CC8=O)(C)C)C)c4)C(=O)N(C)C)C7(CC9OC(=O)NC(O)(C(OC)C=CC=C(0	2)C)C8)C)C)C)C			
		chirality		origin	chemist	notebook	salt form						
		(12S;16S;74R;76S	3;77S;78S;83S;85P	Internal synthesis	Philip Hughes	PFH-007-004A	None: Free base						
		amount available		program	primary target	percent purity	elemental analysis						
		0.017		Purine_inhib	1.010.1	95-100	1945 4445						
	.o - 0 N	mening point		NINK Gala	on.	See chemist for s	amole						
		LCMS datafile					mini toʻsampi						
		VAR											
204.	HS-100184-02	chemic	al regist	ry									
		registry id		mol wt	formula	date	SMILES						
		HS-100184-02		1422.087	CI1S1O19N8C70H9	2015-06-25	Clc1c(cc2cc1N(C(=O)CC(OC(=O)C(	4(C(=O)CCSC3C(=O)N(C(=O)C3)CCCO0	2C0CC0CC0CC0CCCNc4c(ccc(n5nc(c8c5CC(CC8=0)(C)C)C)c4C(=0)N)C)C)C7(0C7C(C80C(=0)NC(0)(C(0C)C=CC=C(C2)C)	C8)C)C)C)OC			
		chirality		origin	chemist	notebook	salt form						
	0 0 N'0	{12S;16S;74R;76S	3;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							
	O N	melting point		NMR data	LCMS data	comment	NMR datafile						
		LONG detelle			on	Sent to UNC							
		LCMS datanie											
205.	HS-100185-01	chemic	al regist	ry									
		registry id	mol wt	formula	date	SMILES							
		HS-100185-01	1512.964	S2O13N7C86H10	9 2015-04-02	S(=O)(=O)([O-]	CCCC[N+]1=C(C=CC2=C(C(=CC=C3)	l(c4c(c5c(cccc5)cc4)C3(C)C)CCCCS(=O)	)(=0)0)CCC2)e6ccc(cc6)CNCCCOCCOCCOCCOCCCCCCCCre7e(cccc/n8ne(e9e8CC(CC9=0)(C)C)C)c7)C(=0)N(C)C)C(e1e1e1e(ccc	1)cc1)(C)C			
	0	chirality	origin	chemist	notebook	salt form							
			Internal synthesis	Philip Hughes	PFH-007-006A	None: Free bas	e						
		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										
200.		registry id	mol wt	formula	date	SMILES						
		HS-100186-01	1412.846	S2O13N7C78H105	2015-04-02	S(=0)(=0)([0-])CCCC[I	+)1=C(C=CC2=C(C(=CC=C3N	I(c4c(cccc4)C3(C)C)CCCCS(=O)	=O)O)CCC2)	c5ccc(cc5)CNCCCOCCOCCOCCCCCccce6c(ccc(n7nc(c8c7CC(CC8=O)(C)C)c6)c(=O)N(C)C)C(c9c1cccc9)(C)C		
		chirality	origin	chemist	notebook	salt form						
	©oo		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						
	-N C O N				HS-117 control							
	¥	LCMS datafile										
		Ville										
		,										
207	HS-100187-01	chemica	al registi	'y								
201.		registry id		mol wt	fc	rmula	date		SMILES			
		HS-100187-01		738.292	738.292 CI*		2015-04-07		Clc1c(cc2c	c1N(C(=O)CC(0C(=O)C(N(C(=O)CCS)C)C3(OC3C(C4OC(=O)NC(O)(C(OC)C=CC=C(C2)C)C4)C)C)OC		
	o ↓	chirality		origin	d	hemist	notebook		salt form			
	0. ↓ ↓ ▲	{12S;16S;25R;27S;	28S;29S;34S;36R;}	Internal synthesis	P	hilip Hughes	PFH-007-004StM_DM-1		None: Free	i base		
	ĴŎ <sup>°</sup> ĤĮ	D H amount available		program	р	rimary target	percent purity		elemental a	analysis		
		0.300					95-100					
	N N N	melting point		NMR data	L	CMS data	comment		NMR datafi	ie		
	Ļ, μ <sub>cι</sub> ö				0	n	DM-1; Mertansine; Tubulin in	hibitor; gift of Genentech				
	_o	LCMS datafile										
		yes										
l												
208.	HS-100188-01	chemica	al registi	у								
		registry id mol wt			formula	1	date		SMILES			
		HS-1001	88-01	363.824	363.824		02N5C15H14	2015-04-09		Clc1cc(n2ncc3c(nc(nc23)SC(C(=O)OC)C)N)ccc1		
	Ν	chirality		origin		chemis	t	notebook		salt form		
	$\sim$			Internal	synthesis	3 Dave C	arlson	3DAC088_1		None: Free base		
		amount	available	program	I	primary	r target	percent puri	ty	elemental analysis		
	N <sup>×</sup> N <sup>×</sup> S <sup>×</sup> Y <sup>×</sup>	0.040		Purine_i	nhib	DAPK/	PIMK	95-100				
	0	melting p	point	NMR da	ta	LCMS	data	comment		NMR datafile		
						on		Analog of H	S38			
		LCMS datafile										
	110 400400 04	chomical registry										
209.	HS-100189-01	registry i	d registi	y mol wt		formula		date	12	SMILES		
		HS-1001	180-01	407 877		CI1S103		2015-04-09				
	_	chirality	105 01	origin		chemist		notebook	6	alt form		
	N_O	Crinality		Internal s	wathoeie		rlson		N			
	N I	amount	availahle	nrogram	synthesis	Dave Ca	arget	percent purity		emental analysis		
		0.040	availabio	Purine in	hih		MK	95-100				
		melting r	oint	NMR dat	a	LCMS da	ata	comment	NI	MR datafile		
	ci-	inolang p	John	T thin C dat	u	on		Analog of HS?	8			
		LCMS d	atafile			0.1.						
l				1								
210.	HS-100190-01	chemica	al registi	у								
		registry id		mol wt	forr	nula	date		SMI	ILES		
	N O	HS-10019	90-01	366.459	O2	N4C21H26	2015-04-23		O=c	c1n(c2c([nH]1)cccc2)C3CCN(CC(=O)c4c(n(c(c4)C)C)C)CC3		
	N N	chirality		origin	che	emist	notebook		salt	form		
				Internal synth	nesis Dav	ve Carlson	4DAC005_1		Nor	ne: Free base		
	$\langle \cdot \cdot \rangle$	amount av	vailable	program	prir	nary target	percent purity		eler	nental analysis		
	~NO	0.5		Purine_inhib	NL	RP3	95-100					
	T I	melting po	pint	NMR data	LCI	MS data	comment		NM	R datafile		
					on		Synthesis for J	lustin Macdonald				
	Ņ	LCMS dat	tafile									
	/											

