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From bedside to bench: Use of patient-derived xenograft models to develop novel therapeutic strategies for triple-negative breast cancer

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University.

By

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February 2020

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ACKNOWLEDGEMENTS

First and foremost, I would like to thank Dr. Chuck Harrell for his outstanding mentorship and guidance throughout my time in his lab. In addition to imparting his expertise and guiding me towards becoming an independent researcher, as well as his constant encouragement and positivity, Dr. Harrell has always gone above and beyond to support my training and provide me with multiple opportunities to advance my career development as a future physician scientist. In addition to being a brilliant and enthusiastic scientist, he is an amazing person who truly cares about his students. I could not have wished for a better mentor in all respects. I am truly honored to be Dr. Harrell's first graduate student and to have had the opportunity to train in his lab. Every aspect of what I've learned from him I will certainly carry with me throughout my career.

I would like to thank all the current and past members of the Harrell lab: Mohammad Alzubi, Sahib Sohal, Madelyn Esquivel, Narmeen Rashid, David Boyd, and Madhu Sriram, for always being eager to assist me with my experiments and taking care of lab responsibilities, for helping me strengthen my mentoring skills, and for being wonderful lab-mates and friends who have made my experience in the lab even more enjoyable.

I would like to thank the members of my thesis committee: Drs. Charles Clevenger, Jennifer Koblinski, Mikhail Dozmorov, and Alicia Zukas, for their incredible guidance, support, and feedback throughout my research projects. I would like to additionally thank Dr. Zukas for her clinical mentorship which has greatly inspired and solidified my clinical aspirations in the field of neuro-oncology. I am grateful to have such brilliant and inspirational role models.

I would like to thank the VCU MD-PhD Program for all its support, with a special thanks to Dr. Michael Donnenberg, Dr. Gordon Archer, Dr. Clive Baumgarten, Dr. Ross Mikkelsen, and Sandra Sorrell for always being there for guidance and for always being great advocates for the MD-PhD students.

I would like to thank the CCTR CaMM Program for providing me with a solid foundation in translational research that has and will continue to help inform my work throughout my training and career, with a special thanks to Dr. Joyce Lloyd, Dr. Devanand Sarkar, Dr. Pamela Dillon, and all the administrative personnel for their incredible support throughout my graduate training.

I would like to thank the NIH National Cancer Institute for funding my F30 fellowship grant (F30CA228393), as well as the VCU Massey Cancer Center, METAvivor, Susan G. Komen, and all other funding sources that helped make this research possible. I would also like to thank the VCU Core Facilities that contributed significantly to this work: the Cancer Mouse Models Core, the FACS Core, and the Microscopy Core.

I would like to thank all members of the VCU Pathology Department for always providing support and assistance when I needed it. I would also like to thank all our collaborators, both within and outside our department, for the opportunity to contribute to other research projects and for also assisting me with my work: Dr. Jason Reed, Graeme Murray, Dr. Senthil Radhakrishnan, Amy Northrop, Dr. Janakiram Vangala, Alex Feygin, Dr. Youngman Oh, Dr. Charles Clevenger, Alicia Woock, Jackie Gible, Justin Craig, Dr. Anthony Faber, Dr. Sheeba Jacob, Dr. Steve Grossman, Kranthi Kumar Chougoni, Dr. Sarah Spiegel, Dr. Mikhail Dozmorov, Dr. Amy Olex, and Dr. Richard Young.

I would like to specially thank my previous research mentor and colleagues from the Feinstein Institute for Medical Research, Drs. Marc Symons, Maria Ruggieri, and Ian Miller, my undergraduate research mentor and professor from Hofstra University, Dr. Beverly Clendening, as well as Dr. Justin DiAngelo, Dr. Rodney Finzel, and my other science professors from Hofstra University, for helping me establish a solid foundation of scientific knowledge and research experience that prepared me immensely for my graduate training, and for their guidance and support throughout college, MD-PhD program applications, and beyond. The impact they all had on me continues to inspire me throughout my training.

Lastly, I would like to give a special thanks to my family (particularly my mom and dad, sister Tara, and Uncle Ed), my boyfriend Rob, and all my friends both inside and outside of VCU, for their unwavering support and encouragement throughout this challenging yet exhilarating endeavor.

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LIST OF ABBREVIATIONS

ADORA3	adenosine A3 receptor
AR	androgen receptor
ATCC	American Type Culture Collection
BCL2	B-cell lymphoma 2
BCRP	breast cancer resistance protein
BIRC5	baculoviral inhibitor of apoptosis repeat-containing 5
BL1	basal-like 1
BL2	basal-like 2
CCLC	Cancer Cell Line Encyclopedia
CCTR	Center for Clinical and Translational Research
CDK	cyclin-dependent kinase
CI	combination index
CMV	cytomegalovirus
CNS	central nervous system
COMT	catechol-O-methyltransferase
CRMPC	castration-resistant metastatic prostate cancer
CYP17A1	cytochrome P450 family 17 subfamily A member 1
CYP27A1	cytochrome P450 family 27 subfamily A member 1
DHP	dihydropyridine
DHT	dihydrotestosterone
DMEM/F12	Dulbecco's Modified Eagle Medium/Nutrient Mixture F12
DMSO	dimethylsulfoxide
DRI	dose reduction index
ECM	extracellular matrix
EGCG	epigallocatechin gallate
EGFR	epidermal growth factor receptor
EMEM	Eagle's Minimum Essential Medium
EMT	epithelial-to-mesenchymal transition
ER	estrogen receptor
Fa	fraction affected (fraction inhibition)
FACS	fluorescence-activated cell sorting
FBS	fetal bovine serum
FDA	U.S. Food and Drug Administration
FKBP1A	FK506 binding protein 1A
GABA	gamma aminobutyric acid
GBM	glioblastoma multiforme
GEO	Gene Expression Omnibus
GFP	green fluorescent protein
GGCX	gamma-glutamyl carboxylase
GIRK	G-protein-coupled inwardly-rectifying potassium channel
H&E	hematoxylin and eosin
HBEC	human breast epithelial cell

HDAC	histone deacetylase
HER2	human epidermal growth factor receptor 2
HIST1H3B3	phosphohistone-H3
HMS	Harvard Medical School
HSP90	heat shock protein 90
IACUC	Institutional Animal Care and Use Committee
IAP	inhibitor of apoptosis
IHC	immunohistochemistry
IM	immunomodulatory
IP	intraperitoneal
KCNA7	potassium voltage-gated channel subfamily A member 7
KCNJ5	potassium inwardly rectifying channel subfamily J member 5
LAR	luminal androgen receptor
LINCS	Library of Integrated Network-based Cellular Signatures
M	mesenchymal-like
MAPK	mitogen-activated protein kinase
MFS	metastasis-free survival
MSL	mesenchymal stem-like
mTOR	mammalian target of rapamycin
NSC	non-silencing control
NSG	non-obese diabetic severe combined immunodeficient gamma
p/s	photons per second
PARP	poly ADP-ribose polymerase
PD-1	programmed cell death protein 1
PDL-1	programmed cell death ligand 1
PDX	patient-derived xenograft
PI3K	phosphoinositide 3-kinase
poly-HEMA	poly-2-hydroxyethyl-methylacrylate
PR	progesterone receptor
PSMB5	proteasome subunit beta 5
PTGS2	prostaglandin endoperoxide synthase 2
QNBC	quadruple-negative breast cancer
RFP	red fluorescent protein
RPKM	reads per kilobase of transcript per million mapped reads
RPMI-1640	Roswell Park Memorial Institute 1640
S1P	sphingosine 1-phosphate
SDS-PAGE	sodium dodecyl sulfate polyacrylamide gel electrophoresis
SERD	selective estrogen receptor degrader
SERM	selective estrogen receptor modulator
SMAC	second mitochondria-derived activator of caspases
SSRI	selective serotonin reuptake inhibitor
TBS	Tris-buffered saline
TBS-T	Tris-buffered saline + Tween-20
TCGA	The Cancer Genome Atlas

TNBC	triple-negative breast cancer
TPM	transcripts per million
TROP-2	trophoblast cell-surface antigen 2
UCSC	University of California Santa Cruz
VCU	Virginia Commonwealth University
VCF	Variant Call Format
VDR	vitamin D receptor
VEGF	vascular endothelial growth factor
VKOR	vitamin K epoxide reductase
XIAP	X-linked inhibitor of apoptosis

ABSTRACT

FROM BEDSIDE TO BENCH: USE OF PATIENT-DERIVED XENOGRAFT MODELS TO DEVELOP NOVEL THERAPEUTIC STRATEGIES FOR TRIPLE-NEGATIVE BREAST CANCER

By Tia Hara Turner, M.D., Ph.D.

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University.

Virginia Commonwealth University, 2020.

Director: J. Chuck Harrell, Ph.D., Assistant Professor, Department of Pathology

Triple-negative breast cancer (TNBC) is a clinically aggressive disease that is associated with bleak outcomes due to its metastatic propensity, frequent failure to respond to chemotherapy, and lack of alternative treatment options. Despite decades of major translational research efforts, there has been very little success thus far in the development of effective targeted therapies for this disease. It is imperative to develop novel therapeutic strategies to improve patient outcomes, as well as minimize the toxicity associated with standard-of-care chemotherapeutics. Given that metastatic disease accounts for the vast majority of TNBC-related deaths, a better understanding of therapeutic responses within common sites of metastasis is crucial for developing effective treatment strategies. Given the molecular heterogeneity of TNBC, the clinical success of new therapies additionally depends on the identification of reliable drug targets within each TNBC subtype for more effective patient stratification. The studies presented herein sought to address these matters, using clinically relevant patient-derived xenograft (PDX) models to characterize chemotherapeutic efficacy in distinct metastatic sites, to identify promising targeted therapeutic candidates and combination strategies, and to assess the translational potential of these therapeutic strategies, with a focus on both the basal-like and luminal androgen receptor (LAR) subtypes of TNBC. We hypothesized that therapeutic efficacy in the primary tumor setting would be maintained in the metastatic setting, and that PDXs of distinct TNBC subtypes would respond to particular targeted therapies based on the distinct molecular pathways that drive their progression. We therefore expected that therapies targeting the epidermal growth factor receptor (EGFR) and the androgen receptor (AR) would have efficacy in basal-like TNBC and LAR TNBC, respectively, and would be ideal for incorporation into novel combination regimens for these specific disease subtypes. Using a combination of *in vitro* and *in vivo* drug response studies, we identified a drug combination, co-targeting EGFR and survivin, that was synergistic across multiple PDX models of basal-like TNBC, despite some of these models responding differently to standard chemotherapies, thus revealing potential pathways that may serve as reliable drug targets in this subset of patients. Furthermore, we identified several potential drug targets and therapeutic candidates for combination with AR-targeted therapies in LAR TNBC. In addition to identifying novel therapeutic strategies that have potential to provide clinical benefit for these subsets of TNBC patients, these studies highlight the utility of PDX models for *in vitro* and *in vivo* drug development studies, and demonstrate that the molecular and drug response profiles of primary tumors are maintained in the metastatic setting, indicating that studies employing PDX mammary tumor models can be applicable in advanced disease. Collectively, the data generated in these studies have the potential not only to directly provide clinical benefit for TNBC patients, but also to inspire and inform countless future research endeavors seeking to improve the therapeutic landscape in breast cancer.

VITA

Tia Hara Turner was born on December 14, 1989 in Mamou, Evangeline Parish, Louisiana, and is an American citizen. She grew up in Hewlett, New York and graduated from George W. Hewlett High School in 2007. She graduated *summa cum laude*, with a Bachelor of Science in Pre-Medical Studies and a minor in Psychology, from Hofstra University in 2013, with high departmental honors in the Department of Biology as well as two awards for completing her undergraduate studies with a cumulative 4.0 grade point average: the Outstanding Senior Scholar Award and the Albert I. DaSilva Memorial Endowed Scholarship. During her undergraduate studies, Tia conducted research with Dr. Beverly Clendening at Hofstra University, as well as Dr. Marc Symons at the Feinstein Institute for Medical Research. After graduating from Hofstra University, Tia spent one year doing full-time research in the Symons lab, studying the role and pharmacologic targeting of microglia in the context of glioblastoma multiforme, leading to a co-authorship publication, before beginning her MD-PhD studies at Virginia Commonwealth University (VCU) School of Medicine in the summer of 2014. In 2016, after finishing her first two years of medical school, she joined the lab of Dr. Chuck Harrell, in the VCU Department of Pathology, to pursue her PhD studies as part of the C. Kenneth and Dianne Wright Center for Clinical and Translational Research (CCTR), Cancer and Molecular Medicine graduate program. During her graduate studies, she received an F30 fellowship grant from the NIH National Cancer Institute, authored or co-authored 8 publications, and became a co-inventor on a patent application, in addition to presenting her work at institutional, local, and national conferences.

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CHAPTER 1: Introduction

1.1 Introduction to breast cancer

1.1.1 Breast cancer history and statistics

The first documented cases of breast cancer date back to ancient times, when cancer was deemed an incurable illness [1, 2]. Throughout ancient Egyptian and Greek history, breast cancer and other cancers were treated surgically, with palliative intent, as cancer was poorly understood apart from its invasive nature [2, 3]. Although early centuries saw gradual improvements in diagnostic and surgical techniques, it was not until the 18th and 19th centuries that scientists and physicians began working towards advancing our understanding of breast cancer with the intent to develop curative treatments, the first of which was the radical mastectomy [2, 4]. During the 20th century, major cancer research efforts resulted in a vast expansion in our comprehension of breast cancer biology and pathogenesis, leading to the discovery of the roles of the estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) in breast cancer [5] and the development of ER- and HER2-targeted therapeutics [6–8], along with the development of chemotherapy [9, 10]. Tailoring of therapeutic regimens to accommodate the individual patient, along with advancements in molecular biology and genomic analysis techniques, resulted in the concept of personalized medicine. This has more recently been facilitated by the identification of the intrinsic molecular subtypes of breast cancer [11–14], which are now known to have significant therapeutic and prognostic implications [15–18]. The development of improved treatment strategies and patient stratification protocols, along with the implementation of routine diagnostic screening, has led to a steady decline in breast cancer mortality over the past several decades [19].

Although the field of breast cancer has come a long way, the disease remains a significant medical problem in the U.S. and the rest of the world in the 21st century [20].

Breast cancer is currently the second most common cancer and the second leading cause of cancer-related mortality in women in the U.S., and it is estimated that 1 in 8 women will develop breast cancer over the course of life [19]. Each year, over 268,000 Americans are diagnosed with invasive breast cancer, and over 41,000 die as a result of disease burden [19]. It is therefore imperative to continue our research efforts to further advance our understanding and improve the treatment and outcomes of this disease.

1.1.2 *Breast cancer subtype classification and clinical implications*

Significant advancements in the field of breast cancer research over the past several decades can largely be attributed to the identification and characterization of the distinct molecular subtypes of breast cancer [11–14], which govern treatment and predict prognosis [15–18]. In the clinic, breast cancer is most commonly subtyped based on ER, PR, and HER2 status, and this is one of the primary determining factors for pharmacologic treatment decisions as well as prognosis [21–23]. ER-positive breast cancer is typically well-differentiated, less proliferative, and less likely to bear oncogenic mutations compared to ER-negative disease [24–26]. Patients with ER-positive tumors are treated with ER-targeted therapeutics, including selective estrogen receptor modulators (SERMs) such as tamoxifen or selective estrogen receptor degraders (SERDs) such as fulvestrant. These are administered with or without adjuvant or neoadjuvant chemotherapy, depending on other tumor characteristics such as tumor stage. Given its association with lower tumor grade and the availability of targeted therapies, ER-positive disease is associated with relatively favorable outcomes, particularly when PR is co-expressed with ER [27–29]. HER2-positive breast cancer is associated with less favorable outcomes compared to ER-positive disease [30–32], however prognosis is substantially improved when patients are treated with HER2-targeted therapeutics, including the anti-HER2 monoclonal antibody trastuzumab, along with chemotherapy. Hormone receptor and/or HER2 positive disease

collectively account for approximately 85% of breast cancers, largely contributing to the current overall breast cancer 5-year survival rate of nearly 90% [19, 33].

Triple-negative breast cancer (TNBC), which accounts for the remaining 15% of breast cancers, is negative for ER, PR, and HER2 [22, 23], and no reliable therapeutic targets have yet been identified despite decades of translational research [34]. Therefore, treatment for this subtype is currently limited to adjuvant or neoadjuvant chemotherapy. TNBC is associated with the worst prognosis of all histologic subtypes [35], as these tumors are typically high grade with a greater propensity to metastasize to visceral organs [36–38]. TNBC tumors are also more likely to be associated with oncogenic mutations [39, 40], and approximately 20% of TNBCs are associated with BRCA1 mutations [41]. Despite aggressive chemotherapeutic regimens consisting of highly toxic anthracyclines, taxanes, and/or alkylating agents, TNBC often fails to respond or acquires resistance to chemotherapy, leading to refractory and recurrent disease, and contributing largely to the poor prognosis associated with this subtype [38].

Breast cancer is classified not only histologically based on ER/PR/HER2 status, but also molecularly based on gene expression profiling. Differential expression of a 50-gene signature divides breast tumors into five distinct intrinsic subtypes (luminal A, luminal B, HER2-enriched, basal-like, and claudin-low) as well as a normal-like subtype, in which expression of the gene signature resembles that of the normal breast tissue [11–14]. PAM50 analysis (now known as Prosigna), the genomic test performed to assess these expression profiles in tumors, has been demonstrated as valuable in predicting therapeutic response and prognosis [42, 43]. Although receptor status alone cannot accurately predict intrinsic subtype, there is considerable overlap between the histologic and intrinsic subtypes of breast cancer. Over 70% of ER-positive tumors are classified as luminal A or B, over 60% of HER2-positive tumors are HER2-enriched, and nearly 80% of TNBC tumors are basal-like [42, 44]. Likewise, luminal tumors are associated with less aggressive

disease and favorable outcomes, while basal-like tumors are associated with highly aggressive disease and poor outcomes [15, 18].

Luminal A and B tumors are characterized by high expression of luminal epithelial markers including keratins 8 and 18 [11], and are usually ER-positive. Luminal A tumors are associated with more favorable outcomes relative to luminal B tumors, as luminal B tumors are characterized by a higher proliferation index and metastatic propensity, particularly to bone [18]. HER2-enriched tumors are characterized by overexpression of the ERBB2 amplicon [11], and are typically HER2-positive. HER2-enriched disease has a propensity to metastasize to the liver [18] and is associated with poorer outcomes than luminal disease. Basal-like tumors are characterized by high expression of basal epithelial markers including keratins 5, 6, and 17 [11], and are typically triple-negative [44]. These tumors have a high proliferation index, are poorly differentiated, and aggressively metastasize to the brain and lung [18]. Basal-like disease is consequently associated with very poor outcomes compared to other intrinsic subtypes. Claudin-low tumors are characterized by high expression of mesenchymal and extracellular matrix (ECM) genes as well as immune-related genes [12, 45], and are also usually triple-negative, highly metastatic, and associated with a poor prognosis [18]. Given the clinically important distinctions between these intrinsic subtypes that cannot be discerned solely by ER/PR/HER2 status, stratification of patients by tumor gene expression profiling is a crucial step towards improving targeted treatment strategies.

1.1.3 *Breast cancer metastasis*

Metastasis, one of the hallmarks of cancer [46], is the process by which cancer cells travel away from the primary tumor site and colonize distant organs. This involves a cascade of cancer cell detachment, migration, and local tissue invasion, intravasation of tumor cells into blood vessels or lymphatics, circulation of tumor cells, and extravasation followed by colonization and growth of tumor cells in distant tissues [47]. There are several

mechanisms by which cancer cells may develop the potential to metastasize [47], the most common being the clonal acquisition of mutations by subpopulations of tumor cells throughout tumor progression [48, 49]. Genomic alterations have also been shown to promote metastasis of cancer cells to specific organs [50–53], providing a molecular basis for the “seed and soil” hypothesis originally described in 1889 [54].

Breast cancer preferentially metastasizes to the brain, liver, lung, and bone, and distinct breast cancer subtypes have differential organ tropism [18, 50–53, 55], as described above. There are currently over 150,000 women living with metastatic breast cancer in the U.S. [19], and metastatic disease accounts for over 90% of cancer-related deaths, including those due to breast cancer [56–59]. Overall survival rates for patients with metastatic breast cancer have improved over the past three decades [60–62], largely due to therapeutic advancements in ER-positive/luminal and HER2-positive disease, which make up the majority of breast cancers. However, metastatic breast cancer remains a clinical challenge, particularly for triple-negative/basal-like disease, as this subtype is both the most clinically aggressive and the most difficult to treat.

Patients with TNBC are more likely to have distant recurrences compared to those with other subtypes [36]. TNBC tumors preferentially metastasize to visceral organs [36, 38], and basal-like tumors (80% of TNBCs) in particular have a high propensity to spread to the brain and lung [18]. TNBC patients have the highest risk of developing brain metastases, and metastatic disease in the brain is particularly aggressive when it results from TNBC [63–66]. The bleak prognosis and very limited therapeutic strategies for metastatic disease in the central nervous system (CNS) emphasize the critical need for novel TNBC treatments that not only are more effective than current therapies but also cross the blood-brain barrier. Although this may further complicate drug development efforts, it is imperative to develop new treatments that can effectively treat both intracranial and extracranial disease.

1.2 Triple-negative breast cancer

1.2.1 *Triple-negative breast cancer: a challenge in cancer therapeutics*

As aforementioned, TNBC (which is most commonly basal-like) has the worst prognosis of all the breast cancer subtypes [35, 36]. This is due not only to the highly malignant features of triple-negative tumor cells, but also to the current lack of reliable molecular markers that can be targeted with pharmacological agents. Whereas ER-positive and HER2-positive disease can be treated with drugs specifically targeting those receptors, no equivalent proteins have yet been identified in TNBC. Thus, despite major translational research efforts, pharmacologic treatment for patients with TNBC is largely limited to chemotherapy. Patients with early-stage or locally advanced TNBC are currently treated with adjuvant or neoadjuvant, respectively, regimens including anthracyclines, taxanes, and/or alkylating agents, along with surgery and radiation. Although TNBC patients have better initial responses to neoadjuvant chemotherapy compared to non-TNBC subtypes, they have significantly shorter progression-free survival and a greater risk of metastasis [36, 38]. Patients with metastatic disease, after confirming the maintenance of TNBC status via a repeat biopsy, receive combination or single-agent chemotherapy, depending on the extent of disease progression. This is sometimes known as a therapeutic rechallenge, as patients with recurrent or metastatic disease may be treated with the same chemotherapeutics they were given previously, given the limited treatment options for triple-negative disease.

Because chemotherapeutics nonspecifically target rapidly-dividing cells, these drugs are highly toxic to normal tissue in addition to cancer cells, and consequently lead to adverse effects involving multiple organ systems. Furthermore, TNBC tumors are often intrinsically refractory or acquire resistance to these drugs [38, 67, 68], leaving patients who develop advanced or recurrent disease with multidrug-resistant tumors and very few alternative treatment options. In addition to the toxicity and limited/inconsistent

effectiveness of chemotherapy, it has been shown that several chemotherapeutics currently approved for breast cancer can promote early steps in the metastatic cascade, despite their anti-proliferative effects on primary tumors [69]. For all these reasons, it is imperative to develop new therapeutic strategies that are both more effective and less toxic for patients with TNBC. The success of this endeavor will likely depend on the identification of reliable targets and more effective patient stratification.

1.2.2 *Triple-negative breast cancer subtypes and clinical implications*

The clinical challenge of treating TNBC can be attributed not only to the lack of reliable drug targets, but also to the molecular heterogeneity of this breast cancer subtype. Given the clinical importance of stratifying patients based on molecular tumor characteristics, the identification of distinct TNBC subtypes [70] was a major advancement in the field of translational breast cancer research. TNBC tumors have been classified into six subtypes based on gene expression profiling: basal-like 1 (BL1), basal-like 2 (BL2), immunomodulatory (IM), mesenchymal-like (M), mesenchymal stem-like (MSL), and luminal androgen receptor (LAR) [70]. BL1 tumors are characterized by expression of genes involved in the cell cycle, proliferation, and DNA repair, whereas BL2 tumors express genes involved in growth factor pathways and glucose metabolism; IM tumors are characterized by expression of immune cell markers and genes indicative of medullary breast cancer; M and MSL tumors highly express genes involved in cell motility, differentiation, growth factor signaling, and epithelial-to-mesenchymal transition (EMT), however MSL tumors are less proliferative; and LAR tumors are characterized by androgen receptor (AR) signaling and have a luminal gene expression profile [70]. These subtypes have more recently been refined into four types (BL1, BL2, M, and LAR), as the IM and MSL types were found to have resulted from infiltrating immune and stromal cells, respectively [71]. BL1 and BL2 tumors make up the majority of TNBCs (60%) and have the worst prognosis; 25% of TNBCs are M subtype and 15% are LAR subtype [70, 71]. AR is

a particularly important marker, and AR-negative TNBCs (the majority of which are basal-like) have been coined quadruple-negative breast cancer (QNBC), which is associated with therapeutic resistance and very poor outcomes [72–74].

The distinct gene signatures and characteristics of each of these TNBC subtypes explain why certain populations of TNBC patients respond to particular therapies while others do not; importantly, these distinctions are crucial to predict which patients will respond to specific therapeutics and to identify pathways that may be effective targets within each subset of TNBC patients. For instance, BL1 and BL2 tumors respond better than other subtypes to taxanes given their high expression of cell cycle and proliferation markers, whereas LAR tumors respond to AR inhibitors given they are driven by AR signaling [70, 71, 75]. There are likely additional pathways driving tumor progression within each TNBC subtype that remain to be identified and may serve as effective drug targets.

1.2.3 *The search for successful targeted therapies for triple-negative breast cancer*

Currently, there are only three targeted treatments approved for select subsets of TNBC patients [76]. Nearly 60% of TNBC tumors are positive for programmed cell death ligand 1 (PDL-1) [77], and patients with PDL-1 positive advanced TNBC are candidates for treatment with PDL-1 inhibitors such as atezolizumab, recently approved by the U.S. Food and Drug Administration (FDA) for use in conjunction with standard chemotherapy in this subset of patients [78]. The poly ADP-ribose polymerase (PARP) inhibitors talazoparib and olaparib have recently been FDA-approved for patients with BRCA1-mutated advanced TNBC [79, 80]. However, these drugs offer no benefit for patients with PDL-1-negative and BRCA1-wildtype disease. Thus, the search for effective targeted therapies in TNBC continues.

Many other targeted therapies have shown promise in preclinical studies, but thus far none of these agents have demonstrated enough success in clinical trials to be approved for TNBC [34, 81, 82]. These include drugs and/or antibodies that target epidermal growth

factor receptor (EGFR) [83–88], AR [89, 90], vascular endothelial growth factor (VEGF) (angiogenesis) [91–94], trophoblast cell-surface antigen 2 (TROP-2) [95], phosphoinositide 3-kinase (PI3K) and mammalian target of rapamycin (mTOR) [96, 97], beta-adrenergic receptor [98–101], heat shock protein 90 (HSP90) and histone deacetylases (HDACs) [102, 103], and programmed cell death protein-1 (PD-1) [77]. Many of these proteins are overexpressed or mutated in TNBC or specific TNBC subtypes, and/or have been shown to play important roles in TNBC progression, making them appealing drug targets. However, given the results of clinical studies combining such drugs with standard-of-care chemotherapies, it is likely that synergistic combinations with other targeted agents are needed to achieve clinical benefit.

1.3 Patient-derived xenograft models

1.3.1 Utility and relevance of patient-derived xenograft models in cancer research

Preclinical studies of cancer biology, and the development and testing of new therapies, rely heavily upon the use of *in vivo* models that accurately recapitulate the characteristics and progression of tumors in humans. Patient-derived xenograft (PDX) models, in which tumor cells derived from human surgical specimens are transplanted into immunodeficient mice, have emerged as preclinical models to study the molecular biology and *in vivo* treatment responses of cancers of various organs [104–114], including the breast [115]. PDXs have been shown to more faithfully maintain the characteristics, behavior, and drug response profiles of human primary tumors and metastases compared to xenograft models utilizing immortalized human cancer cell lines [116–123]. Consequently, preclinical drug development studies using PDX models are more likely to be predictive of clinical success compared to other types of models [124], which is why PDX models were utilized for the therapeutic response studies reported herein.

1.3.2 *Patient-derived xenograft models of primary and metastatic breast cancer*

As described above, breast cancer is a heterogeneous disease, which poses significant therapeutic challenges. Most drugs that show promise in preclinical studies end up failing in clinical trials due to lack of efficacy. This highlights the importance of utilizing preclinical models that faithfully represent the spectrum of breast cancer seen in humans. Indeed, PDX models have been established for all breast cancer subtypes, providing clinically relevant models that represent the heterogeneity of this disease. Some of the first breast cancer PDXs were not initially successful due to instability of tumor engraftments in mice [125–134], however this has improved considerably with the development of better immunodeficient mouse strains [118, 119, 135]. Importantly, breast cancer PDX models have been shown to retain the heterogeneity, histology, molecular profiles, hormone-dependency, drug responses, growth patterns, metastatic behavior, and disease outcomes of human breast cancer, even after multiple passages in mice [116–120, 136–138]. PDX models are therefore considered to be superior to immortalized cell line models regarding their clinical relevance and translational potential in breast cancer [139, 140].

PDX models of metastatic breast cancer are particularly valuable for studying advanced disease. Whereas cell line xenografts do not accurately emulate the metastatic patterns of human disease, orthotopic PDX tumors have been shown to spontaneously metastasize to the same distant sites in the mouse as in the patient from which the PDX models were originally derived [116]. It should be noted that, while spontaneous metastasis models are suitable for studying metastatic disease in the lymph nodes and lungs, experimental metastasis models, in which tumor cells are injected directly into the circulation or organ, are relatively more robust for generating brain and liver metastases in mice [52, 141–143]. Although such experimental models do not mimic the entire metastatic cascade, they provide an efficient and reliable means of studying drug response in the setting of established metastatic disease. This is especially important for TNBC, as this subtype

tends to metastasize early in the disease course, and, consequently, patients often present with TNBC that has already disseminated to distant sites. It is therefore important that drug development efforts focus on identifying therapeutic strategies that are effective in treating established metastases in vital organs. Given that PDX tumors retain many of the properties of their human counterparts, the use of these models for experimental metastasis studies is justified.

1.3.3 *Use of patient-derived xenograft models for preclinical drug screening studies*

In addition to utilizing PDX models for *in vivo* studies, PDX cells obtained from digested tumor tissue can be cultured in suspension [135] and used for *in vitro* drug screening assays. The non-adherent conditions in which the PDX cells are suspended prevent these cells from undergoing genetic and epigenetic changes associated with adaptation to growth on plastic [144–146]. Studies have shown that, whereas established cell lines do not faithfully maintain the transcriptional profiles of corresponding clinical samples [147], short-term *in vitro* cultures of breast cancer PDXs maintain the molecular characteristics and heterogeneity of their *in vivo* counterparts and are therefore suitable models for studying tumor biology and drug response, both *in vivo* and *ex vivo/in vitro* [107, 110, 112, 121–123, 148, 149].

1.4 Overview of dissertation

1.4.1 *Overall goals of this research*

The research presented herein collectively sought to: 1) characterize breast cancer PDX suspension culture, mammary tumor, and metastasis models, 2) characterize chemotherapeutic responses in these models, 3) identify targeted/non-chemotherapeutic drug candidates for TNBC, and 4) identify and test synergistic combination therapies *in vitro* and *in vivo*. The overall goal of this research was to use clinically relevant PDX models to develop novel therapeutic strategies for TNBC, with a focus on both the basal-like and LAR subtypes.

1.4.2 *Part One*

The first part of this work employs two basal-like TNBC PDX models to optimize *in vitro* suspension cultures for use in drug screening assays, and to characterize responses to currently approved chemotherapeutics *in vitro* and *in vivo* in both the primary and metastatic setting, with a particular focus on relative efficacy in distinct metastatic sites.

1.4.3 *Part Two*

The next part of this work focuses on identifying currently FDA-approved or late-stage investigational therapeutic compounds with efficacy in basal-like TNBC through screening of a wide range of drugs in multiple PDX models, and further investigating drugs of interest to identify novel synergistic drug combinations with promise in treating this subset of patients.

1.4.4 *Part Three*

The final part of this work focuses on characterizing responses of AR-positive breast cancer PDX and cell line models to AR-targeted drugs, and identifying genes of interest and potential drug candidates for combination with AR-targeted therapeutics in LAR TNBC.

CHAPTER 2: Characterizing the efficacy of cancer therapeutics in patient-derived xenograft models of metastatic breast cancer [149]

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2.1 Background and rationale

Each year, over 40,000 patients die due to invasive breast cancer [19]. TNBC is associated with a particularly poor prognosis relative to other breast cancer subtypes due to the frequent failure of chemotherapy and lack of alternative treatment strategies, as well as its metastatic propensity [36, 37]. Prior to surgical resection, TNBC tumors often metastasize to vital organs, including the brain, liver, and lungs [18, 65, 150], and it is unclear why some metastases respond to chemotherapeutic treatment whereas others do not. A better understanding of relative therapeutic efficacy in distinct metastatic sites is an important step towards improving therapeutic strategies for TNBC, given that metastatic disease accounts for virtually all TNBC-related deaths.

2.2 Experimental approach

This study sought to evaluate the efficacy of cancer therapeutics in primary and metastatic breast cancer using two PDX models, WHIM2 and WHIM30, obtained from separate patients with basal-like TNBC [117, 120]. We initially tested the effects of twelve different cancer therapeutics, currently FDA-approved for various types of cancer, on the viability of WHIM2 and WHIM30 cells cultured *in vitro*. Selected drugs were then tested in the mammary tumor and metastatic setting to evaluate their efficacy *in vivo* and compare responses between the two PDXs, between primary tumors and metastases, and between distinct metastatic sites (brain, liver, lung).

2.3 Materials and methods

2.3.1 *PDX mouse models and preparation of tumor cell suspensions*

Two basal-like, TNBC PDX lines, WHIM2 and WHIM30, were obtained from the Institute of Clinical and Translational Sciences, Washington University, St. Louis. Cells were resuspended 1:1 in Matrigel (Corning) and injected into the fourth mammary fat pads of non-obese diabetic severe combined immunodeficient gamma (NSG) mice. Mammary tumors were digested with a solution of Dulbecco's Modified Eagle Medium/Nutrient Mixture F12 (DMEM/F12), 5% fetal bovine serum (FBS), 300 U/ml collagenase (Sigma) and 100 U/ml hyaluronidase (Sigma). Digested tissue was resuspended in NH₄Cl, and trypsinized to generate single cells, which were transduced with lentivirus (BLIV101PA-1; Systems Biosciences) encoding green fluorescent protein (GFP) and luciferase. Tumor growth was monitored by luciferase expression using the IVIS Spectrum In Vivo Imaging System (Xenogen IVIS-200) and Living Image software (PerkinElmer). Prior to imaging, mice were injected subcutaneously with 150 mg/kg D-luciferin (Gold Biotechnology).

2.3.2 *Optimization of culture conditions and in vitro drug studies*

WHIM2 and WHIM30 cells were plated in M87 or human breast epithelial cell (HBEC) media [135], in triplicate (25,000 cells/100µl per well) in 96-well plates coated with poly-2-hydroxyethyl-methylacrylate (poly-HEMA) [151] to provide a low-attachment surface, and incubated at 37°C, 5% CO₂ for 3 or 7 days. It should be noted that these suspension cultures were distinct from organoid or spheroid models, as the cells were not suspended in an ECM-like matrix or subjected to centrifugation to encourage spheroid formation once plated; instead, the cells were simply plated in medium and allowed to freely interact with each other three-dimensionally. Cells were imaged and analyzed using a Zeiss AxioObserver A1 Inverted Microscope and Zeiss AxioCam 503 mono, and ZEN2 software. To assess cell viability over time, D-luciferin (15 mg/ml, 10µl/well) was added and plates were IVIS imaged on days 0, 3 and 7. Twelve pharmaceutical-grade cancer therapeutics

(Table 2.1) were obtained from VCU Dalton Oncology Clinic. Cells were treated for 72h with three concentrations of each drug (Table 2.2), determined from prior *in vitro* studies. Cell viability was measured by luciferase activity and CellTiter-Glo assay (Promega).

Table 2.1: Twelve clinically approved cancer therapeutics tested in WHIM2 and WHIM30 PDXs *in vitro*. Adapted by permission from Springer Nature: [149] © Springer Science+Business Media, LLC (2018)

Drug	Mechanism of action	Current clinical use
Carboplatin	Alkylating agent	Testicular, bladder, ovary, lung carcinomas
Dacarbazine	Alkylating agent	Melanoma, Hodgkin's lymphoma, sarcomas, pancreatic adenocarcinoma
Cyclophosphamide	Alkylating agent	Hematologic malignancies, brain cancer, various solid tumors
Gemcitabine	Pyrimidine analog	Pancreatic, breast, bladder, non-small cell lung carcinomas
Cytarabine	Pyrimidine analog	Leukemias and lymphomas
Doxorubicin	Anthracycline, intercalates DNA	Various carcinomas, hematologic malignancies
Cetuximab	EGFR inhibitor	Colorectal cancer, non-small cell lung carcinoma, head and neck cancers
Rituximab	Anti-CD20 monoclonal antibody	Hematologic malignancies, autoimmune disorders
Bevacizumab	VEGF inhibitor	Colorectal, lung, renal cancers
Bortezomib	Proteasome inhibitor	Multiple myeloma
5-Fluorouracil	Antimetabolite, thymidylate synthase inhibitor	Various gastric and head and neck cancers
Irinotecan	Topoisomerase I inhibitor	Colon cancer

Table 2.2: Concentrations and dosing of drugs for *in vitro* and *in vivo* studies in WHIM2 and WHIM30. Adapted by permission from Springer Nature: [149] © Springer Science+Business Media, LLC (2018)

Drug	In vitro concentrations	In vivo dosages^a	Human equivalent doses	Human clinical doses
Carboplatin	1 μM, 10μM, 100μM	90 , 160 mg/kg	270, 480 mg/m ²	300-360 mg/m ²
Dacarbazine	1mM, 5mM, 10mM	60 , 100 mg/kg	180, 300 mg/m ²	150-375 mg/m ²
Cyclophosphamide	1mM, 10mM, 20mM	75 , 150 mg/kg	225, 450 mg/m ²	600 mg/m ²
Gemcitabine	100nM, 1μM, 10μM			
Cytarabine	100nM, 1μM, 10μM			
Doxorubicin	10nM, 100nM, 1μM			
Cetuximab	500nM, 1μM, 5μM			
Rituximab	100nM, 1μM, 10μM			
Bevacizumab	1μM, 10μM, 50μM			
Bortezomib	100nM, 500nM, 1μM	0.3 , 0.75 mg/kg	0.9, 2.25 mg/m ²	1.3 mg/m ²
5-Fluorouracil	1μM, 10μM, 100μM			
Irinotecan	100nM, 1μM, 10μM			

^aBolded dosages for *in vivo* studies indicate the optimal dose determined by initial *in vivo* experiments.

2.3.3 *RNA preparation and sequencing*

Mammary tumor and brain tissues were homogenized in lysis buffer using an electric tissue homogenizer. Cells were plated at 1.5×10^6 cells/well in poly-HEMA-coated 6-well plates and collected 7 days later. RNA was isolated from tissue/cell lysates using the RNeasy Mini Kit (Qiagen). Samples were sequenced on the Illumina Hi-Seq 2500 according to Illumina's sequencing-by-synthesis protocol. KAPA Stranded mRNA-Seq Kit was used for library preparation. 125bp paired-end reads were generated, yielding on average 17M reads per sample. These data have been deposited in the NCBI Gene Expression Omnibus (GEO) (GSE110626). RNA-sequencing data were processed and analyzed by Amy Olex, as described in Turner et al. 2018 [149]. Gene expression data are represented as \log_2 (TPM+1) (transcripts per million) values.

2.3.4 *Analysis of BRCA1 variants in WHIM2 and WHIM30 tumors*

The Integrated Genome Browser [152] version 9.0.0 was used to search for BRCA1 mutations in WHIM2 and WHIM30 tumor samples. The coding region of the BRCA1 gene (human chromosome 17: 43,044,194-43,125,583) in WHIM2 and WHIM30 sequences was aligned to the corresponding region in the human reference genome (GRCh38) [153]. WHIM2 and WHIM30 BRCA1 sequences were then scanned for mutations, using a threshold of 10 or more reads distinct from the reference genome to indicate a mutation at a particular position in the sequence. The specific mutations observed were searched for using the University of California Santa Cruz (UCSC) Genome Browser [154] and compared with established ClinVar [155] variants. Additional analysis of BRCA1 variants in the PDXs was performed by Amy Olex, as described in Turner et al. 2018 [149].

2.3.5 *In vivo mammary tumor studies*

WHIM2 and WHIM30 cells in HF buffer were resuspended 1:1 in Matrigel and injected (500,000 cells) into the fourth mammary fat pads of NSG mice. Mice were anesthetized prior to and during injection using 4% isoflurane, 1 L/min oxygen flow. For initial studies,

drug treatment was initiated when tumors reached 20mm² by caliper measurement. To determine optimal dosing, mice were treated via intraperitoneal (IP) injection with low- or high-dose bortezomib, dacarbazine, carboplatin, or cyclophosphamide (**Table 2.2**), determined based on human-to-mouse dose conversions (<https://www.fda.gov/downloads/drugs/guidances/ucm078932.pdf>) [156] and previous *in vivo* studies. Mice were divided into 5 groups: vehicle (normal saline), bortezomib, dacarbazine, carboplatin, and cyclophosphamide (2 low-dose, 3 high-dose per treatment group). Carboplatin and cyclophosphamide were administered 1x/week; bortezomib 2x/week; dacarbazine 3x/week. Mice were IVIS imaged weekly to monitor tumor growth; luciferase activity of the tumor area was quantified as total flux (photons/second, p/s). Mice were euthanized when tumors reached burden and/or mice displayed signs of drug toxicity, such as weight loss, trembling or hunching behavior, and/or difficulty with ambulation. A single dose of each drug (**Table 2.2**) was chosen for subsequent studies based on efficacy versus toxicity. Subsequent single-dose studies were performed in multiple cohorts of mice: WHIM30 bilateral tumors with treatment initiation at 20mm² (5 mice per group), WHIM2 bilateral tumors with treatment initiation at 20mm² (5 mice per group), WHIM30 unilateral tumors with treatment initiation at 50mm² (5 mice per group), and WHIM2 unilateral tumors with treatment initiation one week after tumor cell injection (4 mice per group). An additional study was conducted in which mice bearing bilateral WHIM30 tumors were treated with cyclophosphamide (5 low-dose, 4 high-dose) with treatment initiation at 100mm². For all studies, tumor growth was monitored as described above. For select studies, tumors were excised, photographed, and harvested for histological analysis.

2.3.6 *In vivo metastasis studies*

PDX cells were injected into the left ventricle of the heart in NSG mice (WHIM2: 15 mice total, 1 cohort; WHIM30: 62 mice total, 5 cohorts). For intracardiac injection, mice were anesthetized using 4% isoflurane, 1 L/min oxygen flow, and maintained on 2.5% isoflurane,

1 L/min oxygen flow throughout the procedure. Prior to injection, the skin overlying the chest was sterilized with betadine followed by ethanol. Subsequently, 500,000 cells in 100µl HF buffer were mixed with D-luciferin and injected into the left ventricle using a 1cc syringe. Following injection, each mouse was immediately IVIS imaged to verify proper seeding of tumor cells in the brain. Drug treatments were initiated 10 days post-injection. Each experimental cohort of mice was randomized into 3 groups and treated weekly with IP vehicle (normal saline), carboplatin, or cyclophosphamide, at a single dose per drug (**Table 2.2**). Collectively, this consisted of 5 mice per treatment group for WHIM2; and 18 vehicle, 22 carboplatin, 22 cyclophosphamide for WHIM30. Mice were imaged weekly to monitor metastases; brain luciferase activity was quantified as total flux (p/s). Mice were euthanized when the vehicle group displayed signs of drug toxicity and/or became moribund; brains, livers, and lungs were excised and imaged *ex vivo* for each treatment group. These tissues were also harvested for histology.

2.3.7 Histology

Hematoxylin and eosin (H&E) staining and immunohistochemistry (IHC) were performed on WHIM2 and WHIM30 mammary tumors, brain, liver, and lung tissues. All tissues were fixed in 10% formalin, paraffin-embedded, and sectioned using a Kedeer KD-2258 rotary microtome, at 10µm per section. H&E staining was performed according to standard procedures. IHC was performed by standard procedures, using the following primary antibodies: rabbit anti-pan-cytokeratin (1:100; ThermoFisher #PA1-27114), rabbit anti-vimentin (1:800; Cell Signaling Technology #5741), rabbit anti-Ki67 (1:100; Cell Signaling Technology #9027), rabbit anti-HIST1H3B3 (phosphohistone-H3) (1:500; One World Lab #42033), and rabbit anti-cleaved caspase-3 (1:200; Cell Signaling Technology #9661). Heat-induced antigen retrieval was conducted using a pressure cooker, in pH 9 Tris-EDTA. Detection was performed using the rabbit Dako EnVision system (Agilent K406511-2). Stained tissue sections were observed and photographed using a Zeiss AxioLab Upright

Microscope and Zeiss AxioCam ICc 5 camera. Image analysis was performed using the ZEN2 software, blue edition.

2.3.8 Statistics

For *in vitro* studies testing the twelve cancer therapeutics, unpaired two-tailed t-tests were performed between control and drug treatment conditions to determine statistical significance. For *in vitro* studies testing suspension cultures in two different media, and for all *in vivo* studies, differences between treatment groups were analyzed at each timepoint using a randomized block design ANOVA, with experimental cohort as a blocking factor. Treatment-time interactions were included in the model. Post-hoc Tukey's Honest Significant Difference tests were performed to detect pairwise differences. All analyses were performed in R computing environment v.3.4.0, with the assistance of Dr. Mikhail Dozmorov.

2.4 Results

2.4.1 PDX cells can be maintained in suspension culture for up to 7 days

Luciferase-expressing WHIM2 and WHIM30 mammary tumors were used for these studies (**Fig. 2.1a**). When cultured in suspension, the tumor cells clustered together over time (**Fig. 2.1b**). Luciferase activity (total photon flux emitted per second after addition of luciferin substrate) was used to assess cell viability. Over time, in two different media formulations (M87 and HBEC) [135], WHIM2 cells showed an increase ($p < 5.0 \times 10^{-5}$) followed by a decline ($p < 5.0 \times 10^{-4}$) in viability, with no significant change in viability over 7 days ($p > 0.6$) (**Fig. 2.1c**); WHIM30 cell viability initially decreased ($p < 6.0 \times 10^{-5}$) and then remained relatively constant ($p > 0.7$), with an overall decrease in viability over 7 days ($p < 6.0 \times 10^{-6}$) (**Fig. 2.1d**). These effects were irrespective of the culture media for both WHIM2 ($p > 0.3$) and WHIM30 ($p = 0.9$). Data shown in **Fig. 2.1c,d** are from one representative experiment per PDX line, however statistical analyses incorporated two independent experiments per

line; absolute flux values varied between experiments, however they showed similar trends in cell viability over time for both PDXs (**Fig. 2.2**).

2.4.2 PDX gene expression is maintained in suspension culture and in the metastatic setting

Pearson correlation analyses, performed on RNA-sequencing data from tumor tissue and cell suspensions, revealed strong correlations between parental mammary tumors and suspension cultures over time, for both WHIM2 and WHIM30 (**Fig. 2.3**). WHIM2 and WHIM30 brain metastases also correlated strongly with mammary tumors and cell suspensions (**Fig. 2.3**).

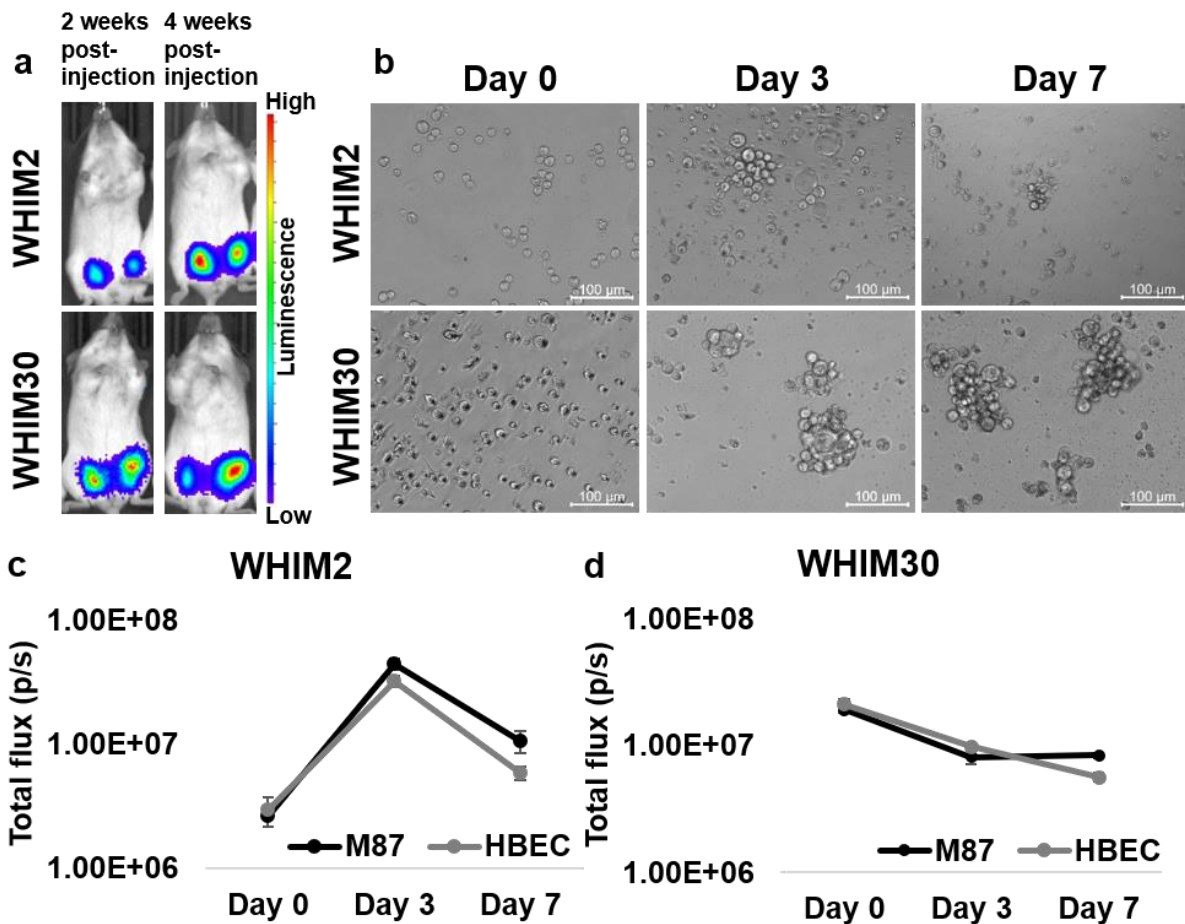


Figure 2.1: WHIM2 and WHIM30 PDX cells can be maintained in suspension culture for up to 7 days. **(a)** IVIS images depicting luciferase-positive mammary gland tumors in mice, 2 and 4 weeks post-injection of WHIM2 or WHIM30 PDX cells. **(b)** Microscopic images (20X) of WHIM2 and WHIM30 cells in suspension culture on days 0, 3, and 7 after plating. **(c,d)** Viability of WHIM2 **(c)** and WHIM30 **(d)** cells in suspension culture in two different media (M87 or HBEC) over time, as measured by luciferase activity in total photon flux per second (p/s), showing one representative experiment per PDX line. Graphs are shown in log₁₀ scale. Error bars represent standard deviation of triplicate values for each condition. Reprinted by permission from Springer Nature: [149] © Springer Science+Business Media, LLC (2018)

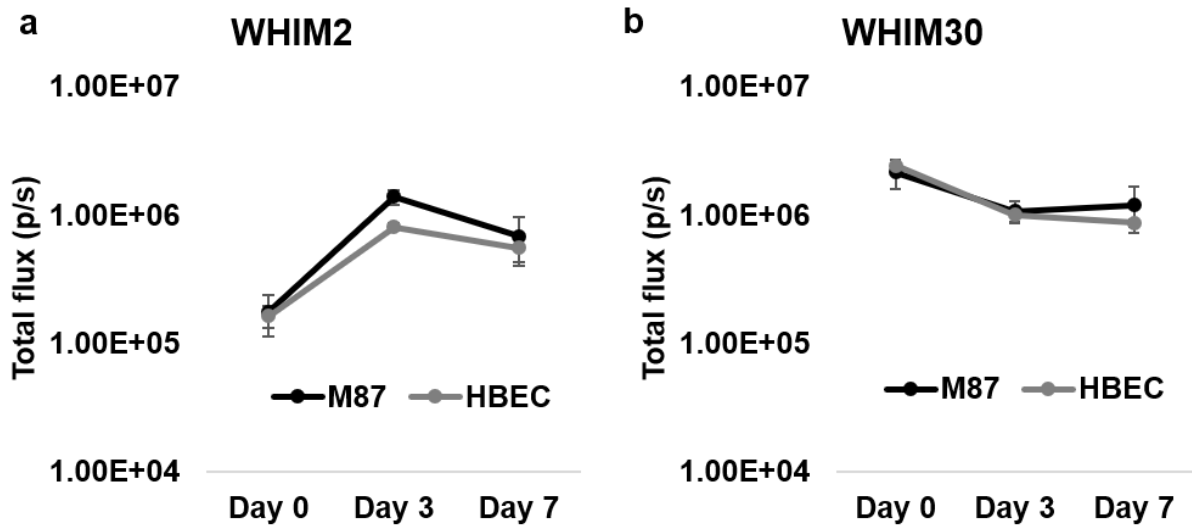


Figure 2.2: WHIM2 and WHIM30 cell viability in suspension culture over time. Viability of WHIM2 (**a**) and WHIM30 (**b**) cells cultured in suspension in two different media (M87, HBEC) immediately after plating (day 0), and after 3 and 7 days in culture. These graphs represent one of two independent experiments per PDX line, the others of which are shown in Fig. 2.1. Graphs are shown in log₁₀ scale. Error bars represent standard deviation of triplicate values for each condition. Reprinted by permission from Springer Nature: [149] © Springer Science+Business Media, LLC (2018)

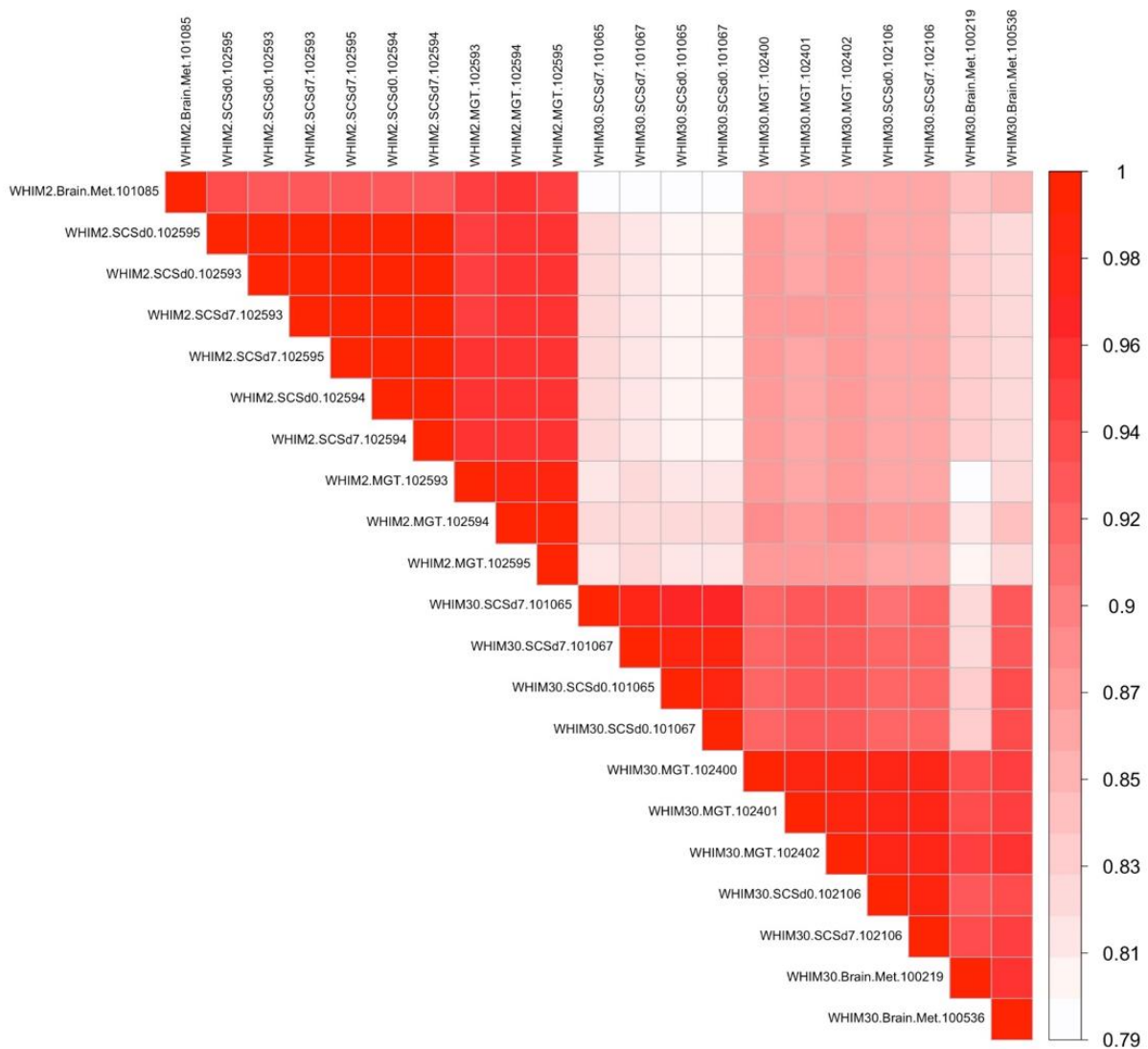


Figure 2.3: Gene expression is maintained when WHIM2 and WHIM30 mammary tumor cells are cultured in suspension over time. RNA-sequencing was performed on WHIM2 and WHIM30 mammary tumors and cells cultured in suspension immediately after processing (SCSd0) and after 7 days in culture (SCSd7); 3 tumors and matched day 0 and day 7 suspension culture samples were sequenced and analyzed for each PDX line. The correlation plot was generated by calculating all-by-all Pearson's correlation coefficient matrix using the filtered log2 TPM expression profiles of each sample, which was then clustered using Hierarchical clustering, average linkage, and Euclidean distance as the dissimilarity measure. The color bar indicates correlation between indicated sample expression profiles, which were all above 0.79 positive correlation. Reprinted by permission from Springer Nature: [149] © Springer Science+Business Media, LLC (2018)

2.4.3 Drug efficacy varies across basal-like PDX lines *in vitro*

To determine the optimal measure of cell viability for *in vitro* drug screening, WHIM30 cultures were treated with four cancer therapeutics: carboplatin, gemcitabine, cytarabine, and bortezomib. Both luciferase and ATP generation (CellTiter-Glo) assays yielded similar percent decreases in cell viability in response to each drug, however CellTiter-Glo produced more inter-experiment variability (**Fig. 2.4a**), likely due to contaminating mouse stromal cells. We next tested twelve cancer therapeutics on WHIM2 and WHIM30 suspension cultures. Some of these drugs (carboplatin, gemcitabine, 5-fluorouracil, doxorubicin, cyclophosphamide) were chosen based on their clinical use or prior testing in breast cancer and their blood-brain barrier permeabilities, whereas some drugs indicated for other types of cancer (e.g. rituximab for hematological malignancies) were expected to be ineffective in our breast cancer models and were therefore used as controls. Cytotoxicity varied greatly across the drugs and the PDX lines (**Fig. 2.4b-d**). The PDXs responded differently to several drugs; for example, carboplatin was cytotoxic to WHIM30 but not WHIM2 cells (**Fig. 2.4c,d**). Bortezomib, dacarbazine, and cyclophosphamide were cytotoxic to both lines (**Fig. 2.4c,d**).

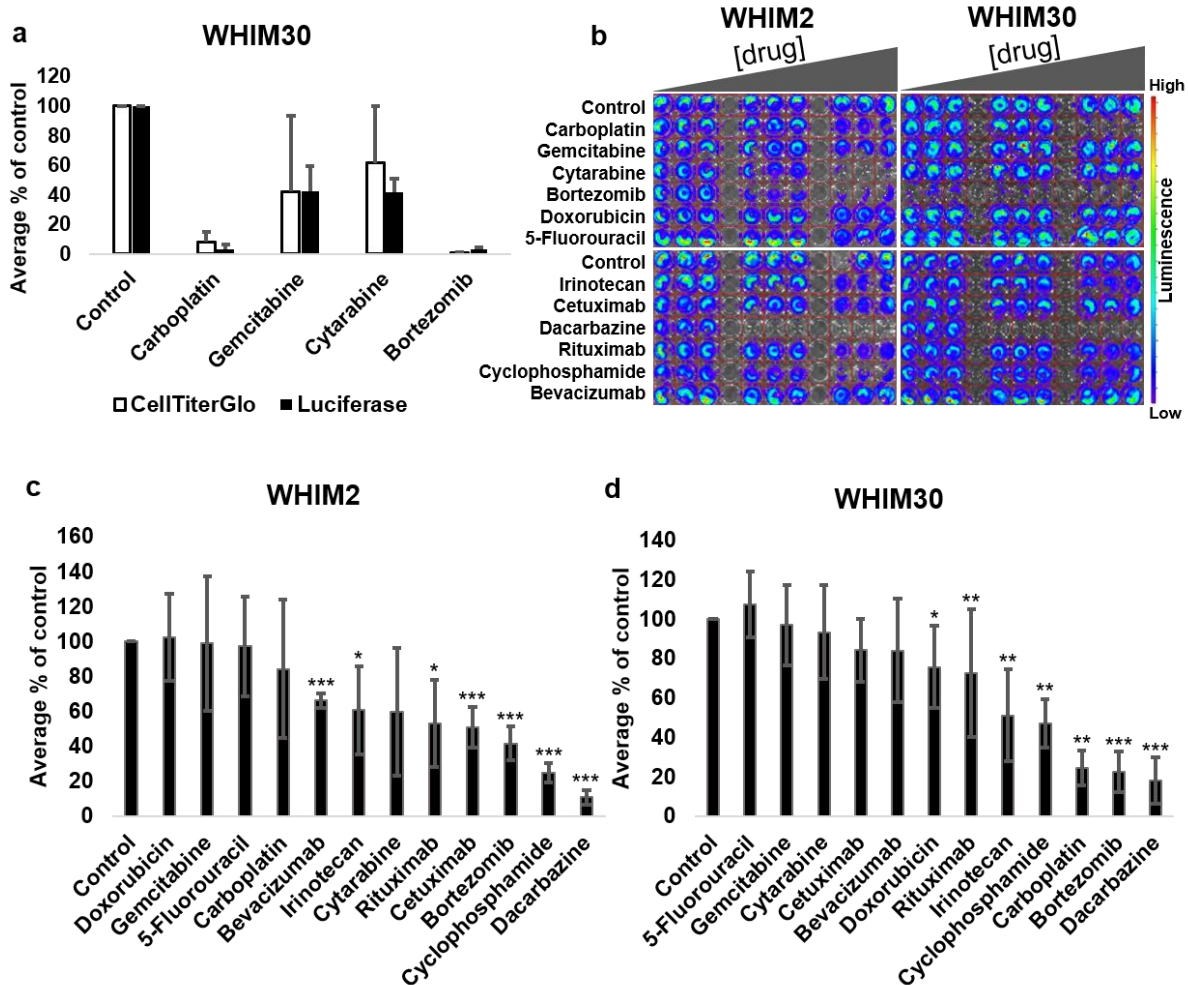


Figure 2.4: Cancer therapeutics are differentially cytotoxic to WHIM2 and WHIM30 cells *in vitro*. **(a)** Comparison of luciferase activity versus ATP production (CellTiter-Glo) to measure cell viability in response to carboplatin (100 μ M), gemcitabine (10 μ M), cytarabine (10 μ M), and bortezomib (100nM). Data represent two independent experiments in which WHIM30 cells were plated in triplicate for each condition; error bars represent standard deviation. **(b)** IVIS images of WHIM2 and WHIM30 cells in suspension culture treated for 72h with increasing concentrations (see Table 2.2) of twelve cancer therapeutics. Cells were plated in triplicate, with one column of wells skipped between sets of triplicates for each condition. **(c,d)** Effect of cancer therapeutics on the viability of WHIM2 **(c)** and WHIM30 **(d)** cells in suspension culture, as measured by luciferase activity (total flux). Concentrations used were as follows: carboplatin 100 μ M, dacarbazine 1mM, cyclophosphamide 20mM, gemcitabine 10 μ M, cytarabine 10 μ M, doxorubicin 1 μ M, cetuximab 5 μ M, rituximab 10 μ M, bevacizumab 50 μ M, bortezomib 100nM, 5-fluorouracil 100 μ M, and irinotecan 10 μ M. Data shown represent three independent experiments for WHIM2 and four independent experiments for WHIM30; error bars represent standard deviation. Significance of treatment effects of each drug compared to control was determined by unpaired two-tailed t-tests: * p <0.05, ** p <0.01, *** p <0.001. Reprinted by permission from Springer Nature: [149] © Springer Science+Business Media, LLC (2018)

2.4.4 BRCA1 status differs between two basal-like PDX lines

Given the differential efficacy of carboplatin between the PDXs *in vitro*, and the association of BRCA1 mutations with sensitivity to platinum agents [157, 158], we became interested in the BRCA1 status of WHIM2 and WHIM30 tumors. Dr. Shunqiang Li (Washington University, St. Louis) confirmed that WHIM30 carries BRCA1 mutations whereas WHIM2 does not. We verified this using our tumor RNA-sequencing data. Variant analyses revealed a total of 7 BRCA1 mutations in WHIM30 that were absent in WHIM2: 3 synonymous mutations (rs16940, Leu-to-Leu; rs1799949, Ser-to-Ser; rs1060915, Ser-to-Ser), 3 missense mutations (rs1799966, Ser-to-Gly; rs16942, Lys-to-Arg; rs16941, Glu-to-Gly), and 1 mutation in the 3'-UTR (rs8176318) (**Table 2.3; Fig. 2.5**). According to our database searches, these specific mutations have been associated with familial breast and ovarian cancer.

Table 2.3: Results of BRCA1 variant analyses in WHIM2 and WHIM30 mammary tumors. Adapted by permission from Springer Nature: [149] © Springer Science+Business Media, LLC (2018)

POSITION ON CHR17 (BRCA1 GENE)	MUTATION ID ^a	REF ^b	ALT ^c	WHIM30 T1 ^d	WHIM30 T2 ^d	WHIM30 T3 ^d	WHIM2 T1 ^d	WHIM2 T2 ^d	WHIM2 T3 ^d	Variant Function
43092919	rs799917	G	A	1/1:13 4,30,0	1/1:12 1,27,0	1/1:14 5,42,0	1/1:18 3,60,0	1/1:16 0,39,0	1/1:11 6,30,0	missense P [Pro] ⇒ L [Leu]
43093449	<i>rs1799949</i>	G	A	1/1:15 5,60,0	1/1:14 5,42,0	1/1:11 7,24,0	.	.	.	cds-synon
43091983	<i>rs16942</i>	T	C	1/1:14 6,45,0	1/1:14 6,48,0	1/1:13 2,36,0	.	.	.	missense K [Lys] ⇒ R [Arg]
43092418	<i>rs16941</i>	T	C	1/1:11 2,27,0	1/1:15 2,42,0	1/1:14 4,39,0	.	.	.	missense E [Glu] ⇒ G [Gly]
43093220	<i>rs16940</i>	A	G	1/1:14 6,33,0	1/1:16 1,45,0	1/1:14 9,36,0	.	.	.	cds-synon
43071077	<i>rs1799966</i>	T	C	1/1:14 6,48,0	1/1:17 1,45,0	1/1:13 2,36,0	.	.	.	missense S [Ser] ⇒ G [Gly]
43082453	<i>rs1060915</i>	A	G	1/1:19 0,72,0	1/1:19 4,66,0	1/1:12 8,16,0	.	.	.	cds-synon
43045257	<i>rs8176318</i>	C	A	1/1:19 3,99,0	1/1:19 9,90,0	1/1:16 9,54,0	.	.	.	UTR function
43044391	rs12516	G	A	1/1:89, 33,0	1/1:79, 21,0	UTR-3

^aIDs for mutations present in WHIM30 samples but not WHIM2 samples are bolded and italicized.

^bREF refers to the normal base in the human reference genome sequence.

^cALT refers to the altered base for each specific mutation.

^dThe labels T1, T2, and T3 represent the 3 tumor samples analyzed for each PDX line. Data are in Variant Call Format (VCF).

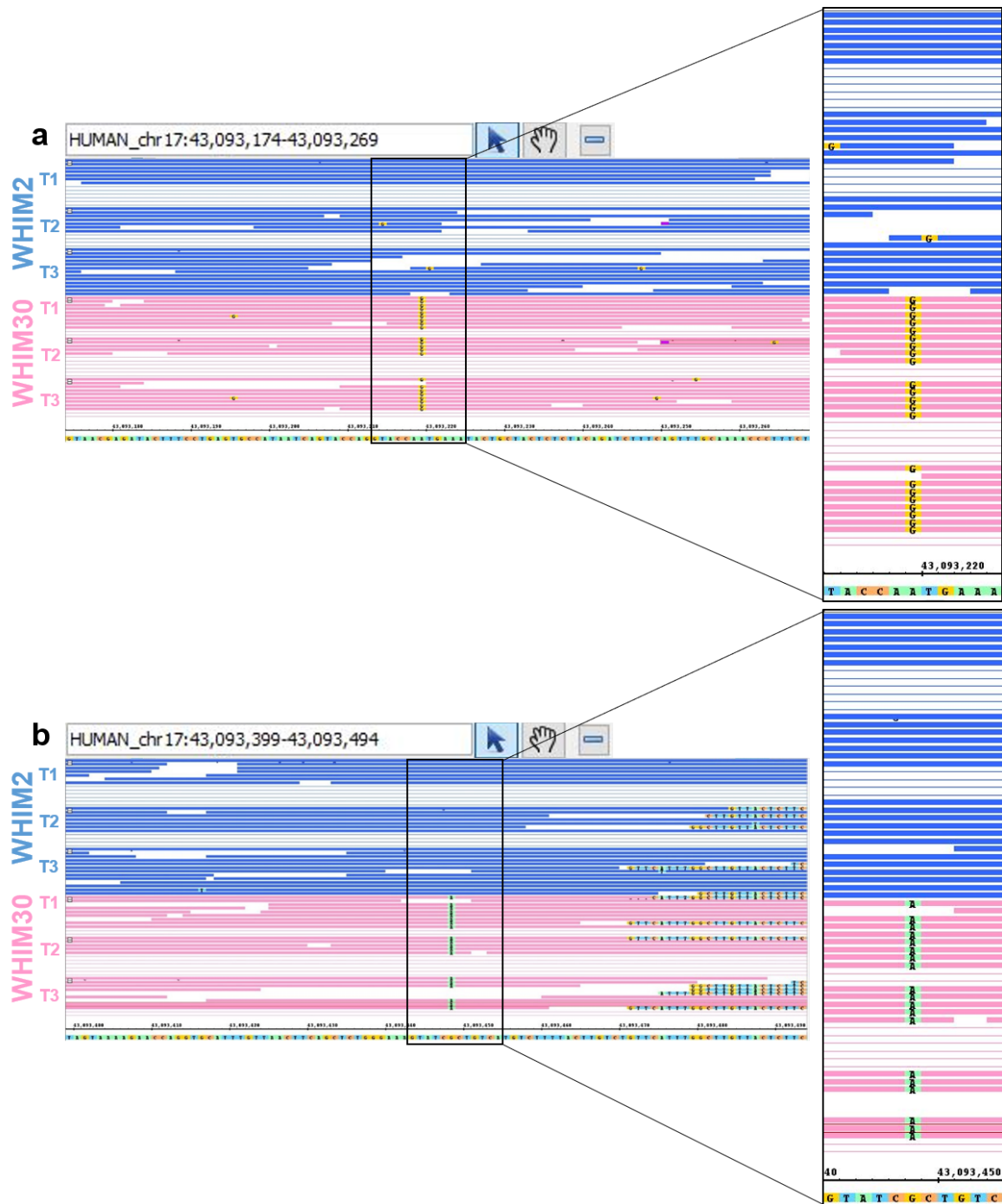


Figure 2.5: BRCA1 status differs between WHIM2 and WHIM30 tumors. Using the Integrated Genome Browser, the BRCA1 gene (human chromosome 17: 43,044,194-43,125,583) in WHIM2 and WHIM30 sequences was aligned to a human reference genome and scanned for mutations, defined as 10 or more reads distinct from the reference genome. Point mutations were observed at positions 43,093,219 (rs16940) **(a)** and 43,093,448 (rs1799949) **(b)** in WHIM30, but not in WHIM2, tumor sequences. The labels T1, T2, and T3 represent the 3 tumor samples analyzed for each PDX line. Reprinted by permission from Springer Nature: [149] © Springer Science+Business Media, LLC (2018)

2.4.5 Cancer therapeutics are differentially efficacious in treating PDX mammary tumors *in vivo*

Based on *in vitro* studies, bortezomib, dacarbazine, carboplatin, and cyclophosphamide were administered to mice bearing PDX mammary tumors. The drugs were ineffective in shrinking WHIM2 tumors when treatment was initiated at 20mm² (**Fig. 2.6a**) or just one week post-inoculation, when tumors were beginning to become palpable (**Fig. 2.6b**); for both studies, $p > 0.2$ with each drug compared to vehicle at week 2. Treatment-week interactions, indicating treatment effects on tumor growth rate, were significant for cyclophosphamide ($p < 0.005$) in both WHIM2 studies and for dacarbazine ($p < 0.03$) and carboplatin ($p < 0.003$) in the latter study, but insignificant otherwise ($p > 0.2$). Carboplatin and cyclophosphamide were significantly effective, at both doses, in shrinking WHIM30 mammary tumors when treatment was initiated at 20mm² (**Fig. 2.6c,d**); with each drug compared to vehicle at week 3, carboplatin: $p < 0.001$, cyclophosphamide: $p < 0.003$. WHIM30 tumors treated with carboplatin or cyclophosphamide were eradicated by the study endpoint; however, bortezomib and dacarbazine were ineffective *in vivo* (**Fig. 2.6d**). Treatment-week interactions were significant for bortezomib ($p < 2.0 \times 10^{-6}$), dacarbazine ($p = 0.0498$), carboplatin ($p < 3.0 \times 10^{-13}$), and cyclophosphamide ($p < 3.0 \times 10^{-16}$). Bortezomib, though initially effective, was toxic at its most effective dose, with mice displaying signs of neurotoxicity. When WHIM30 tumors were treated starting at 50mm², carboplatin and cyclophosphamide had similar efficacy compared with studies on smaller tumors, whereas bortezomib and dacarbazine were still ineffective (**Fig. 2.6e**); treatment-week interactions were insignificant ($p > 0.4$). Cyclophosphamide was equally effective in treating WHIM30 tumors when initiated at 100mm² (**Fig. 2.6f**), with insignificant treatment-week interactions ($p = 0.06$). Mice treated with high-dose cyclophosphamide were tumor-free by the endpoint of the study and for up to 8 weeks following cessation of treatment.

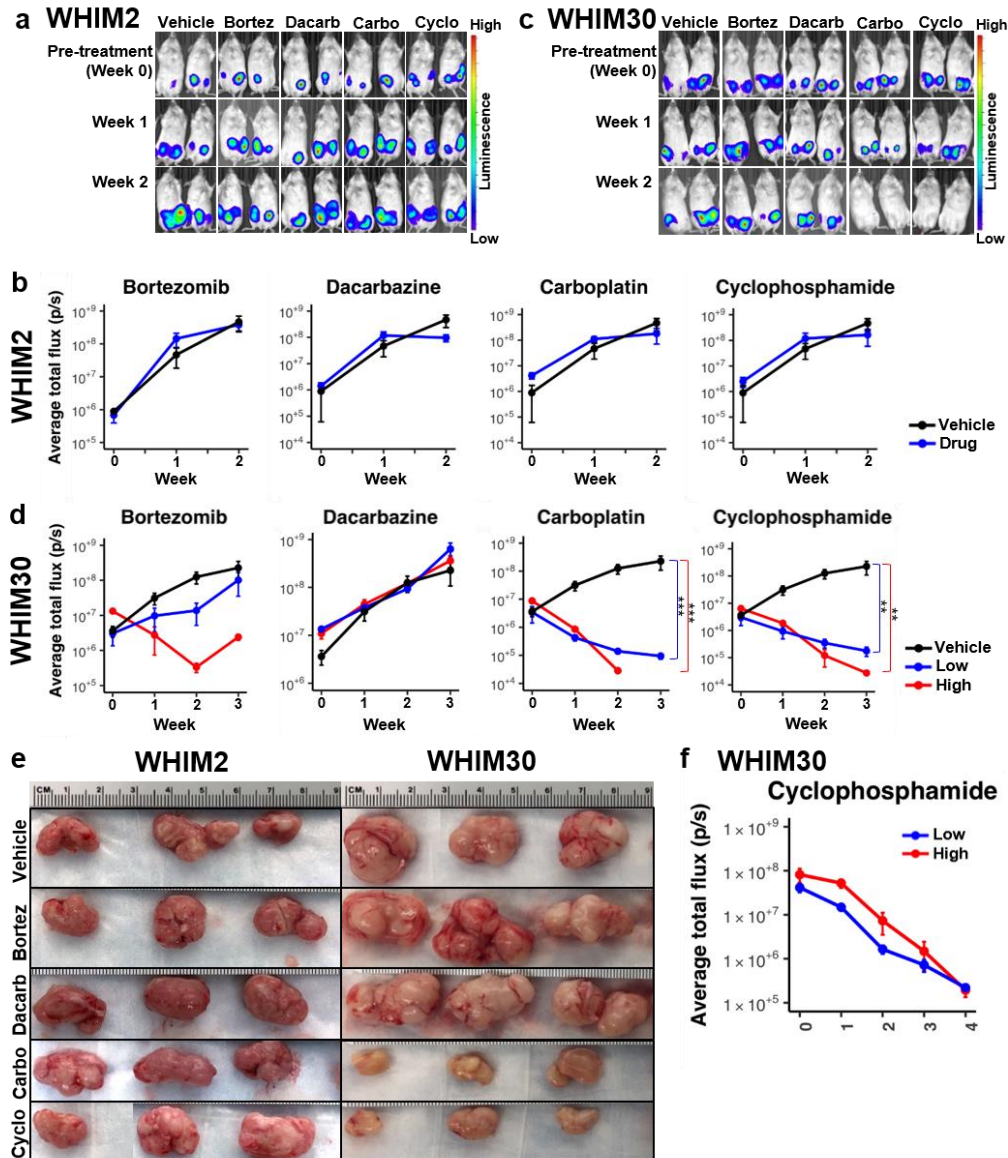


Figure 2.6: Cancer therapeutics are differentially efficacious in treating WHIM2 and WHIM30 mammary tumors *in vivo*. Mice were treated IP with vehicle (normal saline), bortezomib, dacarbazine, carboplatin, or cyclophosphamide (high and low dosages indicated in Table 2.2). **(a,c)** IVIS images depicting WHIM2 **(a)** and WHIM30 **(c)** mammary tumors prior to treatment (Week 0), when tumors were approximately 20mm², and after 1 and 2 weeks of treatment; images show two representative mice from each treatment group (bortezomib 0.3 mg/kg, dacarbazine 60 mg/kg, carboplatin 90 mg/kg, cyclophosphamide 75 mg/kg). **(b,d)** Effects of the four drugs on WHIM2 **(b)** and WHIM30 **(d)** tumor growth over time as measured by luciferase activity of the tumor region (bilateral tumors were considered one region of interest); values at each timepoint were averaged for all mice in each treatment group. Significance of treatment effects of each drug compared to vehicle was determined by Post-hoc Tukey's Honest Significant Difference tests: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. **(e)** Gross images of WHIM2 and WHIM30 mammary tumors after 4 weeks of treatment with the four drugs, when treatment was initiated at 50mm². **(f)** Effect of low and high dose cyclophosphamide (Table 2.2) on the growth of near-burden WHIM30 mammary tumors over time, as measured by luciferase activity of the tumor region. Reprinted by permission from Springer Nature: [149] © Springer Science+Business Media, LLC (2018)

2.4.6 Cancer therapeutics are differentially efficacious in treating PDX metastases in vivo

Given their efficacy in treating mammary tumors, carboplatin and cyclophosphamide were tested in treating metastases generated by intracardiac injection of PDX cells. Using this model, the frequency of metastasis to specific organs was as follows: for WHIM2, 100% of mice develop metastases in the brain, 50% in the liver, 33% in the lung, 83% in the ovary, and 25% in the adrenal glands; for WHIM30, 100% of mice develop metastases in the brain, 100% in the liver, 78% in the lung, and 66% in the femur. Neither drug reduced WHIM2 metastasis burden in general (**Fig. 2.7a**), or specifically in the brain ($p > 0.5$) (**Fig. 2.7b**); treatment-week interactions were insignificant ($p > 0.06$). Both drugs were effective in reducing WHIM30 brain metastases (**Fig. 2.7c,d**); with each drug compared to vehicle at week 5, $p < 2.0 \times 10^{-4}$ for carboplatin and $p < 3.0 \times 10^{-4}$ for cyclophosphamide, both with significant treatment-week interactions ($p < 4.0 \times 10^{-10}$). Whole-body IVIS images (**Fig. 2.7c**) depicted differential efficacy of the drugs in treating WHIM30 metastases, therefore endpoint necropsies were performed on all mice to image the brain, liver, and lungs *ex vivo*. In some cohorts of mice, carboplatin and cyclophosphamide were equally effective in eliminating lung metastases, whereas carboplatin appeared to be superior to cyclophosphamide in treating liver metastases; both showed similar activity towards brain metastases (**Fig. 2.7e**). However, other cohorts showed considerably different efficacy profiles, with similar efficacy of the drugs in the three sites, or lacking efficacy (**Fig. 2.8**). Collectively, despite this variability, quantification of *ex vivo* luciferase activity in the three organs demonstrated that carboplatin and cyclophosphamide were each efficacious in reducing WHIM30 metastatic burden in the brain, liver, and lung (**Fig. 2.7f**); p-values for carboplatin and cyclophosphamide, respectively, compared to vehicle, were 0.04 and 0.04 in the brain, 1.78×10^{-7} and 2.42×10^{-5} in the liver, and 3.09×10^{-8} and 4.48×10^{-8} in the lung. Carboplatin and cyclophosphamide had similar efficacy profiles, when compared to each other, in all three organs (**Fig. 2.7f**). Treatment efficacy in the liver was particularly striking

in some cohorts, in which we observed protruding tumor growths off the liver in vehicle-treated mice, whereas the livers of drug-treated mice did not have grossly visible metastases (**Fig. 2.7g**). As aforementioned, some cohorts of mice did not show a complete treatment response (**Fig. 2.8**), which explains the smaller, albeit significant, treatment effects observed when all *ex vivo* luciferase activity data were analyzed collectively (**Fig. 2.7f**).

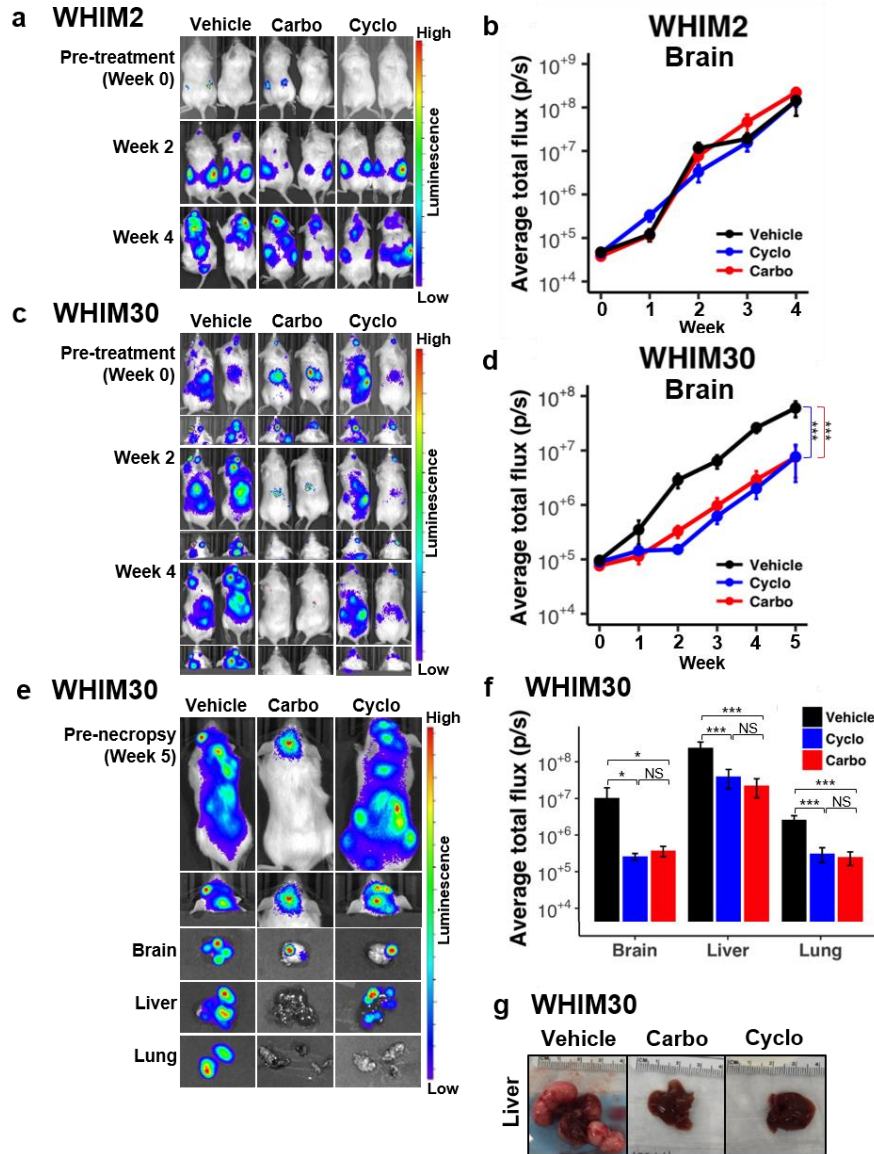


Figure 2.7: Cancer therapeutics are differentially efficacious in treating WHIM2 and WHIM30 metastases *in vivo*. For metastasis studies, mice were injected with tumor cells in the left ventricle of the heart. Drug treatment was initiated 10 days following inoculation, allowing for proper seeding of metastases. Mice were treated IP weekly with vehicle (normal saline), carboplatin 90 mg/kg, or cyclophosphamide 75 mg/kg. **(a,c)** IVIS images depicting WHIM2 **(a)** and WHIM30 **(c)** metastases prior to treatment (Week 0), and after 2 and 4 weeks of treatment; images show two representative mice from each treatment group. **(b,d)** Effects of the four drugs on the growth of WHIM2 **(b)** and WHIM30 **(d)** brain metastases over time as measured by luciferase activity in the brain region of the live mouse; values were averaged for all mice in each treatment group. **(e)** IVIS images of mice bearing WHIM30 metastases *in vivo* prior to euthanasia, and of brain, liver, and lung *ex vivo*, after 5 weeks of treatment with vehicle, carboplatin, or cyclophosphamide. Images are from one representative mouse per treatment group. **(f)** Effects of carboplatin and cyclophosphamide compared to vehicle on WHIM30 brain, liver, and lung metastases, as measured by luciferase activity of each organ *ex vivo*. Significance of treatment effects of each drug compared to vehicle was determined by Post-hoc Tukey's Honest Significant Difference tests: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. **(g)** Gross images of livers from WHIM30 mice after treatment with vehicle, carboplatin, or cyclophosphamide. Reprinted by permission from Springer Nature: [149] © Springer Science+Business Media, LLC (2018)

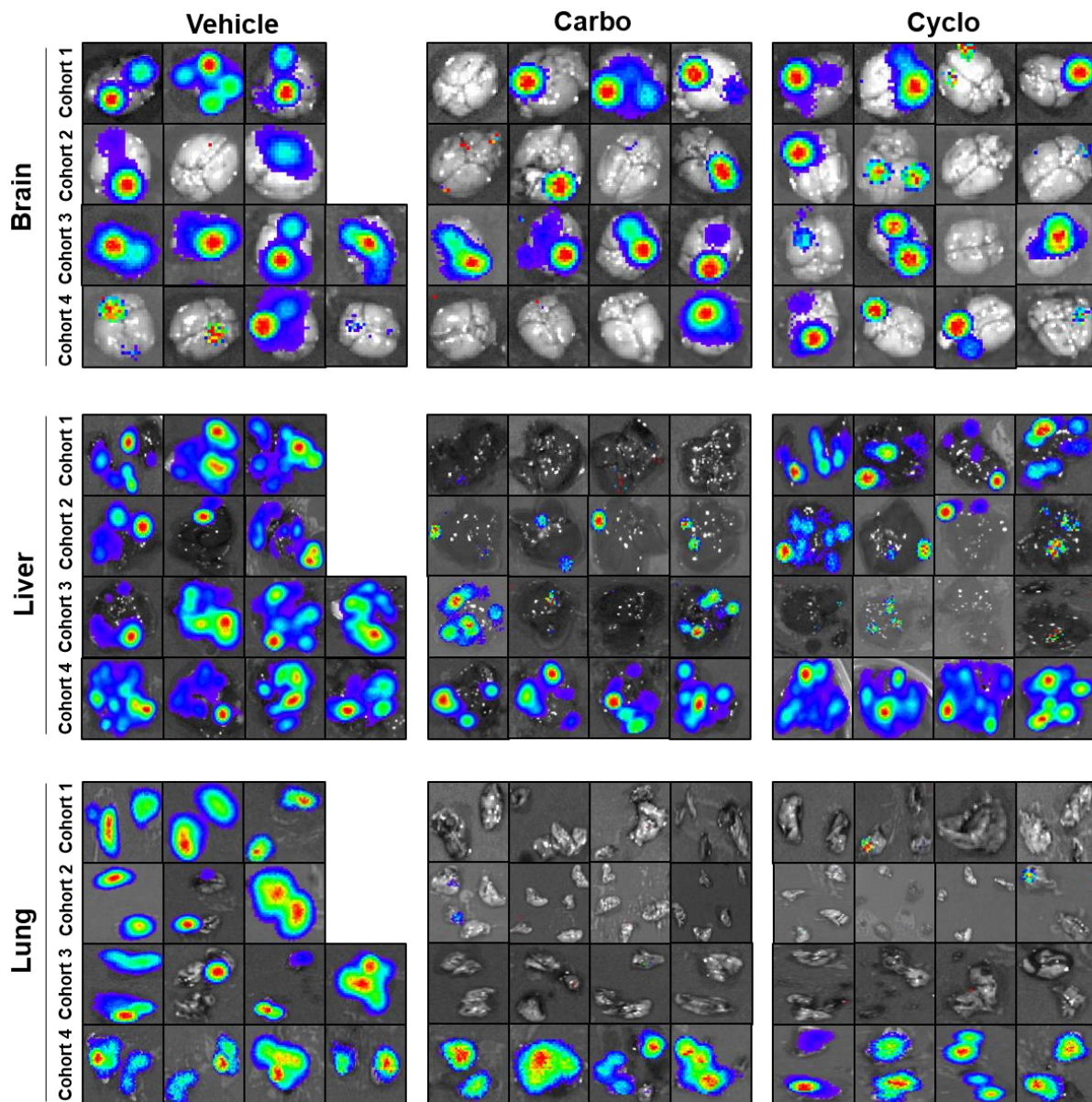


Figure 2.8: IVIS images of *ex vivo* brain, liver, and lungs from all mice used in WHIM30 metastasis studies evaluating the response to carboplatin and cyclophosphamide as compared to vehicle. Cohorts represent groups of mice used in each individual experiment. In each experiment, mice were intracardiac injected with WHIM30 tumor cells and treatment with vehicle or drug was initiated 10 days later, and continued until the vehicle group reached metastatic burden. At this endpoint, all mice were necropsied and brains, livers, and lungs were removed for IVIS imaging and analysis. Reprinted by permission from Springer Nature: [149] © Springer Science+Business Media, LLC (2018)

2.4.7 *Carboplatin and cyclophosphamide reduce the number and size of metastatic lesions*

H&E staining of WHIM30 metastases revealed differences in number and size of metastatic lesions between vehicle and both treatment groups, with larger lesions in the vehicle group; no tumor cells or metastatic lesions were observed in livers from carboplatin-treated mice (**Fig. 2.9a**). No metastases were observed in lungs from carboplatin- or cyclophosphamide-treated mice (data not shown). Per whole-organ section, vehicle-treated mice had an average of 7.5 metastatic lesions in the brain (n=2) and 15.5 in the liver (n=2). Carboplatin-treated mice had an average of 3.33 metastatic lesions in the brain (n=3) and 0 in the liver (n=3). Cyclophosphamide-treated mice had an average of 3.67 metastatic lesions in the brain (n=3) and 1 in the liver (n=3).