211.	HS-100191-01	chemical registry										
		registry id	mol wt	formula	date	SMILES						
		HS-100191-01 348.813		CI1S1O1N6C14H13	2015-04-30	Clc1cc(n2ncc3c(nc(nc23)SC(C(=O)N)C)N)ccc1						
	N	chirality	origin	chemist	notebook	salt form						
	N N		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	NMP datafile						
	ci 🗸		Nivii Cata									
		LCMS datafile			Analog of 11330							
	HE 100102 01	chemical registry										
212.	H3-100192-01	registry id	molwt	formula	date	SMILES						
	_	HS-100192-01	302 866		2015-04-30							
	0	chirolity	origin	chomiet	2013-04-30							
		Chirality		Chemist Deve Cerleen								
	N 		internal synthesis	Dave Canson	4DAC002_1	None. Free base						
	N	amount available	program	primary target	percent purity	elemental analysis						
		0.035	Purine_innib		95-100							
		melting point	NMR data	LCMS data	comment	NMR datafile						
				on	Analog of HS38							
		LCMS datafile										
	HE 100102 01	chemical registry										
213.	113-100133-01	registry id	mol wt	formula	date	SMILES						
		HS-100193-01	275 306	01N3C17H13	2015-05-12	O = c1[nH]c2c(nccc2)c1 = Cc3cn(c4c3cccc4)C						
		chirality	origin	chemist	notebook	salt form						
	$\langle \rangle$		Internal synthesi	s Dave Carlson	2DAC080_1	None: Free base						
	$\rangle = \langle$	amount available	program	primary target	percent purity	elemental analysis						
		0.050	Purine inhib	ACC	95-100							
		melting point	NMR data	L CMS data	comment	NMR datafile						
					GW441756							
		LCMS datafile										
	<b>~</b>											
l						1						
[			chemical registry									
214.	HS-100193-02	chemical registry										
214.	HS-100193-02	chemical registry registry id	mol wt	formula	date	SMILES						
214.	HS-100193-02	chemical registry registry id HS-100193-02	mol wt 275.306	formula O1N3C17H13	date 2015-06-25	SMILES O=c1[nH]c2c(nccc2)c1=Cc3cn(c4c3cccc4)C						
214.	HS-100193-02	chemical registry registry id HS-100193-02 chirality	mol wt 275.306 origin	formula O1N3C17H13 chemist	date 2015-06-25 notebook	SMILES O=c1[nH]c2c(nccc2)c1=Cc3cn(c4c3cccc4)C salt form						
214.	HS-100193-02	chemical registry registry id HS-100193-02 chirality	mol wt 275.306 origin Internal synthesi	formula O1N3C17H13 chemist s Dave Carlson	date 2015-06-25 notebook 4DAC012_1	SMILES         O=c1[nH]c2c(nccc2)c1=Cc3cn(c4c3cccc4)C         salt form         None: Free base						
214.	HS-100193-02	chemical registry registry id HS-100193-02 chirality amount available	mol wt 275.306 origin Internal synthesi program	formula O1N3C17H13 chemist s Dave Carlson primary target	date 2015-06-25 notebook 4DAC012_1 percent purity	SMILES         O=c1[nH]c2c(nccc2)c1=Cc3cn(c4c3cccc4)C         salt form         None: Free base         elemental analysis						
214.	HS-100193-02	chemical registry registry id HS-100193-02 chirality amount available 0.450	mol wt 275.306 origin Internal synthesi program Purine_inhib	formula O1N3C17H13 chemist s Dave Carlson primary target ACC	date 2015-06-25 notebook 4DAC012_1 percent purity 95-100	SMILES         O=c1[nH]c2c(nccc2)c1=Cc3cn(c4c3cccc4)C         salt form         None: Free base         elemental analysis						
214.	HS-100193-02	chemical registry registry id HS-100193-02 chirality amount available 0.450 melting point	mol wt 275.306 origin Internal synthesi program Purine_inhib NMR data	formula O1N3C17H13 chemist s Dave Carlson primary target ACC LCMS data	date 2015-06-25 notebook 4DAC012_1 percent purity 95-100 comment	SMILES         O=c1[nH]c2c(nccc2)c1=Cc3cn(c4c3cccc4)C         salt form         None: Free base         elemental analysis         NMR datafile						
214.	HS-100193-02	chemical registry registry id HS-100193-02 chirality amount available 0.450 melting point	mol wt 275.306 origin Internal synthesi program Purine_inhib NMR data	formula O1N3C17H13 chemist s Dave Carlson primary target ACC LCMS data on	date 2015-06-25 notebook 4DAC012_1 percent purity 95-100 comment GW441756	SMILES         O=c1[nH]c2c(nccc2)c1=Cc3cn(c4c3cccc4)C         salt form         None: Free base         elemental analysis         NMR datafile						