2.4.8 *PDX mammary tumors and metastases have distinct patterns of cytokeratin and vimentin expression*

To examine the effects of chemotherapeutic treatment on markers of malignant cellular processes at the tissue level, as well as differences in these markers between the two PDXs, WHIM2 and WHIM30 mammary tumors and metastases were analyzed by IHC for expression of pan-cytokeratin and vimentin as respective markers of epithelial and mesenchymal cell states, Ki67 and phosphohistone-H3 as markers of proliferation, and cleaved caspase-3 as a marker of apoptotic activity. All tissues were positive for Ki67 and phosphohistone-H3, and clusters of cleaved caspase-3-positive tumor cells were observed in many of the tissues; however, no differences were observed between treatment groups (data not shown). Patterns of cytokeratin and vimentin expression were distinct in WHIM2 versus WHIM30 tissues. WHIM30 mammary tumors contained cells expressing either pan-cytokeratin or vimentin (**Fig. 2.9b**). Regardless of treatment, WHIM30 brain metastases were cytokeratin-positive/vimentin-negative, surrounded by vimentin-positive stromal cells (**Fig. 2.9b**); 35/36 brain lesions were cytokeratin-positive, 36/36 were vimentin-negative. Liver metastases were either cytokeratin-positive/vimentin-negative or cytokeratin-

negative/vimentin-positive (**Fig. 2.9b**); 26/35 liver lesions were cytokeratin-positive, 14/35 were vimentin-positive. In contrast, WHIM2 tumors and metastases were all cytokeratin-positive/vimentin-positive (**Fig. 2.9c**).

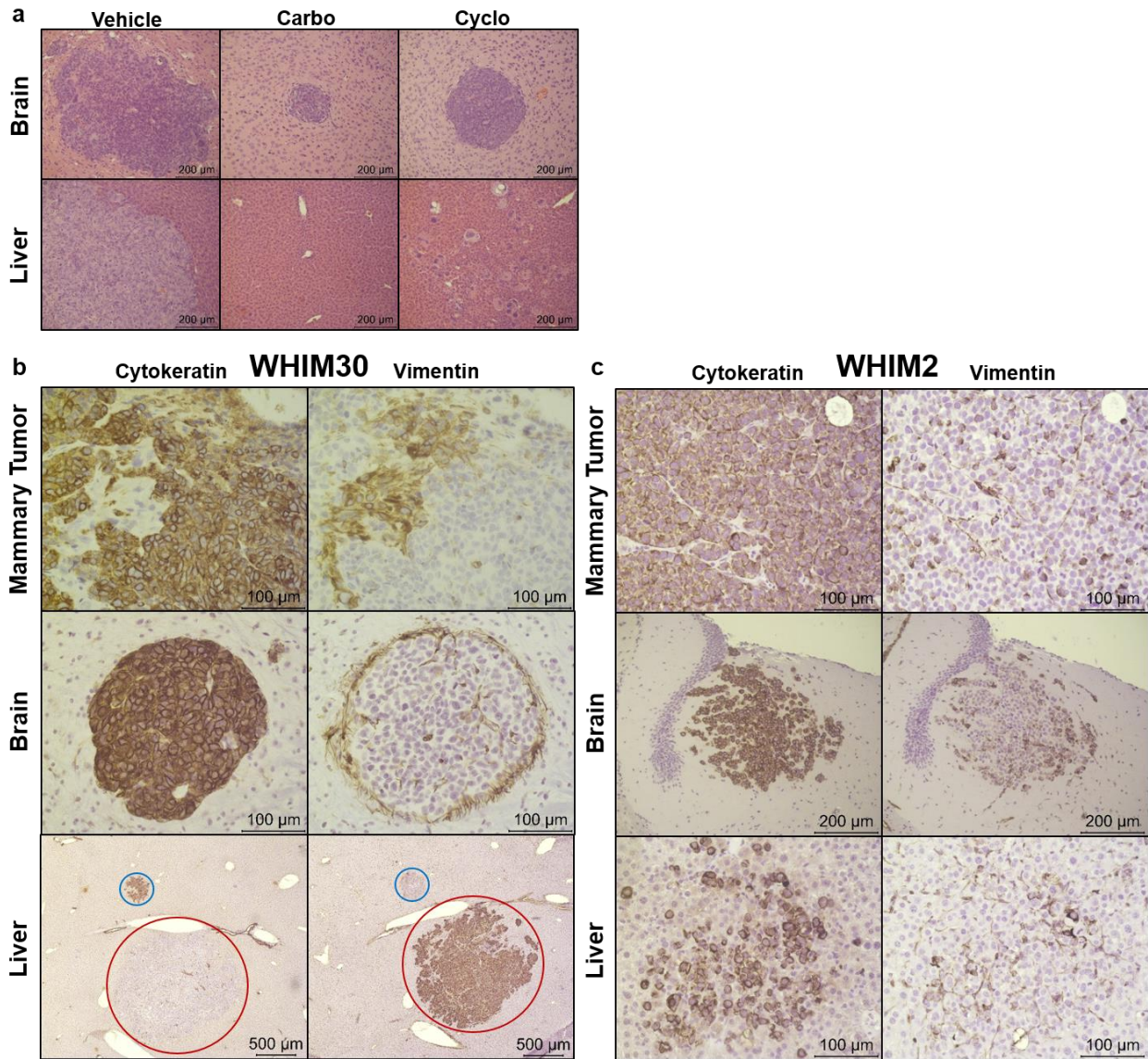


Figure 2.9: WHIM30 metastases show a histological response to chemotherapeutics and have distinct patterns of cytokeratin and vimentin expression, in contrast to WHIM2 metastases. **(a)** H&E staining of WHIM30 brain and liver metastases after treatment with vehicle, carboplatin, or cyclophosphamide. All H&E images are 20X. **(b)** IHC analysis of cytokeratin and vimentin expression in WHIM30 mammary tumor, brain and liver metastasis tissue. Mammary tumor and brain images are 40X, liver images are 5X. **(c)** IHC analysis of cytokeratin and vimentin expression in WHIM2 mammary tumor, brain and liver metastasis tissue. Mammary tumor and liver images are 40X, brain images are 20X. Adapted by permission from Springer Nature: [149] © Springer Science+Business Media, LLC (2018)

2.5 Discussion and conclusions

Our goal was to determine if cancer therapeutics are equally effective in treating TNBC mammary tumors and metastases in the brain, liver, and lung, using two PDX models of basal-like TNBC. We first screened drugs on PDX cells in suspension culture to identify those that may be effective *in vivo*. Cells in suspension culture clustered together over time, forming emboli-like aggregates, which recapitulate physiological tumor cell morphology, gene expression, signaling, microenvironment, and drug responses better than two-dimensional monolayers [159–161]. Other studies have demonstrated that PDX cultures maintain the characteristics and drug response profiles of their *in vivo* counterparts [148]; we found that mammary tumor and brain metastasis gene expression profiles were broadly maintained in suspension cultures over time. Of the twelve cancer therapeutics tested *in vitro*, some drugs were cytotoxic to both PDX lines, some were not cytotoxic to either line, and others were differentially effective between the two lines. Carboplatin was cytotoxic to WHIM30 cells but not to WHIM2 cells, likely attributable, at least in part, to BRCA1 status; BRCA1 mutations, present in WHIM30 but absent in WHIM2, are indeed associated with sensitivity to platinum-based agents [157, 158].

Surprisingly, efficacy profiles were not consistently comparable between *in vivo* and *in vitro* studies. WHIM30 mammary tumors could be eliminated by carboplatin or cyclophosphamide; the latter was equally effective when treatment was delayed until tumors were near-burden, recapitulating the clinical scenario in which a patient presents with an established, potentially high-grade tumor prior to receiving therapy. Bortezomib, despite its toxicity, slowed the growth of WHIM30 tumors. However, in contrast to *in vitro* results, all four drugs were ineffective in treating WHIM2 mammary tumors. Dacarbazine has a short physiological half-life [162] and may have greater efficacy if dosing parameters were altered. Of note, both the WHIM2 and WHIM30 PDXs were treatment naïve in origin—the original tumor samples were obtained from the patients prior to initiation of chemotherapy [117]. Therefore, prior exposure to

chemotherapeutics cannot explain the differential drug sensitivities observed in these models. However, the lack of treatment response in the WHIM2 model parallels clinical data indicating that the WHIM2 patient was treated with neoadjuvant doxorubicin, cyclophosphamide, and paclitaxel, which did not achieve a pathologic complete response; the patient developed metastatic disease in the brain less than one year following chemotherapy, whereas the WHIM30 patient was not reported to develop any post-treatment recurrences [117, 138].

Basal-like tumors tend to metastasize to the brain, liver, and lungs [18]. Brain metastasis is a particularly significant cause of morbidity and mortality due to its severe neurological effects and the lack of effective treatment strategies [163, 164]. We therefore chose to generate metastases in mice via intracardiac injection, which has been used previously to study brain metastasis [53, 142, 143, 165, 166] and is a more efficient method of seeding tumor cells in the brain, liver, and lungs compared to spontaneous metastasis models. Although this model only mimics the later stages of metastasis, not initial intravasation, in our experience, mice bearing PDX mammary tumors only sporadically develop spontaneous brain metastases after primary tumor resection. We hypothesized that carboplatin and cyclophosphamide would have similar efficacy profiles in the metastatic setting as compared to the primary setting, especially given their abilities to cross the blood-brain barrier [167–169] and the similarities in overall gene expression profiles that we observed between primary tumors and metastases. Indeed, both drugs were effective in treating WHIM30 metastases in the brain, liver, and lung, suggesting that these metastatic tumor cells, despite growing in foreign microenvironments, retained properties of primary tumor cells that conferred sensitivity to certain drugs.

To examine the effects of carboplatin and cyclophosphamide on mammary tumors and metastases at the cellular level, we evaluated the expression of markers of proliferation (Ki67, phosphohistone-H3) and apoptosis (cleaved caspase-3), as well as cytokeratin and vimentin. All tissues were positive for proliferation markers, with scattered tumor cells expressing cleaved caspase-3, without notable differences between treatment groups. Thus, the drugs did not

affect proliferation or apoptosis in remaining cells within the primary or metastatic setting. However, histologically, metastases in the brain and liver were smaller, and fewer or nonexistent, in drug-treated mice compared to vehicle-treated mice. Thus, the drugs were effective in reducing both the number and size of metastatic lesions, confirming the reduction in *ex vivo* luciferase activity, reflecting metastatic burden, in these organs in response to these treatments.

Cytokeratin and vimentin—markers of epithelial cells and mesenchymal cells, respectively—are often used to reflect EMT, throughout which tumor cells downregulate cytokeratin and upregulate vimentin, transitioning from an adhesive phenotype to a migratory, invasive phenotype. Vimentin expression, particularly a high vimentin/keratin ratio, has been associated with basal-like tumors and is a poor prognostic indicator [170–172]. Neither carboplatin nor cyclophosphamide influenced cytokeratin or vimentin expression in any tissue, suggesting that neither drug induced or deterred EMT. However, we observed remarkably distinct patterns of cytokeratin and vimentin expression in WHIM2 and WHIM30 mammary tumors and metastases in the brain and liver, regardless of treatment, illuminating the possible existence of distinct tumor cell subpopulations within each PDX line. WHIM2 tumors and metastases were positive for both cytokeratin and vimentin, whose co-expression has been associated with more invasive tumor behavior [173]. In contrast, WHIM30 metastatic lesions were either cytokeratin-positive/vimentin-negative or cytokeratin-negative/vimentin-positive. Brain metastases were all cytokeratin-positive/vimentin-negative, with a ring of vimentin-positive stromal cells surrounding each lesion. Reactive astrocytes are known to localize to sites of brain injury or tumor/metastasis growth and upregulate vimentin and other filament proteins [174–176]. Of note, these rings of vimentin-positive stromal cells were absent in WHIM2 brain metastases, which may indicate an impaired response of glial cells to these tumor cells, potentially affecting tumor behavior and treatment response [177–179]. High vimentin expression has been associated with drug resistance in breast cancer [180, 181] and other

cancer types [182–184]. Tumor cell subpopulations with distinct intermediate filament expression patterns may have differential sensitivities to therapeutics, in addition to their tendencies to form metastases in certain tissue types. Recent studies have demonstrated that different subpopulations of cells within primary tumors can co-migrate, seed, and invade distant tissues, resulting in heterogeneous metastatic lesions [185–188]. Based on our findings in the two models tested, we believe that distinct subpopulations of primary tumor cells may preferentially seed and thrive in different organs, and it appears that the brain may be more selective than the liver in terms of providing a microenvironment suitable for the colonization of particular subpopulations. Alternatively, certain subpopulations of tumor cells may have an enhanced ability to penetrate the blood-brain barrier.

These studies highlight the importance of conducting *in vivo* studies of cancer therapeutics in different metastatic sites, as drug response can be impacted by physiological factors such as drug transport, metabolism, and microenvironment. Although *in vitro* screening assays are widely accepted in preclinical research, *in vivo* studies are superior when evaluating drug responses for advanced disease [189]. We have demonstrated that treatment responses can vary considerably between basal-like TNBC tumors derived from two different patients. This recapitulates the clinical challenges faced in cancer treatment, as patients with the same histologic or molecular subtype often respond differently to the same therapies. It is imperative to discover better ways to predict subsets of patients who will respond to particular therapies, just as we can now predict that the majority of patients with ER- and PR-positive tumors will respond to tamoxifen.

2.6 Future directions

Future studies will focus on investigating the mechanisms underlying the differential responses of WHIM2 and WHIM30 to chemotherapeutics, as well as employ additional PDX models to study chemotherapeutic resistance. These studies will assess differential gene expression in PDX cells with intrinsic sensitivity, intrinsic resistance, and acquired resistance to

chemotherapies such as carboplatin, to identify genes and pathways that may play a role in differential responses to these drugs. Future studies will also focus on characterizing subpopulations of tumor cells with distinct cytokeratin and vimentin expression patterns and exploring their potential roles in metastatic propensity/tropism and treatment efficacy using additional TNBC PDX models. This will involve single-cell RNA sequencing of tumors to determine differential gene expression profiles within each distinct tumor cell subpopulation. Insights gained from this study will help design future *in vivo* studies evaluating the efficacy of combination therapies in reducing both metastatic burden and chemotherapeutic toxicity.

CHAPTER 3: Identification of synergistic drug combinations using breast cancer patient-derived xenografts [190]

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3.1 Background and rationale

It is estimated that each year over 268,000 American women will be diagnosed with invasive breast cancer, and over 41,000 will have fatal outcomes from the disease [19, 33]. Survival rates have considerably improved over the past several decades due to the identification and characterization of distinct histologic and molecular subtypes of breast cancer [11–14], which predict patient outcomes and have led to the development of targeted therapeutics, allowing treatment regimens to be tailored based on specific tumor characteristics [15–18]. ER/PR-positive (predominantly luminal) tumors or HER2-positive (HER2-enriched) tumors, which collectively make up the majority of breast cancer cases, are treated with ER- or HER2-targeted drugs, respectively, largely contributing to the current overall breast cancer 5-year survival rate of nearly 90% [19, 33]. However, for the approximately 15% of breast cancers that are histologically triple-negative, few clinically successful targeted therapies have yet been developed, despite major translational research efforts [34]. Patients with TNBC, a relatively aggressive and highly metastatic subtype, are therefore limited to treatment with chemotherapy, which is highly toxic and often ineffective in treating advanced disease, leading to relatively poor outcomes compared to patients with other subtypes of breast cancer [36, 37, 191]. Development of successful therapeutic strategies for TNBC is a challenge due not only to the current lack of reliable drug targets, but also to the heterogeneity of the disease; TNBC can be classified based on gene expression profiles into four distinct subtypes, each of which is dominated by distinct molecular pathways, contributing to differential responses to chemotherapy and investigational targeted therapies [70, 71]. Nearly 60% of TNBCs are basal-

like [70, 71], which is characterized by a high propensity to metastasize to vital organs and is associated with a particularly poor prognosis [15, 17, 18]. In the realm of translational breast cancer research, there is a critical need to identify reliable molecular targets in each subtype of TNBC, particularly basal-like, to enable the development of tailored therapeutic regimens with superior efficacy and less toxicity than current standard-of-care chemotherapeutic cocktails. Given the lack of clinical success with targeted therapies as single agents or combined with chemotherapies in TNBC, it is likely that novel combination strategies are needed to successfully treat this disease.

3.2 Experimental approach

To identify novel therapeutic candidates, we performed *in vitro* screening of 1,363 drugs in ten breast cancer PDX models. Using this approach, we generated a dataset that can be used to quickly assess and compare responses of breast cancer PDXs of varying subtypes to many different drugs, most of which are approved by the FDA for various cancer or non-cancer indications. From these data, we identified 176 drugs that were consistently effective across four basal-like TNBC PDXs, encompassing a wide variety of molecular targets and mechanisms of action. Several of these drugs have shown promising efficacy in TNBC and other solid tumors, however it is likely that incorporation into combination regimens is needed to maximize their efficacy and thus their likelihood of clinical success. Through a series of *in vitro* drug response assays, we selected four drugs to test in various two-drug combinations: carfilzomib (proteasome inhibitor), afatinib (EGFR inhibitor), and YM155 (inhibitor of baculoviral inhibitor of apoptosis repeat-containing 5 (BIRC5; survivin) expression), along with carboplatin, a chemotherapeutic that is part of the current standard-of-care for TNBC and that we have previously tested in several PDXs [149]. Given the overexpression of EGFR in basal-like TNBC, and the involvement of its downstream pathways in multiple protumorigenic processes, we hypothesized that EGFR inhibition would be efficacious and have synergistic effects with several drugs due to the potential crosstalk of many drug target pathways with

EGFR signaling. Of the six drug combinations tested, we found that the combination of afatinib and YM155 was synergistically cytotoxic across four basal-like TNBC PDXs, and this drug combination significantly reduced PDX mammary tumor growth *in vivo*, without observable toxicity. We then analyzed the expression of the targets of these drugs (EGFR and BIRC5) across breast cancer PDXs, cell lines, and patients, and explored the effects of EGFR and BIRC5 co-expression on metastasis-free survival (MFS), to determine whether co-targeting of these genes may be a promising strategy for effective treatment of advanced basal-like TNBC. Through Western blotting for EGFR, we also gained preliminary insight into a potential mechanism of synergism between afatinib and YM155 in the context of this disease.

3.3 Materials and methods

3.3.1 Breast cancer PDX models and preparation of tumor cell suspensions

Breast cancer PDX models of varying subtypes were used in these studies: triple-negative, basal-like (HCI01, HCI16, UCD52, WHIM2, WHIM30); triple-negative, LAR type (HCI09); ER-positive, luminal (HCI03, HCI11, HCI13); and HER2-enriched (HCI08). HCI01, HCI03, HCI08, HCI09, HCI11, HCI13, and HCI16 were obtained from the Huntsman Cancer Institute, University of Utah; WHIM2 and WHIM30 were obtained from Washington University, St. Louis; UCD52 was obtained from the University of Colorado. All studies involving mice were approved by the VCU Institutional Animal Care and Use Committee (IACUC) (Protocol# AD10001247; approved June 29, 2018), and all experiments were performed in accordance with IACUC guidelines and regulations. Tumor fragments were grown in the fourth mammary fat pads of female NSG mice. Established tumors were removed from mice, finely chopped, and digested for 1h at 37°C in DMEM/F12 containing 5% FBS, 300 U/ml collagenase (Sigma), and 100 U/ml hyaluronidase (Sigma). Digested tumor tissue was then resuspended in ammonium chloride and trypsinized to generate single cell suspensions. Tumor cells were transduced with a lentivirus (BLIV101PA-1, Systems Biosciences) encoding GFP and luciferase, and GFP-luciferase expressing tumor

cells were suspended 1:1 in Matrigel (Corning) and injected into the fourth mammary fat pads of NSG mice (500,000 cells per injection). Mammary tumors were removed for experimental use once they reached approximately 100mm² by caliper measurement. Tumors were processed into single cell suspensions as described above.

3.3.2 *Breast cancer cell lines*

Three basal-like TNBC cell lines, MDA468, HCC1143, and HCC1937, were employed to validate the results of PDX studies. MDA468 cells were provided by Dr. Youngman Oh (VCU Department of Pathology); HCC1143 and HCC1937 cells were obtained from the American Type Culture Collection (ATCC) and used within 10 passages of the original stocks. Cell lines were cultured in Roswell Park Memorial Institute 1640 (RPMI-1640) GlutaMAX medium (ThermoFisher Scientific) supplemented with 10% FBS and penicillin/streptomycin.

3.3.3 *Cell viability assays*

For PDX cell viability assays, PDX cell suspension cultures were plated in 96-well plates at 25,000 cells per well in M87 medium [135] and treated with drugs for 72h, followed by imaging and measurement of luciferase activity (total photon flux per second) two minutes after the addition of D-luciferin (15 mg/ml; Gold Biotechnology) to each well (1/10 of total volume per well), using the IVIS Spectrum In Vivo Imaging System (Xenogen IVIS-200) and Living Image software (PerkinElmer), as described in our previous work [149]. For cell line viability assays, MDA468, HCC1143, or HCC1937 cells were plated in 96-well plates at 5,000 cells per well in complete RPMI-1640 GlutaMAX medium, cultured overnight to allow for adherence, and subsequently treated with drugs for 72h. Viability of cell lines was measured using the CellTiter-Glo Luminescent Viability Assay (Promega), according to the provided protocol.

3.3.4 *In vitro* drug screening studies

PDX tumor cells (HCI01, HCI16, UCD52, WHIM2, WHIM30, HCI08, HCI09, HCI03, HCI11, HCI13) were treated with 1,363 drugs (ApexBio DiscoveryProbe FDA-approved Drug Library), at 10 μ M per drug, and cell viability was measured after 72h as described above. Drug response was assessed and compared between drugs and PDXs by calculating the percent of vehicle (0.1% dimethylsulfoxide (DMSO)) viability for each drug-treated well. Replicates were then averaged for each PDX and analyzed based on breast cancer subtype, with a focus on identifying promising targeted therapeutic candidates for basal-like TNBC using four PDXs of this subtype (HCI01, UCD52, WHIM2, WHIM30). To select drug candidates for further studies, drug response data for each of these four PDXs were ranked in order of increasing efficacy (decreasing % of vehicle viability), and the 200 most effective drugs were chosen for each individual PDX line. We then used a Venn diagram (<https://bioinfoqp.cnb.csic.es/tools/venny/>) to determine the extent of overlap in the most effective drugs across the four PDXs. Based on this analysis, we selected 176 drugs for further testing in basal-like TNBC models, consisting of: 1) 71 drugs that overlapped across all four PDXs, 2) 53 drugs that overlapped in three of the PDXs, 3) 48 drugs that overlapped in two of the PDXs, 4) two drugs that were exclusive to one of the PDXs (erlotinib and carboplatin), and 5) two drugs that were not included on these lists but were of interest from a mechanistic standpoint, to compare with other drugs with similar mechanisms of action (birinapant and bortezomib). All subsequent drug studies were performed using the same drug stock solutions purchased from ApexBio.

3.3.5 *Single-dose drug combination studies*

All drug combination studies were carried out *in vitro* using the same cell viability assay methods described above. For initial combination studies, the 176 selected drugs were tested on PDX cells (HCI01, UCD52, WHIM2, WHIM30) at 1 μ M alone and in combination with the proteasome inhibitor carfilzomib (10nM for HCI01, UCD52, and WHIM30; 100nM

for WHIM2) or the EGFR inhibitor afatinib (10nM for HCl01, UCD52, and WHIM2; 1 μ M for WHIM30). To assess for additive/supra-additive/sub-additive trends (defined here based on whether the efficacy of a combination was equal to/greater than/less than the sum of the efficacies of each drug alone), percent cell viability values were used to calculate the difference in percent inhibition between each drug as a single agent and in combination: (percent inhibition of combination) – [(percent inhibition of drug 1 alone) + (percent inhibition of drug 2 alone)]. Using this approach, if the calculated value for a combination is greater than zero, the combination has supra-additive trends; if it is zero, it has additive trends; if it is less than zero, it has sub-additive trends. The data generated in these studies were used to help select drugs of interest for more expansive combination testing, described below.

3.3.6 *Multiple-dose drug combination studies*

Based on initial screening and single-dose drug combination data, as well as drug target gene expression data, 13 drugs were selected for dose response analysis: three proteasome inhibitors (carfilzomib, bortezomib, ixazomib), five drugs that target apoptosis pathways (YM155, navitoclax, ABT-199, embelin, birinapant), an EGFR inhibitor (afatinib), a cyclin-dependent kinase 4/6 (CDK4/6) inhibitor (abemaciclib), a selective serotonin reuptake inhibitor (SSRI) (fluoxetine), synthetic vitamin D3 (calcitriol), and an antiarrhythmic agent (dronedarone). These drugs included the two drugs tested in combination with the 176 drugs in the single-dose combination screen (carfilzomib and afatinib), one of the most effective of the 176 drugs in the prior screening studies (YM155), drugs with similar mechanisms of action (two additional proteasome inhibitors and four additional drugs that target apoptosis pathways), and drugs with mechanisms that are not typically targeted in cancer therapy (calcitriol, dronedarone, and fluoxetine). Basal-like TNBC PDX cells (HCl01, UCD52, WHIM2, WHIM30) were treated with increasing concentrations of each of the 13 drugs (ranging from 0.1-10 μ M) for 72h, followed by cell

viability measurement. Based on potency and efficacy across the four PDXs, three of these drugs (carfilzomib, YM155, and afatinib) were selected for subsequent combination testing, along with carboplatin, a chemotherapeutic agent that is part of the standard-of-care regimen for TNBC and that we have previously tested in several PDXs [149]. Pharmaceutical-grade carboplatin was obtained from the VCU Dalton Oncology Clinic. PDX cells (HCI01, UCD52, WHIM30) were treated for 72h *in vitro* with 7 doses of each drug alone, and with all possible two-drug combinations: carboplatin+carfilzomib, carboplatin+afatinib, carboplatin+YM155, carfilzomib+afatinib, carfilzomib+YM155, afatinib+YM155. Afatinib+YM155 was additionally tested in the WHIM2 PDX model, as well as three breast cancer cell lines (MDA468, HCC1143, HCC1937). Two independent experiments, each in triplicate, were performed for each PDX/cell line. Fraction inhibition (Fa) values were calculated using percent viability values for each drug and drug combination. Triplicate Fa values were averaged, and data were analyzed for drug combination effects using the CompuSyn software, which employs the Chou-Talalay method [192–194]. Combination index (CI) and dose reduction index (DRI) values, generated by CompuSyn software simulation, were averaged for each PDX/cell line and used to generate Fa-CI and Fa-DRI plots for each constant-ratio drug combination.

3.3.7 Data clustering

Data were hierarchically clustered using Cluster 3.0, and heatmaps were generated using Java Treeview. This was performed for drug response data (percent cell viability in response to the 176 drugs selected from initial screening, and difference in percent inhibition of the 176 drugs alone and in combination with carfilzomib or afatinib), as well as gene expression data (\log_2 (TPM+1) values) to assess drug target expression across the PDXs. The latter data were obtained from previous RNA-sequencing of PDXs [141], and are publicly available in the NCBI Gene Expression Omnibus (GEO Accession: GSE118942). Data were clustered by both drugs/genes and PDX line.

3.3.8 *In vivo PDX drug treatment studies*

HCI01 cell suspensions were prepared from mammary tumors as described above and injected into the fourth mammary fat pads of NSG mice. After 12 days of tumor growth, monitored by weekly caliper measurements, mice were divided into four treatment groups: untreated (n=3), afatinib (n=3), YM155 (n=3), and afatinib+YM155 (n=3). Afatinib (AChemBlock) was dissolved in 1% methylcellulose + 0.1% Tween-80 and administered at 25 mg/kg via daily oral gavage for 7 days. YM155 (Adooq Bioscience) was dissolved in saline and administered at 5 mg/kg as a 7-day continuous subcutaneous infusion via Alzet pump (Alzet 1007D). Alzet pumps were implanted subcutaneously on the back, posterior to the scapulae. During and following the treatment period, tumor growth was monitored via biweekly caliper measurements. Mice were weighed and observed regularly throughout the study for signs of illness or distress related to tumor growth and/or drug toxicity. All mice were euthanized by CO₂ asphyxiation followed by cervical dislocation once tumors of untreated mice reached near protocol-defined tumor size limits. Tumors were then immediately removed, weighed *ex vivo*, and photographed. Alzet pumps were also removed and examined to confirm that all their contents were administered to the mice.

3.3.9 *Western blot studies*

HCI01 PDX cell suspensions were prepared from mammary tumors as described above, plated in 100mm dishes at 5 million cells per dish in M87 medium, and treated for 24h with vehicle (DMSO) or YM155 (1 or 10 nM). For protein extraction, treated HCI01 cell suspensions were pelleted and resuspended in Pierce RIPA buffer (ThermoFisher Scientific, 89900) + protease inhibitor (ThermoFisher Scientific, A32963) for cell lysis, and centrifuged at max speed at 4°C for 15 min to collect protein lysates. Protein concentrations were determined using Pierce BCA Protein Assay Kit (ThermoFisher Scientific, 23225). Proteins were resolved by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and transferred to Immobilon-FL membranes (Millipore), which were then

blocked in Odyssey Blocking Buffer in Tris-buffered saline (TBS) (Li-Cor) for 1h at room temperature. Primary and secondary antibodies were diluted in Odyssey Blocking Buffer in TBS (Li-Cor) + 0.1% Tween-20. Membranes were incubated for 1h at room temperature with rabbit anti- β -actin (1:1000; Cell Signaling Technology #4970) and overnight at 4°C with rabbit anti-EGFR (1:1000; Cell Signaling Technology #4267). For detection, membranes were incubated with IRDye 680RD donkey anti-rabbit secondary antibody (1:10,000; Li-Cor 926-68073) for 1h at room temperature. All washes were performed using TBS-T (TBS + 0.1% Tween-20). Membranes were imaged using the Odyssey Fc Imaging System (Li-Cor). Densitometry analysis was performed using ImageJ software; EGFR was normalized to actin.

3.3.10 Analysis of EGFR and BIRC5 gene expression in PDXs, cell lines, and patients

Expression levels of EGFR and BIRC5 were assessed using a PDX RNA-sequencing dataset [141], as well as RNA-sequencing data from two publicly available breast cancer cell line gene expression databases: the Harvard Medical School (HMS) Library of Integrated Network-based Cellular Signatures (LINCS) Breast Cancer Profiling Project (<http://lincs.hms.harvard.edu/db/datasets/20348/>) and the Broad Institute Cancer Cell Line Encyclopedia (CCLE) (<https://portals.broadinstitute.org/ccle>). Gene expression data from LINCS are represented as RPKM (reads per kilobase of transcript, per million mapped reads) values, and those from CCLE are represented as log₂ RPKM values. Expression of the two genes was also assessed using a breast cancer patient dataset consisting of microarray gene expression data and clinical data [53, 195] from 855 patients; this dataset was generated by combining four breast cancer microarray datasets (GSE2034, GSE12276, GSE2603, and NKI295) [18]. PDXs, cell lines (from each database separately), and the 855-patient data were each grouped based on breast cancer intrinsic subtype, and EGFR and BIRC5 expression values were averaged for each subtype.

3.3.11 Assessment of the effects of EGFR and BIRC5 expression on patient clinical parameters and outcomes

The 855-patient dataset was used to assess the relationships between EGFR/BIRC5 expression and clinical parameters/outcomes. Pearson correlations were performed to determine correlations between EGFR/BIRC5 expression and clinical characteristics (breast cancer intrinsic subtype, ER/PR/HER2 status, patient age, lymph node status, differentiation and proliferation scores, MFS time, as well as relapse-free survival in the brain, liver, and lung). The 140 patients with basal-like tumors were ranked and divided based on EGFR and BIRC5 expression separately: EGFR^{high} (top 50%) or EGFR^{low} (bottom 50%) and BIRC5^{high} (top 50%) or BIRC5^{low} (bottom 50%). These patients were subsequently divided into four groups based on the designated expression levels (high or low) for each gene: EGFR^{high}BIRC5^{high} (N=32), EGFR^{high}BIRC5^{low} (N=38), EGFR^{low}BIRC5^{high} (N=38), EGFR^{low}BIRC5^{low} (N=32). Kaplan-Meier analysis was performed to determine the differences across these four groups in terms of MFS time, liver relapse-free survival, and lung relapse-free survival.

3.3.12 Statistical analyses

Statistical analyses were performed using unpaired two-tailed student's t-tests to determine the significance of differences in cell viability between control and drug-treated conditions *in vitro*, the significance of differences in drug target gene expression between PDXs, as well as the significance between all treatment conditions *in vivo*; $p < 0.05$ was considered statistically significant. For the single-dose drug combination studies, we performed unpaired two-tailed t-tests to determine the significance of differences between mean differences in percent inhibition across PDXs, and we calculated 95% confidence intervals of the mean differences in percent inhibition and of the proportion of PDXs showing supra-additive or sub-additive trends based on our analysis method. Where appropriate, data are presented as means \pm standard deviations. Tukey's multiple comparisons tests were

performed to analyze differences in EGFR and BIRC5 expression between breast cancer subtypes using the 855-patient dataset. Relationships between EGFR and BIRC5 expression and clinical characteristics in the 855-patient dataset were analyzed by Pearson correlation. The effects of EGFR and BIRC5 expression on MFS in patients with basal-like breast cancer were statistically analyzed using log-rank tests. All statistical tests were performed using GraphPad Prism 8.

3.4 Results

3.4.1 *Drug screening of breast cancer PDXs reveals potential targeted therapeutic candidates for TNBC*

Given the lack of successful targeted therapies currently available for the treatment of TNBC, and the superior clinical relevance of using PDX cultures as opposed to cell lines for assessing drug response in cancer [189], we first sought to identify effective targeted agents through drug screening of breast cancer PDXs: basal-like TNBC (HCI01, HCI16, UCD52, WHIM2, WHIM30), LAR subtype TNBC (HCI09), luminal ER-positive (HCI03, HCI11, HCI13), and HER2-enriched (HCI08). We characterized response profiles, in terms of percent cell viability, of these PDXs of varying breast cancer subtypes to 1,363 drugs, most of which are FDA-approved for various cancer/non-cancer indications (**Appendix A**). This dataset is most appropriately useful for assessing drugs that are cytotoxic to tumor cells (less than 100% viability in response), as several drugs or classes of drugs, most notably HDAC inhibitors, appeared to increase tumor cell viability, due to activation of the cytomegalovirus (CMV) promoter responsible for luciferase expression in the PDX models; HDACs are known to inactivate viral promoters [196], and HDAC inhibitors have been shown to enhance CMV promoter activity [197–199]. It is possible that other drugs may affect CMV promoter activity as well. Using this drug screening dataset, we identified 176 drugs that were most cytotoxic across four of the basal-like PDXs (HCI01, UCD52, WHIM2, WHIM30) (**Fig. 3.1a**), encompassing an interestingly wide range of molecular targets,

mechanisms of action, and indications (**Appendix A**, bolded drugs). The variety of proteins and pathways targeted by these drugs include the cell cycle, proteasome, ion channels, apoptosis pathways, calcium/vitamin D receptor (VDR) signaling, EGFR and mitogen-activated protein kinase (MAPK) signaling, and serotonin signaling, as well as several non-human, microbial pathogen targets, indicating these drugs for treatment of a range of diseases, including cancer, cardiac arrhythmias, calcium imbalance, depression, and bacterial/viral/parasitic infections. Although several drugs of similar classes or with similar mechanisms of action (e.g. doxorubicin and epirubicin, fluoxetine and duloxetine, benidipine and amlodipine) clustered together in terms of PDX drug response profiles, most drugs of similar classes or mechanisms were part of distinct clusters. Analysis of previous RNA-sequencing data [141] revealed that about half of the genes encoding human targets of the 176 drugs are highly expressed across TNBC PDXs (**Fig. 3.1b**). Among the highly expressed genes in TNBC PDXs were CDK4, proteasome subunit beta 5 (PSMB5), EGFR, BIRC5 (survivin), and VDR, which encode the targets of abemaciclib (LY2835219), carfilzomib/bortezomib/ixazomib, afatinib, YM155, and calcitriol, respectively. Conversely, many of the drug target genes were differentially expressed to some extent between the TNBC PDXs (**Appendix B**), which may provide insight into their differential responses to certain drugs. For example, many of these genes were differentially expressed between WHIM2 and WHIM30, which we previously showed were differentially responsive to chemotherapeutics [149]. Most notably, ABCG2 and PTGS2 (prostaglandin endoperoxide synthase 2), which respectively encode a multidrug efflux transporter and a pro-inflammatory enzyme that has been associated with breast cancer brain and lung metastasis [52, 53], were more highly expressed in WHIM2 than in WHIM30.

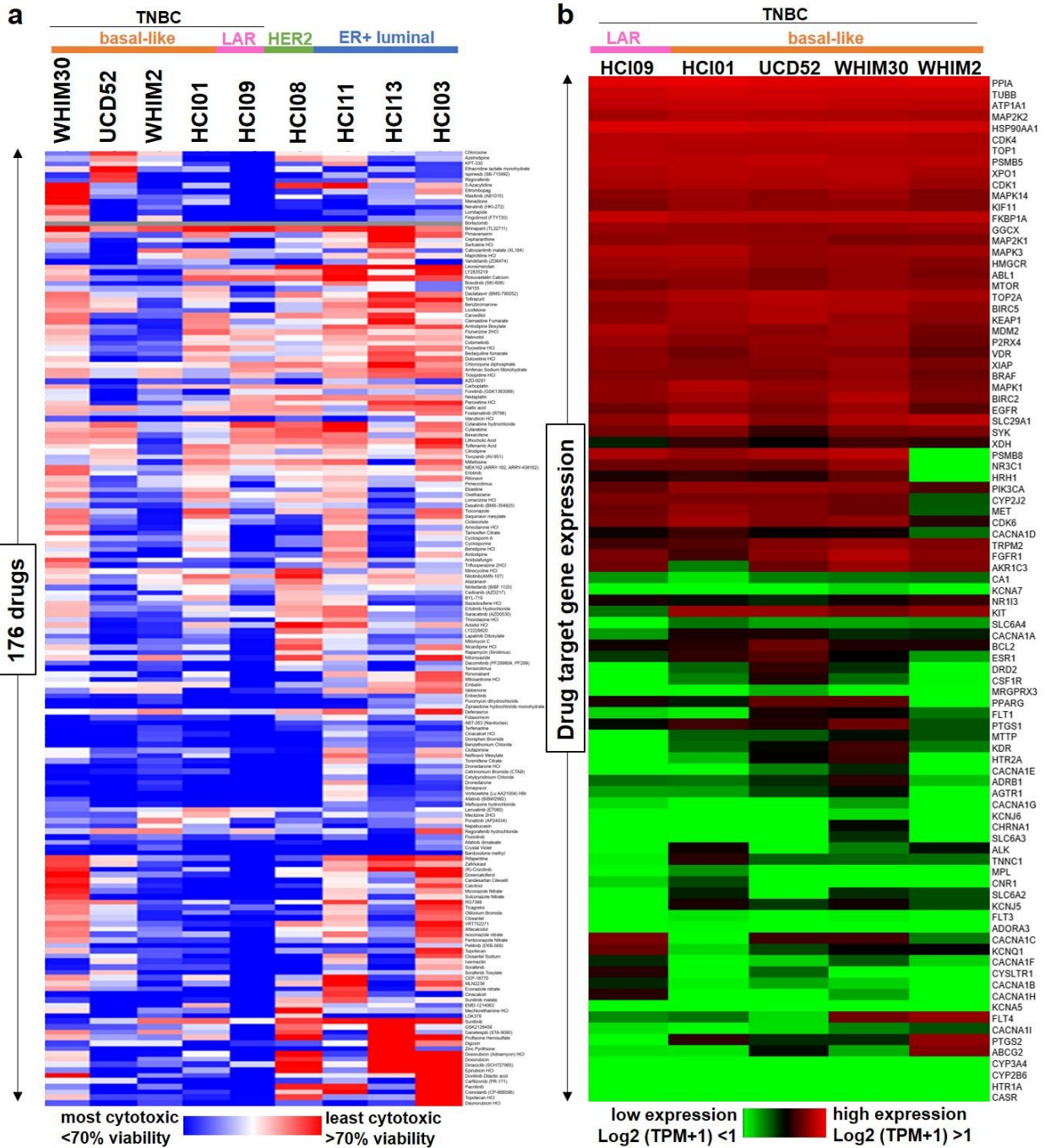


Figure 3.1: Selection of targeted drug candidates in TNBC PDXs based on a 1,363-drug screen. **(a)** Heatmap showing relative response to 176 drugs across PDXs of varying subtypes, selected based on efficacy in basal-like TNBC PDXs (HCl01, UCD52, WHIM2, WHIM30) on initial screening of 1,363 drugs at 10 μ M. Hierarchical clustered cell viability data (average percent of vehicle) are represented in the heatmap for comparison of drug response across PDXs (n=2 per PDX). The 1,363-drug screening data are provided in Appendix A, with the 176 selected drugs bolded. **(b)** Heatmap showing relative expression of target genes of the 176 selected drugs across TNBC PDXs. Clustered log₂ (TPM+1) values from PDX RNA-sequencing data (averaged for each PDX) are represented in the heatmap for analysis of target gene expression levels across PDXs. Comparisons of gene expression between the PDXs are provided in Appendix B. Reprinted from [190]

3.4.2 *Carfilzomib and afatinib have supra-additive trends when combined with other select targeted agents*

Although proteasome and EGFR inhibitors have demonstrated preclinical efficacy in TNBC, it is likely that synergistic combinations with other targeted agents are necessary to achieve efficacy that is sufficient for clinical success [200–206]. We therefore tested carfilzomib and afatinib in combination with each of the 176 selected drugs, at a 10-fold lower dose (1 μ M) relative to prior screening assays, in four basal-like PDXs (HCI01, UCD52, WHIM2, WHIM30) (**Appendices C,D**). Drug combination effects were assessed by calculating the difference in percent inhibition (efficacy) between each combination and each drug alone, with positive values indicating supra-additivity (efficacy of combination > sum of efficacies of each drug alone), zero indicating additivity (efficacy of combination = sum of efficacies of each drug alone), and negative values indicating sub-additivity (efficacy of combination < sum of efficacies of each drug alone). There was considerable heterogeneity in drug combination effects between the PDXs (**Fig. 3.2**), which is reflective of the heterogeneity in drug response seen in patients with the same tumor subtypes in the clinic. Given our goal of identifying treatments that have the potential to provide maximal clinical benefit for TNBC patients, we chose to focus on drugs that were effective across multiple PDX models of basal-like TNBC. Several drugs were found to have additive or supra-additive trends in at least two of the four basal-like PDXs when combined with carfilzomib (including benidipine, bexarotene, carvedilol, isoconazole, embelin, dronedarone, and abemaciclib) (**Fig. 3.2a**) or afatinib (including benidipine, bexarotene, carvedilol, isoconazole, fluoxetine, amiodarone, candesartan, and dovitinib) (**Fig. 3.2b**), providing several drugs/drug classes of interest for further studies. When mean differences in percent inhibition were analyzed across all four PDXs (relative to a difference in percent inhibition of zero), only isoconazole and meclizine were significantly supra-additive when combined with carfilzomib and only

bexarotene was significantly supra-additive when combined with afatinib; all other drugs were either significantly sub-additive or not significant in either direction (**Appendices E,F**).

3.4.3 *Carfilzomib, afatinib, and YM155 are cytotoxic to TNBC PDX cells*

Given that the prior combination studies consisted of a single dose of each drug, this posed a significant limitation in that it was not possible to assess additive or supra-additive trends in combination with drugs that were highly cytotoxic as single agents at 1 μ M, such as YM155 (**Appendices C,D**). Therefore, several drugs/classes of drugs were selected for dose response testing to assess both potency and efficacy across the four basal-like PDX lines: carfilzomib, bortezomib, and ixazomib (proteasome inhibitors) (**Fig. 3.3a**); YM155 (survivin inhibitor), navitoclax and ABT-199 (B-cell lymphoma 2 (BCL2) inhibitors), embelin (X-linked inhibitor of apoptosis (XIAP) inhibitor), and birinapant (inhibitor of apoptosis (IAP) inhibitor/second mitochondria-derived activator of caspases (SMAC) mimetic), all of which promote apoptosis (**Fig. 3.3b**); afatinib (EGFR inhibitor), abemaciclib (CDK4/6 inhibitor), fluoxetine (SSRI), calcitriol (synthetic vitamin D3), and dronedarone (ion channel blocker) (**Fig. 3.3c**). All p-values are listed in **Table 3.1**. Proteasome inhibitors were significantly effective across the PDXs in the micromolar range; it should be noted that certain doses of ixazomib and/or bortezomib appeared to cause an increase in cell viability in HCl01 and WHIM2 at lower doses, followed by a decrease in viability with higher doses, which we believe to be due to proteasome inhibitor activity at CMV promoters causing an increase in expression of luciferase, as seen with HDAC inhibitors in the 1,363-drug screen. The survivin inhibitor YM155 was the most potent drug tested and was significantly effective across all four PDXs in the nanomolar range. Carfilzomib, YM155, and afatinib were selected for subsequent multiple-dose combination studies, given their efficacy across basal-like TNBC PDXs and the high expression of their drug targets in these tumor cells (**Fig. 3.1b**).