214.	HS-100193-02	chemical registry registry id HS-100193-02 chirality amount available 0.450 melting point LCMS datafile	mol wt 275.306 origin Internal synthesi program Purine_inhib NMR data	formula O1N3C17H13 chemist s Dave Carlson primary target ACC LCMS data on	date 2015-06-25 notebook 4DAC012_1 percent purity 95-100 comment GW441756	SMILES         O=c1[nH]c2c(nccc2)c1=Cc3cn(c4c3cccc4)C         salt form         None: Free base         elemental analysis         NMR datafile						
214.	HS-100193-02	chemical registry registry id HS-100193-02 chirality amount available 0.450 melting point LCMS datafile	mol wt 275.306 origin Internal synthesi program Purine_inhib NMR data	formula O1N3C17H13 chemist s Dave Carlson primary target ACC LCMS data on	date 2015-06-25 notebook 4DAC012_1 percent purity 95-100 comment GW441756	SMILES         O=c1[nH]c2c(nccc2)c1=Cc3cn(c4c3cccc4)C         salt form         None: Free base         elemental analysis         NMR datafile						
214.	HS-100193-02	chemical registry registry id HS-100193-02 chirality amount available 0.450 melting point LCMS datafile	mol wt 275.306 origin Internal synthesi program Purine_inhib NMR data	formula O1N3C17H13 chemist s Dave Carlson primary target ACC LCMS data on	date 2015-06-25 notebook 4DAC012_1 percent purity 95-100 comment GW441756	SMILES         O=c1[nH]c2c(nccc2)c1=Cc3cn(c4c3cccc4)C         salt form         None: Free base         elemental analysis         NMR datafile						
214.	HS-100193-02	chemical registry registry id HS-100193-02 chirality amount available 0.450 melting point LCMS datafile	mol wt 275.306 origin Internal synthesi program Purine_inhib NMR data	formula O1N3C17H13 chemist s Dave Carlson primary target ACC LCMS data on	date 2015-06-25 notebook 4DAC012_1 percent purity 95-100 comment GW441756	SMILES         O=c1[nH]c2c(nccc2)c1=Cc3cn(c4c3cccc4)C         salt form         None: Free base         elemental analysis         NMR datafile						
214. 215.	HS-100193-02	chemical registry registry id HS-100193-02 chirality amount available 0.450 melting point LCMS datafile chemical registry registry id HS-100194-01	mol wt 275.306 origin Internal synthesi program Purine_inhib NMR data NMR data	formula O1N3C17H13 chemist s Dave Carlson primary target ACC LCMS data on International Cl1S1O2N5C16H16	date           2015-06-25           notebook           4DAC012_1           percent purity           95-100           comment           GW441756	SMILES           O=c1[nH]c2c(nccc2)c1=Cc3cn(c4c3cccc4)C           salt form           None: Free base           elemental analysis           NMR datafile           SMILES           Clc1cc(n2ncc3c(nc(nc23))SC(C(=0))C()C))N(C)ccc1						
214.	HS-100193-02	chemical registry registry id HS-100193-02 chirality amount available 0.450 melting point LCMS datafile chemical registry registry id HS-100194-01 chirality	mol wt 275.306 origin Internal synthesi program Purine_inhib NMR data NMR data	formula O1N3C17H13 chemist s Dave Carlson primary target ACC LCMS data on on	date 2015-06-25 notebook 4DAC012_1 percent purity 95-100 comment GW441756 GW441756 date 2015-05-20 potebook	SMILES         O=c1[nH]c2c(nccc2)c1=Cc3cn(c4c3cccc4)C         salt form         None: Free base         elemental analysis         NMR datafile         SMILES         Clc1cc(n2ncc3c(nc(nc23)SC(C(=O)OC)C)NC)ccc1         salt form						
214.	HS-100193-02	chemical registry registry id HS-100193-02 chirality amount available 0.450 melting point LCMS datafile chemical registry registry id HS-100194-01 chirality	mol wt 275.306 origin Internal synthesi Program Purine_inhib NMR data NMR data MIR d	formula O1N3C17H13 chemist s Dave Carlson primary target ACC LCMS data on LCMS data on Cl1S1O2N5C16H16 chemist Dave Carlson	date 2015-06-25 notebook 4DAC012_1 percent purity 95-100 comment GW441756 GW441756 date 2015-05-20 notebook 4DAC006 1	SMILES         O=c1[nH]c2c(nccc2)c1=Cc3cn(c4c3cccc4)C         salt form         None: Free base         elemental analysis         NMR datafile         Image: SMILES         Clc1cc(n2ncc3c(nc(nc23)SC(C(=0)OC)C)NC)ccc1         salt form         None: Free base						
214.	HS-100193-02	chemical registry registry id HS-100193-02 chirality amount available 0.450 melting point LCMS datafile chemical registry registry id HS-100194-01 chirality amount available	mol wt       275.306       origin       Internal synthesi       program       Purine_inhib       NMR data       Internal synthesis       program	formula O1N3C17H13 chemist s Dave Carlson primary target ACC LCMS data on LCMS data on cl1S102N5C16H16 chemist Dave Carlson primary target	date 2015-06-25 notebook 4DAC012_1 percent purity 95-100 comment GW441756 GW441756 date 2015-05-20 notebook 4DAC006_1 percent purity	SMILES         O=c1[nH]c2c(nccc2)c1=Cc3cn(c4c3cccc4)C         salt form         None: Free base         elemental analysis         NMR datafile         NMR datafile         SMILES         Clc1cc(n2ncc3c(nc(nc23)SC(C(=O)OC)C)NC)ccc1         salt form         None: Free base         elemental analysis						
214.	HS-100193-02 N = 0 HS-100194-01 HS-100194-01	chemical registry registry id HS-100193-02 chirality amount available 0.450 melting point LCMS datafile chemical registry registry id HS-100194-01 chirality amount available 0.050	mol wt       275.306       origin       Internal synthesi       program       Purine_inhib       NMR data       Internal synthesi       mol wt       377.851       origin       Internal synthesis       program	formula O1N3C17H13 chemist s Dave Carlson primary target ACC LCMS data on LCMS data on cl1S102N5C16H16 chemist Dave Carlson primary target DAPK/PIM3	date 2015-06-25 notebook 4DAC012_1 percent purity 95-100 comment GW441756 GW441756 date 2015-05-20 notebook 4DAC006_1 percent purity 95-100	SMILES         O=c1[nH]c2c(nccc2)c1=Cc3cn(c4c3cccc4)C         salt form         None: Free base         elemental analysis         NMR datafile         SMILES         SMILES         Clc1cc(n2ncc3c(nc(nc23)SC(C(=O)OC)C)NC)ccc1         salt form         None: Free base         elemental analysis						
214.	HS-100193-02 N = 0 HS-100194-01 HS-100194-01	chemical registry registry id HS-100193-02 chirality amount available 0.450 melting point LCMS datafile chemical registry registry id HS-100194-01 chirality amount available 0.050 melting point	mol wt         275.306         origin         Internal synthesi         program         Purine_inhib         NMR data         a         a         a         a         a         a         b         a         b         b         b         c         c         c         c         c         c         c         c         c         c         c         c         c         c         c         c         c         c         c         c         c         c         c         c         c         c         c         c         c         c         c         c         c         c         c         c         c <th>formula O1N3C17H13 chemist s Dave Carlson primary target ACC LCMS data on LCMS data on Cl1S102N5C16H16 chemist Dave Carlson primary target DAPK/PIM3 LCMS data</th> <th>date 2015-06-25 notebook 4DAC012_1 percent purity 95-100 comment GW441756 3 4 2015-05-20 notebook 4DAC006_1 percent purity 95-100 comment</th> <th>SMILES         O=c1[nH]c2c(nccc2)c1=Cc3cn(c4c3cccc4)C         salt form         None: Free base         elemental analysis         MR datafile         SMILES         Clc1cc(n2ncc3c(nc(nc23)SC(C(=O)OC)C)NC)ccc1         salt form         None: Free base         elemental analysis</th>	