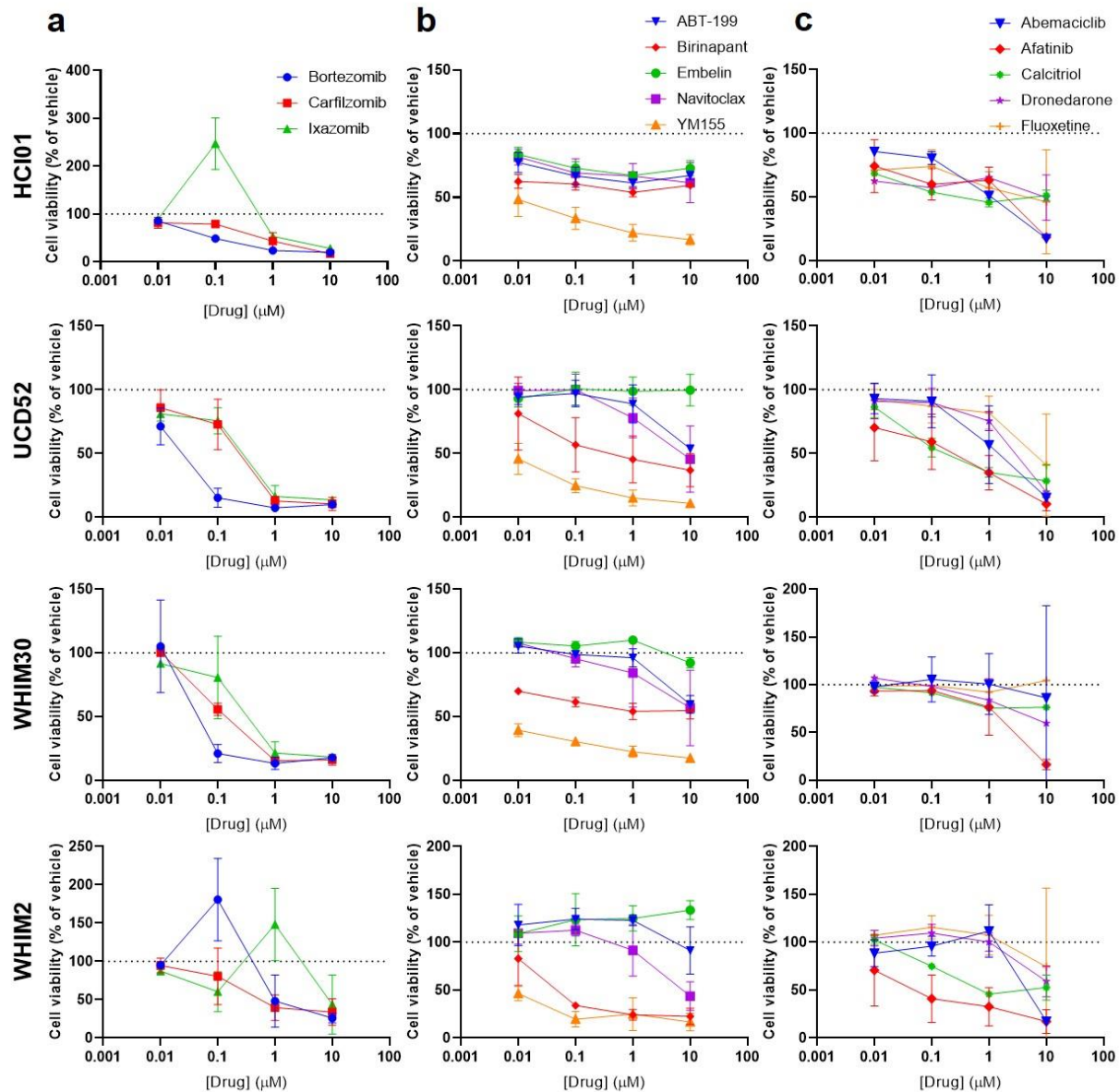


Figure 3.3: Dose responses of basal-like TNBC PDXs to selected classes of targeted therapeutics. Graphs depict cell viability (percent of vehicle) in response to increasing concentrations of the indicated drugs for each of four basal-like PDX lines (HCl01, UCD52, WHIM30, WHIM2): **(a)** proteasome inhibitors (carfilzomib, bortezomib, ixazomib); **(b)** drugs targeting apoptosis pathways (YM155, navitoclax, ABT-199, embelin, birinapant); and **(c)** EGFR inhibitor (afatinib), CDK4/6 inhibitor (abemaciclib), SSRI (fluoxetine), synthetic vitamin D3 (calcitriol), antiarrhythmic (dronedaron). Experiments were performed in triplicate. Error bars represent standard deviation between independent experiments. p-values are listed in Table 3.1. Reprinted from [190]

Table 3.1: P-values for *in vitro* dose response experiments shown in Figure 3.3. *t*-tests were performed to compare each drug treatment condition with vehicle controls for each PDX line. Significant values ($p < 0.05$) are bolded and italicized. Adapted from [190]

HCI01	N^a	0.01μM	0.1μM	1μM	10μM
Bortezomib	2	0.063381	<i>0.005474</i>	<i>0.000043</i>	<i>0.000092</i>
Carfilzomib	3	<i>0.04963</i>	<i>0.007833</i>	<i>0.005388</i>	<i><0.000001</i>
Ixazomib	2	0.110962	0.06093	<i>0.001144</i>	<i>0.001801</i>
ABT-199	3	<i>0.007255</i>	<i>0.001172</i>	<i>0.00003</i>	<i>0.000083</i>
Birinapant	3	<i>0.000288</i>	<i>0.00015</i>	<i>0.000021</i>	<i>0.000003</i>
Embelin	3	<i>0.007419</i>	<i>0.000892</i>	<i>0.000018</i>	<i>0.001437</i>
Navitoclax	4	<i>0.001159</i>	<i>0.001534</i>	<i>0.000527</i>	<i>0.002758</i>
YM155	4	<i>0.000238</i>	<i>0.000005</i>	<i><0.000001</i>	<i><0.000001</i>
Abemaciclib	2	<i>0.014298</i>	<i>0.03196</i>	<i>0.000116</i>	<i>0.000001</i>
Afatinib	2	0.221783	<i>0.044243</i>	<i>0.036208</i>	N/A
Calcitriol	2	<i>0.000008</i>	<i>0.000193</i>	<i>0.002056</i>	<i>0.003609</i>
Dronedarone	2	<i>0.000991</i>	<i>0.002264</i>	<i>0.000811</i>	0.057112
Fluoxetine	2	<i>0.000008</i>	0.104927	<i>0.041811</i>	0.20296
UCD52	N^a	0.01μM	0.1μM	1μM	10μM
Bortezomib	3	<i>0.026413</i>	<i>0.000039</i>	<i><0.000001</i>	<i><0.000001</i>
Carfilzomib	4	0.091647	<i>0.032814</i>	<i><0.000001</i>	<i><0.000001</i>
Ixazomib	3	<i>0.004423</i>	<i>0.014659</i>	<i>0.000068</i>	<i><0.000001</i>
ABT-199	3	0.183095	0.652814	0.268487	<i>0.000003</i>
Birinapant	3	0.319556	<i>0.024892</i>	<i>0.006759</i>	<i>0.001068</i>
Embelin	3	0.156021	0.937212	0.868763	0.962227
Navitoclax	4	0.830949	0.996264	<i>0.029684</i>	<i>0.005872</i>
YM155	4	<i>0.000112</i>	<i><0.000001</i>	<i><0.000001</i>	<i><0.000001</i>
Abemaciclib	4	0.29377	0.41761	<i>0.030087</i>	<i><0.000001</i>
Afatinib	4	0.062199	<i>0.009366</i>	<i>0.000071</i>	<i><0.000001</i>
Calcitriol	3	0.050349	<i>0.000418</i>	<i>0.000007</i>	<i>0.000643</i>
Dronedarone	3	0.317764	0.200828	<i>0.004828</i>	<i>0.000084</i>
Fluoxetine	3	0.16584	0.160174	0.073714	0.062933
WHIM30	N^a	0.01μM	0.1μM	1μM	10μM
Bortezomib	3	0.815718	<i>0.000042</i>	<i>0.000006</i>	<i><0.000001</i>
Carfilzomib	4	0.746654	<i>0.000106</i>	<i><0.000001</i>	<i>0.000004</i>
Ixazomib	3	<i>0.000619</i>	0.361073	<i>0.000107</i>	<i><0.000001</i>
ABT-199	2	0.301903	0.333421	0.534922	<i>0.014036</i>
Birinapant	2	<i>0.00193</i>	<i>0.004334</i>	<i>0.009629</i>	<i>0.011227</i>
Embelin	2	0.087373	0.168851	<i>0.031747</i>	0.114093
Navitoclax	2	<i>0.03891</i>	0.420622	0.490906	0.175765
YM155	2	<i>0.003486</i>	<i>0.000422</i>	<i>0.001594</i>	<i>0.000244</i>
Abemaciclib	2	0.686389	0.769689	0.97588	0.858871
Afatinib	2	0.208958	0.158912	0.378832	<i>0.001984</i>

Table continues on next page

Table 3.1, continued

Calcitriol	1	N/A	N/A	N/A	N/A
Dronedarone	1	N/A	N/A	N/A	N/A
Fluoxetine	1	N/A	N/A	N/A	N/A
WHIM2	N^a	0.01μM	0.1μM	1μM	10μM
Bortezomib	3	0.068183	0.059901	0.058861	0.000033
Carfilzomib	4	0.310044	0.333459	0.000359	0.000278
Ixazomib	3	0.000784	0.05822	0.15067	0.06533
ABT-199	2	0.355539	0.089689	0.028295	0.669916
Birinapant	2	0.482637	0.000351	0.002711	0.006058
Embelin	2	0.572152	0.347313	0.115227	0.040586
Navitoclax	3	0.231318	0.024578	0.617452	0.002852
YM155	3	0.000252	0.000069	0.001651	0.000426
Abemaciclib	4	0.153799	0.459897	0.422449	<0.000001
Afatinib	4	0.167517	0.003227	0.000542	0.000036
Calcitriol	2	0.529639	0.009585	0.002376	0.037265
Dronedarone	2	0.534513	0.280651	0.977216	0.070761
Fluoxetine	2	0.175073	0.214316	0.663944	0.702763

^a N indicates number of independent experiments for each drug tested.

3.4.4 Afatinib and YM155 are synergistically cytotoxic across TNBC PDXs

We next sought to identify synergistic combinations among drugs we have established as consistently effective with highly expressed drug targets in basal-like TNBC PDXs (carfilzomib, YM155, and afatinib), as well as carboplatin, a standard-of-care chemotherapeutic agent. HCl01, UCD52, and WHIM30 cells were treated with seven doses of each of these four drugs (WHIM2 cells with afatinib and YM155 only), and all possible two-drug combinations. Percent viability values were converted into fraction inhibition values (Fa). Drug doses were tailored for each PDX (**Table 3.2**) based on prior dose response data to achieve a consistent dose response for each drug across the PDXs, and, as established previously, the four drugs were significantly cytotoxic to these PDX cells, and YM155 was the most potent of the four drugs tested in the PDXs (**Fig. 3.4**); all p-values are listed in **Table 3.3**.

Table 3.2: Drug doses used for *in vitro* dose response experiments shown in Figure 3.4. Adapted from [190]

Carboplatin (μM)	Dose 1	Dose 2	Dose 3	Dose 4	Dose 5	Dose 6	Dose 7
HCI01	0.4	2	10	50	250	500	1000
UCD52	0.04	0.2	1	5	25	125	625
WHIM30	0.16	0.8	4	20	100	200	400
Carfilzomib (μM)	Dose 1	Dose 2	Dose 3	Dose 4	Dose 5	Dose 6	Dose 7
HCI01	0.004	0.02	0.1	0.5	2.5	12.5	62.5
UCD52	0.0016	0.008	0.04	0.2	1	5	25
WHIM30	0.0008	0.004	0.02	0.1	0.5	2.5	12.5
Afatinib (μM)	Dose 1	Dose 2	Dose 3	Dose 4	Dose 5	Dose 6	Dose 7
HCI01	0.004	0.02	0.1	0.5	2.5	12.5	62.5
UCD52	0.0004	0.002	0.01	0.05	0.25	1.25	6.25
WHIM30	0.04	0.2	1	5	10	20	40
WHIM2	0.0004	0.002	0.01	0.05	0.25	1.25	6.25
YM155 (μM)	Dose 1	Dose 2	Dose 3	Dose 4	Dose 5	Dose 6	Dose 7
HCI01	0.00008	0.0004	0.002	0.01	0.05	0.25	1.25
UCD52	0.00004	0.0002	0.001	0.005	0.025	0.125	0.625
WHIM30	0.00004	0.0002	0.001	0.005	0.025	0.125	0.625
WHIM2	0.00008	0.0004	0.002	0.01	0.05	0.25	1.25

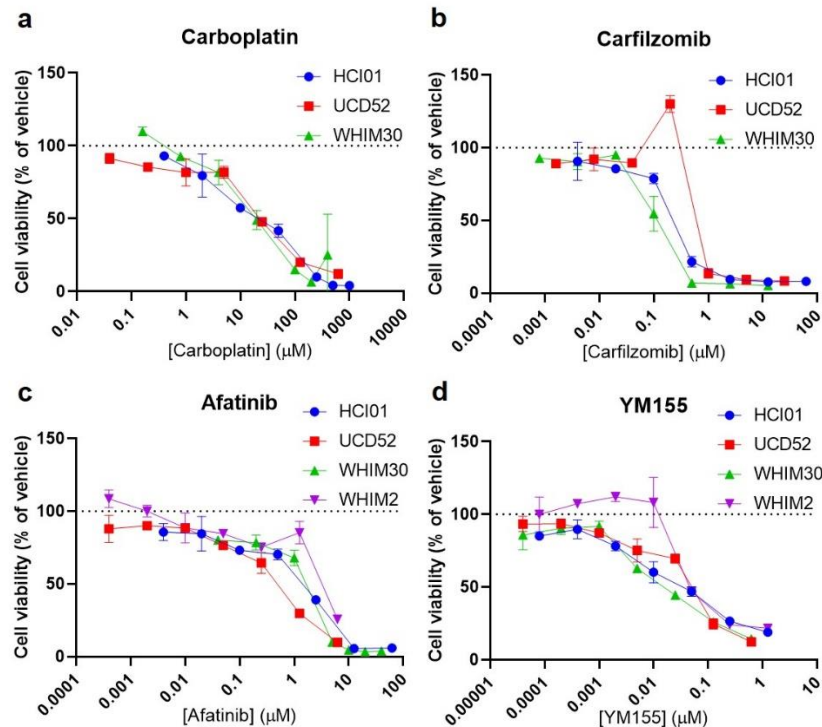


Figure 3.4: Dose responses of basal-like TNBC PDXs to four promising drug candidates. Graphs depict cell viability (percent of vehicle) in response to increasing concentrations of carboplatin (a), carfilzomib (b), afatinib (c), or YM155 (d) for each PDX line (HCI01, UCD52, WHIM30, WHIM2). Each experiment was performed in triplicate. Error bars represent standard deviation between independent experiments ($n=2$ for each PDX); drug doses are listed in Table 3.2, and p-values are listed in Table 3.3. Reprinted from [190]

Table 3.3: P-values for *in vitro* dose response experiments shown in Figure 3.4. *t*-tests were performed to compare each drug treatment condition with vehicle controls for each PDX line. Significant values ($p < 0.05$) are bolded and italicized. Adapted from [190]

Carboplatin	Dose 1	Dose 2	Dose 3	Dose 4	Dose 5	Dose 6	Dose 7
HCI01	<i>0.011969</i>	0.188374	<i>0.000454</i>	<i>0.003011</i>	<i>0.000032</i>	<i>0.000084</i>	<i>0.000222</i>
UCD52	0.073298	<i>0.018515</i>	0.108632	<i>0.024821</i>	<i>0.000717</i>	<i>0.000519</i>	<i>0.000599</i>
WHIM30	<i>0.046447</i>	<i>0.000012</i>	0.090614	<i>0.008275</i>	<i>0.000309</i>	<i><0.000001</i>	0.063431
Carfilzomib	Dose 1	Dose 2	Dose 3	Dose 4	Dose 5	Dose 6	Dose 7
HCI01	0.425251	<i>0.007535</i>	<i>0.013284</i>	<i>0.001064</i>	<i>0.000463</i>	<i>0.000027</i>	<i>0.000004</i>
UCD52	<i>0.000417</i>	0.291974	<i>0.023256</i>	<i>0.017735</i>	<i>0.000731</i>	<i>0.000625</i>	<i>0.000382</i>
WHIM30	<i>0.00319</i>	0.131364	<i>0.000132</i>	<i>0.0323</i>	<i>0.000143</i>	<i>0.000083</i>	<i><0.000001</i>
Afatinib	Dose 1	Dose 2	Dose 3	Dose 4	Dose 5	Dose 6	Dose 7
HCI01	0.076782	0.210436	<i>0.001735</i>	<i>0.007566</i>	<i>0.000711</i>	<i>0.000058</i>	<i>0.000073</i>
UCD52	0.210197	<i>0.007077</i>	<i>0.009177</i>	<i>0.002972</i>	<i>0.019954</i>	<i>0.000267</i>	<i>0.000522</i>
WHIM30	<i>0.00052</i>	<i>0.028389</i>	<i>0.013618</i>	<i>0.000322</i>	<i>0.000013</i>	<i>0.000003</i>	<i>0.000002</i>
WHIM2	0.187042	0.99756	0.257375	<i>0.012296</i>	<i>0.001094</i>	0.115623	<i>0.000009</i>
YM155	Dose 1	Dose 2	Dose 3	Dose 4	Dose 5	Dose 6	Dose 7
HCI01	<i>0.000167</i>	0.154071	<i>0.011395</i>	<i>0.016656</i>	<i>0.00195</i>	<i>0.000156</i>	<i>0.000009</i>
UCD52	0.217038	0.099011	<i>0.009378</i>	<i>0.047491</i>	<i>0.005413</i>	<i>0.001095</i>	<i>0.000506</i>
WHIM30	0.18806	0.088101	0.08598	<i>0.000325</i>	<i>0.000149</i>	<i>0.000179</i>	<i>0.000579</i>
WHIM2	0.994948	<i>0.00007</i>	<i>0.032879</i>	0.572891	<i>0.001695</i>	<i>0.000122</i>	<i>0.000029</i>

To identify synergistic drug combinations, data were analyzed using CompuSyn [192–194] to determine CI and DRI values for each drug combination tested at a constant dose ratio. CI values indicate the effect of combining multiple drugs (synergistic, additive, or antagonistic); DRI values represent the fold decrease in the dose of a drug needed when in a combination to achieve the same efficacy (F_a) as the drug alone. Using this approach, drug combinations with CI values < 1 are synergistic, and DRI values > 1 are favorable given the concern for toxicity when combining multiple drugs. When assessing drug combinations for cancer treatment, these criteria are most important if met at high effect (F_a) levels, when the drug combinations are killing most of the tumor cells, as this is the goal of cancer therapy. We therefore considered any drug combination with $CI < 1$ and $DRI > 1$ (for both drugs in the combination) at $F_a > 0.75$ to be a promising combination. Based on CI values: carboplatin was synergistic with carfilzomib, afatinib, and YM155 in UCD52 and WHIM30;

carfilzomib was synergistic with afatinib in WHIM30 and with YM155 in UCD52; and afatinib was synergistic with YM155 in HCl01, UCD52, WHIM30, and WHIM2 (**Fig. 3.5**). DRI values were favorable for carboplatin when combined with carfilzomib, afatinib, or YM155 in UCD52 and WHIM30; for carfilzomib when combined with carboplatin, afatinib, or YM155 in HCl01, UCD52, and WHIM30; for afatinib when combined with carboplatin, carfilzomib, or YM155 in HCl01, UCD52, and WHIM30, and with YM155 in WHIM2; and for YM155 when combined with carboplatin, carfilzomib, or afatinib in HCl01, UCD52, and WHIM30, and with afatinib in WHIM2 (**Fig. 3.6**). Collectively, these data indicate that the combination of afatinib and YM155 is synergistic, with favorable dose reductions, across all four basal-like PDX lines tested. Afatinib and YM155 were also found to be effective as single agents (**Fig. 3.7a,b**) and synergistic (**Fig. 3.7c**) with favorable dose reductions (**Fig. 3.7d,e**) in three basal-like TNBC cell lines (MDA468, HCC1143, HCC1937), further confirming the efficacy and synergism of afatinib and YM155 in basal-like TNBC. All p-values for data shown in **Fig. 3.7a,b** are listed in **Table 3.4**.

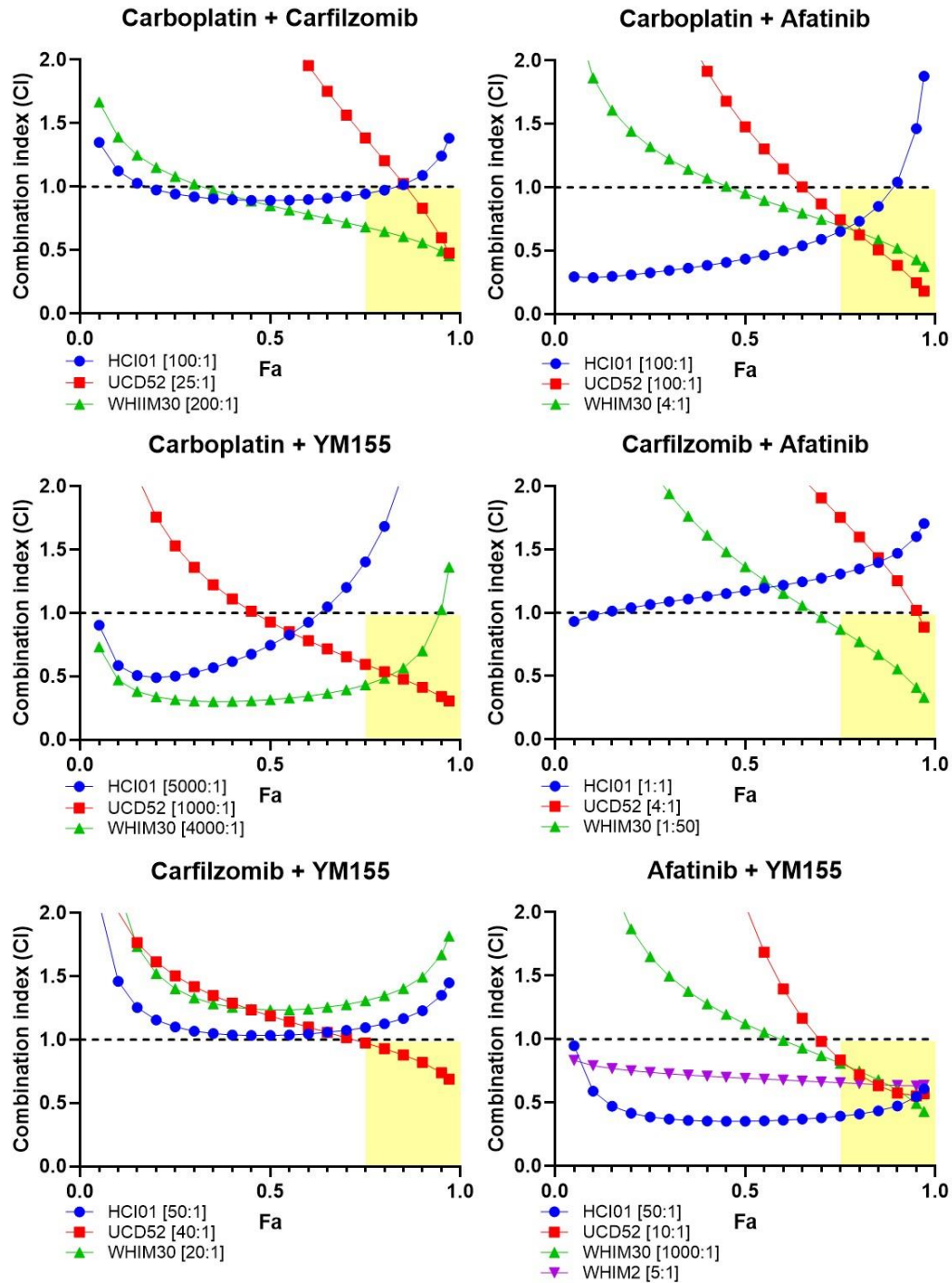


Figure 3.5: Drug combination analysis reveals synergism between afatinib and YM155 across four basal-like TNBC PDXs. PDX cells were treated with four drugs (carboplatin, carfilzomib, afatinib, and YM155), seven doses each, alone and in all possible two-drug combinations. Combination index (CI) values were generated using CompuSyn software, and Fa-CI plots were generated using constant dose ratio combination data for each of the six drug combinations in each of the PDXs. CI<1 indicates synergism; CI=1 indicates additivity; CI>1 indicates antagonism. The regions highlighted in yellow are synergistic (CI<1) at optimal effect levels (Fa>0.75). Dose ratios (Drug1:Drug2) for each drug combination and PDX are indicated in the legend of each graph. Reprinted from [190]

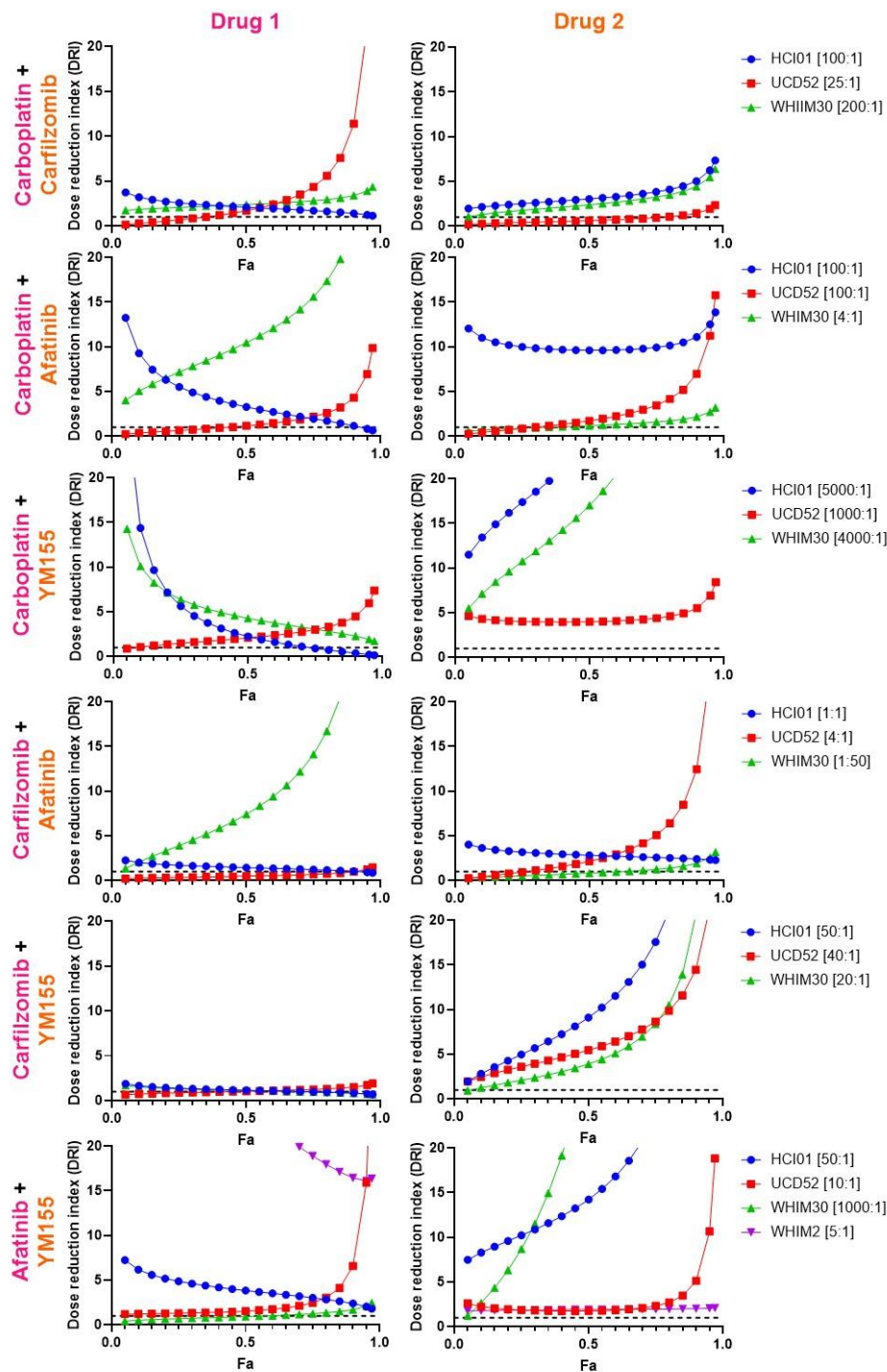


Figure 3.6: Drug combination analysis reveals favorable dose reduction of several drugs when combined with other agents in basal-like TNBC PDXs. PDX cells were treated with four drugs (carboplatin, carfilzomib, afatinib, and YM155), seven doses each, alone and in all possible two-drug combinations. Dose reduction index (DRI) values were generated using CompuSyn software, and Fa-DRI plots were generated using constant dose ratio combination data for each of the six drug combinations in each of the PDXs. DRI indicates the fold decrease in drug dose needed to achieve a given effect when in combination with another drug vs. as a single agent. $DRI > 1$ indicates favorable dose reduction; $DRI < 1$ indicates unfavorable dose reduction. Dose ratios (Drug1:Drug2) for each drug combination and PDX are indicated in the legend of each graph. Reprinted from [190]

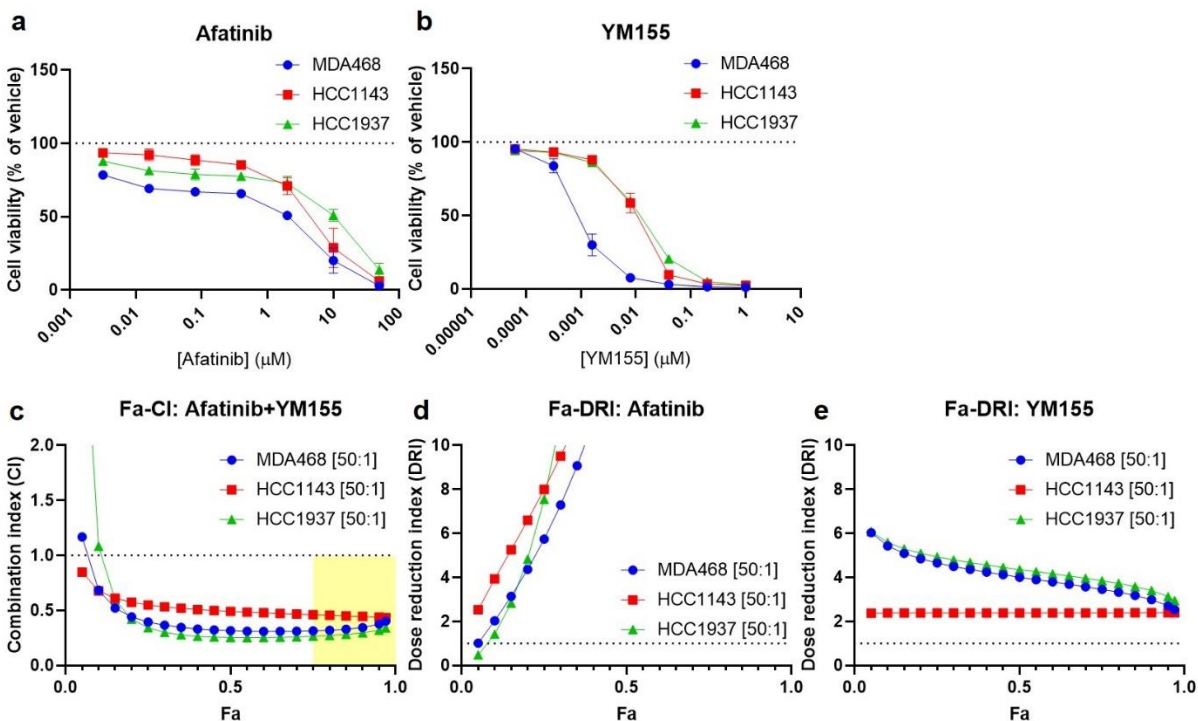


Figure 3.7: Afatinib and YM155 are synergistically cytotoxic to three basal-like TNBC cell lines. MDA468, HCC1143, and HCC1937 cells were treated in triplicate for 72h *in vitro* with seven doses of afatinib or YM155, as well as all possible dose combinations of the two drugs. Graphs depict cell viability (percent of vehicle) of each of the three cell lines in response to afatinib (a) or YM155 (b). Two independent experiments were performed for each cell line; error bars represent standard deviation; p-values are listed in Table 3.4. Data were analyzed using CompuSyn software, and constant dose ratio combination data were used to generate a Fa-CI plot (c) and Fa-DRI plots for both afatinib (d) and YM155 (e). Dose ratios (Drug1:Drug2) for each cell line are indicated in the graph legends. CI<1 indicates synergism; CI=1 indicates additivity; CI>1 indicates antagonism. The region highlighted in yellow is synergistic (CI<1) at optimal effect levels (Fa>0.75). DRI indicates the fold decrease in drug dose needed to achieve a given effect when in combination with another drug vs. as a single agent. DRI>1 indicates favorable dose reduction; DRI<1 indicates unfavorable dose reduction. Reprinted from [190]

Table 3.4: P-values for *in vitro* dose response experiments shown in Figure 3.7a,b. *t*-tests were performed to compare each drug treatment condition with vehicle controls for each cell line. Significant values ($p<0.05$) are bolded and italicized. Adapted from [190]

Afatinib	0.0032 μ M	0.016 μ M	0.08 μ M	0.4 μ M	2 μ M	10 μ M	50 μ M
MDA468	<i>0.005145</i>	<i>0.00005</i>	<i>0.000268</i>	<i>0.000776</i>	<i>0.000685</i>	<i>0.005603</i>	<i>0.000036</i>
HCC1143	<i>0.003195</i>	0.107024	<i>0.048012</i>	<i>0.004614</i>	<i>0.018885</i>	<i>0.016815</i>	<i>0.000443</i>
HCC1937	<i>0.028664</i>	<i>0.007818</i>	<i>0.015839</i>	<i>0.000845</i>	<i>0.014367</i>	<i>0.003326</i>	<i>0.001422</i>
YM155	0.000064 μ M	0.00032 μ M	0.0016 μ M	0.008 μ M	0.04 μ M	0.2 μ M	1 μ M
MDA468	<i>0.046448</i>	<i>0.041252</i>	<i>0.005506</i>	<i>0.000008</i>	<i><0.000001</i>	<i><0.000001</i>	<i><0.000001</i>
HCC1143	<i>0.002632</i>	<i>0.008782</i>	<i>0.026343</i>	<i>0.012459</i>	<i>0.000029</i>	<i>0.000006</i>	<i><0.000001</i>
HCC1937	<i>0.015797</i>	<i>0.003415</i>	<i>0.0013</i>	<i>0.001102</i>	<i>0.000002</i>	<i>0.000008</i>	<i><0.000001</i>

3.4.5 Afatinib and YM155 reduce PDX mammary tumor growth *in vivo*

To validate the efficacy of afatinib and YM155 *in vivo*, mice bearing HCI01 PDX mammary tumors were either untreated or treated with afatinib alone, YM155 alone, or afatinib+YM155. Both afatinib and YM155 as single agents, as well as afatinib and YM155 combined, significantly reduced mammary tumor growth over time compared to the control group (**Fig. 3.8a**). YM155 was significantly more effective as a single agent in reducing tumor growth compared to afatinib as a single agent, and the combination of afatinib+YM155 was significantly more effective than afatinib alone; there was no significant difference in tumor growth between YM155 alone and afatinib+YM155 treated groups (**Fig. 3.8a**). All p-values are listed in **Table 3.5**. Importantly, mice did not display any signs of drug toxicity throughout or following the treatment period, and no considerable changes in mouse weight were observed in treated mice compared to control mice (**Fig. 3.8b**). Once tumors in control mice reached near protocol-defined burden, all mice were euthanized, and mammary tumors were removed. Mammary tumor weights were not significantly different between afatinib-treated and untreated mice, however tumor weights were significantly reduced in mice treated with YM155 as a single agent and combined with afatinib compared to control mice (**Fig. 3.8c**). All p-values are listed in **Table 3.5**. Grossly, afatinib-treated tumors appeared slightly smaller, and YM155- and afatinib+YM155- treated tumors appeared considerably smaller, than control tumors (**Fig. 3.8d**).

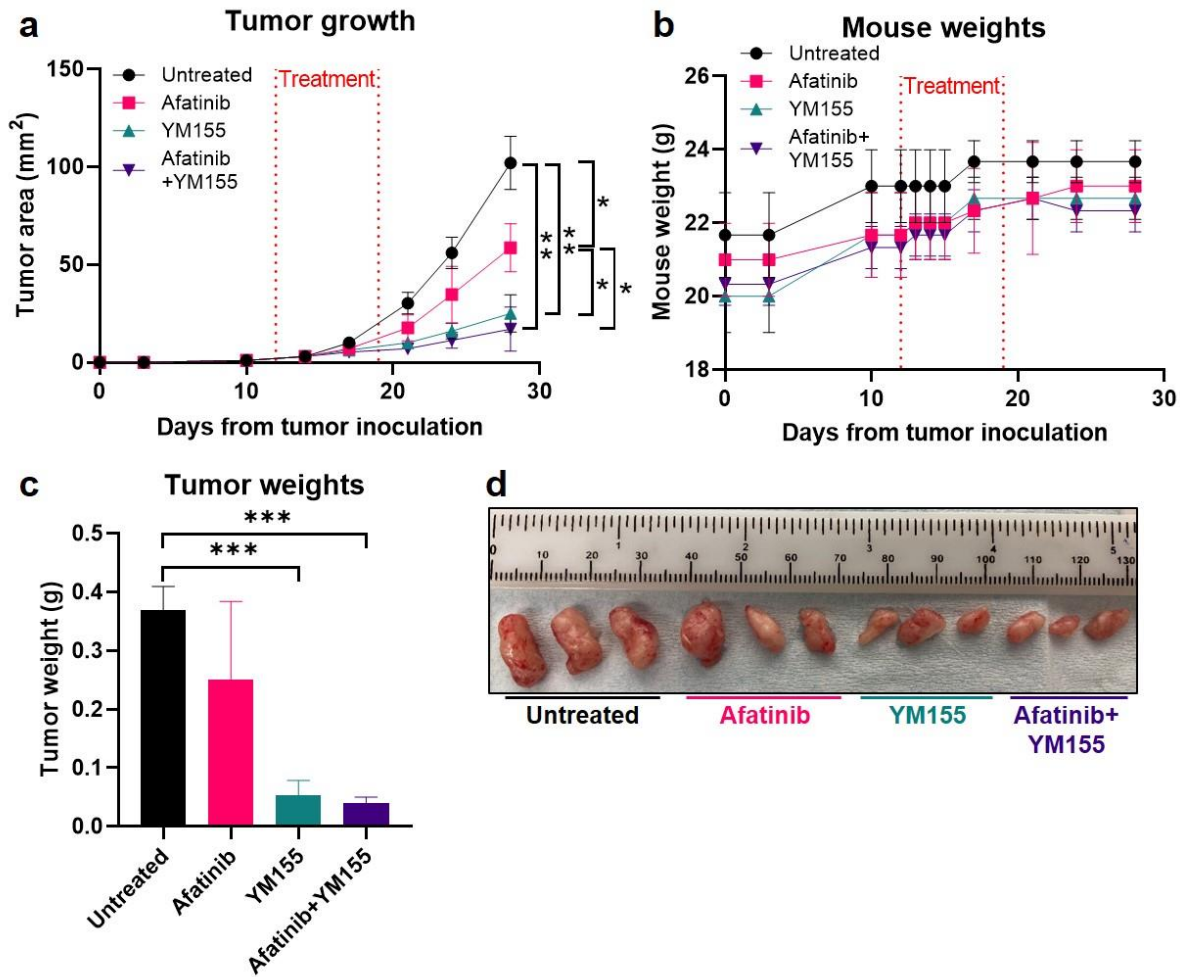


Figure 3.8: Afatinib and YM155 reduce PDX mammary tumor growth in vivo. HC101 PDX cells were injected into the mammary fat pads of NSG mice. After 12 days of tumor growth, mice were divided into four groups (n=3 mice per group): untreated, afatinib (25 mg/kg, daily oral gavage for 7 days), YM155 (5 mg/kg, 7-day continuous subcutaneous infusion via Alzet pump), and afatinib + YM155 (same doses and routes of administration as monotherapy groups). **(a)** Tumor area (length x width) over time for each treatment group, monitored via caliper measurements. The treatment period is indicated by red dotted lines. Error bars represent standard deviation. Significance is shown only for endpoint measurements (*p<0.05, **p<0.01); p-values for all timepoints are listed in Table 3.5. **(b)** Mouse weights over time for each treatment group. The treatment period is indicated by red dotted lines. **(c)** Tumor weights for each treatment group, obtained after tumor removal at the study endpoint; ***p<0.001; p-values are listed in Table 3.5. **(d)** Photographs of mammary tumors for each treatment group at the study endpoint; ruler scale is mm. Reprinted from [190]

Table 3.5: P-values for *in vivo* drug treatment experiments shown in Figure 3.8a,c. *t*-tests were performed to compare all treatment conditions at each timepoint for tumor growth and at the study endpoint for tumor weights. Significant values ($p < 0.05$) are bolded and italicized. Adapted from [190]

Treatment group comparison	Tumor growth					Tumor weights
	Day 14	Day 17	Day 21	Day 24	Day 28	Endpoint
Untreated vs. Afatinib	>0.999999	0.101192	0.06405	0.089521	<i>0.015093</i>	0.212763
Untreated vs. YM155	>0.999999	0.106166	<i>0.003654</i>	<i>0.001496</i>	<i>0.001343</i>	<i>0.000315</i>
Untreated vs. Afatinib+YM155	>0.999999	<i>0.017797</i>	<i>0.002192</i>	<i>0.000991</i>	<i>0.001174</i>	<i>0.000157</i>
Afatinib vs. YM155	>0.999999	0.724659	0.125798	0.098082	<i>0.01975</i>	0.067574
Afatinib vs. Afatinib+YM155	>0.999999	0.237796	0.054921	0.054978	<i>0.012391</i>	0.054311
YM155 vs. Afatinib+YM155	>0.999999	0.565533	0.101192	0.228229	0.403088	0.441823

3.4.6 YM155 reduces EGFR expression in basal-like TNBC PDX cells

To preliminarily explore potential crosstalk between the pathways targeted by afatinib and YM155, we performed Western blots to assess the effects of YM155 treatment on EGFR expression in the HCl01 PDX line. Interestingly, we found that YM155 treatment (at 10 nM) resulted in reduced EGFR protein expression in HCl01 cells compared to vehicle controls (**Fig. 3.9a,b**), indicating that YM155 has activity against the molecular target of afatinib in these basal-like TNBC cells.

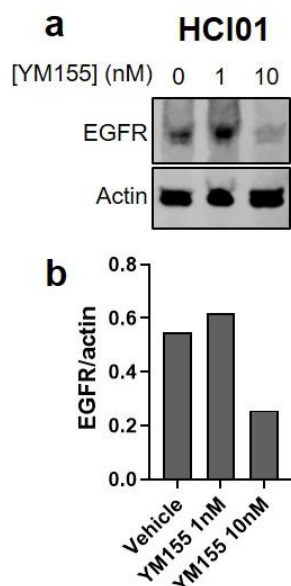


Figure 3.9: YM155 reduces EGFR expression in basal-like TNBC PDX cells. **(a)** Western blot showing EGFR expression in HCl01 cells treated with vehicle (DMSO) or YM155 (1 or 10 nM); actin was used as a loading control (100 μ g per sample). Images are cropped blots showing proteins from different parts of the same gel. **(b)** Densitometry graph showing EGFR normalized to actin for each treatment condition. Samples were run on the same gel, and loading controls were run on the same blot. Reprinted from [190]

3.4.7 *EGFR and BIRC5 are highly expressed in basal-like PDXs, cell lines, and patient tumors*

EGFR and BIRC5 (survivin) mRNA expression levels were assessed based on breast cancer intrinsic subtype using our PDX RNA-sequencing data, as well as RNA-sequencing data from two different breast cancer cell line gene expression databases: the HMS LINCS Breast Cancer Profiling Project (<http://lincs.hms.harvard.edu/db/datasets/20348/>) and the Broad Institute CCLE (<https://portals.broadinstitute.org/ccle>). These analyses found that EGFR is most highly expressed in the basal-like subtype compared to the other subtypes in PDXs and cell lines (**Fig. 3.10a**), while BIRC5 expression is consistently high across all of the intrinsic subtypes in PDXs and cell lines (**Fig. 3.10b**). Analyses using an 855-patient breast cancer gene expression dataset [18, 53, 195] identified that both EGFR and BIRC5 have significantly higher expression levels in basal-like patient tumors compared to those of other subtypes (**Fig. 3.10c,d**).