formula O1N3C17H13 chemist s Dave Carlson primary target ACC LCMS data on LCMS data on Cl1S102N5C16H16 chemist Dave Carlson primary target DAPK/PIM3 LCMS data	date 2015-06-25 notebook 4DAC012_1 percent purity 95-100 comment GW441756 3 4 2015-05-20 notebook 4DAC006_1 percent purity 95-100 comment	SMILES         O=c1[nH]c2c(nccc2)c1=Cc3cn(c4c3cccc4)C         salt form         None: Free base         elemental analysis         MR datafile         SMILES         Clc1cc(n2ncc3c(nc(nc23)SC(C(=O)OC)C)NC)ccc1         salt form         None: Free base         elemental analysis						
214.	HS-100193-02 N = 0 HS-100194-01 HS-100194-01	chemical registry registry id HS-100193-02 chirality amount available 0.450 melting point LCMS datafile chemical registry registry id HS-100194-01 chirality amount available 0.050 melting point	mol wt         275.306         origin         Internal synthesi         program         Purine_inhib         NMR data         Image: synthesis         77.851         origin         Internal synthesis         program         Purine_inhib	formula O1N3C17H13 chemist s Dave Carlson primary target ACC LCMS data on cl1S102N5C16H16 chemist Dave Carlson primary target DAPK/PIM3 LCMS data on	date 2015-06-25 notebook 4DAC012_1 percent purity 95-100 comment GW441756 GW441756 2015-05-20 notebook 4DAC006_1 percent purity 95-100 comment Analog of HS38	SMILES         O=c1[nH]c2c(nccc2)c1=Cc3cn(c4c3cccc4)C         salt form         None: Free base         elemental analysis         MR datafile         SMILES         Clc1cc(n2ncc3c(nc(nc23)SC(C(=O)OC)C)NC)ccc1         salt form         None: Free base         elemental analysis						
214.	HS-100193-02 I = I = I = I = I = I = I = I = I = I =	chemical registry         registry id         HS-100193-02         chirality         amount available         0.450         melting point         LCMS datafile         chirality         registry id         HS-100194-01         chirality         amount available         0.050         melting point	mol wt 275.306 origin Internal synthesi program Purine_inhib NMR data NMR data NMR data NT7.851 Origin Internal synthesis program Purine_inhib NMR data	formula O1N3C17H13 chemist s Dave Carlson primary target ACC LCMS data on club CI1S102N5C16H16 chemist Dave Carlson primary target DAPK/PIM3 LCMS data on	date 2015-06-25 notebook 4DAC012_1 percent purity 95-100 comment GW441756 GW441756 2015-05-20 notebook 4DAC006_1 percent purity 95-100 comment Analog of HS38	SMILES         O=c1[nH]c2c(nccc2)c1=Cc3cn(c4c3cccc4)C         salt form         None: Free base         elemental analysis         MR datafile         SMILES         Clc1cc(n2ncc3c(nc(nc23)SC(C(=O)OC)C)NC)ccc1         salt form         None: Free base         elemental analysis						
214.	HS-100193-02 I = I = I = I = I = I = I = I = I = I =	chemical registry         registry id         HS-100193-02         chirality         amount available         0.450         melting point         LCMS datafile         chemical registry         registry id         HS-100194-01         chirality         amount available         0.050         melting point         LCMS datafile	mol wt         275.306         origin         Internal synthesi         program         Purine_inhib         NMR data         a         mol wt         377.851         origin         Internal synthesis         program         Purine_inhib         NMR data	formula O1N3C17H13 chemist s Dave Carlson primary target ACC LCMS data on club CANS data ON Cl1S102N5C16H16 chemist Dave Carlson primary target DAPK/PIM3 LCMS data on	date 2015-06-25 notebook 4DAC012_1 percent purity 95-100 comment GW441756 2015-05-20 notebook 4DAC006_1 percent purity 95-100 comment Analog of HS38	SMILES         O=c1[nH]c2c(ncc2)c1=Cc3cn(c4c3cccc4)C         salt form         None: Free base         elemental analysis         NMR datafile						