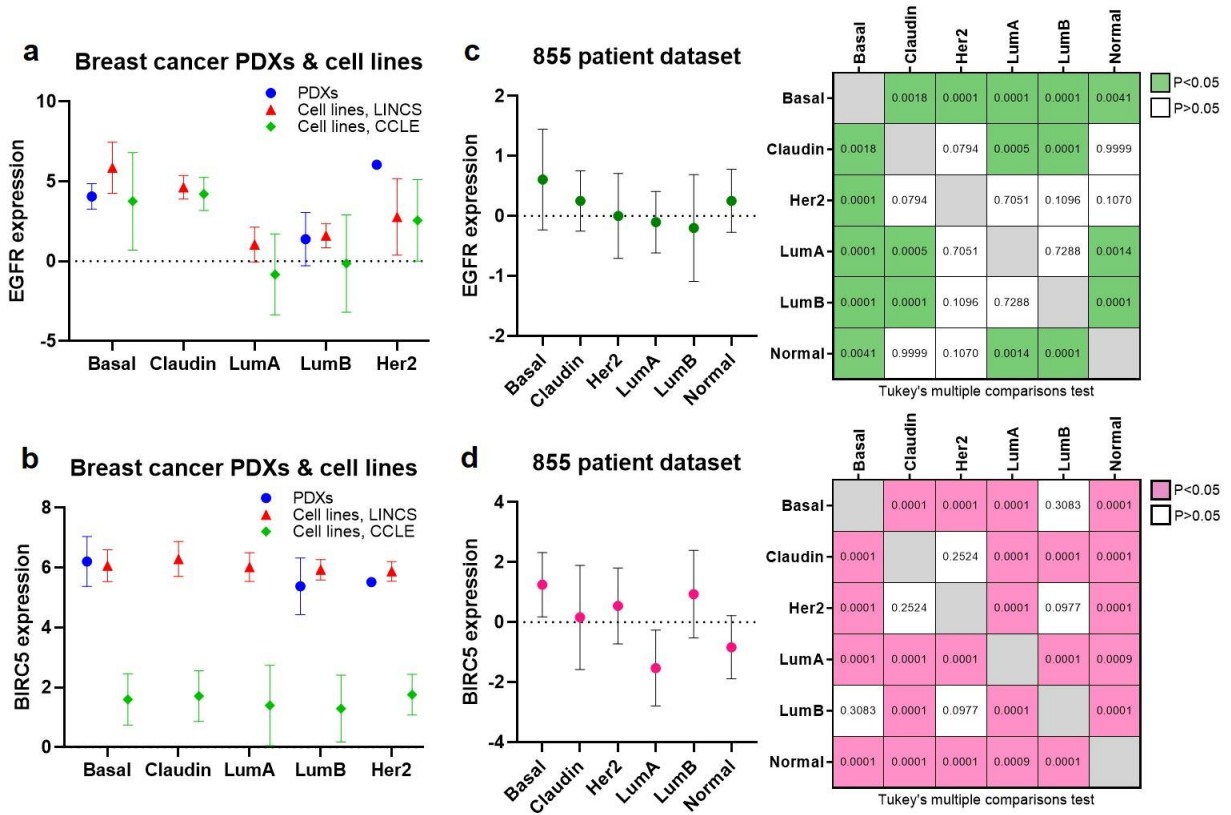


Figure 3.10: EGFR and BIRC5 are highly expressed in basal-like PDXs, cell lines, and patient tumors. RNA-sequencing data from breast cancer PDXs (log₂ TPM+1) and cell lines (LINCS and CCLE databases, RPKM and log₂ RPKM, respectively) were used to assess expression levels of EGFR (**a**) and BIRC5 (**b**) according to intrinsic subtype: basal-like (Basal), claudin-low (Claudin), luminal A (LumA), luminal B (LumB), HER2-enriched (Her2). Gene expression data from 855 breast cancer patients were used to assess expression levels of EGFR (**c**) and BIRC5 (**d**) in patients according to intrinsic subtype: basal-like (Basal), claudin-low (Claudin), luminal A (LumA), luminal B (LumB), HER2-enriched (Her2), normal-like (Normal). Tukey's multiple comparisons tests were used to analyze differences in expression levels of each gene between each subtype; tables in right panels depict p-values. PDX, cell line, and patient datasets were each grouped by breast cancer intrinsic subtype, and expression values for each gene were averaged; graphs depict the average (marker) and range (bars) of expression of EGFR or BIRC5 in each breast cancer subtype. Reprinted from [190]

Pearson correlation analysis was performed to assess the relationships between EGFR and BIRC5 expression and clinical characteristics of breast cancer patients using the 855-patient dataset. This revealed positive correlations of both EGFR and BIRC5 expression with basal-like triple-negative tumors, and negative correlations of both EGFR and BIRC5 expression with luminal ER/PR-positive tumors and differentiation score (**Fig. 3.11**). In addition, BIRC5 expression showed a strong positive correlation with proliferation score (**Fig. 3.11**).

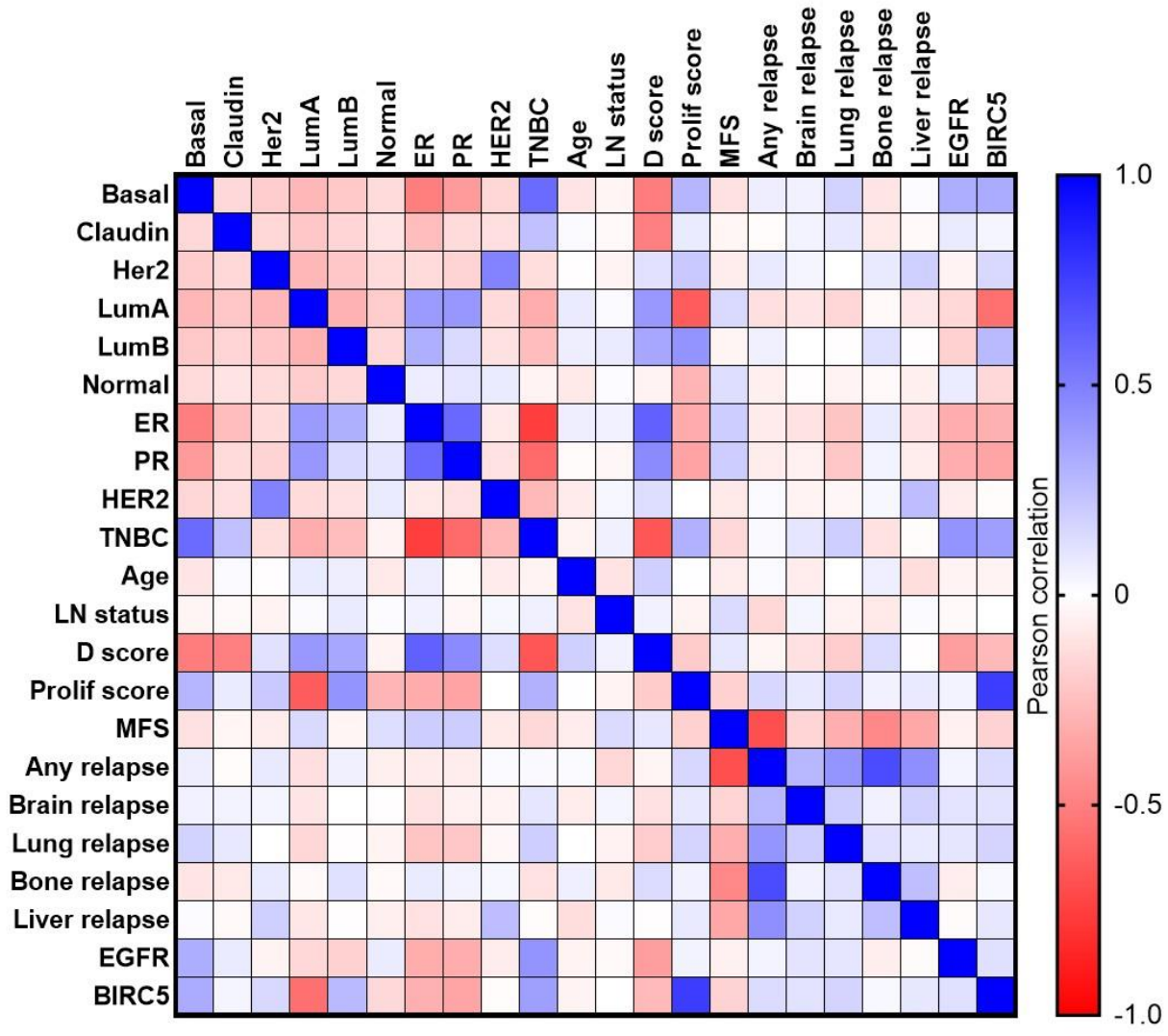


Figure 3.11: EGFR and BIRC5 expression correlate with clinical characteristics of patient tumors. Using an 855-patient dataset consisting of gene expression data as well as clinical information, Pearson correlations were performed to assess the relationships of EGFR and BIRC5 expression with clinical parameters. Intrinsic subtype: basal-like (Basal), claudin-low (Claudin), luminal A (LumA), luminal B (LumB), HER2-enriched (Her2), normal-like (Normal). Receptor status: estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), triple-negative breast cancer (TNBC). Other parameters: patient age, lymph node (LN) status, differentiation (D) score, proliferation (Prolif) score. Clinical outcomes: metastasis-free survival (MFS), relapse-free survival (any relapse, brain, liver, lung, bone). Heatmap depicts Pearson correlation values for each comparison of parameters: negative correlation (red), no correlation (white), positive correlation (blue). Reprinted from [190]

3.4.8 *EGFR and BIRC5 expression are negatively associated with patient outcomes*

The 855-patient dataset was used to determine the effect of EGFR and BIRC5 expression levels on clinical outcomes for patients with basal-like tumors (N=140) in terms of MFS time, as well as relapse-free survival pertaining to liver and lung metastases. Basal-like patients were divided into four groups based on EGFR/BIRC5 expression levels: EGFR^{high}BIRC5^{high}, EGFR^{high}BIRC5^{low}, EGFR^{low}BIRC5^{high}, EGFR^{low}BIRC5^{low}. Kaplan-Meier analyses revealed that patients with EGFR^{high}BIRC5^{high} tumors had significantly reduced liver relapse-free survival relative to those with EGFR^{low}BIRC5^{high} tumors (**Fig. 3.12a**) as well as significantly reduced lung relapse-free survival compared to those with EGFR^{high}BIRC5^{low}, EGFR^{low}BIRC5^{high}, and EGFR^{low}BIRC5^{low} tumors (**Fig. 3.12b**). Patients with EGFR^{high}BIRC5^{high} tumors also had significantly shorter MFS times compared to those with EGFR^{high}BIRC5^{low}, EGFR^{low}BIRC5^{high}, and EGFR^{low}BIRC5^{low} tumors (**Fig. 3.12c**). All p-values are listed in **Table 3.6**. Collectively, these results indicate that high tumor expression levels of both EGFR and BIRC5 are associated with more rapid development of liver and lung metastases in patients compared to tumors with low expression of one or both of these genes.

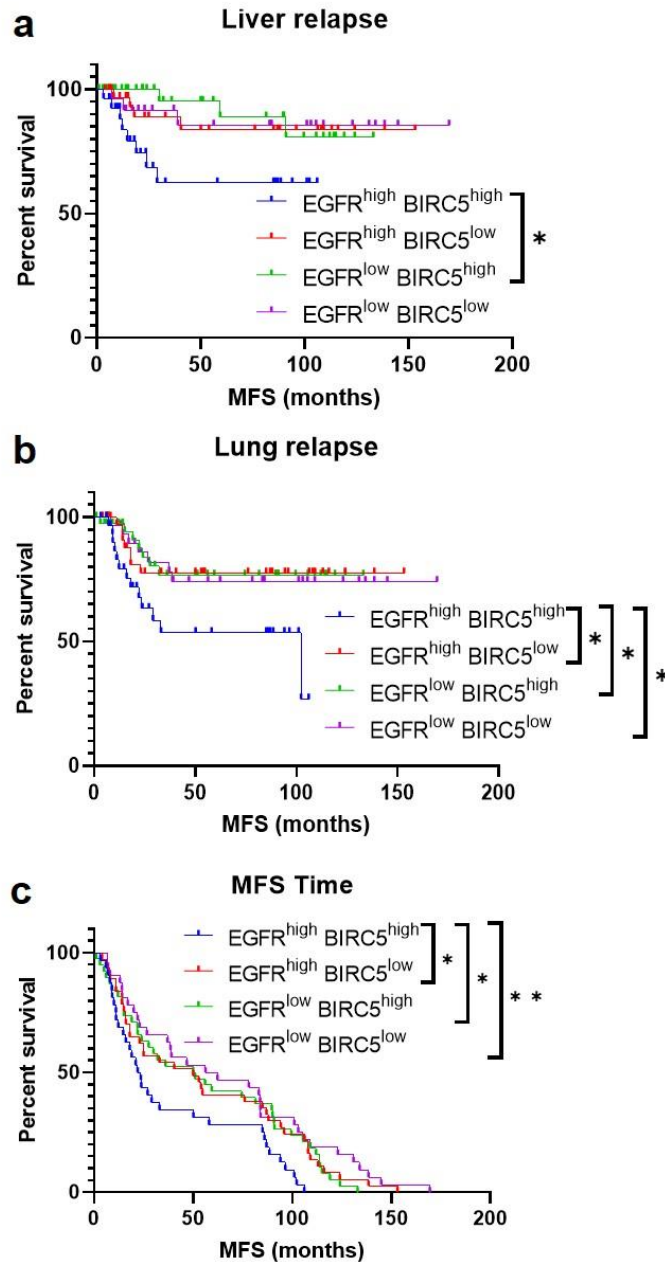


Figure 3.12: EGFR and BIRC5 expression are negatively associated with metastasis-free survival in patients with basal-like tumors. Using an 855-patient breast cancer dataset, patients with basal-like tumors (N=140) were divided into four groups based on expression levels of EGFR and BIRC5: EGFR^{high}BIRC5^{high}, EGFR^{high}BIRC5^{low}, EGFR^{low}BIRC5^{high}, EGFR^{low}BIRC5^{low}. Kaplan-Meier curves were generated to assess the effect of high versus low expression of the two genes on (a) liver relapse-free survival, (b) lung relapse-free survival, and (c) metastasis-free survival (MFS) time. Log-rank tests were performed to determine statistical significance (*p<0.05, **p<0.01); p-values are listed in Table 3.6. Reprinted from [190]

Table 3.6: P-values for Kaplan-Meier survival curves shown in Figure 3.12. Log-rank tests were performed between all basal-like patient groups (based on EGFR/BIRC5 expression levels) for relapse-free survival (liver and lung) and metastasis-free survival (MFS) time. Significant values ($p < 0.05$) are bolded and italicized. Adapted from [190]

Liver relapse			P-value
EGFR ^{high} /BIRC5 ^{high}	vs	EGFR ^{high} /BIRC5 ^{low}	0.0764
EGFR ^{high} /BIRC5 ^{high}	vs	EGFR ^{low} /BIRC5 ^{high}	<i>0.0153</i>
EGFR ^{high} /BIRC5 ^{high}	vs	EGFR ^{low} /BIRC5 ^{low}	0.0787
EGFR ^{high} /BIRC5 ^{low}	vs	EGFR ^{low} /BIRC5 ^{high}	0.627
EGFR ^{high} /BIRC5 ^{low}	vs	EGFR ^{low} /BIRC5 ^{low}	0.9262
EGFR ^{low} /BIRC5 ^{high}	vs	EGFR ^{low} /BIRC5 ^{low}	0.8038
Lung relapse			P-value
EGFR ^{high} /BIRC5 ^{high}	vs	EGFR ^{high} /BIRC5 ^{low}	<i>0.0284</i>
EGFR ^{high} /BIRC5 ^{high}	vs	EGFR ^{low} /BIRC5 ^{high}	<i>0.0204</i>
EGFR ^{high} /BIRC5 ^{high}	vs	EGFR ^{low} /BIRC5 ^{low}	<i>0.0337</i>
EGFR ^{high} /BIRC5 ^{low}	vs	EGFR ^{low} /BIRC5 ^{high}	0.9187
EGFR ^{high} /BIRC5 ^{low}	vs	EGFR ^{low} /BIRC5 ^{low}	0.9291
EGFR ^{low} /BIRC5 ^{high}	vs	EGFR ^{low} /BIRC5 ^{low}	0.8673
MFS time			P-value
EGFR ^{high} /BIRC5 ^{high}	vs	EGFR ^{high} /BIRC5 ^{low}	<i>0.022</i>
EGFR ^{high} /BIRC5 ^{high}	vs	EGFR ^{low} /BIRC5 ^{high}	<i>0.0178</i>
EGFR ^{high} /BIRC5 ^{high}	vs	EGFR ^{low} /BIRC5 ^{low}	<i>0.009</i>
EGFR ^{high} /BIRC5 ^{low}	vs	EGFR ^{low} /BIRC5 ^{high}	0.8503
EGFR ^{high} /BIRC5 ^{low}	vs	EGFR ^{low} /BIRC5 ^{low}	0.42
EGFR ^{low} /BIRC5 ^{high}	vs	EGFR ^{low} /BIRC5 ^{low}	0.213

3.5 Discussion and conclusions

Despite decades of translational research, no reliable targeted therapeutics have yet been FDA-approved for the treatment of TNBC. Although several classes of targeted drugs have shown promise in preclinical studies, most of these drugs have failed in clinical trials, and it is likely that effective synergistic combination regimens are needed to successfully combat this disease [34]. One factor that certainly can contribute to the discrepancy in results between preclinical studies and clinical trials is the use of immortalized cell line models for preclinical drug response testing. Cell lines have been shown to undergo considerable changes while in

culture that can affect drug response, whereas three-dimensional PDX cultures have been shown to more faithfully maintain tumor cell morphology, gene expression, and drug response profiles [159–161]. Indeed, we have previously found that two of the breast cancer PDXs employed in the present studies maintain the gene expression profiles of their *in vivo* counterparts after seven days in cell culture [149]. Therefore, preclinical drug screening studies using PDXs are more likely than those using cell lines to be indicative of *in vivo* efficacy, and *in vivo* PDX drug studies are more likely to predict clinical potential [189]. Thus, the studies presented herein employ breast cancer PDX models, in addition to cell lines, to assess drug response.

Through screening of 1,363 drugs in ten PDXs of varying breast cancer subtypes, we have generated a drug response dataset that can be used to assess and compare drug response profiles of patient-derived breast cancer cells to many specific drugs or classes of drugs, currently approved for a wide range of clinical indications. From this dataset, we identified 176 drugs that were most effective in four basal-like TNBC PDXs, and through a series of subsequent drug screening assays, we selected four drugs of interest for combination testing and Chou-Talalay analysis: carfilzomib (proteasome inhibitor), afatinib (EGFR inhibitor), YM155 (survivin inhibitor), and carboplatin (standard-of-care chemotherapeutic). In addition to their efficacy in screening experiments, the former three drugs were of interest given the high level of expression of the genes encoding their targets. Of the six two-drug combinations, only afatinib and YM155 were found to be synergistic in the four basal-like PDXs tested, as well as in three cell lines. Notably, this combination was also favorable given the reduced dose of each drug required to achieve a given level of efficacy when combined with one another, suggesting that this drug combination could potentially minimize toxicity associated with combining multiple drugs. Indeed, our *in vivo* study employing the HCI01 PDX model demonstrated not only that both drugs, as single agents and in combination, were efficacious in reducing

mammary tumor growth, but also that both drugs were very well-tolerated, with no observable signs of toxicity.

It should be noted that, although the *in vivo* study showed a greater reduction in HClO1 tumor growth when afatinib was combined with YM155 compared to afatinib treatment alone, there was no significant difference in tumor growth between mice treated with the combination versus YM155 alone—both YM155-containing treatment groups showed a marked reduction in tumor growth, regardless of the presence or absence of afatinib. This indicates that the efficacy of the drug combination was dominated by the effects of YM155, therefore synergism was not discernible. Future studies incorporating lower doses of YM155 would be needed to detect synergism *in vivo*. Furthermore, prolonged drug administration may have caused tumor shrinkage rather than slowed growth, however this type of study design would be difficult to implement using these PDX models given the rapid growth rates of untreated tumors. Nevertheless, the efficacy of both afatinib and YM155 *in vivo*, and their minimal toxicity profiles, further suggest that these drugs are promising candidates for TNBC treatment.

YM155 is an investigational inhibitor of survivin expression that has shown promise in preclinical models of TNBC [207, 208], drug-resistant ER-positive breast cancer [209, 210], and other solid tumor types [211–216]. BIRC5, the gene encoding survivin, is upregulated in many human cancers [217], and in the breast cancer PDXs and cell lines employed in our study, and has been shown to have low levels of expression in normal tissue types [218, 219], which makes survivin an appealing drug target. The preclinical success of YM155 has led to its testing in several clinical trials, one of which was focused on combining YM155 with docetaxel in HER2-negative breast cancer (including TNBC), however this trial did not find significant benefit of the combination relative to docetaxel as a single agent [220]. The failure of preclinical drug studies to translate into clinical success is not uncommon. Thus, although YM155 was highly effective as a single agent in reducing mammary tumor growth in the *in vivo* study presented herein, its clinical track record to date suggests that its preclinical

monotherapeutic efficacy would be unlikely to translate into success in clinical trials, whether or not it is combined with standard-of-care chemotherapeutics. It is likely that identification of synergistic combinations incorporating YM155 would maximize its efficacy and potential for clinical benefit.

Our present findings indicate that, in several basal-like TNBC PDX models, YM155 is synergistic with afatinib, an EGFR inhibitor currently approved for the treatment of non-small cell lung cancer. EGFR is expressed in a large percentage of TNBCs [71, 221], including TNBC PDX models and the cell lines used in this study, and it has been explored as a potential therapeutic target in this disease [34, 222, 223]. However, EGFR inhibitors and anti-EGFR antibodies have thus far been unsuccessful in TNBC clinical trials [83–88], suggesting that, like for YM155, more effective combinations must be identified to maximize its efficacy. Based on our collective findings, we propose that YM155 and afatinib could potentially enhance each other's efficacy in TNBC. Interestingly, YM155 has been shown to reduce EGFR expression and tumor cell proliferation and survival in pancreatic cancer [224] as well as EGFR-positive non-small cell lung cancer, in which YM155 was found to be synergistic with afatinib [225] and other EGFR inhibitors [226], to reverse resistance to the EGFR inhibitor erlotinib in EGFR-mutant lung cancer [227], and to inhibit EGFR autophosphorylation which promotes lung cancer stemness [228]. The EGFR inhibitor lapatinib was also found to enhance the efficacy of YM155 in neuroblastoma by inhibiting drug efflux through the ABCB1 transporter [229].

Mechanisms of synergism between YM155 and EGFR inhibitors such as afatinib have not yet been extensively explored in breast cancer. We have demonstrated herein that YM155 reduces EGFR expression in a PDX model of basal-like TNBC, consistent with the aforementioned studies in pancreatic and lung cancer. Based on this finding, and on the aforementioned studies in other cancer types, we can postulate that YM155, in addition to promoting tumor cell apoptosis by inhibiting survivin, downregulates EGFR expression in breast cancer cells that highly express both BIRC5 and EGFR. When YM155 and afatinib are

combined, this may potentiate the inhibition of EGFR-mediated pathways, leading to enhanced inhibition of tumor cell proliferation and survival. In turn, afatinib may enhance the efficacy of YM155 in breast cancer cells by inhibiting YM155 efflux; indeed, afatinib has been shown to inhibit the ABCB1 drug efflux transporter in ovarian cancer [230] and the ABCG2 drug efflux transporter in other cancer types [231]. Notably, ABCG2 is known to be expressed and contribute to drug resistance in breast cancer cells, hence it is also known as breast cancer resistance protein (BCRP) [232]. Further investigation of the mechanisms underlying the synergism between afatinib and YM155 in basal-like TNBC is warranted to explore these and alternative possibilities.

Our studies collectively provide compelling evidence that the combination of afatinib and YM155 holds promise for potential clinical benefit in the treatment of basal-like TNBC. This is further supported by our analyses of the 855-patient gene expression and clinical dataset. Both EGFR and BIRC5 were found to have the highest expression levels in basal-like tumors compared to other subtypes. In addition, both genes were positively correlated with basal-like triple-negative tumor status, and negatively correlated with luminal ER/PR-positive tumor status and differentiation score. BIRC5 was also positively correlated with proliferation score, as this is one of the 11 proliferation markers that is included in the PAM50 gene list, which is used clinically for breast cancer subtyping and predicting patient prognosis [42]. Taken together with the aforementioned studies demonstrating the prevalence and functions of these genes in cancer, these findings suggest that both EGFR and BIRC5 may be important drug targets in basal-like TNBC. Our analyses of the 855-patient dataset further revealed that high co-expression of EGFR and BIRC5 was associated with significantly reduced MFS time and relapse-free survival specifically in the liver and lung. This suggests that co-targeting of EGFR and BIRC5 may have significant clinical impacts for patients with advanced basal-like TNBC, who currently face considerable limitations in treatment options and bleak outcomes relative to patients with tumors of other, currently targetable, subtypes. Based on our collective findings,

the combination of afatinib and YM155, and combinations incorporating other EGFR and survivin inhibitors, warrant further investigation as novel therapeutic regimens for the treatment of basal-like TNBC.

In conclusion, the studies reported herein provide a valuable 1,363-drug response dataset, employing clinically relevant PDX models, that has the potential to inspire and inform many future studies focusing on therapeutic development in breast cancer. Using this dataset to inform more focused follow-up screening studies, with an emphasis on basal-like TNBC, we have uncovered a promising drug combination that, to our knowledge, has not yet been established or explored in the context of this disease. Based on our collective findings and on previous research in other cancers, we believe that, upon further preclinical investigation, the combination of afatinib and YM155, and perhaps other EGFR and survivin inhibitors, could potentially be incorporated into novel therapeutic regimens for eventual clinical testing in humans. Furthermore, additional therapeutic strategies that may be explored based on our drug screening dataset, such as the repurposing of non-cancer therapeutics for breast cancer treatment, have the potential to make major translational impacts on treatment decisions, clinical outcomes, and quality of life for patients with advanced breast cancer.

3.6 Future directions

Future studies will focus on investigating the mechanisms of synergism between afatinib and YM155 in the context of basal-like TNBC, and potentially in other subtypes of breast cancer, beginning with known mechanisms of synergism in other cancer types (the reduction of EGFR protein levels by YM155 and the inhibition of drug efflux by afatinib). This would be particularly interesting to study in the WHIM2 PDX model, which has the highest expression of ABCG2 compared to the other basal-like TNBC PDXs. To identify other potentially important genes that are up- or down-regulated in response to the drugs, mechanistic studies will also involve global gene expression profiling of cells and/or tumor samples with and without treatment. In addition, it would be of interest to explore potential mechanisms of resistance to afatinib and

YM155 and strategies for sensitizing tumor cells to these drugs, as resistance to targeted therapeutics is a common occurrence in advanced disease. Furthermore, given the efficacy, potency, and tumor cell specificity of YM155, high-throughput *in vitro* combination studies will be performed to identify other drugs this survivin inhibitor may synergize with. In order to pursue the goal of translating the combination of afatinib and YM155 into the clinic, further *in vivo* studies with dose escalations will be performed to validate the efficacy, detect synergism, and assess the toxicity profile of this drug combination in multiple PDX models, with a particular focus on detecting *in vivo* synergism using lower doses of YM155. Lastly, afatinib and YM155 will be tested in the metastatic setting using PDX metastasis models to evaluate their efficacy in treating brain, liver, and lung metastases. This is especially important given that advanced or recurrent TNBC is often resistant to current standard-of-care therapies, and also that brain metastases in particular pose a unique challenge in cancer drug development. Afatinib is known to cross the blood-brain barrier [233, 234] and has demonstrated efficacy in the context of brain metastasis in lung cancer [235, 236], although it was not efficacious in treating HER2-positive breast cancer brain metastases [237]. Although YM155 does not effectively penetrate the blood-brain barrier [238], it is a therapeutic candidate in glioblastoma multiforme (GBM) based on its efficacy in *in vitro* and *in vivo* studies using intratumoral delivery of the drug [239–241]. However, the activity of YM155 against metastatic disease in the CNS is unknown. Given the propensity of basal-like TNBC to metastasize to the brain, and the challenges in pharmacologic management of brain metastases, it is especially important to investigate the potential efficacy of afatinib and YM155 in this specific context. In testing the efficacy of afatinib and YM155 in treating metastases, particularly those in the brain, it would be important to compare this treatment regimen to the current standard of care, including chemotherapy and radiation. The latter is especially important in breaking down the blood-brain barrier to enhance drug penetration into the brain. This type of study, designed like a clinical trial, would help determine whether the combination of afatinib and YM155 has superior efficacy to the standard

of care. Given the minimal toxicity profiles of afatinib and YM155, efficacy that is equivalent to the standard of care would still be quite promising given the relative toxicity of chemotherapeutics.

CHAPTER 4: Targeting the androgen receptor in triple-negative breast cancer

4.1 Background and rationale

As aforementioned, TNBC is a highly aggressive subtype of breast cancer with a propensity to metastasize to vital organs. Treatment for TNBC is limited to chemotherapy, which is toxic and often ineffective in eliminating disease and/or preventing recurrence, and, consequently, this subtype is associated with a particularly poor prognosis. There is a critical need for the development of targeted therapeutic strategies, as well as methods for stratifying TNBC patients based on tumor characteristics to predict therapeutic responses.

One potential therapeutic target in TNBC is AR, a current therapeutic target in castration-resistant metastatic prostate cancer (CRMPC) [242, 243]. Enzalutamide, a nonsteroidal small molecule AR inhibitor, is one of the AR-targeted agents currently FDA-approved to treat CRMPC [244–248] and has demonstrated efficacy in preclinical and clinical TNBC studies [89, 249–251]. Approximately 70% of all primary breast cancers, and 30-40% of TNBCs, are positive for AR expression [252]. Although the majority of TNBC tumors are classified as basal-like [44, 70, 71] and are AR-negative [72–74], approximately 15% of TNBCs are classified as the LAR subtype, which defines tumors that are triple-negative, AR-positive, with luminal gene expression profiles [70, 71]. LAR TNBCs are driven by AR signaling and are associated with a poor prognosis [70, 71], suggesting that patients within this subset may clinically benefit from AR-targeted therapies. There is some controversy regarding the role of AR in breast cancer, given the discrepancies between studies showing that AR expression is associated with better [253, 254] or worse [249, 255] clinical outcomes in breast cancer patients, which may involve differences in preclinical models and/or expression of other tumor markers such as ER. Regardless of these discrepancies, there is ample evidence to suggest that AR may be a suitable target in LAR TNBC, and it is likely that the development of synergistic combination regimens containing AR-targeted agents would increase the likelihood of clinical success in this subpopulation of TNBC patients.

4.2 Experimental approach

This study sought to investigate AR as a therapeutic target in LAR TNBC and other AR-positive PDX models and breast cancer cell lines, and to identify currently FDA-approved drugs that are potential candidates for combination with AR inhibitors for this subset of TNBC patients. After characterizing the expression of AR in several breast cancer PDXs and cell lines, we evaluated the effects of pharmacologic AR inhibition, inducible AR knockdown, and AR stimulation on the cell viability of those lines that were found to be AR-positive, and tested the efficacy of AR inhibition and knockdown on PDX mammary tumor growth *in vivo*. We expected that AR inhibition/knockdown would have cytotoxic effects in the LAR TNBC models. To identify potential therapeutic candidates for combination with AR inhibitors, we utilized the PDX 1,363-drug screening dataset in conjunction with patient gene expression data to identify drugs and drug targets of interest for further exploration in LAR TNBC.

4.3 Materials and methods

4.3.1 *Breast cancer PDX models and preparation of tumor cell suspensions*

Breast cancer PDX models of varying subtypes were used in these studies: triple-negative, basal-like (HCI01, HCI02, HCI04, HCI16, UCD18, UCD52, WHIM2, WHIM30); triple-negative, LAR type (HCI09); ER-positive, luminal (HCI03, HCI11, HCI13); and HER2-enriched (HCI08). HCI01, HCI02, HCI03, HCI04, HCI08, HCI09, HCI11, HCI13, and HCI16 were obtained from the Huntsman Cancer Institute, University of Utah; WHIM2 and WHIM30 were obtained from Washington University, St. Louis; UCD18 and UCD52 were obtained from the University of Colorado. All experiments were performed in accordance with IACUC guidelines and regulations. Tumor fragments were grown in the fourth mammary fat pads of female NSG mice. Established tumors were removed from mice, finely chopped, and digested for 1h at 37°C in DMEM/F12 containing 5% FBS, 300 U/ml collagenase (Sigma), and 100 U/ml hyaluronidase (Sigma). Digested tumor tissue was then resuspended in ammonium chloride and trypsinized to generate single cell suspensions.

Tumor cells were transduced with a lentivirus (BLIV101PA-1, Systems Biosciences) encoding GFP and luciferase, and these tumor cells were suspended 1:1 in Matrigel (Corning) and injected into the fourth mammary fat pads of NSG mice (500,000 cells per injection). Mammary tumors were removed for experimental use once they reached approximately 100mm² by caliper measurement. Tumors were processed into single cell suspensions as described above.

4.3.2 *Breast cancer cell lines*

Seven breast cancer cell lines were employed for these studies: MDA453, MDA468, MDA231, MCF7, T47D, ZR751, and BT549. Cell lines were originally obtained from the ATCC and were cultured according to ATCC guidelines in the following media: Leibovitz's L15 supplemented with 10% FBS (MDA453, MDA468, MDA231); RPMI-1640 supplemented with 10% FBS (ZR751) or 10% FBS and bovine insulin (0.2 U/ml T47D, 0.023 U/ml BT549); and Eagle's Minimum Essential Medium (EMEM) supplemented with 10% FBS and 0.01 mg/ml bovine insulin (MCF7); all media were additionally supplemented with penicillin/streptomycin. Cell lines were maintained in complete media, and both cell lines and PDX cell suspensions were cultured in charcoal-stripped phenol red-free media for drug response experiments (cell viability and Western blots). MDA453, MCF7, and T47D cells were transduced with a lentivirus (LVP323, GenTarget Inc.) encoding GFP and luciferase, followed by selection using blasticidin (Gemini Bio) (15 µg/ml for MDA453, 12.5 µg/ml for MCF7 and T47D).

4.3.3 *AR knockdown*

Tetracycline-inducible lentiviral shRNAs were generated using TRIPZ Lentiviral shRNA Transfection Starter Kit with DharmaFECT kb (Dharmacon, RHS11852-EG367 glycerol kit), including one non-silencing control (NSC) shRNA and three shRNAs targeting AR (V3THS_367658, V3THS_367662, V3THS_367663; subsequently abbreviated as AR658, AR662, AR663, respectively). Lentiviral particles were generated in HEK293T cells using

the Trans-Lentiviral shRNA Packaging Kit with Calcium Phosphate and HEK293T (Dharmacon, TLP5917). MDA453, MCF7, and T47D cells were transduced with lentivirus (NSC, AR658, AR662, AR663, or all three AR shRNAs combined (ARall3)) according to the provided protocols, followed by selection with puromycin (Gemini Bio) (2 µg/ml for MDA453, 1 µg/ml for MCF7 and T47D) to generate stable cell lines. HCl09 cell suspension cultures were transduced with lentivirus according to the provided protocols, followed by fluorescence-activated cell sorting (FACS) for red fluorescent protein (RFP) and subsequent injection into the fourth mammary fat pads of NSG mice to generate tumors. AR knockdown was induced *in vitro* using 0.5 µg/ml doxycycline (Sigma, D9891) and *in vivo* using doxycycline chow (625 mg/kg; Envigo Teklad Diets).

4.3.4 Western blotting

PDX cell suspensions were prepared from mammary tumors as described above and plated in 6-well plates at 1.5 million cells per well in M87 medium. Cell lines were plated in 6-well plates (500,000 cells per well for MDA453; 250,000 cells per well for MCF7 and T47D) in their corresponding ATCC-recommended media and incubated overnight to allow for adherence. To assess AR expression levels, protein extracts were collected from frozen PDX mammary tumors (WHIM2, WHIM30, HCl03, HCl08, HCl09, HCl11, HCl13) and from cell lines (MCF7, ZR751, T47D, MDA453, MDA468, MDA231, BT549) after 24h in culture. To assess the effects of TOK-001 treatment on AR expression, HCl09, MDA453, MCF7, and T47D cells were treated for 72h with vehicle (DMSO) or TOK-001 (10µM), followed by protein extraction. For AR knockdown verification, previously transduced (all shRNAs) and selected MDA453, MCF7, and T47D cells, and HCl09 cell suspensions generated from control or AR658 shRNA-expressing mammary tumors, were treated for 72h with or without doxycycline (0.5 µg/ml), followed by protein extraction. For protein extraction, PDX mammary tumors were homogenized, cell suspensions were pelleted and resuspended, and adherent cell lines were scraped, in Pierce RIPA buffer (ThermoFisher Scientific,

89900) + protease inhibitor (ThermoFisher Scientific, A32963) for cell lysis, and centrifuged at max speed at 4°C for 15 min to collect protein lysates. Protein concentrations were determined using Pierce BCA Protein Assay Kit (ThermoFisher Scientific, 23225). Proteins were resolved by SDS-PAGE and transferred to Immobilon-FL membranes (Millipore), which were then blocked in Odyssey Blocking Buffer in TBS (Li-Cor) for 1h at room temperature. Primary and secondary antibodies were diluted in Odyssey Blocking Buffer in TBS (Li-Cor) + 0.1% Tween-20. Membranes were incubated overnight at 4°C with rabbit anti- β -actin (1:1000; Cell Signaling Technology #4970) or rabbit anti-AR (1:1000; Cell Signaling Technology #5153). For detection, membranes were incubated with IRDye 680RD donkey anti-rabbit secondary antibody (1:10,000; Li-Cor 926-68073) for 1h at room temperature. All washes were performed using TBS-T. Membranes were imaged using the Odyssey Fc Imaging System (Li-Cor).

4.3.5 *Immunohistochemistry*

HCI03, HCI08, HCI09, HCI11, and HCI13 mammary tumor tissues were fixed in 10% formalin, paraffin-embedded, and sectioned using a Kedeer KD-2258 rotary microtome, at 10 μ m per section. IHC was performed by standard procedures, using the following primary antibodies: rabbit anti-AR (1:100; Cell Signaling Technology #5153), rabbit anti-ER (1:50; One World Lab #59347), rabbit anti-PR (1:1000; Cell Signaling Technology #8757), and rabbit anti-HER2 (1:100; Cell Signaling Technology #2242). Heat-induced antigen retrieval was conducted using a pressure cooker, in pH 9 Tris-EDTA. Detection was performed using the rabbit Dako EnVision system (Agilent K406511-2). Stained tissue sections were observed and photographed using a Zeiss AxioLab Upright Microscope and Zeiss AxioCam ICc 5 camera. Image analysis was performed using the ZEN2 software, blue edition.

4.3.6 *Cell viability assays*

For PDX cell viability assays, PDX cells were plated in 96-well plates at 25,000 cells per well in M87 medium [135] and treated with drugs for 72h, followed by imaging and

measurement of luciferase activity (total photon flux per second) two minutes after the addition of D-luciferin (15 mg/ml; Gold Biotechnology) to each well (1/10 of total volume per well), using the IVIS Spectrum In Vivo Imaging System (Xenogen IVIS-200) and Living Image software (PerkinElmer), as described in our previous work [149]. For cell line viability assays, cell lines were plated in 96-well plates at 5,000 cells per well (MCF7, T47D) or 10,000 cells per well (MDA453), cultured overnight to allow for adherence, and subsequently treated with drugs for 72h. Viability of cell lines was measured using luciferase activity as described above (for luciferase-expressing cells) or the CellTiter-Glo Luminescent Viability Assay (Promega), according to the provided protocol.

4.3.7 *1,363-drug screening analyses*

The 1,363-drug screening dataset consisting of drug response data for 10 PDXs (**Appendix A**; described in Chapter 3, Section 3.3.4) [190] was utilized to assess response to AR-targeting drugs across multiple breast cancer subtypes. A heatmap was generated using GraphPad Prism 8 to show the relative responses (cell viability as percent of vehicle) of the 10 PDXs to AR agonists and AR antagonists from the screening dataset. Graphs were generated for comparison of enzalutamide and TOK-001 responses across the individual PDXs using averaged duplicate data for each PDX. Data were then averaged for AR-positive PDXs and AR-negative PDXs to compare overall responses of the two groups to enzalutamide and TOK-001, and unpaired two-tailed t-tests were performed to assess for significant differences between responses to enzalutamide vs. TOK-001 and between responses of AR-positive vs. AR-negative PDXs to each of the two drugs.

4.3.8 *In vitro AR-targeting studies*

For dihydrotestosterone (DHT) and enzalutamide dose response experiments, AR-positive PDXs (HCI09, HCI08, HCI13) and cell lines (MDA453, MCF7, T47D) were treated in triplicate for 72h with DHT (1, 5, 10, 25, 50 nM) or enzalutamide (1, 10, 50, 75, 100 μ M), followed by measurement of cell viability as described above (luciferase activity for PDXs,

CellTiter-Glo for cell lines). For AR knockdown experiments, MDA453, MCF7, and T47D cells expressing both luciferase and lentiviral shRNAs (NSC, AR658, AR662, AR663, or ARall3) were treated in triplicate with or without doxycycline (0.5 µg/ml) for 72h, followed by measurement of cell viability using luciferase activity. To assess the effects of AR knockdown on response to DHT and enzalutamide, the three cell lines expressing all three AR-targeted lentiviral shRNAs (ARall3) were treated in triplicate for 72h with DHT (25nM) +/- doxycycline (0.5 µg/ml) or enzalutamide (100µM) +/- doxycycline (0.5 µg/ml), followed by measurement of cell viability using luciferase activity. To compare the effects of TOK-001 vs. enzalutamide, HCl08, HCl09, HCl13, MDA453, MCF7, and T47D cells were treated in triplicate for 72h with TOK-001 (0.01, 0.1, 1, 10 µM) or enzalutamide (0.01, 0.1, 1, 10 µM), followed by measurement of cell viability using luciferase activity. To assess the effects of AR knockdown on response to TOK-001 vs. enzalutamide, T47D cells expressing all three AR-targeted lentiviral shRNAs (ARall3) or NSC shRNA were treated in triplicate for 72h with TOK-001 (0.01, 0.1, 1, 10 µM) or enzalutamide (0.01, 0.1, 1, 10 µM) after induction of AR knockdown with doxycycline (0.5 µg/ml), followed by measurement of cell viability using luciferase activity. For all these studies: DHT, enzalutamide, and TOK-001, were obtained from Sigma, Selleck Chemicals, and MedChemExpress, respectively.

4.3.9 *In vivo AR-targeting studies*

HCl09 PDX mammary tumors were processed into single cell suspensions as described above, and tumor cells diluted 1:1 with Matrigel (Corning) were injected into the fourth mammary fat pads of NSG mice (500,000 cells per tumor). For all experiments, treatments were initiated once tumors became palpable and continued until control tumors reached protocol-defined burden. For enzalutamide studies, mice were treated with enzalutamide (10 mg/kg or 30 mg/kg; Selleck Chemicals) or vehicle (DMSO) every 2 days via IP injection. For TOK-001 studies, mice were treated with TOK-001 (90 mg/kg; MedChemExpress) or vehicle (0.5% hydroxyethyl cellulose) 5 days per week via oral gavage. For AR knockdown

studies, mammary tumors were generated in mice using HCl09 cells expressing inducible lentiviral shRNA targeting AR (AR658), and, once tumors became palpable, mice were given doxycycline chow (625 mg/kg; Envigo Teklad Diets) or maintained on control chow. For all experiments, tumor growth was monitored over time via caliper measurements.

4.3.10 Analyses using patient clinical and gene expression datasets

AR expression in breast cancer patients was analyzed using the 855-patient clinical and gene expression dataset [18, 53, 195] employed for studies described in Chapter 3, Section 3.3.10. AR expression was assessed across the intrinsic breast cancer subtypes, and Tukey's multiple comparisons test was used to determine the significance of differences in AR expression between each subtype. Also using the 855-patient dataset, ER-negative patients (n=256) were ranked by AR expression and divided into two groups: high AR expression (top 50%) and low AR expression (bottom 50%); Kaplan-Meier analysis was performed to determine the effect of AR expression level on relapse-free survival in this group of patients. To identify potential drug targets correlating with AR expression in patients with AR-positive TNBC, breast cancer patient gene expression (RNA-sequencing) data from The Cancer Genome Atlas (TCGA) were utilized along with the PDX 1,363-drug screening dataset [190]. First, all TNBC patients included in the TCGA dataset (n=115) were ranked according to AR expression levels. TNBC patients with the highest AR expression (n=9) were selected for Pearson correlation analyses between AR expression and the expression of all other genes in the TCGA dataset. Subsequently, the HCl09 1,363-drug screening dataset was used to compare Pearson correlations for particular genes with HCl09 cell viability in response to drugs that target the proteins encoded by those genes. Genes/drug targets with the strongest correlations with AR expression (Pearson correlation >0.50) and corresponding drugs with the highest efficacy (percent of vehicle viability <50%) in HCl09 cells were considered to be potential drug targets of interest for future studies in AR-positive TNBC. To further explore the seven identified genes of interest, Pearson

correlations between these genes and AR expression within the high-AR patient group (n=9) were compared with the same analyses performed within all other (low-AR) patients (n=106) and within all TNBC patients (n=115). Additionally, heatmaps were generated to compare expression levels (TPM values) of AR and the seven genes in the high-AR versus low-AR groups, as well as across the nine high-AR patients individually.

4.3.11 RNA-sequencing analyses

PDX mammary tumor RNA-sequencing data [141] (GEO Accession: GSE118942) were used to assess expression levels of AR and the seven genes of interest identified above across 13 PDXs: HCI01, HCI02, HCI03, HCI04, HCI08, HCI09, HCI10, HCI13, HCI16, UCD18, UCD52, WHIM2, WHIM30. Log₂ (TPM+1) values were averaged across replicates for each PDX. Expression of these genes was also assessed in breast cancer cell lines using the two RNA-sequencing databases described in Chapter 3, Section 3.3.10: the HMS LINCS Breast Cancer Profiling Project (<http://lincs.hms.harvard.edu/db/datasets/20348/>) and the Broad Institute CCLE (<https://portals.broadinstitute.org/ccle>). For these analyses, specific cell lines were selected such that TNBC subtypes, along with ER-positive status for comparison, were each represented by at least one cell line: LAR TNBC (MDA453), basal-like TNBC (MDA468, HCC1143, HCC1187, HCC1937, CAL851), mesenchymal TNBC (MDA231, CAL51), and luminal ER-positive (T47D, MCF7). It should be noted that HCC1187 data were only available in the CCLE database. Gene expression heatmaps were generated separately for data from each cell line database as well as the PDX data to assess and compare expression levels of the genes of interest across PDXs and cell lines of varying subtypes, with a particular focus on comparing AR-positive with AR-negative models.

4.3.12 Statistics

Unpaired two-tailed t-tests were performed to assess significant differences between control and drug treated conditions for both *in vitro* and *in vivo* experiments, as well as

between AR-positive vs. AR-negative PDXs and TOK-001 vs. enzalutamide in the 1,363-drug screening analyses. Tukey's multiple comparisons test was used to analyze differences in AR expression across intrinsic subtypes using patient data. Log rank test was used to assess the effect of AR expression level on relapse-free survival using patient data. For all analyses, $p < 0.05$ was considered statistically significant.

4.4 Results

4.4.1 *AR expression across breast cancer cell lines, PDXs, and patients*

To determine how the expression of AR relates to breast cancer intrinsic subtype, we utilized a publicly available 855-patient breast cancer dataset consisting of clinical and gene expression data. AR expression was lowest in basal-like and claudin-low tumors and highest in HER2-enriched, luminal A, and luminal B tumors (**Fig. 4.1a**). To determine whether AR expression is related to clinical outcome, we analyzed the relationship between AR expression level and MFS using the same dataset. Interestingly, when stratified by ER status, high AR expression was associated with significantly reduced total relapse-free survival in ER-negative patients (**Fig. 4.1b**).

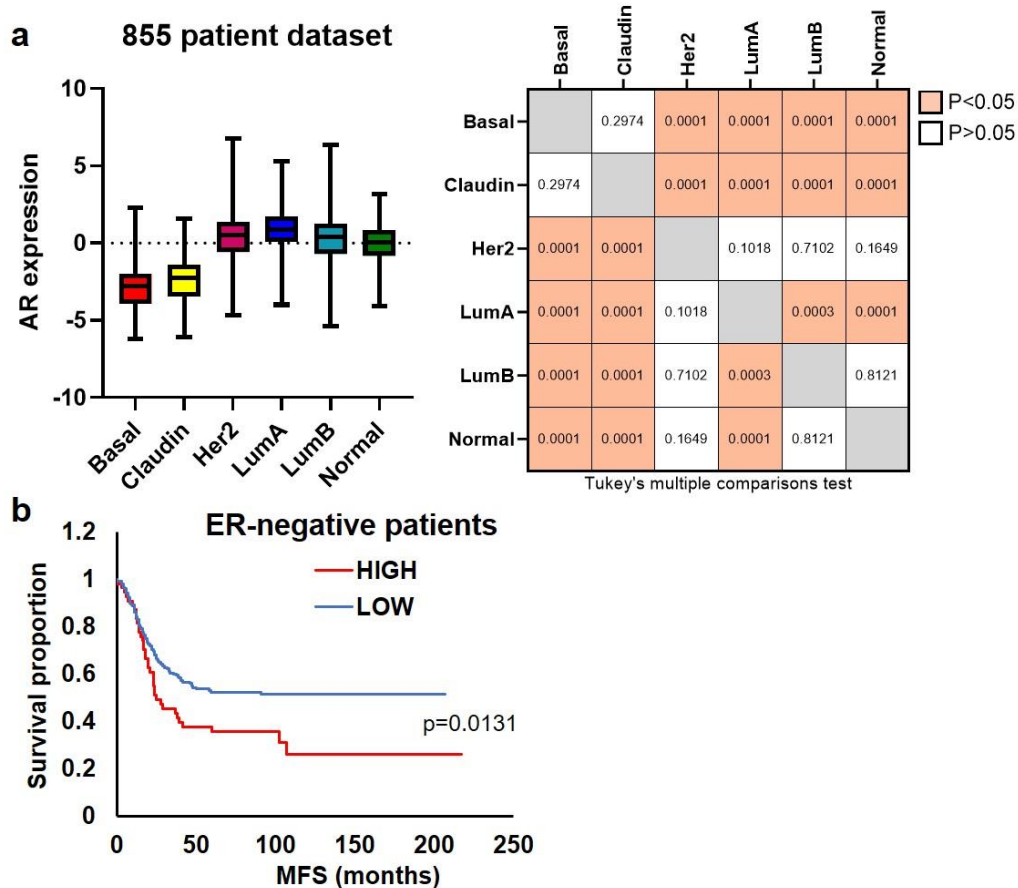


Figure 4.1: AR expression is correlated with breast cancer intrinsic subtype and reduces metastasis-free survival in ER-negative patients. **(a)** Gene expression microarray data from 855 breast cancer patients were used to assess expression levels of AR in patients according to intrinsic subtype: basal-like (Basal), claudin-low (Claudin), luminal A (LumA), luminal B (LumB), HER2-enriched (Her2), normal-like (Normal). Tukey's multiple comparisons test was used to analyze differences in expression levels between each subtype; table in right panel depicts p-values. **(b)** Patients with ER-negative disease (n=256) were ranked by AR expression level and divided into high vs. low AR expression (top and bottom 50% of patients, respectively). Graph shows Kaplan-Meier analysis for effect of high vs. low AR expression on metastasis-free survival (MFS) in ER-negative patients.

To identify breast cancer cell lines and PDX lines that express AR, we performed Western blot analyses which revealed AR protein expression in four cell lines (ER-positive: MCF7, ZR751, T47D; ER-negative: MDA453) and five PDX lines (ER-positive: HCI03, HCI11, HCI13; ER-negative: HCI08, HCI09) (**Fig. 4.2a**). AR expression and ER/PR/HER2 status in PDX mammary tumor tissues were confirmed by IHC (**Fig. 4.2b**); note that HCI09 is triple-negative whereas HCI08 is ER/PR-negative but HER2-positive. Collectively, these studies identified two AR-positive TNBC models (HCI09 and MDA453), several AR-positive

ER-positive models (HCI03, HCI11, HCI13, MCF7, ZR751, T47D), and one AR-positive HER2-positive model (HCI08). HCI09 and MDA453 can both be classified as LAR TNBC models. HCI09 liver metastasis tissue was also positive for AR by IHC (**Fig. 4.2c**), indicating that the AR status of primary tumors is maintained in the metastatic setting in this LAR TNBC model. Consistent with AR protein analyses, analysis of previous PDX RNA-sequencing data revealed that AR mRNA expression in mammary tumors was highest by far in HCI03, HCI08, HCI09, and HCI13, with zero to minimal expression of the AR transcript in the other nine PDXs included in the dataset, which are all basal-like TNBC models (HCI01, HCI02, HCI04, HCI10, HCI16, UCD18, UCD52, WHIM2, WHIM30) (**Fig. 4.3**).

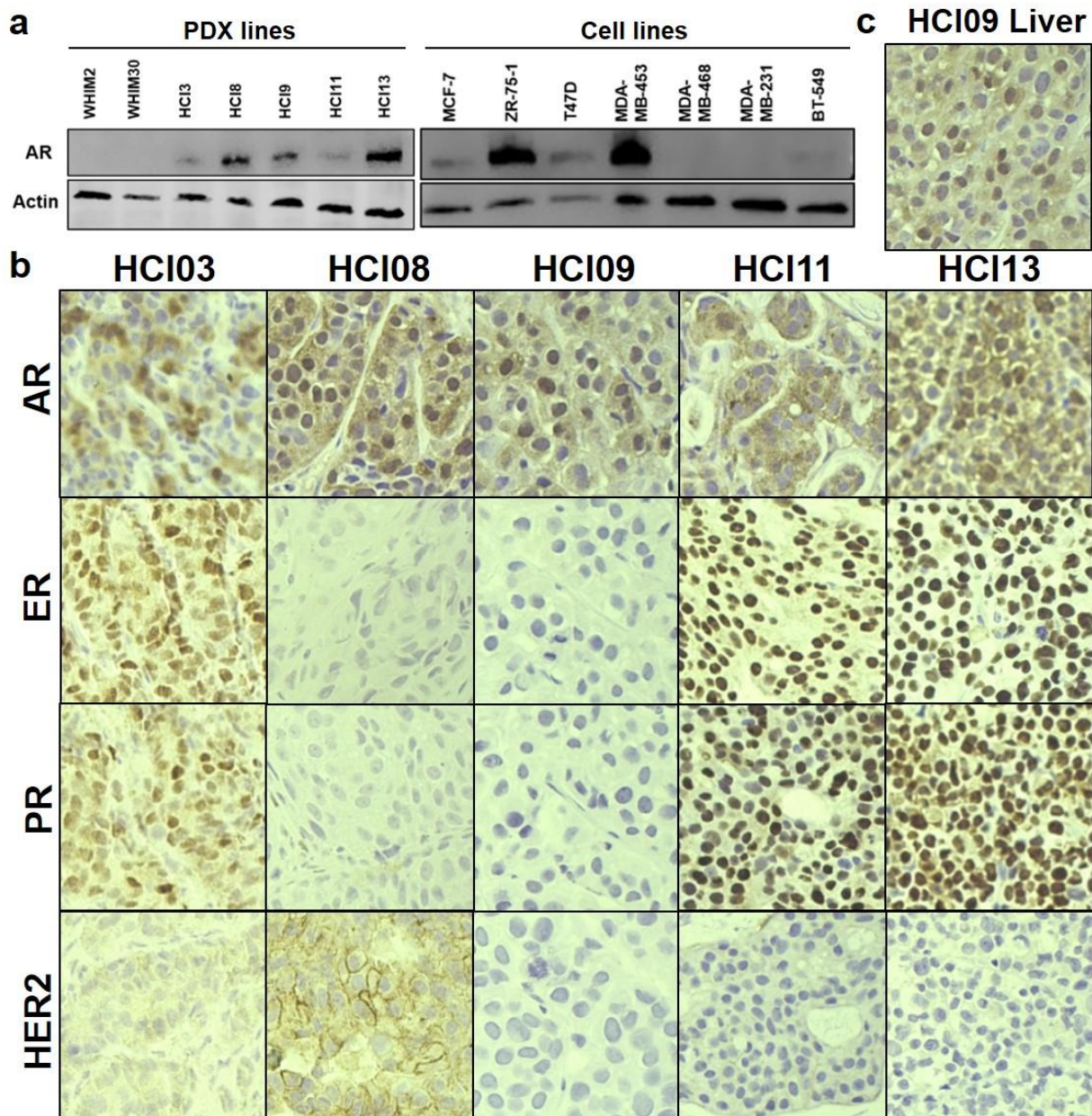


Figure 4.2: Identification of AR-positive breast cancer PDXs and cell lines. **(a)** Western blots depicting AR expression across breast cancer PDXs (WHIM2, WHIM30, HCl03, HCl08, HCl09, HCl11, HCl13) and cell lines (MCF7, ZR751, T47D, MDA453, MDA468, MDA231, BT549). **(b)** IHC for AR, ER, PR, and HER2 in PDX mammary tumor tissue (HCl03, HCl08, HCl09, HCl11, HCl13). **(c)** IHC for AR in HCl09 liver metastasis tissue.

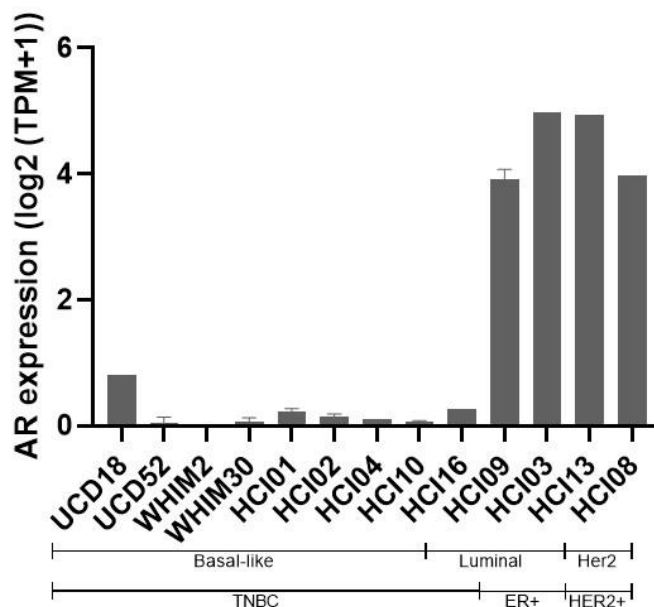


Figure 4.3: AR gene expression in breast cancer PDX tumors. RNA-sequencing data were used to assess AR expression across 13 PDXs of varying breast cancer histologic and intrinsic subtypes, as labeled beneath the graph. Log2 (TPM+1) values for each PDX were averaged when applicable across mammary tumor samples (UCD18 n=1, UCD52 n=6, WHIM2 n=3, WHIM30 n=5, HCI01 n=3, HCI02 n=3, HCI04 n=1, HCI10 n=2, HCI16 n=1, HCI09 n=4, HCI03 n=1, HCI13 n=1, HCI08 n=1). Error bars represent standard deviation between replicate samples, where applicable.

4.4.2 DHT and enzalutamide variably affect viability of AR-positive breast cancer cells

AR-positive breast cancer PDXs (HCI09, HCI08, HCI13) and cell lines (MDA453, MCF7, T47D) were treated *in vitro* with DHT to determine the effect of AR stimulation on cell viability, and with enzalutamide to determine the effect of AR inhibition on cell viability. DHT caused an increase in viability of HCI08 cells, which tapered off with increasing doses, whereas it caused a dose-dependent reduction in viability of HCI09 cells and did not considerably affect HCI13 cells (**Fig. 4.4a**). DHT also increased the viability of T47D cells and slightly but insignificantly increased the viability of MDA453 cells, whereas it did not affect the viability of MCF7 cells (**Fig. 4.4b**). In contrast, the AR inhibitor enzalutamide dose-dependently reduced cell viability in all three PDX lines (**Fig. 4.4c**) and all three cell lines (**Fig. 4.4d**), although these cytotoxic effects of enzalutamide reached significance only for HCI09, MDA453, and T47D cells. All p-values are listed in **Table 4.1**.

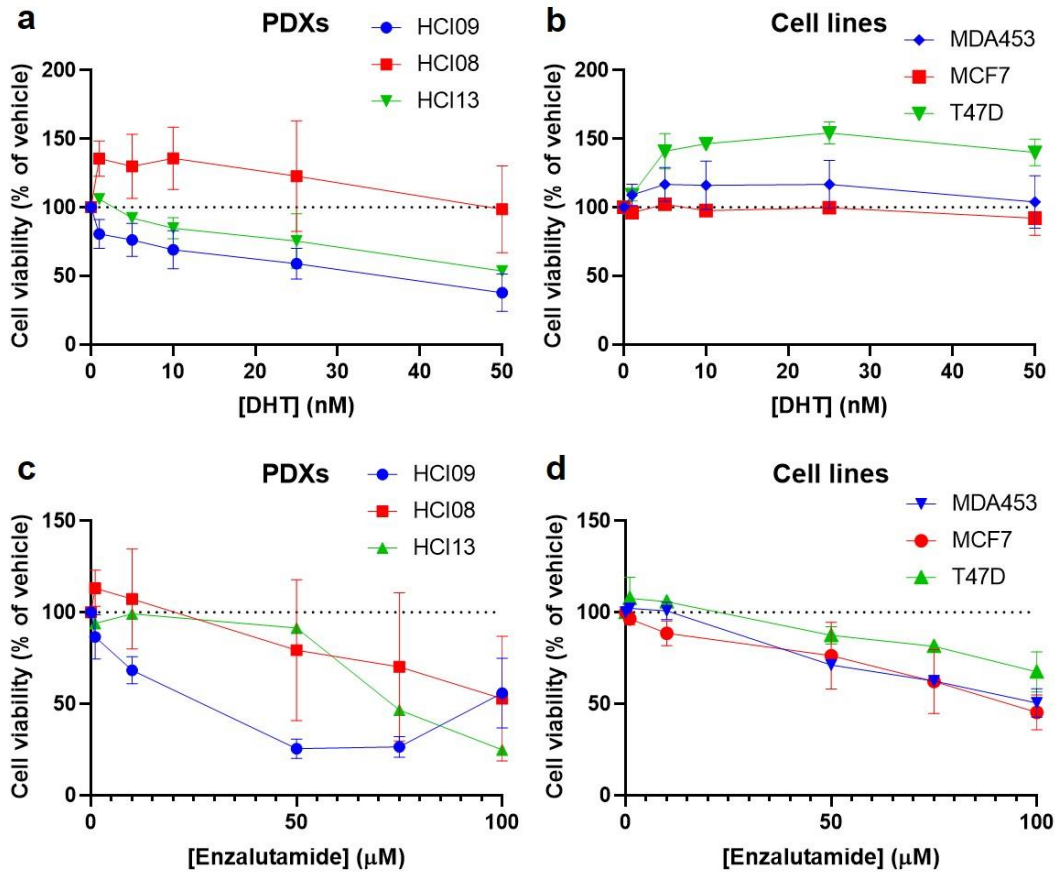


Figure 4.4: DHT and enzalutamide variably affect viability of AR-positive breast cancer cells. Upper panel graphs depict cell viability (% of vehicle) in response to dihydrotestosterone (DHT) in breast cancer PDXs (HCI09, HCI08, HCI13) **(a)** and cell lines (MDA453, MCF7, T47D) **(b)**. Lower panel graphs depict cell viability (% of vehicle) in response to enzalutamide in breast cancer PDXs (HCI09, HCI08, HCI13) **(c)** and cell lines (MDA453, MCF7, T47D) **(d)**. For cell viability assays, cells were treated in triplicate for 72h with either DHT or enzalutamide, followed by IVIS imaging (PDXs) or CellTiter-Glo assay (cell lines). Error bars represent standard deviation. For DHT experiments: HCI09 N=9, HCI08 N=5, HCI13 N=2, MDA453 N=2, MCF7 N=2, T47D N=2. For enzalutamide experiments: HCI09 N=3, HCI08 N=2, HCI13 N=1, MDA453 N=2, MCF7 N=2, T47D N=2. All p-values are listed in Table 4.1.

Table 4.1: P-values for *in vitro* dose response experiments shown in Figure 4.4. *t*-tests were performed to compare each drug treatment condition with vehicle controls for each PDX/cell line. Significant values ($p < 0.05$) are bolded and italicized.

DHT (nM)	1	5	10	25	50
HCI09	<i>4.6E-05</i>	<i>2.3E-05</i>	<i>5E-06</i>	<i><0.000001</i>	<i><0.000001</i>
HCI08	<i>0.00027</i>	<i>0.02092</i>	<i>0.00807</i>	0.244171	0.909225
HCI13	0.11027	<i>0.0219</i>	0.10809	0.222232	N/A
MDA453	0.24435	0.19399	0.32604	0.310154	0.799312
MCF7	0.05721	0.44613	0.06034	<i>0.039903</i>	0.464411
T47D	0.10724	<i>0.0468</i>	<i>0.00135</i>	<i>0.010914</i>	<i>0.027876</i>
Enzalutamide (μ M)	1	10	50	75	100
HCI09	0.12828	<i>0.00178</i>	<i>1.6E-05</i>	<i>0.000023</i>	<i>0.015842</i>
HCI08	0.19913	0.74295	0.52782	0.408143	0.190043
HCI13	N/A	N/A	N/A	N/A	N/A
MDA453	0.32959	0.84274	<i>5.9E-05</i>	<i>0.001341</i>	<i>0.01215</i>
MCF7	0.24955	0.13743	0.20944	0.092788	<i>0.014661</i>
T47D	0.4449	<i>0.00047</i>	0.06659	<i>0.012222</i>	0.052188

4.4.3 AR knockdown does not reduce viability of AR-positive breast cancer cells or abrogate the effects of enzalutamide

To determine the effect of reduced AR expression on cell viability, we used a doxycycline-inducible system to knockdown AR in MDA453, MCF7, and T47D cells using three different AR-targeted shRNAs (AR658, AR662, AR663), separately and in combination, and one NSC shRNA; the combination of all three AR-targeted shRNAs (ARall3) produced the most efficient knockdown in all three cell lines (**Fig. 4.5a**). In contrast to pharmacological inhibition with enzalutamide, doxycycline-induced AR knockdown did not reduce the viability of MDA453 cells (**Fig. 4.5b**), MCF7 cells (**Fig. 4.5c**), or T47D cells (**Fig. 4.5d**) compared to NSC conditions, although doxycycline itself had cytotoxic effects on the three cell lines. We next sought to determine the effect of AR knockdown on responses to DHT and enzalutamide in the three cell lines. Doxycycline-induced AR knockdown inhibited the DHT-induced increase in viability of MDA453 cells but did not abrogate the cytotoxic effects of enzalutamide (**Fig. 4.5e**). However, AR knockdown did not alter the effects of DHT or enzalutamide in MCF7 cells (**Fig. 4.5f**) or T47D cells (**Fig. 4.5g**).

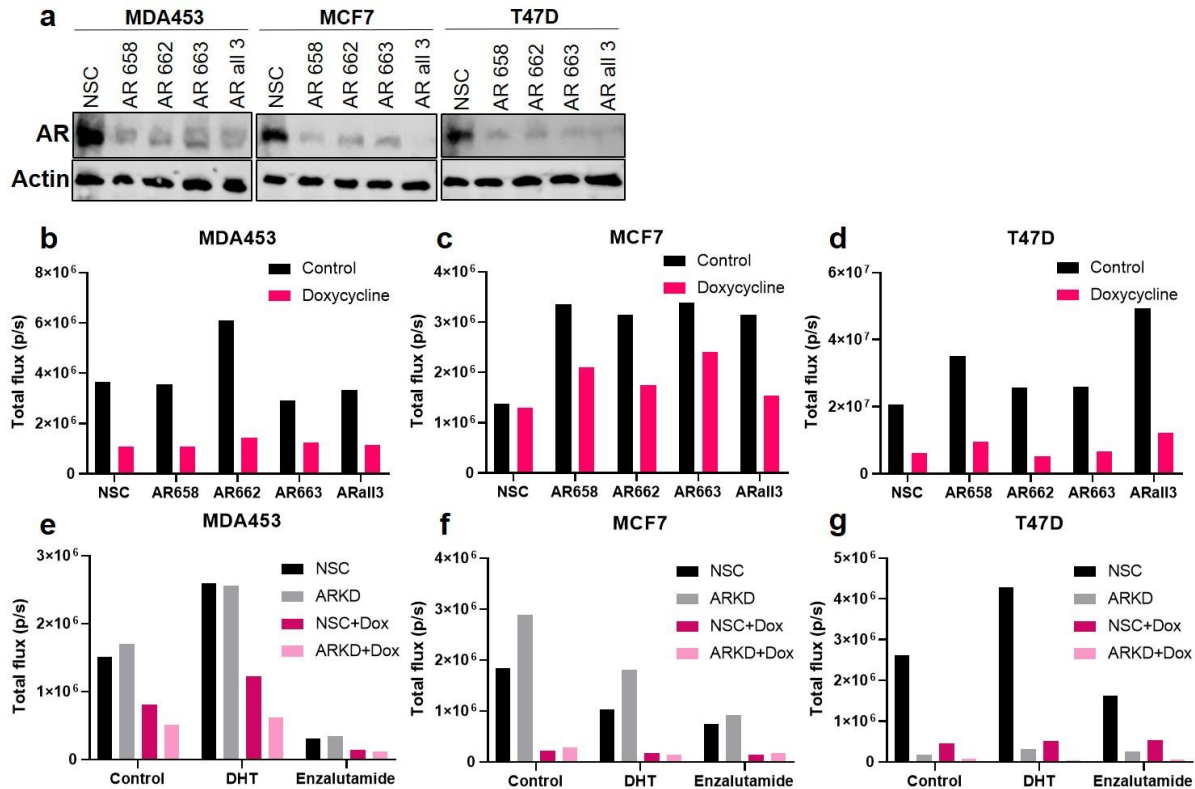


Figure 4.5: AR knockdown does not reduce viability of AR-positive breast cancer cells or abrogate the effects of enzalutamide. AR knockdown was performed using an inducible knockdown system with three lentiviral shRNAs targeting AR (AR658, AR662, AR663), separately and in combination (ARall3), as well as one non-silencing control (NSC) shRNA. **(a)** Western blots showing AR knockdown efficiency in breast cancer cell lines (MDA453, MCF7, T47D) after 72h of induction with doxycycline (0.5 μ g/ml). Middle panel graphs show effect of doxycycline-induced AR knockdown on viability of luciferase-expressing MDA453 cells **(b)**, MCF7 cells **(c)**, and T47D cells **(d)**; cell viability was measured as total flux (p/s) using IVIS imaging. Graphs in lower panel show the effect of doxycycline-induced AR knockdown (ARall3) on response to DHT (25nM) and enzalutamide (100 μ M) in luciferase-expressing MDA453 cells **(e)**, MCF7 cells **(f)**, and T47D cells **(g)**; cell viability was measured as total flux (p/s) using IVIS imaging.

4.4.4 Drug screening reveals TOK-001 as a promising antiandrogen for AR-positive breast cancer

To identify drugs other than enzalutamide with efficacy in AR-positive breast cancer, we utilized the 1,363-drug screening dataset (10 μ M) consisting of drug response data for ten PDX lines (**Appendix A**; described in Chapter 3, Section 3.3.4) [190]: AR-positive (HCl08, HCl09, HCl03, HCl11, HCl13) and AR-negative (HCl01, HCl16, UCD52, WHIM2, WHIM30). Interestingly, of the eight AR antagonists included in the screening library, TOK-001 was the most effective AR inhibitor in AR-positive PDXs, with the most consistent differential responses between AR-positive vs. AR-negative disease and the highest efficacy in the LAR TNBC PDX HCl09 (**Fig. 4.6a**). Notably, TOK-001 had efficacy superior to that of enzalutamide in four out of the five AR-positive PDXs, including HCl09 (**Fig. 4.6b**). When data were averaged for AR-positive vs. AR-negative PDXs, TOK-001 was significantly more effective than enzalutamide in AR-positive PDXs ($p=0.0106$) but not in AR-negative PDXs ($p=0.2109$), and TOK-001 was significantly more effective in AR-positive PDXs than in AR-negative PDXs ($p=0.0229$) whereas enzalutamide showed no difference in response between AR-positive vs. AR-negative disease ($p=0.5086$) (**Fig. 4.6c**). These data suggest that the dual AR/CYP17A1 (cytochrome P450 family 17 subfamily A member 1) inhibitor TOK-001 is a promising candidate for treatment of AR-positive breast cancer, more so than the AR inhibitor enzalutamide.

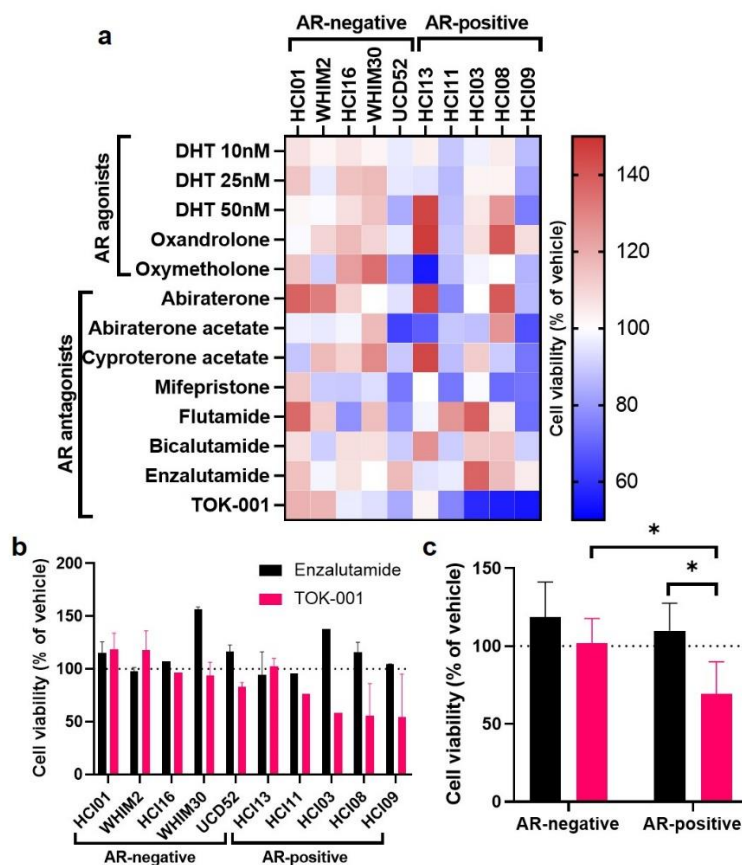


Figure 4.6: Drug screening reveals TOK-001 as a promising antiandrogen for AR-positive breast cancer. PDX cells were treated for 72h with 1,363 drugs (10 μ M) as well as the indicated concentrations of DHT, followed by measurement of cell viability using IVIS imaging (luciferase activity); all screening data are provided in Appendix A. **(a)** Heatmap depicting cell viability of ten PDXs (AR-negative: HCI01, WHIM2, HCI16, WHIM30, UCD52; AR-positive: HCI13, HCI11, HCI03, HCI08, HCI09) in response to drugs targeting AR (agonists and antagonists). Color scale represents cell viability as percent of vehicle controls. **(b)** Comparison of responses of the ten PDXs to enzalutamide vs. TOK-001 in the drug screen. **(c)** Comparison of averaged responses of AR-negative vs. AR-positive PDXs to enzalutamide vs. TOK-001 in the drug screen; * p <0.05.

Given the promising results with TOK-001 in the 1,363-drug screen, we performed follow-up dose response testing to further compare the efficacies of TOK-001 and enzalutamide in AR-positive PDXs (**Fig. 4.7a-d**) and cell lines (**Fig. 4.7e-g**). In this set of studies, TOK-001 and enzalutamide did not show considerable cytotoxicity or differential efficacy, except slightly in HCI09 and HCI13. Notably, however, AR knockdown abrogated the dose-dependent effects of TOK-001 in T47D cells, whereas it did not completely abrogate the dose-dependent effects of enzalutamide in these cells (**Fig. 4.7h**), indicating that TOK-001 may target AR more specifically than enzalutamide. P-values are listed in **Table 4.2**.

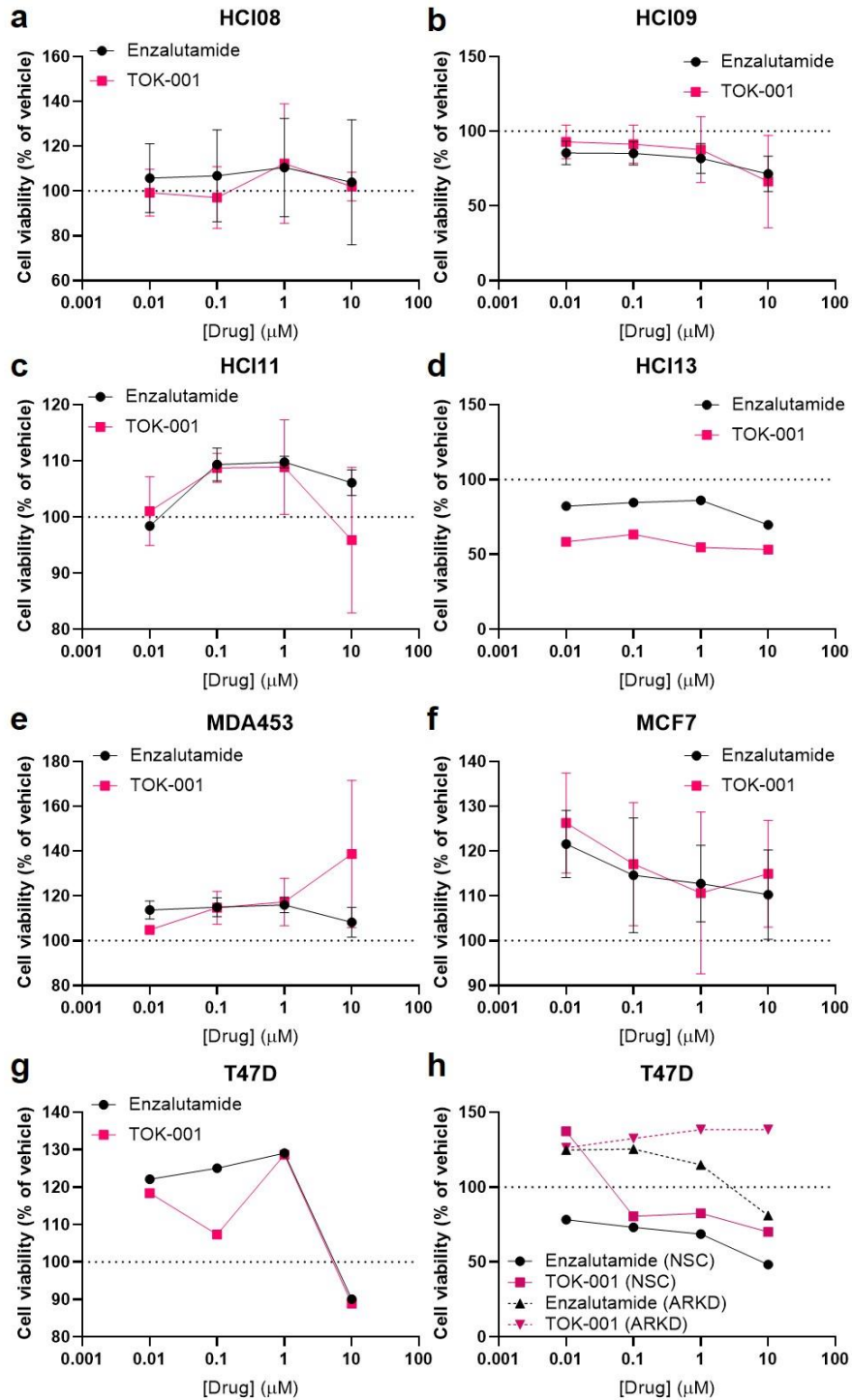


Figure 4.7: Comparison of the effects of TOK-001 vs. enzalutamide on the viability of AR-positive breast cancer cells. Luciferase-expressing PDXs and cell lines were treated for 72h with increasing concentrations of TOK-001 or enzalutamide, followed by measurement of cell viability using IVIS imaging (luciferase activity); cell viability is shown as percent of vehicle controls. Graphs depict TOK-001 and enzalutamide dose responses for HCl08 (N=3) (a), HCl09 (N=6) (b), HCl11 (N=2) (c), HCl13 (N=1) (d), MDA453 (N=3) (e), MCF7 (N=2) (f), and T47D (N=1) (g). P-values are provided in Table 4.2. (h) Graph depicts enzalutamide vs. TOK-001 responses of T47D cells expressing inducible lentiviral shRNAs (non-silencing control, NSC; AR knockdown, ARKD, using ARall3), after 72h induction with doxycycline (0.5 μg/ml); N=1.

Table 4.2: P-values for *in vitro* dose response experiments shown in Figure 4.7. *t*-tests were performed to compare each drug treatment condition with vehicle controls, and enzalutamide with TOK-001, for each PDX/cell line. Significant values ($p < 0.05$) are bolded and italicized.

HCI08	Enzalutamide vs. Vehicle	TOK-001 vs. Vehicle	Enzalutamide vs. TOK-001
0.01 μ M	0.556252	0.904131	0.579418
0.10 μ M	0.595403	0.728114	0.530294
1 μ M	0.456948	0.472687	0.933487
10 μ M	0.821107	0.623669	0.912847
HCI09	Enzalutamide vs. Vehicle	TOK-001 vs. Vehicle	Enzalutamide vs. TOK-001
0.01 μ M	<i>0.001011</i>	0.146192	0.220968
0.10 μ M	<i>0.000903</i>	0.125972	0.334094
1 μ M	<i>0.001238</i>	0.201266	0.564059
10 μ M	<i>0.000154</i>	<i>0.023465</i>	0.706398
HCI11	Enzalutamide vs. Vehicle	TOK-001 vs. Vehicle	Enzalutamide vs. TOK-001
0.01 μ M	0.079189	0.828885	0.603979
0.10 μ M	<i>0.045337</i>	<i>0.040966</i>	0.848208
1 μ M	<i>0.005748</i>	0.273786	0.896136
10 μ M	0.065693	0.696617	0.386816
MDA453	Enzalutamide vs. Vehicle	TOK-001 vs. Vehicle	Enzalutamide vs. TOK-001
0.01 μ M	<i>0.004067</i>	<i>0.008552</i>	<i>0.025064</i>
0.10 μ M	<i>0.003472</i>	<i>0.025758</i>	0.956975
1 μ M	<i>0.001261</i>	<i>0.047788</i>	0.840493
10 μ M	0.098693	0.110526	0.189615
MCF7	Enzalutamide vs. Vehicle	TOK-001 vs. Vehicle	Enzalutamide vs. TOK-001
0.01 μ M	0.056139	0.080027	0.668425
0.10 μ M	0.248165	0.220171	0.868294
1 μ M	0.16994	0.491889	0.897054
10 μ M	0.28278	0.219452	0.713895

As TOK-001 is a dual inhibitor of both AR and CYP17A1 that has been reported to reduce AR expression levels in prostate cancer [256], we were interested in determining the effect of TOK-001 on AR expression in AR-positive breast cancer cells. Interestingly, TOK-001 reduced AR expression in MDA453 cells, but did not affect AR expression in MCF7, T47D, or HCI09 cells (**Fig. 4.8**).

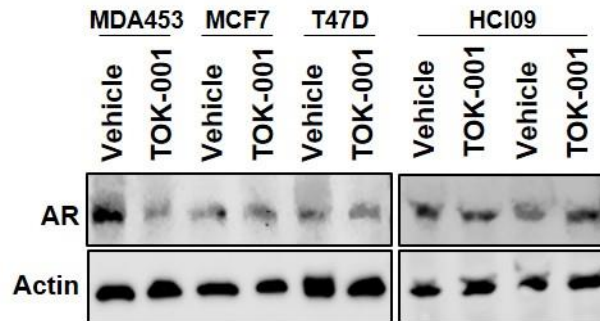


Figure 4.8: TOK-001 reduces AR expression in a luminal AR TNBC cell line. MDA453, MCF7, T47D, and HCl09 cells were treated for 72h with vehicle (DMSO) or TOK-001 (10 μ M), followed by Western blotting for AR, with actin as a loading control.

4.4.5 AR inhibition/knockdown does not reduce AR-positive mammary tumor growth *in vivo*

To determine the effects of targeting AR *in vivo*, we tested the efficacy of enzalutamide, TOK-001, and AR knockdown in mice bearing HCl09 mammary tumors. Tumor growth was only very slightly reduced by enzalutamide (**Fig. 4.9a**) and not at all reduced by TOK-001 (**Fig. 4.9b**). Although a successful knockdown of AR expression was achieved in HCl09 mammary tumor cells (**Fig. 4.9c**), doxycycline-induced AR knockdown did not reduce mammary tumor growth (**Fig. 4.9d**). All p-values are listed in **Table 4.3**. Thus, the efficacy of targeting AR in this LAR TNBC model was not validated *in vivo*.

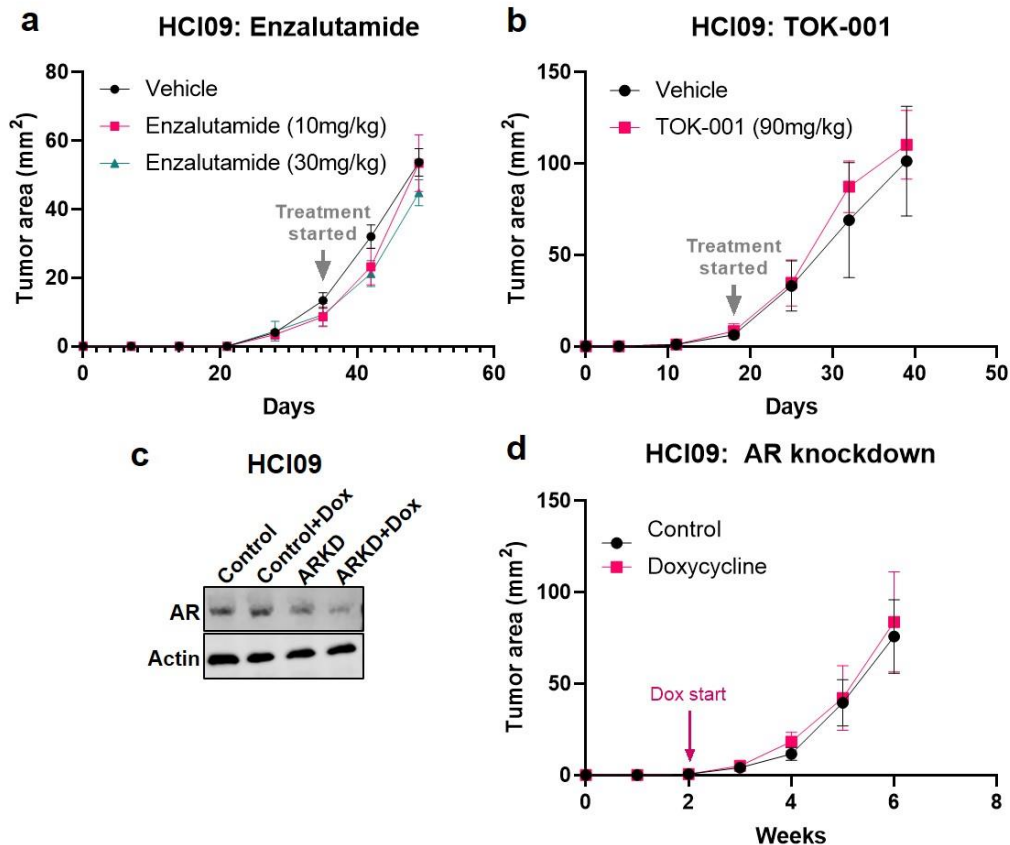


Figure 4.9: Targeting AR does not reduce PDX mammary tumor growth *in vivo*. **(a)** Mice bearing HCl09 mammary tumors were treated with enzalutamide (n=5) or vehicle (n=5) at the indicated doses. Graph depicts tumor area over time. **(b)** Mice bearing HCl09 mammary tumors were treated with TOK-001 (n=3) or vehicle (n=3) at the indicated doses. Graph depicts tumor area over time. **(c)** Western blot showing efficiency of doxycycline-induced AR knockdown in HCl09 cells expressing lentiviral shRNA (AR knockdown, ARKD, using AR658) vs control cells. **(d)** Mice bearing HCl09 mammary tumors expressing AR658 shRNA were fed control chow (n=2) or doxycycline chow (n=3) to induce AR knockdown. Graph depicts effect of AR knockdown on tumor growth (tumor area) over time. All p-values are listed in Table 4.3.

Table 4.3: P-values for *in vivo* experiments shown in Figure 4.9. *t*-tests were performed to compare each treatment condition (enzalutamide, TOK-001, or doxycycline-induced AR knockdown (ARKD)) with controls, at each indicated timepoint. Significant values ($p < 0.05$) are bolded and italicized.

Timepoint (Enza/TOK/ARKD)	Treatment (vs. control)			
	Enza 10mg/kg	Enza 30mg/kg	TOK 90mg/kg	ARKD Dox
Day 28/Day 18/Week 3	0.481618	0.823621	0.507158	0.581718
Day 35/Day 25/Week 4	0.05351	0.106762	0.885221	0.206605
Day 42/Day 32/Week 5	<i>0.046194</i>	<i>0.007275</i>	0.411243	0.86834
Day 49/Day 39/Week 6	0.961	<i>0.020859</i>	0.682492	0.748667

4.4.6 *AR expression correlates with expression of other potential drug targets in patients with AR-positive TNBC*

Given the prior findings, it is likely that AR inhibitors need to be combined with other drugs in order to achieve efficacy that is likely to translate into clinical success for patients with AR-positive disease. To search for potential candidates for combination with AR inhibitors, focusing particularly on AR-positive TNBC, we utilized the 1,363-drug screening dataset [190] along with the breast cancer TCGA dataset to identify drug targets whose genes correlate with AR expression and whose inhibitors are cytotoxic to LAR TNBC cells. Of the 115 TNBC patients in the TCGA dataset, we selected the patients with high AR expression (n=9) (**Fig. 4.10a**). Within this subset of patients, we performed Pearson correlation analyses between the expression of AR and the expression of all other genes in the dataset. We subsequently plotted these values against HCl09 cell viability data from the 1,363-drug screen, where a Pearson correlation value for a particular gene corresponded to the HCl09 cell viability in response to a drug targeting the protein encoded by that gene (**Fig. 4.10b**). Drug targets of interest, with the highest correlation with AR expression and the lowest cell viability (highest efficacy), were selected using a cutoff Pearson correlation value of 0.5 or higher and a cutoff cell viability value of 50% or lower (**Fig. 4.10c**). This analysis identified seven drug targets of interest, listed in order of decreasing correlation with AR expression: VDR, catechol-O-methyltransferase (COMT), potassium inwardly rectifying channel subfamily J member 5 (KCNJ5), FK506 binding protein 1A (FKBP1A), gamma-glutamyl carboxylase (GGCX), adenosine A3 receptor (ADORA3), and potassium voltage-gated channel subfamily A member 7 (KCNA7). These drug targets corresponded to 11 drugs of interest, which were cytotoxic to HCl09 cells: doxercalciferol/calcitriol/alfacalcidol, tolcapone/entacapone, fingolimod, rapamycin (sirolimus)/pimecrolimus, menadione, nifedipine, and amiodarone, respectively. Notably, most of these drugs were more effective in HCl09 than in PDX models of other breast

cancer subtypes (**Appendix A**). Pearson correlations for each gene of interest are shown in **Fig. 4.11a**, and expression levels for each gene across the nine patients are shown in **Fig. 4.11b**. Expression of all seven genes increased with increasing AR expression, although this was most robust for VDR, COMT, FKBP1A, and GGCX, which were consistently more highly expressed across the patients compared to KCNJ5, ADORA3, and KCNA7 (**Fig. 4.11b**).