216.	HS-100195-01	registry id mol ut formula data SMILES										
		registry	id	mol v	vt	formula	date	SMILES				
		HS-100	0195-01	362.8	39	CI1S1O1N6C15	-115 2015-05	5 2015-05-20 Clc1cc(n2ncc3c(nc(nc23)SC(C(=O)N)C)NC)cc				
	Ņ	chirality	/	origin	I	chemist	noteboo	notebook salt form				
				Interr	al synthesi	s Dave Carlson	1 4DAC008_1 None: Free base		None: Free base			
	N N N	amount	t available	progr	am	primary target	percent	percent purity elemental analysis				
		0.050		Purin	e_inhib	DAPK/PIM3	95-100					
	Ö	melting	point	NMR	data	LCMS data	comme	comment NMR datafile				
	CI					on	Analog	Analog of HS38				
	2	LCMS of	datafile									
17.	HS-100196-01	chemic	cal regist	у								
		registry id	mol wt	formula	date	SMILES						
	-0	HS-100196-01	HS-100196-01 1544.920 S40		2015-06-03	S(=O)(=O)(O)c1cc2c(cc1)N(C(=CC=C3C(=C	C=CC4=[N+](c5c(cc(cc5)S(=O)(=	0)0)C4(C)C)CCCCS	(=O)(=O)[O-])CCC3)c6ccc(cc6)CNCCCOCCOCCOCCOCCOCCCCCCC?c(ccc(n8nc(c9c8CC(CC9=O)(C)C)C)C)C)=O)N)C2(C)			
	os o	chirality origin che		chemist	notebook	salt form	at form					
			Internal synthesis	Philip Hughes	PFH-007-015D	None: Free base	one: Free base					
		amount available	program	primary target	percent purity	elemental analysis	tal analysis					
		0.043	Purine_inhib		95-100							
		melting point	NMR data	LCMS data	comment	NMR datafile						
	<b>5</b> 0		on	on	See Chemist for sample	yes						
	(80	LCMS datafile										
		yes										
	110 400407 04	chemical registry										
18.	HS-100197-01	registry	id	y mol w	+	formula	date	SMILE	۹			
	<b>o</b> , /	HS-100	197-01	397.4	53	S103N5C19H19	2015-06-10	s1c(nc)	2cc(ccc12)C(-O)OC)NC(-O)C3CN(c4pccpc4)CCC3			
	)ó	chirality	/	origin	50	chemist	notebook	salt for	m			
		ormanty	·	Intern	al synthesis	Dave Carlson		None:	Free base			
	O N	amount	t available	progra	am	primary target	percent purity		nental analysis			
		0.250	available	Purine	inhih	Hsn70	95-100					
	N	melting	point	NMR	data	LCMS data	comment	NMR d	latafile			
		moning	point		aala		Common					
		LCMS	datafile									
	ĽN	201010	aatanic	-								
		][										
219	HS-100198-01 chemical registry											
219.		registry id	mol wt	formula	date	SMILES						
		HS-100198-01	1346 745	\$2013NZC73	199 2015-06-11	S(=0)(=0)((0-))CCCC(IN+11=C(C=	CC(=CC=C2N(c3c(cccc3)C2(C)C)	)CCCCS(=0)(=0)0)c4				