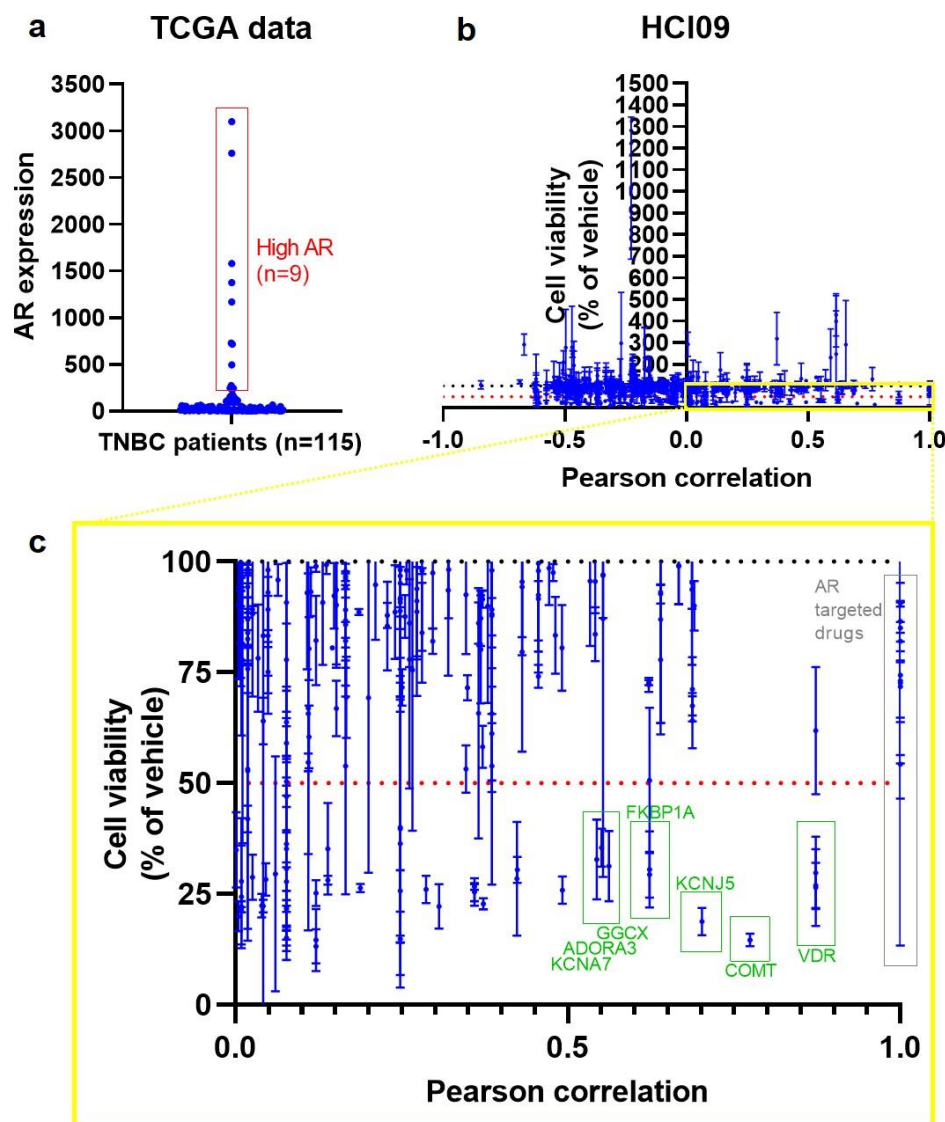


Figure 4.10: Identification of potential drug targets correlating with AR expression in patients with AR-positive TNBC. **(a)** AR expression levels (TPM values) in TNBC patients using the breast cancer TCGA RNA-sequencing dataset. Each point on the graph represents an individual TNBC patient's AR expression level (n=115). The red box indicates the 9 patients considered to have high AR expression compared to the rest of the TNBC patients. **(b)** Pearson correlations were performed between expression of AR and expression of all other genes in TNBC patients with high AR expression (n=9). HCl09 1,363-drug screening data were used to compare Pearson correlations for particular genes with LAR TNBC cell viability in response to drugs that target those genes. Graph depicts Pearson correlation values vs. HCl09 cell viability, with each point representing a particular drug. The region of interest highlighted with a yellow box is shown zoomed in **(c)**; this region depicts high Pearson correlation values and low cell viability values. The gray box represents drugs that target AR (for which Pearson correlation between drug target expression and AR expression is 1.0). The green boxes represent effective drugs whose target genes correlate strongly with AR expression (Pearson correlation > 0.5); labels indicate the genes encoding the proteins that the drugs in each green box target. Vitamin D receptor (VDR): doxercalciferol, calcitriol, alfacalcidol. Catechol-O-methyltransferase (COMT): tolcapone, entacapone. Potassium inwardly rectifying channel subfamily J member 5 (KCNJ5): fingolimod. FK506 binding protein 1A (FKBP1A): rapamycin (sirolimus), pimecrolimus. Gamma-glutamyl carboxylase (GGCX): menadione. Adenosine A3 receptor (ADORA3): nicardipine. Potassium voltage-gated channel subfamily A member 7 (KCNA7): amiodarone.

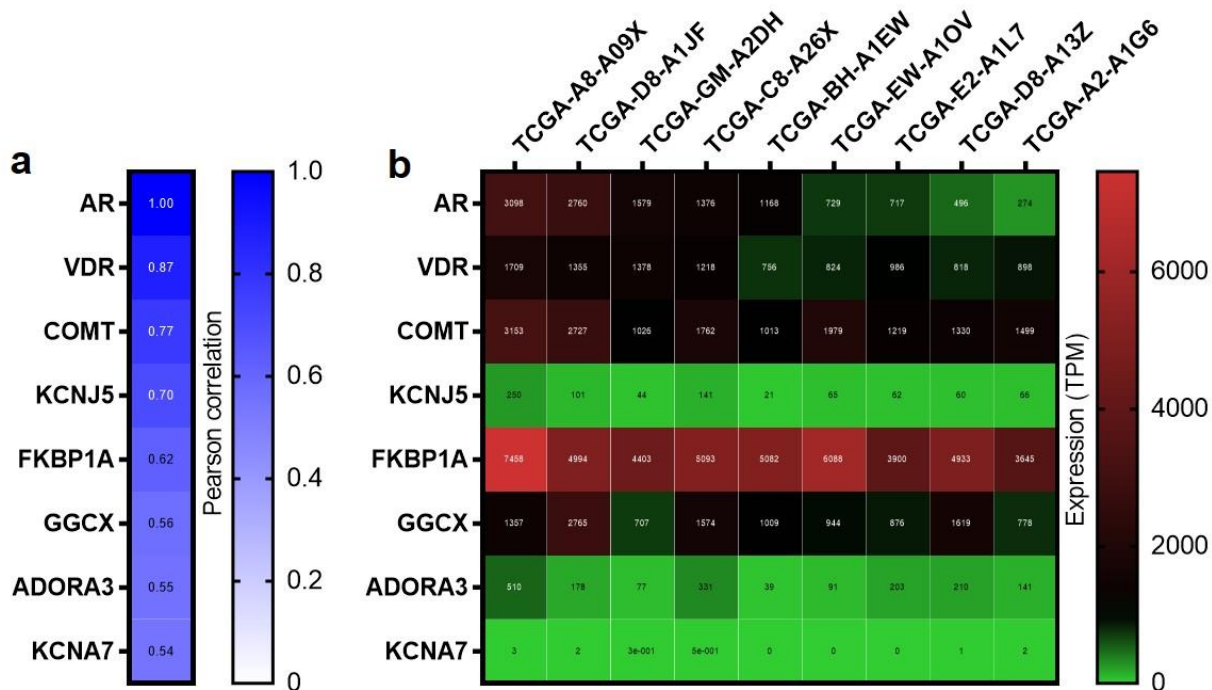


Figure 4.11: Relative expression of select genes of interest in patients with AR-positive TNBC. **(a)** Heatmap showing Pearson correlations between expression of AR and the indicated genes in AR-positive TNBC patients using TCGA data (n=9). Correlation values for each gene are indicated on the heatmap and the range is indicated in the color scale legend. **(b)** Heatmap showing TCGA expression data for the indicated genes in the nine individual patients. Patients are ranked by AR expression, and genes are ranked by correlation with AR expression. Expression values for each gene are indicated on the heatmap and the range is indicated in the color scale legend.

Notably, all seven genes (VDR, COMT, KCNJ5, FKBP1A, GGCX, ADORA3, and KCNA7) were weakly or negatively correlated with AR expression within the low-AR expression subset of TNBC patients and within all TNBC patients in the TCGA dataset (**Fig. 4.12a**). Although AR was expressed to some extent in the low-AR subset, and there were no considerable differences in expression of the seven genes between high-AR and low-AR TNBC groups (**Fig. 4.12b**), these findings indicate that the association of the genes with AR expression is specific to the strongly AR-positive subset of TNBC.

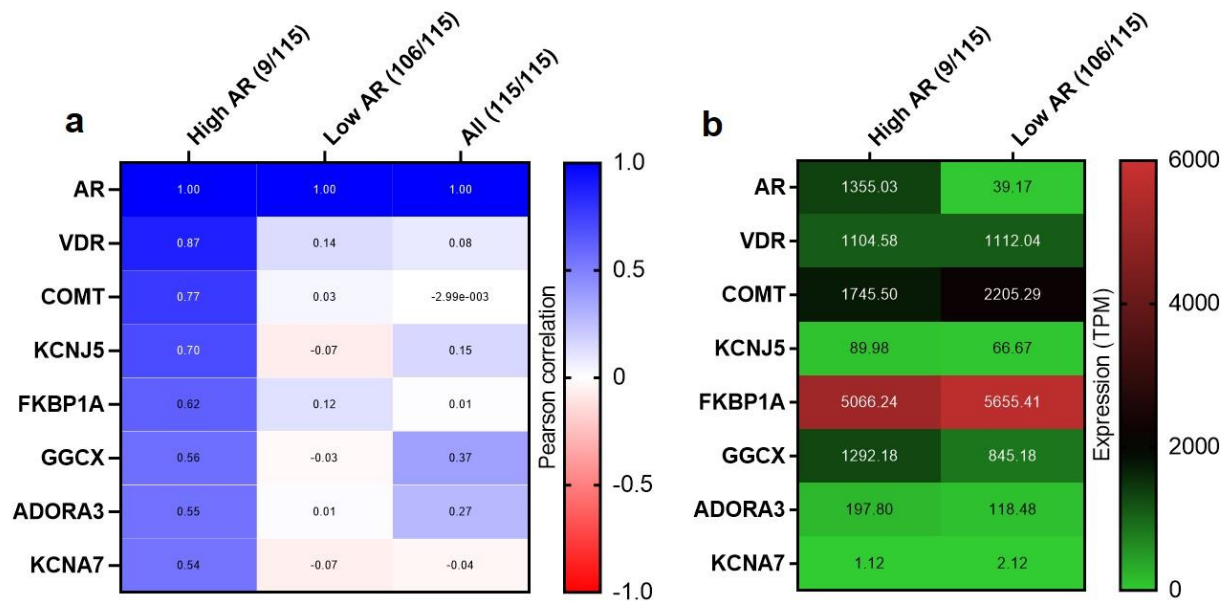


Figure 4.12: Relative expression of select genes of interest based on AR expression across TNBC patients. **(a)** Heatmap showing Pearson correlations between expression of AR and the indicated genes in different populations of TNBC patients from the TCGA dataset: patients grouped based on AR expression (High AR or Low AR) and all TNBC patients (All). **(b)** Heatmap showing relative expression of the indicated genes in High AR vs. Low AR TNBC patients. Fractions of total number of TNBC patients for each group are labeled on each heatmap. Correlation/expression values for each gene are indicated on the heatmaps and the ranges are indicated in the color scale legends.

To gain further insight into the importance of the identified genes, and thus their encoded drug targets, of interest in LAR TNBC, we utilized the PDX RNA-sequencing dataset along with two breast cancer cell line RNA-sequencing databases (CCLE and LINCS) to assess relative expression levels of the genes across breast cancer subtypes (**Fig. 4.13**). Correlation analyses of AR expression with other genes within the LAR TNBC subtype could not be performed using these datasets as each only contains one LAR TNBC model (HCI09 or MDA453), however patterns in gene expression could still be observed and compared between subtypes. As previously shown, AR expression was highest in the HCI03, HCI13, HCI08, and HCI09 PDXs (**Fig. 4.13a**) and MDA453 cell line (**Fig. 4.13b,c**) compared to other PDXs/cell lines, with the lowest expression in basal-like models. The seven genes of interest (VDR, COMT, ADORA3, KCNA7, KCNJ5, FKBP1A, GGCX) had

fairly consistent expression levels across PDXs and cell lines of different subtypes, with relatively higher overall expression of VDR, COMT, FKBP1A, and GGCX than ADORA3, KCNA7, and KCNJ5 (**Fig. 4.13a-c**), consistent with the TCGA data. Note that ADORA3 expression data were not available in the LINCS database, therefore analysis of this gene in cell lines was only performed using the CCLE database. Although, as with the TCGA data, no drastic differences in expression of the seven genes were observed between AR-positive and AR-negative models, COMT expression was moderately higher in the MDA453 model compared to other cell lines (**Fig. 4.13b,c**), and GGCX expression was slightly higher in AR-positive PDXs compared to AR-negative PDXs (**Fig. 4.13a**) and in LAR and mesenchymal TNBC cell lines compared to basal-like TNBC cell lines (**Fig. 4.13b,c**). Thus, although correlated with AR expression exclusively within AR-positive TNBC patients, these genes do not appear to be expressed or upregulated exclusively in LAR TNBC, i.e. the expression of the genes is not dependent on AR expression. These collective findings suggest that these genes may play roles in LAR TNBC that are distinct from their roles in other breast cancer subtypes, and that these distinctions cannot be solely attributed to differences in AR expression levels.

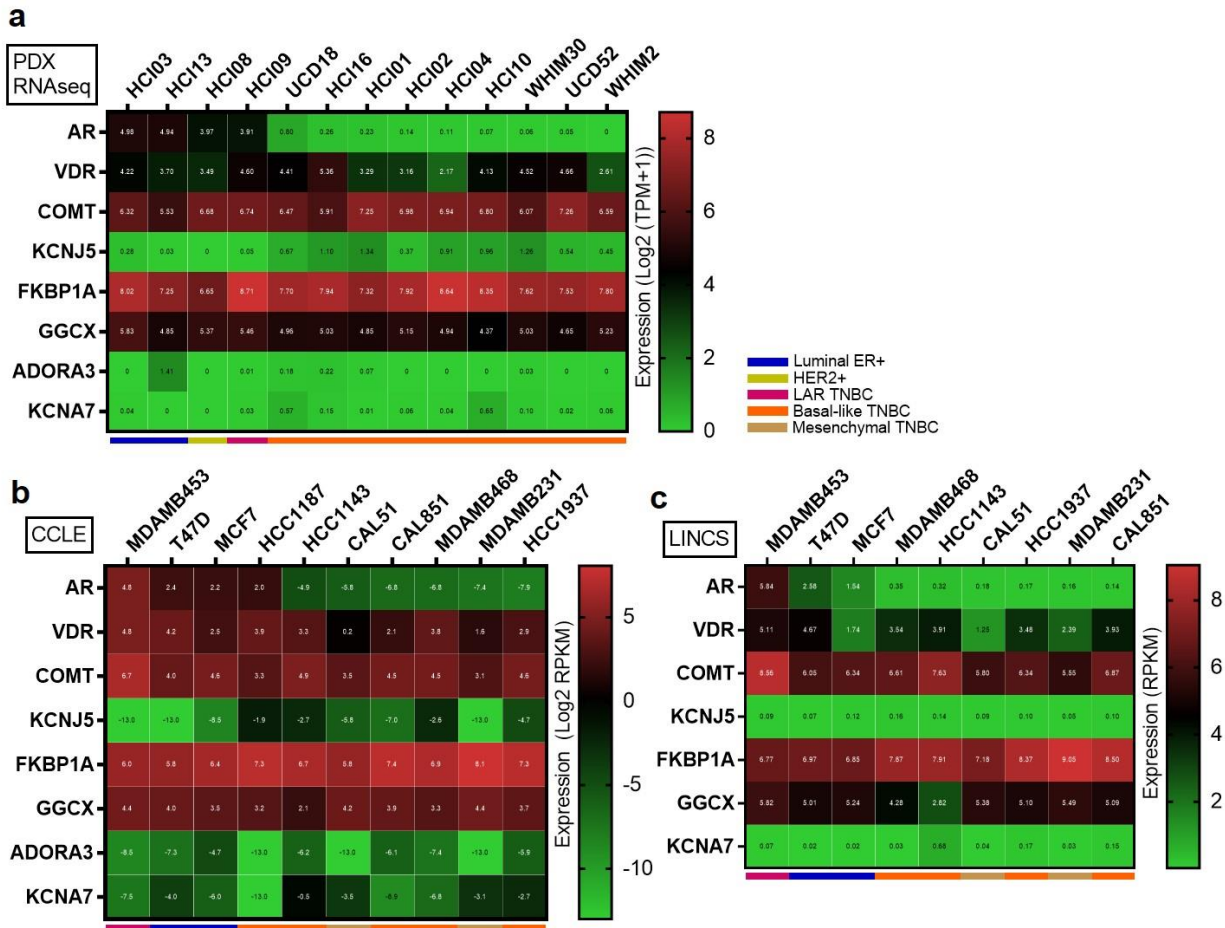


Figure 4.13: Relative expression of select genes of interest across breast cancer PDXs and cell lines. Heatmaps depict expression data for the indicated genes using (a) PDX RNA-sequencing data (averaged replicates where applicable), (b) cell line RNA-sequencing data from the CCLF database, and (c) cell line RNA-sequencing data from the LINC database. PDXs and cell lines are shown ranked by AR expression levels. Expression values for each gene are indicated on each heatmap and ranges are indicated in each color scale legend. Breast cancer subtypes of PDXs and cell lines are indicated by colored bars underneath each heatmap.

4.5 Discussion and conclusions

Previous studies have implicated AR as a potentially important therapeutic target in breast cancer, particularly in the luminal subtypes and the LAR subtype of TNBC, given the high levels of AR expression in these subsets of patients [70, 71, 74, 252]. Our analyses using patient data indicated that AR expression is highest in luminal tumors, which are typically ER-positive and associated with relatively favorable outcomes, and lowest in basal-like tumors, which are typically triple-negative and associated with relatively poor outcomes. However, when stratified

by ER status, AR expression was correlated with reduced relapse-free survival in patients with ER-negative tumors, suggesting that patients with AR-positive/ER-negative disease, many of which would fall into the LAR TNBC category, may be ideal candidates for AR-targeted therapy. These findings highlight the importance of further stratifying patients based on molecular tumor characteristics to predict clinical outcomes and to determine optimal therapeutic strategies.

Of the seven breast cancer PDXs and seven breast cancer cell lines tested, AR was expressed in five PDXs and four cell lines, of varying histologic and intrinsic subtypes. Of these, one PDX line (HCI09) and one cell line (MDA453) could be categorized as suitable models of LAR TNBC, consistent with previous data establishing MDA453 as a LAR TNBC model [70]. Of those remaining, three PDX lines (HCI03, HCI11, HCI13) and three cell lines (MCF7, T47D, ZR751) were classified as AR-positive/ER-positive, and one PDX line (HCI08) was classified as AR-positive/HER2-positive, making the latter an additional model that could be used to study AR in ER-negative disease. To determine the effect of targeting AR in these models, PDXs (HCI08, HCI09, HCI13) and cell lines (MDA453, MCF7, T47D) were treated with DHT (AR agonist) or enzalutamide (AR antagonist). Although DHT had stimulatory effects on the viability of HCI08 and T47D cells, and little to no effect on MDA453 and MCF7 cells, DHT was cytotoxic to HCI09 cells and did not considerably affect HCI13 cells. This was likely due to the intrinsic lack of cell proliferation in PDX suspension cultures, which we have observed previously with several PDX models [149]. In contrast, enzalutamide reduced cell viability across the PDXs and cell lines tested, with the greatest efficacy in the LAR TNBC models, validating the current interest in its use as a targeted therapeutic for AR-positive breast cancer. Given this efficacy of enzalutamide and its approved use as an AR inhibitor, it was therefore surprising that AR knockdown did not affect cell viability or abrogate the effects of enzalutamide in any of the three AR-positive cell lines tested. These findings suggest that enzalutamide may have off-target effects that are responsible for its efficacy in breast cancer cells. Indeed, another study found that enzalutamide and bicalutamide reduced proliferation of breast cancer

cells regardless of AR status [257], which is consistent with this class of drugs possibly having an AR-independent mechanism of action in breast cancer. Many drugs that are currently FDA-approved or undergoing clinical trials are known to have off-target effects [258, 259], and AR antagonists in particular have been shown to additionally inhibit other nuclear hormone receptors [260], gamma aminobutyric acid (GABA) receptors [261], and CYP27A1 (cytochrome P450 family 27 subfamily A member 1) [262]. At least some of these known off-target effects, or perhaps others that have yet to be identified, may be responsible for the AR-independent efficacy of enzalutamide and similar drugs in breast cancer, in contrast to the AR-dependent efficacy of these drugs in prostate cancer. Despite its *in vitro* efficacy, however, enzalutamide did not reduce HCl09 mammary tumor growth *in vivo*. Not surprisingly, AR knockdown also failed to produce anti-tumor effects *in vivo*. These findings suggest that monotherapeutic targeting of AR is not sufficient to treat LAR TNBC.

Using the PDX 1,363-drug screening dataset, we identified TOK-001 as a more effective and more potent AR-targeting agent compared to enzalutamide and other AR inhibitors. The drugs in this screen were tested at 10 μ M, a dose at which enzalutamide was not cytotoxic to any of the models previously tested *in vitro*. The efficacy of TOK-001 was also more specific to AR-positive PDXs, with the greatest efficacy in the LAR TNBC PDX model, HCl09. TOK-001 is a dual inhibitor of AR and CYP17A1 [263, 264], therefore it inhibits both the synthesis of androgens and the activity of AR, making it a drug of keen interest for prostate cancer studies [265] [NCT00959959, NCT01709734, NCT02438007]. Interestingly, this investigational drug has not yet been examined in the context of breast cancer. Although the efficacy of TOK-001 could not be validated through further *in vitro* and *in vivo* studies, the effects of TOK-001 were abrogated by AR knockdown, in contrast to enzalutamide. This finding, along with the differential efficacy of TOK-001 between AR-positive and AR-negative PDXs, suggest that this drug may target AR more specifically than enzalutamide and that its effects in breast cancer are likely AR-dependent. TOK-001 is therefore of great interest for further studies that seek to

identify synergistic combinations with other targeted agents in AR-positive breast cancer. This drug may also be of interest for testing in ER-positive disease, given that CYP17A1 is upstream of the precursor for estrogens, and thus CYP17A1 inhibition would affect the synthesis of estrogens in addition to androgens.

To preliminarily search for potentially promising drug targets and candidates for combination with AR inhibitors in LAR TNBC, we utilized the breast cancer TCGA gene expression dataset to determine genes that correlate strongly with AR expression in patients with AR-positive TNBC, along with the HCl09 drug response data from the 1,363-drug screening dataset to determine which of the drugs that target the proteins encoded by those genes were cytotoxic to LAR TNBC cells. Using this approach, we identified several drugs and drug targets of interest for future combination studies. Interestingly, none of these drugs or their target pathways are currently approved for any type of cancer treatment: vitamin D analogs (doxercalciferol, calcitriol, alfacalcidol), COMT inhibitors used for Parkinson's disease (tolcapone, entacapone), immunosuppressive agents (sirolimus, pimecrolimus), an antiarrhythmic agent (amiodarone), an antihypertensive agent (nicardipine), an immunomodulator used for multiple sclerosis (fingolimod), and a vitamin K precursor (menadione). Although the genes encoding the targets of these drugs (VDR, COMT, FKBP1A, KCNA7, ADORA3, KCNJ5, and GGCX, respectively) were not differentially expressed between AR-positive and AR-negative PDXs, cell lines, and patients, the positive correlation of their expression with AR expression was exclusive to strongly AR-positive TNBC patients. Thus, although the expression of these genes appears to be independent of AR expression levels, the findings suggest potential distinct roles of these genes in AR-positive versus AR-negative TNBC that are not solely due to the extent of expression of AR.

Although the drugs listed above are not currently used clinically to treat cancer, some of their target pathways have been implicated in cancers of the breast and other organs. VDR expression was the most highly correlated with AR expression in AR-positive TNBC patients,

and co-targeting of AR and VDR has been shown to be effective in TNBC cell lines expressing both genes [257]. VDR is expressed in over 25% of TNBCs and has been shown to negatively correlate with proliferation index and tumor grade and positively correlate with overall survival [266], suggesting that VDR agonists, such as calcitriol, may have therapeutic benefit in TNBC patients. Indeed, several studies have demonstrated promising anti-tumor activity of calcitriol and other vitamin D analogs in preclinical TNBC models [267–272]. Interestingly, one of these studies combined calcitriol with menadione [272], another drug of interest identified in the analyses performed herein. Menadione, a vitamin K3 analog, and other vitamin K compounds are known to have anticancer activity in many tumor types, including TNBC, by inhibiting proliferation and migration and promoting apoptosis by inducing oxidative stress [273–277]. The role of vitamin K specifically in AR-positive TNBC is currently unknown. However, one of the major pathways characterizing LAR TNBC tumors is glutathione metabolism [70], and glutathione functions to reduce vitamin K so that it can act as a cofactor for the GGCX enzyme, which catalyzes the gamma-carboxylation and consequent activation of coagulation factors. Interestingly, AR is also gamma-carboxylated by GGCX, which stabilizes the protein [278, 279]; this may explain mechanistically why GGCX expression is correlated with AR expression in AR-positive tumor cells, as the studies herein have revealed to be the case in AR-positive TNBC patients. These findings further suggest that GGCX and vitamin K may play a role in this subtype. Furthermore, studies have shown that inhibition of vitamin K epoxide reductase (VKOR) using the anticoagulant warfarin reduces AR signaling and activity [279], and that vitamin K reduces AR expression and exerts antitumor activity in androgen-dependent prostate cancer [280]. Similarly, the VKOR antagonist phenprocoumon, another anticoagulant, synergizes with the AR inhibitor flutamide in prostate cancer by preventing its gamma-carboxylation, thus leading to AR degradation and sensitizing the cancer cells to AR inhibitor treatment [278]. The same group recently filed a patent application focused on combining AR inhibitors with vitamin K antagonists in prostate cancer and other AR-positive cancers,

including breast cancer [281]. Given the parallels between LAR TNBC and androgen-dependent prostate cancer, these findings collectively suggest that vitamin K pathways may indeed play a role in both diseases.

COMT, whose expression was the second most highly correlated with AR expression, encodes an enzyme which degrades not only catecholamines such as dopamine, but also catechol-estrogens, which are metabolites of estradiol and estrone [282] that have been implicated in carcinogenesis in various hormone-sensitive tissues [283–286]. Although past studies have shown that polymorphisms in the COMT gene are not associated with breast cancer risk [287, 288], the COMT protein has recently been associated with lymph node metastasis and tumor grade in TNBC [289]. Furthermore, COMT inhibition has been shown to enhance the proteasome inhibitor activity of epigallocatechin gallate (EGCG), a component of green tea, in MDA231 cells [290]. These findings collectively suggest that COMT may play different roles in hormone receptor-positive versus triple-negative disease. However, the role of COMT in AR-positive TNBC has not yet been explored.

Amiodarone, a potassium-channel blocker, was identified as a drug of interest for LAR TNBC given the correlation of its drug target (KCNA7) with AR expression and its cytotoxicity in HCl09 cells. Potassium channels have been shown to promote cancer cell proliferation and migration, as well as angiogenesis [291, 292]. Likewise, potassium channel blockers, such as amiodarone, have demonstrated efficacy in several solid tumor types [293, 294], including breast cancer [295, 296], consistent with the PDX drug screening data presented herein. One study found that amiodarone potentiates the cytotoxic effects of tamoxifen in both MCF7 (ER-positive) and MDA231 (TNBC) cells [295]. A more recent study showed that dronedarone was cytotoxic to breast cancer cell lines of varying subtypes *in vitro*, with similar IC₅₀s in both basal-like (MDA468 and others) and LAR (MDA453) TNBC, however *in vivo* validation studies were performed using a HER2-positive cell line model [296]. Follow-up studies focusing on

potassium channel inhibition in TNBC in general or LAR TNBC specifically have not yet been performed.

Fingolimod is currently approved for multiple sclerosis based on its activity as a sphingosine 1-phosphate (S1P) receptor antagonist, however, through initial transient activation of S1P receptors, the drug also activates G-protein-coupled inwardly-rectifying potassium (GIRK) channels, leading to its cardiovascular side effects [297]. In the analyses performed herein, fingolimod was identified as a drug of interest for LAR TNBC due to its efficacy in HCl09 cells as well as the correlation of the expression of KCNJ5 (which encodes GIRK4) with AR expression in AR-positive TNBC patients. Fingolimod has demonstrated promising anticancer activity in TNBC due to its inhibition of S1P receptor signaling [298], which is associated with increased metastasis and reduced patient survival [299, 300]. However, it is possible that its efficacy in breast cancer may additionally be due to its targeting of GIRK channels. GIRK channels are known to be expressed in breast cancer, with GIRK4 being the most common across cell lines of varying breast cancer subtypes, including the LAR TNBC cell line MDA453 [301, 302]. GIRK1 is associated with lymph node metastasis in breast cancer patients, irrespective of subtype [303], and knockdown of GIRK1 in MDA453 cells was shown to inhibit MAPK and PI3K signaling [304], suggesting that inhibition of GIRK1 may have anticancer effects. However, the role of GIRK4 in breast cancer is currently unknown. Further studies are warranted to explain why activation of GIRK4 by fingolimod may be cytotoxic to TNBC cells, and to determine how this mechanism may be related to AR status, given that KCNJ5 (GIRK4) expression was found to be correlated with AR expression in patients.

Sirolimus and pimecrolimus were identified as drugs of interest in LAR TNBC due to their efficacy in HCl09 cells as well as the correlation of FKBP1A expression with AR expression in patients. By forming a complex with FKBP12 (encoded by FKBP1A), these drugs inhibit mTOR, thereby blocking the G1-S transition of the cell cycle and, consequently, proliferation [305, 306]. This makes mTOR inhibitors useful not only for preventing rejection in organ transplant

recipients by suppressing immune cell responses, which is their currently approved indication, but also for hindering cancer progression by blocking cancer cell proliferation and other malignant processes. In breast cancer, mTOR is commonly activated and plays a prominent role in tumor progression, therefore it has been widely studied as a potential therapeutic target in this disease [307–309]. Clinical trials testing the mTOR inhibitor everolimus in TNBC have thus far been unsuccessful [310, 311], however it is possible that stratifying patients based on TNBC subtype, particularly AR status, could increase the likelihood of clinical success. Activating mutations in PI3K, upstream of mTOR, are particularly prevalent in LAR TNBC cells [70], including the HCl09 PDX model used in the studies herein, and co-targeting of AR and PI3K has shown promising efficacy in PIK3CA-mutated LAR TNBC xenograft models [75], thus it stands to reason that mTOR inhibitors may be similarly effective in this subtype. One study using several PDX models found that response to the mTOR inhibitor everolimus was not associated with particular TNBC subtypes or PIK3CA mutation status [312], whereas another study demonstrated that the mTOR inhibitor deguelin had selective activity in LAR TNBC cells (MDA453) compared to all other TNBC subtypes, in addition to showing promising efficacy of combination therapy with sirolimus and enzalutamide in MDA453 xenografts [313]. It is possible that the LAR-selectivity of deguelin in the latter study was due to its dual inhibition of mTOR and AR [313], however further investigation is warranted to validate the findings of both these studies in additional models.

Finally, the dihydropyridine (DHP) calcium channel blocker nifedipine, which is currently approved to treat hypertension, was also identified as a drug of interest for LAR TNBC. Studies on calcium channel blockers in cancer are limited and somewhat conflicting. Efficacy of nifedipine and amlodipine has been demonstrated in GBM [314] and neuroblastoma [315], respectively. In contrast, a study found that nifedipine exerted pro-tumorigenic effects in breast cancer cell lines [316], whereas nifedipine and other DHPs were found to sensitize TNBC cells to proteasome inhibitors [317] through their inhibition of the multidrug efflux transporter

BCRP (ABCG2) [318]. In addition to its targeting of DHP calcium channels (intended target) and BCRP, nicardipine also targets the G protein-coupled A3 adenosine receptor (ADORA3) [319], and DHP calcium channel blockers in general have been shown to interact with adenosine receptors [320]. DHP derivatives such as nicardipine are antagonists of the A3 adenosine receptor specifically [321, 322], and our analyses indicated that ADORA3 expression was positively correlated with AR expression in AR-positive TNBC patients. Adenosine receptors are known to play a role in cancer progression and have been implicated as potential targets in various cancers, with the effects of agonism versus antagonism depending on the target receptor subtype [323–329]. In breast cancer, ADORA3 agonism has been shown to promote apoptosis of breast cancer stem cells [329]. Interestingly, A3 adenosine receptors are also highly expressed in androgen-dependent prostate cancer [330], and the endogenous A3 agonist adenosine is cytotoxic to prostate cancer cells [331]. These findings are paradoxical considering the efficacy of the A3 receptor antagonist nicardipine in the present study. Further studies are needed to determine whether the efficacy of nicardipine in LAR TNBC cells is mediated by ADORA3 and/or DHP calcium channels, and how these pathways may relate to AR signaling.

In conclusion, the studies reported herein suggest that AR inhibition alone is not sufficient to successfully treat LAR TNBC, and it is therefore imperative to identify additional pathways that may be targeted along with AR inhibitors to achieve optimal efficacy. Collectively, our studies provide multiple drug candidates and targets that warrant further investigation in AR-positive TNBC, both alone and in combination with AR-targeted agents. Although other studies have provided evidence that many of these drugs exhibit activity in breast cancer and other cancers, much remains to be explored regarding their efficacy and mechanisms in AR-positive disease. Furthermore, given that all these drugs are currently FDA-approved, albeit for other indications, successful preclinical studies may be more expeditiously translated to the clinic

relative to investigational compounds. Repurposing of such drugs has the potential to provide rapid clinical benefit for this unique subset of TNBC patients.

4.6 Future directions

Future studies will focus on performing further testing of the eleven drugs identified as both cytotoxic in the HCl09 PDX model and related to AR expression in patients, as well as exploring the role of their drug targets and associated pathways in AR-positive TNBC. These studies will employ both the HCl09 PDX model and the MDA453 cell line. The drugs will be tested in dose escalation studies as single agents, followed by combination studies with the AR inhibitor TOK-001, using Chou-Talalay analysis to assess for synergistic effects. It would also be of interest to test TOK-001 analogs that have been shown to have greater efficacy and pharmacokinetic profiles in prostate cancer [332]. Promising combinations will then be validated *in vivo* in both the primary and metastatic setting. Given that AR expression was shown to be maintained in HCl09 liver metastases, we expect that treatments effective in reducing mammary tumor growth will maintain their efficacy in the metastatic setting, consistent with our previous findings regarding chemotherapeutic efficacy in basal-like PDX models [149]. Mechanistic analyses will involve inhibition or ablation of drug targets and key molecules in their associated pathways, especially for the drugs that have been shown to target multiple proteins that may play a role in tumor progression and/or be related to AR activity. Additionally, it would be interesting to perform RNA-sequencing on tumors before and after drug treatment to reveal consequent changes in gene expression. This would not only provide additional mechanistic insights, but also shed light on potential alternative therapeutic targets. Lastly, it would be important to test promising drugs and combinations in AR-positive and AR-negative models of other breast cancer subtypes, which would provide insight into the specificity of these agents for LAR TNBC as well as identify potentially effective agents in other subtypes of the disease, including ER-positive and HER2-positive breast cancers that may be refractory to standard therapies.

CHAPTER 5: Overall impact and implications of this work

The studies presented herein collectively provide valuable tools and insights to the field of translational breast cancer research. Namely, this work highlights the utility of clinically relevant PDX models for both *in vitro* and *in vivo* drug response studies in the primary and metastatic setting, identifies promising pharmacologic candidates for two distinct subtypes of TNBC, and provides data and examples of analytic approaches that can be used to inform many future drug development studies to advance therapeutic strategies for all breast cancer subtypes.

We have demonstrated that breast cancer PDX cells in suspension culture maintain the molecular profiles of parental mammary tumors, validating the use of these models for *in vitro* drug screening studies to rapidly identify drug candidates of interest for further testing. Indeed, using this *in vitro* approach, we generated a dataset compiling the responses of ten breast cancer PDXs, representing each subtype, to 1,363 drugs with a wide variety of mechanisms of action and clinical indications. This led to the identification of a promising drug combination for basal-like TNBC, as well as the identification of several potential therapeutic candidates for combination with AR-targeted therapies in LAR TNBC, each of which shed light on major potential areas of future investigation for translational research in the most clinically challenging subtype of breast cancer. These are merely two examples of the utility of these data. The 1,363-drug screening dataset provides countless opportunities for breast cancer drug development research, as it can inspire and inform research focusing on drug development in particular breast cancer subtypes, repurposing of drugs not currently indicated for cancer, and/or uncovering potentially important pathways in breast cancer, all of which the studies reported herein have exemplified in basal-like and LAR TNBC. The data may also provide insight into drugs or pathways of interest for testing in other cancer types. Furthermore, given that most of the drugs in the screening library are FDA-approved, it is likely that promising preclinical research could be expeditiously translated to the clinical setting to provide immediate benefit to patients.

In addition to highlighting the value of *in vitro* drug screening using PDXs, we have shown that the molecular profiles of mammary tumors are maintained in the metastatic setting, and that PDX metastases have drug response profiles similar to those of primary tumors despite the cells growing in a foreign microenvironment, indicating that the results of drug studies performed using PDX mammary tumor models can be applicable in the setting of advanced disease. Our studies further demonstrated that multiple PDX models of the same histologic and intrinsic subtype respond differently to standard-of-care chemotherapies, mirroring one of the major limitations currently faced in the clinic and emphasizing the critical need for discovery of novel biomarkers with better precision and predictive power. Indeed, these studies shed light on the existence of different subpopulations of tumor cells that preferentially seed and form metastases in distinct sites, and the differential existence of these subpopulations between PDXs of the same breast cancer subtype paralleled the differential responses of these PDXs to chemotherapy. The efficacy of afatinib and YM155 in both of these PDXs as well as others within the basal-like TNBC subtype, along with the impact of co-expression of their drug targets on patient outcomes, provide a good example of how novel therapeutic strategies and potential biomarkers may be discovered by integrating drug screening data with gene expression data. This approach led to the identification of a drug combination that was effective across multiple basal-like TNBC models that respond differently to the therapies that patients with this subtype of breast cancer are currently receiving in the clinic. Furthermore, it led to the identification of several drug candidates whose target pathways may play important roles in LAR TNBC. Given the heterogeneity of TNBC and the failure of many targeted therapies in clinical trials, even when combined with standard-of-care therapeutics, the identification of novel therapeutic combination strategies for distinct TNBC subtypes is critical for improving the likelihood of clinical success. These studies have the potential to provide not only clinical benefit for these subsets of breast cancer patients, but also insights for many future studies that seek to build on these findings or to identify additional therapeutic candidates and strategies for TNBC and other breast cancer subtypes.

We hope that the data presented herein will be useful for many future translational research endeavors both within and outside of our lab, and that the findings resulting from these data will eventually lead to the implementation of therapeutic advancements that will improve clinical outcomes and quality of life for patients with breast cancer.

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APPENDIX A

Adapted from [190]

Appendix A: PDX 1,363 drug screening dataset
Cell viability data are listed for each PDX in response to each drug (10uM). The 176 drugs selected for TNBC studies are **bolded**.