-				
chemic	al registry	/		
registry id	mol wt	formula	date	SMLES
HS-100198-01	1346.745	S2O13N7C73H99	2015-06-11	S(=0)[+0)[[0-]]CCCC[[N+]]=C[C=CC]=CC]=C2N(c3c(cccc3)C2]C]C)CCCCS(=0)(=0)(0)04ccc(cc4)ONCCC0CC0CC0CC0CC0CCCCCCCCCCCCCCCCCCCCC
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 datafie
		on	500 mg sent for MTD etc.	
LCMS datafile				
yes				

220. HS-100199-01



	chemic	al regis	try			]
	registry id	mol wt	formula	date	SMILES	1
	HS-100199-01	1572.974	S4O19N7C78H105	2015-06-23	S(+O))(+O)(O):1ct2ct(ct))N(C(+CC+C3C(+C(+C+C4+(N+)(ctc(cc(xt)S(+O)(+O)()C4(C)C)CCCS(+O)(+O)(O-1)CCC3)ct6cxt(cxt)(NCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC	c)c)ccc
0 0'0	chirality	origin	chemist	notebook	salt form	1
		Internal synthesis	Philip Hughes	PFH-007-032B	None: Free base	1
	amount available	program	primary target	percent purity	elemental analysis	1
	0.017	Purine_inhib		95-100		1
	melting point	NMR data	LCMS data	comment	NMR datafie	1
			on	See Chemist for sample		1
	LCMS datafile					1
	yes					1

HS-100200-01	chemica	chemical registry										
		mol wt	for	nula	date		SMLES					
oo o <sup>s</sup> o	HS-100200-01	887.505	CI1	S4O12N2C38H47	2015-06-29	9	CIC1 = C(C - CC2 = [N + ](c3c(cc(cc3)S(*O)(*O)(*O)(CC)C)CCCCS(*O)(*O)((*O)(CC)C1 = CC = C4N(c5c(cc(cc5)S(*O)(*O)(*O)(CC)C)CCCCS(*O)(*O)(*O)(*O)(*O)(*O)(*O)(*O)(*O)(*O)					
¯ ¯ ¯ ¯ ¯ ¯ ¯	chirality	origin	che	mist	notebook		salt form					
<b>→</b> <sup>N</sup> <sup>→</sup>		Internal synth	iesis Phi	imary target PFH-0	PFH-007-0	27A	None: Free base					
	amount available	program	prir		percent purity		elemental analysis					
	0.409 Purine_inhib											
o š N±	melting point	NMR data	LCI	//S data	comment		NMR datafile					
rst.					See Chemi	ist for sample						
	LCMS datafile											
500												
HS-100201-01	cnemical registry											
	registry id	nol wt	formula	date		SMILES						
	HS-100201-01	1304.536	O14N9C72H89	2015-07-17 O=C(OC)		0-C(0C)C1C2(C3-Cc4[n+]jc(c(xC)CCC(+0)NCCCCCCCCCCCCCCCCCCCCCCcccc(ndinc(c7c8CC(CC7-0)(C)C)C)cb)C(+0)N(C+c8inc(c(x8CCC(+0)OC)C)-c+3[n+]jc(+CC(+N3)C2+CC+C1C(+0)OC)c(c4C+C)(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C2+CC+C1C(+D)C+C1C+C1C+C1C+C1C+C1C+C1C+C1C+C1C+C1C+C						
<u>`0</u>	chirality	origin	chemist	notebook salt form		salt form						
o 8	(5S;6R;) Internal synthesis Philip Hughes PFH-007-046A			None: Free base								
	amount available	orogram	primary target	percent purity								
	0.036	Purine_inhib		95-100								
	melting point	NMR data	LCMS data	comment NMI		NMR datafie						
			on	Mixture of isomers from	verteporfin							
	LCMS datafile											
	yes											
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# 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 12/16/1 <b>6</b>
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

Appendix C

### 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

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

Appendix C

# Future Statement of Work

## Aim 8: Optimize lead NIR contrast agent.

<u>Aim 8. Task 2:</u> 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.

<u>Aim 10. Task 1:</u> 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

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

## Future Statement of Work

### 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

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

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



Brian Pogue, Dartmouth



ID Milestone	2012 2013 2014 2015 2016 2017 2018 2019 2020 2021 2019 2020 2021 2011 2012 2019 2020 2021 2011 201	<u>)tr 1</u>
39 No	Task 4 - Demonstrate detection of NR Hsp99i accumulation in tumor xenografts derived from humional, HR2+ and triple negative human breast cancer and spontaneous murine breast cancer models of breast	
40 No	Task 5 - Demonstrate thermal changes and antitumor effects of R7 mediated thermat therapy in human breast cancer renograf model, syngmetic models, then test antitumor effects	
41 No	Aim 3 - Confirming Hsp90 Expression in specific molecular subtypes of human breast cancer	
42 No	Tysk 1 - Confirm protein expression levels of Hsp90 in breast cancer subtypes including TNBC	
43 No	Task 2 - Analyze breast cancer tissues for additional markers of Hsp90 activity including Hsp70 and caspase 3	
44 No	UT and utransformed and the second a	
45 No	Task 4 - Perform pilot feasibility studies to determine the association of Hsp90 expression with patient outcomes	
46 No	UTH C GMP Mahufacturing of PM Hstp30 Inhibitor	
47 No	0% Albany Molecular Research Inc. Task 1 - Establish synthetic pathways and SOPs for lead molecular	
48 No	82% and Philip Hughes, Dr. Timothy Haystead Task 2 - Engage a grivate pharmaceutical contrador for synthesis of GMP material	
49 No.	8221 Henriffy GMP manifesturer albumy Molecular Revearch Inc (IAMRI)	
50 No	100% Thill Hughes, Dr. Timothy Haystead, Guy Matsumoto (Vsolvit)	
50 140		
51 NO	CUA/MDA.Imitatory, review, and approval 100% - Dr. David Krifly (Duke), Guy Masumoto (Visohit), Henry Hagen (AMRI)	
52 No	Duke-AMR budget, contract, delivier babe, manufacturing timeline meeting 100% prof. Susan Billings (AMR) J.Dr. H. Kim Lyerh, I'VA Team	
53 No	Manufacturing RP Initiation; review, and approval (includes pricing and completion timeline) OR the description of the descript	
54 Yes	PM Hsp90 Inhibiter Manufacturing Process 0K 🛶 9/9	
55 No	Not lot. Of Mark Dr. Philip Hughes, Dr. Susan Billings (AMR), Dr. Timothy Haystead	
56 No	Final Report for InDu Othera Dr. Amy Hobeika,Dr. Michael Morse,Albany Molecular Research Inc.	
57 Yes	Task 3 - Produce <sup>PM</sup> Hsp90 Inhibitor GMP material GNspa, Albany Modecular Research Inc.	
58 No	Ship noh-GMP material for Trainciology Studies at Charles River OStan Albany Molecular Research Inc., Charles River Labs	
59 <b>No</b>	Aim 5 Required GMP Preclinical Toyloo by Studies for Phase I Testing	
60 No	Identify contract company: Piedmint [Charles River]	
61 No	Toxicology CDA (bDA) Documentation	
62 No	Initiation, review, and approval Oxig_L-IP. David Sordys (Duke), Guy Matsumoto (Vsolvit), Lorie Boyd (CR)	
63 No	Task 2 - Preclinical thirdogy studies	
64 No	Determine budget, contract, and leiterables teleconference meeting OKB_CDuarke River Labs.Dc H. Kim Lyerky.Dr. Michael Morse.Dr. Timothy Haystead	
65 No	Develop and finalize to ox protocol (or staged 0r. Timothy Haystead, 0r. Michael Morse	
66 Yes	Pharmacokinetic Studies 0% == 9022e River Labs	
67 No	Muse PK (rodent) (Muse PK (rodent)	
68 No	Rabble PP (inter-there the	
69 Yes	Toxicology Studies (single desc)	
70 No	Moute Tox Study	
71 No	USN 🐨 Early sacrifice (for main study group, est. Day 3-2)	
72 No	Late sacrifice (fbr regivery group, est. Day 14)	
73 No	04sgcCharles River Labs Rubbl Tox Study	
74 No	Early sacrifice (for train is study group, est. Day 1-2)	
	Office Thirds River Labs	
Project: TVA Grant Date: Thu 7/30/15	C11108_Du       Melestone       Project Summary       External Milestone       Inactive Milestone       Manual Task       Manual Summary Rollup       Start-only       Deadline       +         Split       Summary       External Tasks       Inactive Task       Inactive Summary       -       Duration-only       Image: Manual Summary Rollup       Start-only       Deadline       +	



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