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)			ER-positive (luminal)				HER2-enriched				
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	UCD52	WHIM2	WHIM2	WHIM30	WHIM30	WHIM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108	
(+)-Ketozonazole	B1240	KCNA10	112.80	190.12	103.02	42.69	46.53	127.33	140.81	102.71	86.93	33.42	25.59	118.95	87.92	105.77	92.01	64.51	89.21				
(+)-Octopamine HCl	B1995	TAAR1	93.36	108.24	119.82	102.53	79.61	82.56	93.91	149.59	149.19	100.18	85.73	119.00	98.27	130.84	255.84	118.50	97.22				
(6-)-Aminocaproic acid	B2076	PLA	41.57	94.06	101.31	73.57	80.61	83.77	117.63	138.50	170.76	100.95	79.04	135.99	79.60	107.19	100.10	33.90	89.94				
(R)-Crisotinib	A3020	MET	76.48	43.57	41.86	25.67	20.44	36.89	41.62	105.79	144.18	22.09	27.45	134.77	89.56	141.19	142.45	38.69	101.77				
(S)-Flurbiprofen	C5264	PTGS1, PTGS2	98.55	120.36	106.54	104.80	101.40	93.89	112.11	102.40	110.40		83.18	137.95	78.62	97.75	99.63	112.57	78.65				
Deacetylase (CKAP5)	A4395	CKAP5	124.40	151.07	125.74	81.23	77.19	72.36	97.05	120.51	130.67	100.84	97.82	107.37	108.38	95.99	99.61	133.95	118.55				
17-AAG (KOS953)	A4054	HSP90AA1	78.95	130.66	106.15	95.41	87.83	63.16	63.35	79.12	90.99	27.25	26.17	57.08	72.52	371.11	206.18	118.47	110.16				
1-Hexadecanol	B1651	N/A	105.06	110.53	108.75	62.91	71.29	86.67	101.75	90.66	78.76	106.41	89.28	95.89	95.17	166.06	48.04	146.98	69.01				
2-Methoxyestradiol (2-MeOE2)	A4188	HIF 1A	135.58	146.92	120.81	100.17	89.96	108.80	118.66	134.42	165.86	86.04	103.53	110.38	117.44	188.46	174.28	101.02	148.44				
2-Thiouราซิล	B1872	TPO	111.14	102.45	111.82	93.83	89.81	93.33	140.70	182.01	173.69	107.60	81.20	138.88	102.60	88.17	76.59	137.92	102.30				
5-Aminolevulinic acid HCl	B2070	N/A	58.07	108.31	164.08	77.22	87.93	111.46	145.66	141.34	150.71	91.52	88.22	131.81	83.23	96.62	130.18	35.54	143.38				
5-Azacytidine	A1907	N/A	60.47	49.67	102.86	56.06	50.79	24.83	45.31	184.72	211.81	22.76	31.70	85.05	169.62	59.61	46.66	104.35	145.28				
5-Methoxypsoralen	N1304	N/A	85.58	120.16	109.08	94.45	75.91	100.25	105.54	90.79	95.21	102.50	83.69	142.13	93.83	122.76	118.41	147.97	48.73				
8-Methoxypsoralen	N1305	N/A	104.27	128.37	106.42	106.76	88.90	113.51	96.65	99.15	96.65	99.15	104.06	94.88	146.93	104.13	111.65	130.05	160.56	43.71			
Abacavir	A3139	N/A	148.47	197.73	121.24	266.60	241.96	198.82	158.63	455.70	348.59	427.56	260.41	208.52	117.72	214.39	172.37	355.50	198.72				
Abacavir sulfate	B2220	N/A	170.15	151.71	156.56	192.52	124.19	131.52	248.89	227.97	209.08	236.51	207.06	139.00	122.45	145.24	557.19	176.15					
Abiraterone	A4240	CYP17A1	133.02	143.00	110.60	100.66	87.62	126.98	135.61	171.35	139.91	89.40	82.84	167.88	76.60	174.28	115.38	160.33	119.90				
Abiraterone acetate	A8202	CYP17A1	86.71	106.67	97.98	61.28	64.00	81.18	109.86	152.87	80.74	45.79	85.73	87.61	88.74	59.81	76.25	167.61	83.97				
ABT-199	A8194	BCL2	123.04	44.74	80.05	91.26	111.34	173.66	129.13	136.75	62.01	40.52	82.53	279.38	68.36	121.99	136.52	77.87	49.05				
ABT-263 (Navitoclax)	A3007	BCL2	26.61	29.39	29.64	38.13	34.81	29.21	35.05	40.70	29.78	24.07	19.63	44.23	47.09	34.34	33.26	21.75	63.26				
ABT-888 (Veliparib)	A3002	PARP1	104.13	114.77	91.06	92.82	95.60	110.93	90.96	123.55	117.65	111.50	104.07	105.04	109.48	88.25	108.14	125.48	109.92				
Acetabosol	A2431	GAA	105.16	118.81	78.53	100.17	86.45	74.10	97.94	124.41	82.83	92.92	105.04	120.20	100.40	96.49	77.25	109.48	99.52				
Acetaminophen	B1330	ADRB1	128.86	120.72	156.20	92.07	102.04	92.35	104.98	131.64	131.55	117.71	86.31	123.35	106.35	74.10	78.59	118.78	107.91				
Acemetacin	B1440	PTGS1, PTGS2	110.66	105.65	105.63	74.69	81.77	71.42	102.41	84.45	68.80	117.85	77.38	113.20	97.44	104.40	117.12	113.85	73.70				
Acetaminophen	B3532	PTGS1, PTGS2	76.74	111.13	126.29	107.04	97.31	92.37	93.05	99.87	94.97	103.54	93.29	100.69	80.44	106.50	126.21	108.61	78.19				
Acetaminophen	B2071	PTGS1, PTGS2	45.52	107.68	138.39	66.25	84.14	115.99	135.99	222.64	216.46	104.36	94.00	163.10	81.79	116.02	104.51	37.17	105.65				
Acetylcholine Chloride	B1596	Chrm1	87.75	120.77	97.84	70.61	68.09	91.82	101.49	121.93	92.32	100.45	89.81	85.78	87.11	107.61	94.04	117.25	76.98				
Acetylcysteine	A8356	N/A	96.79	86.41	118.15	90.32	89.65	122.84	125.38	106.74	86.91	105.71	82.89	112.59	90.02	116.33	78.35	102.30	106.76				
Acipimox	B2072	HCAR2	44.25	107.92	102.69	75.47	83.76	106.78	108.74	211.84	199.520	110.45	86.55	159.02	78.88	92.43	87.66	93.09	33.89	96.87			
Acitretin	A2415	RARA	106.57	120.34	76.70	124.17	136.45	79.40	101.57	174.29	114.74	81.16	100.68	72.42	86.49	92.11	73.85	161.65	91.13				
Acidinium Bromide	B1609	CHRM1	103.02	122.48	93.87	69.87	89.53	79.26	90.08	113.90	98.40	108.00	99.08	131.46	94.25	180.13	189.01	144.59	75.87				
Acyclovir	A8644	N/A	97.74	107.93	87.83	83.14	99.10	94.04	97.95	121.63	94.56	21.10	90.78	106.89	113.29	163.40	144.69	128.81	90.14				
Adapalene	A1267	RARA	114.40	123.02	82.71	198.23	159.28	75.07	92.62	126.07	101.25	64.20	120.26	81.36	95.52	155.33	122.35	108.40	80.53				
Adapalene sodium salt	B1277	RARA	94.94	135.97	158.07	170.60	143.10	111.73	97.03	101.68	91.99	88.10	140.71	81.89	98.35	181.45	184.90	85.62	107.75				
Adefovir Dipivoxil	B2222	N/A	78.97	139.53	129.49	94.27	107.77	48.01	53.23	250.41	248.26	89.50	35.97	148.31	104.90	50.13	37.09	163.52	88.04				
Adenine HCl	B1471	N/A	117.31	131.01	146.87	161.08	169.39	103.30	109.43	106.48	95.72	115.41	108.85	125.75	117.07	80.39	95.08	134.88	102.56				
Adenosine	B1877	Adora1	97.12	102.24	97.72	98.24	93.23	97.13	145.83	112.93	135.35	101.19	79.53	123.12	96.90	69.33	63.01	144.71	89.49				
Adiphenine HCl	B1878	CHRNA2, CHRNA4, CHRNA6, CHRNA7																					
Adrenalone HCl	B1331	ADRA1A, ADRA1B, ADRA1D	125.94	95.77	151.87	95.97	103.80	86.56	89.01	111.41	101.20	114.54	93.72	115.78	107.33	83.30	93.65	106.91	101.53				
Afatinib (BIBW2992)	A8247	EGFR	25.43	25.78	55.40	18.44	18.97	32.79	36.42	48.71	39.82	16.35	13.84	47.72	73.47	44.50	42.32	23.28	37.60				
Afatinib dimaleate	A3145	EGFR	33.19	37.36	30.70	45.27	34.86	38.23	44.00	59.52	49.66	38.17	32.20	53.82	32.55	33.92	30.89	46.39	30.39				
Agomelatine	B2262	HTR2A	85.33	99.70	104.60	94.46	77.78	75.77	104.12	143.99	127.92	102.97	96.37	138.90	92.43	87.84	90.94	143.57	86.48				
Albendazole	A8358	N/A	192.64	139.25	160.42	77.95	112.87	103.22	142.54	234.38	206.65	196.59	147.26	130.63	93.57	134.87	120.05	430.18	223.70				
Albendazole Oxide	B1880	N/A	107.25	122.89	106.27	94.74	110.48	87.88	135.96	140.75	142.38	135.14	85.74	143.95	104.99	74.92	61.54	172.50	101.38				
Alcathadine	B3518	HRH1	72.29	115.83	123.55	99.63	85.24	100.34	95.52	109.58	119.35	81.71	106.85	117.22	86.86	105.96	133.57	124.36	92.71				
Alendronate	B2073	FDPS	80.79	98.45	109.10	81.17	108.31	108.08	100.88	89.87	105.10	93.96	76.31	123.21	69.49	102.76	109.96	113.96	99.68				
Alendronate sodium	A8359	FDPS	96.20	107.14	97.06	74.93	83.08	84.62	100.84	121.87	110.01	107.58	82.62	111.13	97.32	94.78	100.30	147.07	98.18				

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)			ER-positive (luminal)			HER2-enriched				
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	WHM2	WHM2	WHM30	WHM30	WHM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108	HC108
Alfuzosin HCl	A5173	ADRA1A	101.12	105.35	112.72	85.62	97.55	83.32	87.57	139.03	126.51	111.25	98.79	97.40	112.60	83.39	117.99	83.39	117.99	133.05	133.05	143.20
Alibendol	B1881	N/A	85.83	110.83	133.34	111.45	106.68	98.20	131.35	123.30	152.22	118.88	94.84	139.23	110.03	64.42	71.49	64.42	71.49	171.09	171.09	107.63
Aliskiren Hemifumarate	B2215	REN	109.36	125.26	147.68	98.67	117.22	112.65	132.62	150.09	130.48	100.73	112.75	157.33	97.25	105.12	108.15	105.12	108.15	131.82	131.82	117.86
Allopurinol	A8360	XDH	104.98	117.18	103.48	82.19	86.83	97.14	97.84	116.09	127.51	103.69	84.83	131.72	109.77	106.99	90.75	106.99	90.75	131.60	131.60	97.25
Allylthiourea	B1882	N/A	90.98	101.91	106.93	154.50	104.37	83.31	132.40	124.27	135.57	107.56	80.69	118.28	97.44	74.92	54.76	74.92	54.76	147.60	147.60	95.31
Almotriptan Malate	B2243	HTR1B	108.73	101.70	143.97	84.69	90.73	90.48	90.71	128.75	140.03	98.96	107.44	132.04	86.49	79.30	90.28	79.30	90.28	153.30	153.30	101.99
Allogliptin (SYR-322)	A4038	DPP4	122.02	113.81	113.19	108.82	108.91	107.57	120.54	112.28	121.69	95.75	83.23	112.05	112.39	133.24	96.05	133.24	96.05	108.03	108.03	97.40
Alprostadil	B2154	PTGER1	32.64	140.30	175.12	125.70	122.48	138.25	154.96	144.39	137.47	91.70	197.90	124.31	103.93	289.73	237.43	289.73	237.43	31.68	31.68	142.84
Altretenogest	B1503	PGR	132.36	121.58	149.98	78.47	87.69	98.44	115.04	146.97	134.44	56.11	74.80	124.72	78.66	131.74	142.54	131.74	142.54	142.51	142.51	95.39
Altretenamine	A2559	N/A	86.96	102.63	108.37	81.53	74.55	119.11	111.09	108.87	109.92	87.72	91.47	96.71	96.84	75.48	80.27	75.48	80.27	82.67	82.67	93.55
Alvelestat	B1037	ELANE	106.63	121.55	114.27	99.26	99.90	80.49	102.78	99.07	86.97	193.43	90.85	118.92	134.68	174.40	143.94	174.40	143.94	147.42	147.42	101.29
Alverine Citrate	B1655	HTR1A	101.96	96.93	117.57	60.54	59.31	85.75	91.38	91.74	112.82	110.71	96.34	95.52	94.58	193.22	186.37	193.22	186.37	118.49	118.49	65.60
Amanatadine HCl	B1486	DRD2	123.57	148.08	132.31	94.76	91.83	94.71	118.99	103.83	105.88	105.05	103.11	117.01	98.74	114.47	124.94	114.47	124.94	116.48	116.48	89.99
Ambrisentan	B2075	EDNRA	42.73	116.94	105.76	67.13	82.24	95.22	118.51	244.36	237.47	103.58	82.08	128.16	84.03	92.82	95.41	92.82	95.41	34.40	34.40	100.11
Amlenac Sodium Monohydrate	B1656	PTGS1, PTGS2	94.00	19.16	103.62	68.45	55.84	80.23	85.16	90.63	89.60	101.92	82.89	101.53	92.59	124.93	102.38	124.93	102.38	99.40	99.40	62.88
Amidopyrine	B1883	CYP3A4	87.46	110.67	97.48	102.77	92.73	90.51	143.46	115.75	127.74	107.75	81.26	117.68	93.20	75.89	76.77	75.89	76.77	146.90	146.90	107.54
Amikacin	B3431	N/A	81.96	104.53	114.20	110.52	95.01	80.01	92.12	118.94	115.32	120.78	89.69	144.47	95.27	94.37	116.77	94.37	116.77	126.35	126.35	102.20
Amiloride HCl dihydrate	B2268	ASIC1	94.10	104.39	115.25	96.92	95.79	74.82	97.27	119.38	107.83	119.48	121.60	102.48	89.40	96.21	108.09	96.21	108.09	128.27	128.27	100.65
Aminoglutethimide	B1380	CYP19A1	117.59	99.27	102.87	92.72	93.30	83.23	94.52	106.48	110.35	111.90	94.69	113.45	102.62	120.58	104.09	120.58	104.09	93.73	93.73	100.19
Aminoguanidine hydrochloride	B6452	NOS2	89.03	111.62	118.01	93.04	106.16	80.32	109.92	48.93	57.97	100.06	90.32	105.47	63.96	91.71	88.33	91.71	88.33	118.18	118.18	114.68
Amnophylline	A4346	PDE4A	85.20	110.88	75.78	83.30	60.66	102.71	92.08	109.43	75.62	100.05	87.19	95.17	99.40	104.42	97.16	104.42	97.16	101.16	101.16	87.73
Aminothiazole	B1659	N/A	163.65	129.72	135.77	88.14	95.39	120.09	111.86	92.41	117.91	98.68	103.18	104.93	117.23	103.80	92.74	103.80	92.74	96.61	96.61	92.07
Amiodarone HCl	B1389	KCNA7	58.14	80.82	60.03	35.51	45.83	32.79	41.30	87.16	79.04	26.41	39.21	54.74	74.95	33.31	39.04	33.31	39.04	29.29	29.29	43.97
Amisulpride	B1479	DRD2	166.75	211.70	158.62	105.27	126.17	124.69	119.05	140.52	137.58	117.50	98.39	125.67	100.06	82.15	83.34	82.15	83.34	139.44	139.44	104.04
Amitriptyline HCl	B2231	Htr2a	90.29	115.55	135.38	77.63	71.38	99.56	101.10	112.30	115.91	83.32	91.92	99.25	83.20	97.76	111.80	97.76	111.80	137.50	137.50	90.31
Amlodipine	B1410	CACNA1D	92.32	48.86	69.86	24.83	30.43	24.45	39.31	82.23	64.54	21.21	79.87	86.45	99.97	29.32	35.07	29.32	35.07	32.59	32.59	61.58
Amlodipine Besylate	B1411	CACNA1D	94.08	94.04	102.50	47.78	52.27	35.83	38.23	87.06	75.24	31.71	95.85	115.15	110.02	99.48	96.19	99.48	96.19	51.34	51.34	73.26
Amonafide	A2782	TOP2A, TOP2B	100.17	105.87	196.03	156.44	120.20	59.38	51.56	77.30	79.61	33.21	52.29	69.44	90.36	66.95	62.50	66.95	62.50	80.30	80.30	131.67
Amorfinone HCl	B2077	N/A	39.09	94.26	118.81	54.43	62.14	41.96	87.04	172.11	159.07	82.01	94.84	128.56	83.76	144.21	93.59	144.21	93.59	27.30	27.30	88.02
Amoxapine	B1660	Htr2a	85.94	107.00	94.92	71.63	128.42	86.57	96.84	184.56	209.74	93.68	81.33	104.27	85.02	89.76	86.22	89.76	86.22	87.35	87.35	87.35
Amoxicillin	B1661	N/A	142.73	103.41	119.58	76.43	93.32	169.29	106.93	94.79	109.65	105.76	99.31	112.42	112.28	153.38	129.34	153.38	129.34	112.29	112.29	100.80
Amphotericin B	B1885	N/A	94.60	121.86	107.47	85.98	78.33	78.98	111.46	125.59	127.63	103.12	106.81	115.78	109.48	119.60	94.55	119.60	94.55	144.22	144.22	142.55
Ampicillin	A2510	N/A	101.50	101.44	78.89	80.74	86.23	78.64	77.06	126.54	97.49	96.68	110.53	101.33	84.60	93.12	80.31	93.12	80.31	108.76	108.76	80.64
Ampicillin Trihydrate	B1662	N/A	119.87	156.73	119.81	76.93	87.06	104.05	101.04	93.89	97.64	100.39	88.90	124.43	109.83	148.49	138.00	148.49	138.00	118.24	118.24	100.14
Amprenavir (agenertase)	A8201	N/A	88.51	104.09	144.91	54.56	59.01	84.96	72.67	129.77	94.97	88.81	82.35	99.11	104.39	108.22	97.61	108.22	97.61	107.66	107.66	120.94
Amprolium HCl	B1663	N/A	119.03	139.96	144.53	52.24	90.60	105.33	115.62	89.96	108.93	99.21	105.39	134.73	103.89	133.38	123.41	133.38	123.41	135.25	135.25	91.49
Amuvatinib (MP-470, HPK 56)	A4237	RET	72.48	141.07	84.31	72.18	73.75	146.84	151.46	82.03	68.37	26.98	52.97	119.60	81.75	75.45	88.53	75.45	88.53	63.16	63.16	91.89
Anagrelide HCl	A4352	PDE3A	118.21	123.58	103.24	81.11	87.62	113.28	118.02	99.83	96.32	109.81	96.60	139.92	119.90	136.27	120.63	136.27	120.63	111.49	111.49	90.98
Anastrozole	B1382	CYP19A1	174.65	145.95	102.29	103.27	118.32	115.95	147.70	124.75	123.55	124.10	91.23	149.21	119.55	235.28	234.23	235.28	234.23	118.18	118.18	116.52
Anidulafungin	B1224	N/A	46.65	43.34	55.23	54.06	41.43	71.36	63.37	100.49	123.40	29.98	50.58	67.50	92.44	54.16	62.42	54.16	62.42	40.85	40.85	106.10
Aniracetam	B1210	GRIA1	103.46	100.56	95.39	90.77	101.15	85.25	104.35	90.65	81.49	202.27	91.04	106.59	103.52	140.22	138.14	140.22	138.14	137.09	137.09	88.86
Anizolone HCl	B1664	HRH1	134.54	133.25	144.45	53.68	79.65	91.91	93.13	96.59	108.33	102.10	103.71	123.16	119.47	102.05	115.03	102.05	115.03	124.16	124.16	91.98
Antipyrine	B1886	PTGS1, PTGS2	99.74	120.51	95.94	103.52	92.87	84.62	126.48	117.19	132.50	108.72	93.81	131.31	103.48	87.86	89.40	87.86	89.40	142.94	142.94	105.51
Apalitinib	B2303	CSK	78.02	202.93	119.47	53.08	43.96	81.96	88.71	118.62	91.85	39.30	27.50	108.68	65.43	66.41	63.64	66.41	63.64	114.80	114.80	82.09
Apixaban	A4341	F10	100.33	101.23	82.36	95.02	86.29	91.74	103.55	94.72	75.60	105.36	81.69	112.71	172.99	155.43	142.79	155.43	142.79	110.51	110.51	88.79
Apremilast (CC-10004)	A4317	PDE4A	170.62	151.92	134.96	126.98	108.00	123.85	113.09	151.95	129.04	112.50	112.71	148.89	120.78	161.85	139.15	161.85	139.15	127.14	127.14	104.57
Aprepitant	A1684	TACR1	115.10	46.93	66.07	72.64	78.00	92.17	108.23	81.35	85.80	66.17	88.82	91.54	86.85	38.96	32.59	38.96	32.59	87.56	87.56	73.10
Aprolinin	A2574	PLG	119.82	105.75	86.14	130.31	89.80	186.68	244.89	111.99	113.33	96.06	126.28	128.77	160.34	284.51	95.17	284.51	95.17	88.24	88.24	189.13
Arbidol HCl	A8362	N/A	105.74	59.39	92.32	36.50	34.96	32.84	45.74	80.49	89.95	55.50	61.62	87.29	114.12	72.24	56.58	72.24	56.58	129.80	129.80	147.63
Arbutin	N1714	TYR	86.73	126.59																		

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)			ER-positive (luminal)				HER2-enriched				
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	UCD52	WHM2	WHM2	WHM30	WHM30	WHM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108	HC108
Atipirazole	B2232	HTR1A	93.47	116.76	126.54	80.22	67.64	99.78	108.92	124.39	119.75	119.75	78.14	68.99	127.43	82.05	73.28	73.38	73.38	73.38	117.84	117.84	59.17
Arsonic acid	A8355	N/A	108.57	102.32	105.06	94.53	130.09	84.70	107.51	121.41	142.30	117.00	86.91	143.68	112.22	143.68	112.22	76.41	70.05	70.05	177.53	177.53	114.38
Artemether	N1742	N/A	93.69	107.81	106.17	97.98	93.09	91.82	103.51	75.13	75.24	113.08	75.66	120.73	102.20	102.20	96.24	96.24	96.24	96.24	108.22	108.22	26.54
Artemether (SM-224)	A4014	N/A	113.71	89.73	123.00	73.74	80.25	114.36	118.91	101.98	97.63	96.96	61.59	110.87	74.72	74.72	86.55	81.66	81.66	81.66	101.13	101.13	68.47
Artemisinin	N1827	N/A	98.04	152.38	153.21	97.34	97.56	104.81	83.00	84.55	107.98	92.15	90.03	139.43	102.36	87.70	103.67	103.67	87.70	103.67	85.89	85.89	37.46
Artisanine HCl	B1887	N/A	100.43	107.37	133.13	90.21	98.29	91.82	116.67	133.41	125.32	110.88	120.71	115.31	96.90	72.21	72.21	72.21	72.21	72.21	142.76	142.76	105.05
Asenapine	A5010	HTR1A	86.98	96.91	120.80	67.00	74.96	69.56	89.44	132.16	96.83	65.01	72.70	93.02	93.75	69.29	69.29	69.29	69.29	69.29	108.26	108.26	86.38
Aspartame	B1888	TAS1R2, TAS1R3	125.00	115.43	117.31	115.16	85.18	114.50	147.28	123.67	133.16	100.76	106.24	151.59	119.09	158.08	158.08	158.08	158.08	158.08	164.37	111.98	114.61
Aspirin (Acetylsalicylic acid)	A4013	ASIC3	162.48	185.58	151.36	151.17	132.20	89.78	113.18	143.53	176.41	101.21	95.83	106.60	135.68	169.40	169.40	126.69	126.69	126.69	153.46	153.46	103.51
AT13387	A4056	HSP90AA1	81.45	150.72	109.02	75.02	79.10	73.06	77.51	158.13	192.87	27.62	23.25	43.66	123.76	502.60	502.60	304.81	304.81	304.81	96.85	96.85	120.28
Atazanavir	A8205	N/A	87.84	88.85	151.28	49.38	53.82	74.60	72.81	86.02	78.23	58.88	56.10	80.01	74.50	78.03	78.03	85.31	85.31	85.31	109.18	109.18	93.35
Atazanavir sulfate (BMS-232632-05)	A4040	N/A	140.11	128.52	137.76	122.86	103.23	85.59	94.32	126.29	170.36	72.84	76.85	134.95	140.15	96.21	96.21	104.08	104.08	104.08	116.57	116.57	133.87
Atomoxetine HCl	B2244	SLC6A3	113.11	125.73	129.57	87.67	82.38	100.79	76.63	200.31	160.52	103.07	118.45	102.57	107.74	102.57	107.74	102.57	107.74	102.57	111.26	111.26	121.68
Atorvastatin Calcium	A4367	Hmgcr	86.24	92.20	140.12	46.12	49.36	36.53	50.79	154.28	161.76	71.02	107.33	138.23	213.56	95.94	95.94	95.94	95.94	95.94	90.27	90.27	110.42
Atovaquone	B2078	N/A	57.36	105.84	116.34	68.10	89.64	93.53	105.89	73.74	71.13	24.33	31.03	82.33	54.87	48.66	48.66	51.36	51.36	51.36	54.03	54.03	52.86
Atracurium Besylate	B1666	CHRNA1	114.03	260.93	144.60	127.90	124.02	63.32	79.68	102.03	92.12	45.94	128.33	109.80	80.96	93.59	93.59	66.63	66.63	66.63	125.96	125.96	242.28
Atropine	A8369	CHRM1, CHRM2, CHRM3, CHRM4	109.34	98.71	100.84	87.16	79.42	78.46	104.79	92.87	103.93	119.47	96.66	133.91	113.69	92.13	92.13	98.64	98.64	98.64	177.71	177.71	119.98
Avanafil	A4334	PDE5A	149.92	160.46	120.85	114.31	92.91	131.63	127.94	140.39	129.79	86.04	118.32	116.53	143.26	130.83	130.83	114.83	114.83	114.83	111.97	111.97	131.83
Avobenzone	B2079	N/A	45.57	102.79	119.08	69.90	72.17	79.67	131.57	131.95	149.28	68.16	80.05	126.04	83.46	80.36	80.36	73.06	73.06	73.06	31.24	31.24	87.94
Axitinib (AG 013736)	A8370	KDR	271.16	200.31	150.29	187.33	193.95	233.98	204.86	534.20	376.00	406.16	233.55	336.40	157.67	271.23	225.83	225.83	225.83	225.83	1163.74	1163.74	228.21
Azacyclonol	B1891	N/A	84.73	111.37	110.05	103.04	88.65	84.82	133.12	111.76	114.75	111.77	57.32	137.41	93.79	86.15	86.15	71.88	71.88	71.88	141.82	141.82	90.89
Azaguanine-8	B1667	N/A	123.71	191.40	568.15	63.20	140.55	96.23	95.79	109.30	129.63	122.27	152.57	145.70	332.73	143.07	155.98	165.33	165.33	165.33	145.21	145.21	83.58
Azaperone	B1668	N/A	101.63	137.01	150.63	57.96	75.93	94.99	101.62	87.72	83.83	95.14	98.17	113.50	120.66	221.16	212.08	212.08	212.08	212.08	113.34	113.34	83.58
Azathioprine	B1892	N/A	75.60	120.73	150.83	141.59	116.00	63.99	78.15	103.82	116.29	124.67	88.24	119.03	87.00	71.13	58.84	58.84	58.84	121.66	121.66	70.92	
AZD6244 (Selumetinib)	A8207	MAP2K1	148.47	309.37	244.28	93.29	75.49	85.72	73.70	213.66	288.34	66.98	98.87	83.90	111.61	92.76	91.65	91.65	91.65	163.72	163.72	175.16	
AZD-9291	B1104	EGFR	42.46	41.03	60.69	29.46	30.80	39.03	49.90	43.00	40.33	75.62	25.16	39.93	61.31	54.39	49.00	49.00	49.00	38.66	38.66	30.55	
Azelastine HCl	B1568	HRH1	109.68	175.27	116.49	45.43	69.82	72.78	84.71	99.37	90.45	100.15	102.04	105.98	69.21	128.18	97.24	109.44	109.44	69.35	69.35	69.35	
Azelinidipine	B1414	CACNA1B	32.64	34.50	62.02	89.18	97.78	74.73	47.90	75.88	39.42	21.07	21.89	58.97	80.42	45.76	37.45	37.45	37.45	30.70	30.70	152.25	
Azilastat	B2210	AGTR1	48.33	110.98	96.23	88.31	78.26	88.56	107.30	99.01	95.92	75.37	94.24	142.30	91.97	97.97	101.60	101.60	101.60	18.82	18.82	95.10	
Azisartan Medoxomil	B2218	AGTR1	95.63	105.28	124.43	117.50	105.20	94.05	118.84	125.04	128.91	108.99	105.94	161.95	94.18	96.42	116.42	116.42	116.42	154.08	154.08	114.03	
Azithromycin	B1398	MLNR	166.29	123.24	124.14	86.54	123.42	115.67	114.12	136.49	102.26	120.29	111.94	137.47	121.26	367.80	383.14	383.14	383.14	112.02	112.02	117.24	
Azithromycin Dihydrate	B1669	MLNR	104.08	116.77	104.19	86.43	84.30	99.68	103.50	87.76	90.20	93.25	107.82	114.12	112.41	140.65	147.69	147.69	147.69	115.00	115.00	82.80	
Azlocillin sodium salt	B1893	N/A	80.58	114.56	130.25	97.74	97.79	84.91	126.15	117.01	133.30	116.33	92.66	130.96	103.78	82.85	70.05	70.05	70.05	159.96	159.96	109.37	
Aztreonam	A5931	N/A	106.85	100.86	114.49	98.00	93.76	78.38	90.42	144.15	102.13	101.30	91.70	112.79	108.55	106.82	128.18	128.18	128.18	124.27	124.27	124.27	
Bacitracin	B1670	N/A	86.57	88.99	101.02	79.17	103.97	107.70	98.43	78.22	75.33	82.45	81.54	98.69	90.72	108.68	77.45	78.46	78.46	98.07	98.07	98.07	
BAF312 (Siponimod)	B3225	S1PR1	90.18	104.67	115.42	92.65	94.76	81.55	105.94	117.29	103.86	23.35	64.96	123.69	72.18	76.04	75.24	75.24	75.24	56.89	56.89	51.07	
Balsalazide	B3460	PTGS1, PTGS2	83.68	108.99	114.50	100.78	86.26	88.42	109.14	114.15	105.57	88.47	86.81	119.78	91.08	115.46	124.44	124.44	124.44	157.48	157.48	94.91	
Barasertib (AZD1152-HQPA)	A4112	AURKA	120.92	151.83	142.80	121.48	92.96	86.54	92.17	130.60	131.35	84.06	74.37	117.86	91.53	101.34	93.27	93.27	93.27	136.69	136.69	120.73	
Baradoxolone methyl	A3221	KEAP1	25.72	31.25	30.44	23.87	25.31	30.24	38.08	27.58	25.94	24.36	21.86	33.91	23.15	33.56	29.39	29.39	29.39	24.33	24.33	24.33	
Batimastat (BB-94)	A2577	MMP2, MMP9	102.40	86.13	67.00	139.00	115.64	56.65	87.40	175.60	174.43	64.33	92.01	88.16	95.30	129.81	124.24	124.24	124.24	92.43	92.43	90.00	
Bazedoxifene HCl	B1519	ESR1	33.87	78.83	114.27	43.62	47.68	57.67	84.79	84.28	22.08	21.16	41.56	73.90	42.37	33.72	33.72	33.72	33.72	52.58	52.58	119.58	
Beclomethasone dipropionate	B1248	NR3C1	60.38	201.55	174.73	135.59	130.15	126.00	130.56	130.60	116.22	137.41	149.91	182.06	122.66	334.72	310.40	310.40	310.40	110.17	110.17	140.22	
Bedaquiline	B3492	N/A	76.55	101.23	135.51	70.01	70.26	90.03	83.99	76.11	83.73	66.11	107.12	107.12	87.05	90.43	113.42	113.42	113.42	57.52	57.52	77.63	
Bedaquiline fumarate	B3491	N/A	66.63	91.47	86.96	43.13	42.11	50.19	47.19	67.98	72.10	48.83	80.										

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)			ER-positive (luminal)				HER2-enriched		
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	WHM2	WHM2	WHM30	WHM30	WHM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108
Benidipine HCl	B1409	CACNA1B	70.71	93.41	87.46	46.42	56.43	26.81	35.38	66.93	61.14	17.76	37.97	68.28	83.24	41.63	30.72	28.74	40.63		
Benserazide HCl	B1489	DDC	94.83	96.89	77.17	75.62	63.56	94.03	98.52	99.99	106.20	87.95	79.27	69.08	44.89	87.26	71.23	115.65	92.81		
Benzbromarone	B1673	XDH	100.61	31.17	97.04	70.76	81.26	31.95	48.15	81.26	108.91	16.41	51.13	103.26	98.01	148.18	107.38	55.30	64.36		
Benzethonium Chloride	B1674	N/A	27.31	19.09	38.16	29.34	20.59	36.31	41.00	18.57	25.59	33.34	23.82	44.20	52.78	41.78	42.33	27.40	22.07		
Benzocaine	B1675	SCN10A	134.99	153.00	134.18	123.79	111.11	133.15	150.17	147.25	132.42	124.30	105.11	87.22	116.83	78.68	80.91	120.46	139.01		
Benzoic Acid	B1676	N/A	128.81	157.46	124.44	115.32	103.86	131.16	132.24	121.31	99.85	126.59	91.16	95.57	103.78	77.39	63.25	125.57	133.78		
Benzotropine mesylate	B1554	HRH1, CHRM1	145.88	231.18	125.08	74.99	85.86	75.26	91.57	142.06	139.87	119.91	101.05	108.19	93.98	129.88	109.98	161.39	94.73		
Benzylamine HCl	B1677	PTGS1, PTGS2	117.05	224.16	163.26	99.98	100.60	111.65	120.64	109.93	135.53	90.15	67.86	85.43	103.83	74.05	58.42	103.11	102.52		
Bephenium	A8376	N/A	114.05	127.33	104.14	81.23	97.94	97.22	127.59	164.91	136.48	143.72	111.59	127.45	125.19	117.64	87.89	191.29	114.83		
Hydroxynaphthoate	B1569	HRH1	123.52	186.63	127.63	72.55	102.73	84.09	91.25	144.86	130.30	111.30	113.59	131.38	96.56	125.65	116.32	156.28	86.33		
Betahistine 2HCl	B1555	HRH3	177.58	612.09	223.18	98.88	166.61	72.28	114.78	195.91	175.91	119.74	86.62	134.08	140.35	101.53	77.92	323.87	105.71		
Betaine	N1700	N/A	83.59	130.77	115.88	109.97	101.60	88.69	110.65	98.47	81.43	111.59	95.09	140.13	90.65	140.69	138.60	100.26	40.90		
Betaine hydrochloride	N1700	N/A	107.72	114.47	122.42	86.67	77.30	99.77	91.13	108.54	105.12	98.67	91.98	123.41	103.12	105.01	120.39	98.33	44.35		
Betamethasone	B1896	NR3C1	101.00	158.73	237.21	184.61	181.18	110.80	148.79	157.47	209.56	121.81	167.26	177.14	175.29	307.47	215.95	159.62	153.49		
Betamethasone	A8378	NR3C1	109.40	141.80	223.59	137.65	157.08	73.81	110.83	198.59	206.36	132.44	167.52	138.47	136.26	423.41	372.76	151.54	132.28		
Dipropionate	A8379	NR3C1	111.34	128.60	202.78	153.87	167.86	68.18	109.61	182.44	205.94	123.69	171.53	169.15	123.51	329.65	347.09	168.36	152.27		
Betamipron	B1679	SLC22A6	105.13	136.44	98.92	106.59	93.29	93.41	109.48	111.61	105.22	107.04	67.92	104.63	98.16	77.07	62.51	103.48	103.26		
Betaxolol HCl	B1353	ADRB1	133.28	130.20	148.57	73.03	75.28	90.61	111.68	115.82	117.67	131.46	83.21	134.46	106.97	82.21	91.80	136.20	103.87		
Bethanechol chloride	B1599	CHRM1	89.94	82.57	101.02	104.48	96.16	100.76	109.59	80.72	78.03	99.64	81.96	87.97	82.47	93.94	113.70	111.56	106.60		
Bexarotene	A8380	PPARG	82.65	37.78	84.72	87.83	108.18	34.59	55.10	96.91	90.71	101.16	95.83	85.87	100.08	52.66	55.98	100.19	118.57		
Befarizate	B1680	PPARA	108.61	108.27	123.09	107.07	94.62	102.27	122.45	117.67	108.15	107.25	83.75	100.87	103.69	99.09	95.45	123.19	98.44		
B16727 (Volasertib)	A8558	PLK1	117.63	47.51	572.68	113.05	119.26	37.34	49.67	178.03	175.80	27.06	25.71	85.10	114.97	105.38	63.76	762.51	239.80		
B1BR-1048	A8381	F2	87.48	100.98	106.64	86.76	97.11	84.05	129.82	123.52	107.79	100.26	110.69	124.40	110.72	123.91	112.71	68.68	107.43		
Bicalutamide	A5065	AR	101.32	113.90	107.63	81.67	97.64	85.67	94.74	109.72	105.33	100.01	81.22	113.05	90.19	124.21	129.26	126.27	101.75		
Bifonazole	B1897	N/A	96.44	90.29	108.25	184.44	114.25	122.04	120.09	112.36	140.03	75.16	72.94	107.81	95.26	99.70	68.94	167.76	86.70		
Bimatoprost	B2139	PTGFR	35.49	126.24	143.97	89.48	83.01	82.07	114.81	141.66	155.13	107.70	76.18	154.04	97.49	122.40	112.98	32.47	94.48		
Bimatoprost	B2156	CCL2	38.28	134.63	117.11	80.87	85.27	96.98	123.60	168.40	129.71	97.35	107.30	133.17	86.60	136.12	135.92	26.34	103.88		
BIRB 796 (Doramipimod)	A5639	MAPK11	109.05	167.29	87.45	57.14	67.05	95.41	84.15	115.82	90.32	107.12	79.94	89.62	71.07	50.87	46.09	169.60	102.48		
Birinapant (TL3271)	A4219	BIRC2	128.80	136.76	114.68	99.53	88.00	114.23	113.96	135.50	163.33	120.72	171.90	99.52	128.49	365.00	360.28	98.27	125.94		
Bisacodyl	B1898	ADCYAP1	42.90	63.42	70.89	92.83	69.03	80.78	141.16	75.55	77.54	26.50	35.32	130.14	50.34	195.20	172.82	100.82	105.42		
Bisoprolol fumarate	B1354	ADRB1	130.08	128.76	96.07	92.37	79.74	82.29	105.54	121.74	118.20	123.02	80.54	129.29	112.61	92.28	93.83	144.88	99.74		
Bleomycin Sulfate	A8331	N/A	118.82	114.29	83.44	114.09	104.78	77.90	76.13	80.89	119.04	50.35	71.97	205.37	106.28	55.88	22.55	105.07	155.36		
BMS-708163	A4022	PSEN1	112.42	79.57	96.65	81.01	82.15	107.05	108.09	114.32	132.73	69.01	65.93	141.69	75.54	112.71	90.83	107.94	66.17		
(Avagacestat)	A3261	CTSA	86.59	114.02	65.12	68.47	91.81	70.25	91.06	91.35	78.75	91.61	82.79	83.75	100.68	73.30	71.64	100.64	89.50		
Bocoprevir	B1682	Ednra	99.23	121.49	104.20	108.74	112.69	89.03	139.76	116.27	111.69	85.92	56.26	95.12	86.37	87.72	79.66	102.12	96.17		
Bosentan	B1521	Ednra	288.15	445.53	275.14	131.21	118.67	81.20	93.00	185.57	181.76	106.11	69.51	123.83	100.85	197.76	146.99	407.87	112.03		
Bosutinib (SKI-606)	A2149	ABL1	46.47	50.34	55.85	40.45	33.72	27.78	45.47	58.69	30.41	76.91	47.95	101.28	105.74	37.14	50.27	81.90			
Brexiprazole	B1102	DRD2	150.80	121.23	162.42	73.96	82.70	108.40	121.24	117.37	105.74	78.63	92.74	105.81	102.46	126.50	118.60	54.28	96.75		
Brimonidine Tartrate	B1683	ADRA2A	116.34	129.29	123.82	97.93	83.54	106.80	142.33	99.29	97.45	74.74	81.24	125.02	89.91	91.66	85.30	103.83	124.57		
Brimonidamide	A4359	CA1	99.80	117.09	100.37	87.83	88.52	112.66	96.01	101.60	91.54	108.09	87.19	142.07	139.11	143.10	120.63	118.79	99.59		
Brivaracetam	B4806	Sv2a	93.06	103.02	100.87	106.56	104.54	89.80	106.54	136.46	120.37	98.31	95.83	163.01	89.29	88.36	87.29	121.83	29.11		
Bromfenac Sodium	B1684	PTGS1	109.38	158.00	96.22	91.79	86.14	113.84	149.73	115.25	106.04	91.00	73.20	104.41	102.57	88.18	65.08	108.00	92.56		
Bromhexine HCl	B1899	ELANE, MPO	85.88	105.64	78.62	69.05	33.55	105.60	33.55	105.60	110.22	97.29	88.75	106.49	96.31	66.65	63.16	114.22	69.03		
Brompheniramine hydrochloride	B1545	HRH1	105.01	132.48	118.25	76.56	73.29	95.54	100.26	112.65	114.22	104.76	102.04	117.14	99.53	145.65	139.21	146.77	74.64		
Broxiprinone	B1685	N/A	46.36	116.67	122.37	43.35	102.33	104.00	188.54	95.00	100.95	20.09	30.92	89.08	98.06	37.17	31.43	22.91	25.01		
Bruceine	N1490	CHRM1	83.33	97.27	100.19	106.97	104.80	68.27	98.66	93.21	99.97	118.37	77.96	132.20	94.47	98.63	113.57	132.33	36.99		
Budesonide	B1900	NR3C1	91.87	133.97	173.43	148.01	134.63	59.95	88.82	205.47	202.08	135.83	191.85	101.94	140.39	274.92	279.19	133.60	109.19		
Bufexamac	B1443	HDAC10	181.91	183.66	200.77	127.45	168.56	109.74	113.56	104.48	99.40	135.80	145.11	280.65	173.27	116.39	166.18	126.56	68.18		
Buflomedil HCl	B1889	PF4	93.08	97.80	122.32	103.83	81.18	97.62	136.48	131.97	135.31	105.98	85.23	131.19	94.38	88.38	84.72	138.81	89.10		
Bumetanide	A1855	SLC12A2	101.80	115.41	108.47	98.03	99.93	68.37	88.74	151.54	114.11	102.38	115.01	95.90	91.97	92.35	86.72	114.65	129.85		

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)			ER-positive (luminal)				HER2-enriched			
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	UCD52	WHM12	WHM2	WHM30	WHM30	WHM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108
Bupivacaine HCl	B1420	SCN10A	166.15	124.45	168.89	77.78	100.15	105.98	116.76	125.83	108.74	113.85	93.84	127.80	119.55	107.27	104.23	116.95	118.90	118.90	118.90	118.90
Bupropion hydrochloride	B3326	SLC6A3	102.43	98.95	112.69	100.45	100.48	103.81	104.37	108.03	128.53	113.94	113.67	85.56	103.91	103.91	103.91	103.91	103.91	103.91	103.91	103.91
Bupropion HCl	B1687	HLR1A	99.34	121.43	119.26	108.74	103.81	104.37	108.03	128.53	113.94	113.67	85.56	103.91	103.91	103.91	103.91	103.91	103.91	103.91	103.91	103.91
Busulfin	A8386	N/A	99.97	99.93	108.03	78.74	84.16	94.75	100.48	135.73	150.15	111.94	122.10	115.46	104.77	112.92	106.03	96.41	102.86	102.86	102.86	102.86
Butorafine HCl	B1901	N/A	103.05	105.16	150.86	83.27	79.04	64.76	139.79	144.46	102.89	130.38	99.17	103.65	69.36	75.99	111.54	72.98	72.98	72.98	72.98	72.98
Butoconazole nitrate	B1902	N/A	98.33	96.07	186.37	77.18	72.04	42.74	64.77	195.36	184.21	202.83	43.54	99.55	142.66	38.55	40.60	33.62	31.70	31.70	31.70	31.70
BYL-719	A8346	PIK3CA	79.18	92.17	93.64	36.71	40.28	52.05	79.22	64.50	67.31	25.18	45.82	75.91	39.33	49.13	104.98	59.33	59.33	59.33	59.33	59.33
Cabazitaxel	B2157	TUBB1	42.02	114.13	201.12	73.78	66.91	64.44	79.49	110.45	103.70	70.02	62.41	112.97	89.21	109.73	102.51	19.88	80.93	80.93	80.93	80.93
Cabozantinib (XL184), BMS-907351	A2977	KDR	103.38	112.68	93.81	98.69	77.87	97.97	82.15	118.36	113.58	92.91	90.13	113.96	88.93	88.64	106.76	88.12	93.79	93.79	93.79	93.79
Cabozantinib malate (XL184)	B1401	KDR	79.48	98.00	63.44	36.76	32.24	109.53	100.26	57.27	54.67	61.64	54.84	45.39	43.99	95.58	74.68	80.50	53.09	53.09	53.09	53.09
Caftaric acid	N1735	N/A	83.28	92.64	136.79	101.38	92.94	72.03	101.00	87.71	91.04	124.10	89.76	115.05	93.27	96.55	83.24	95.86	27.83	27.83	27.83	27.83
CAL-101 (Idelalisib, GS-1101)	A3005	PIK3CA	85.68	97.52	68.14	70.43	66.26	64.85	60.71	122.25	121.56	101.35	75.02	80.74	76.75	54.30	49.44	90.80	77.77	77.77	77.77	77.77
Calcitriol	B2141	VDR	19.26	35.90	106.70	56.11	55.23	32.81	45.89	127.15	146.66	23.35	30.64	118.91	73.36	71.27	61.59	8.20	73.99	73.99	73.99	73.99
Calcium Gluceptate	A8387	VDR	136.85	132.15	123.93	96.42	77.89	111.11	106.56	135.18	146.64	108.95	115.88	167.73	126.83	115.92	104.27	118.41	136.54	136.54	136.54	136.54
Camostat Mesilate	B2082	PRSS1	87.75	121.84	112.22	95.04	104.47	113.81	106.54	113.92	113.92	89.81	80.53	133.18	70.73	113.04	104.91	123.15	70.62	70.62	70.62	70.62
Canagliflozin	A8333	SLC5A1	118.53	109.36	123.75	82.50	69.51	29.67	101.25	106.27	114.61	36.90	74.74	149.52	108.43	62.71	91.96	78.39	79.89	79.89	79.89	79.89
Candesartan	A5932	AGTR1	94.11	101.79	109.34	82.35	81.95	80.32	91.53	128.46	96.05	95.20	92.02	121.78	100.90	128.74	126.98	123.22	130.66	130.66	130.66	130.66
Candesartan Cilexetil	B2203	AGTR1	9.60	26.67	75.28	85.45	63.18	32.87	42.24	123.98	131.50	14.98	21.52	94.49	72.30	47.68	47.65	4.69	24.72	24.72	24.72	24.72
Capacetabine	A8647	TYMS	159.69	123.31	119.55	114.62	109.04	102.89	112.66	184.58	138.49	156.29	121.65	113.62	123.81	182.35	147.63	139.97	110.65	110.65	110.65	110.65
Capreomycin Sulfate	B1689	N/A	84.57	88.78	95.72	72.56	67.94	91.69	95.85	51.67	52.37	82.80	80.97	67.66	67.25	95.88	78.44	100.81	87.84	87.84	87.84	87.84
Capsaicin	A3278	CFTR	98.68	110.89	82.37	74.33	82.28	104.85	75.43	99.41	116.17	76.99	74.66	119.86	90.61	112.54	89.10	75.85	91.49	91.49	91.49	91.49
Carbadox	A8388	N/A	108.34	103.92	98.82	63.75	80.95	89.93	103.70	120.22	106.93	91.65	103.98	116.04	107.18	126.19	85.93	115.25	115.25	115.25	115.25	115.25
Carbamazepine	B1390	SCN9A	108.55	104.51	99.64	82.66	88.86	59.39	90.95	101.93	95.60	116.78	71.92	102.85	106.03	91.05	92.54	138.76	102.58	102.58	102.58	102.58
Carbamoylcholine chloride	B7196	CHRM1, CHRM2, CHRM3, CHRM4	99.69	115.68	123.73	93.94	97.29	121.95	131.86	99.88	97.88	90.18	88.66	120.43	71.39	108.73	115.24	119.93	98.13	98.13	98.13	98.13
Carbazochrome sodium sulfonate (AC-17)	B1903	ADRA2A	100.01	99.59	123.67	112.28	85.68	84.43	114.43	126.67	140.45	105.71	105.08	128.54	94.63	93.39	68.58	144.11	92.92	92.92	92.92	92.92
Carbencillin, Disodium Salt	A2511	N/A	96.01	89.99	104.66	87.94	82.83	121.38	97.63	113.64	116.44	93.34	94.73	92.60	103.07	85.89	87.48	84.55	91.66	91.66	91.66	91.66
Carbexolone disodium	A8389	GJE1	89.96	78.58	107.81	83.54	81.14	100.38	116.24	99.66	96.09	85.99	92.37	121.86	102.70	190.74	68.14	147.28	133.83	133.83	133.83	133.83
Carbidopa	B1904	DDC	130.44	102.02	148.71	117.84	130.70	73.84	89.30	129.99	121.23	107.24	134.89	122.29	79.81	120.09	109.33	99.41	96.26	96.26	96.26	96.26
Carbimazole	B1905	TPO	85.25	96.45	101.47	100.82	90.20	82.77	124.76	142.55	126.53	102.73	87.22	144.98	93.37	79.37	53.47	147.05	87.11	87.11	87.11	87.11
Carboplatin	A2171	N/A	86.59	77.52	50.99	44.46	34.83	94.26	75.42	92.89	85.10	88.81	94.49	82.70	86.42	86.72	87.02	93.57	91.87	91.87	91.87	91.87
Carfilzomib (PR-171)	A1933	PSMB5	34.79	29.76	38.93	72.37	56.41	18.33	34.43	66.97	70.62	22.41	29.04	282.41	55.87	29.58	36.28	27.24	54.79	54.79	54.79	54.79
Cariprazine	A3282	DRD2	101.78	141.81	89.71	34.25	42.78	124.34	113.03	118.81	118.32	42.35	45.48	72.06	67.69	61.50	45.35	52.40	51.69	51.69	51.69	51.69
Carmofur	A2548	N/A	114.05	105.89	107.72	80.52	137.98	65.27	119.66	131.64	107.94	74.37	61.10	102.60	131.30	76.08	85.63	80.93	85.95	85.95	85.95	85.95
Carmustine	B3489	N/A	89.52	123.22	212.91	119.51	111.81	96.05	96.42	117.31	128.71	56.35	143.54	166.42	83.91	118.18	149.71	106.87	107.66	107.66	107.66	107.66
Carprofen	B1690	PTGS2	138.52	211.12	138.08	115.66	110.88	130.26	173.37	117.02	117.74	107.29	115.79	106.70	95.30	102.81	101.68	124.07	128.03	128.03	128.03	128.03
Carteolol HCl	B5944	ADRB1, ADRB2	87.15	105.65	114.64	116.92	112.00	75.06	99.62	115.83	117.06	106.89	87.67	144.10	109.84	124.35	121.69	110.36	33.51	33.51	33.51	33.51
Carvedilol	B1332	ADRB1	98.09	97.66	126.66	44.92	43.06	43.82	48.46	101.68	102.52	70.20	81.63	69.92	88.68	123.77	123.86	111.33	81.82	81.82	81.82	81.82
Casopufungin	B4972	N/A	100.97	88.00	141.71	98.30	109.39	92.72	99.14	129.61	125.62	102.13	108.37	141.09	114.38	121.56	131.40	102.32	35.10	35.10	35.10	35.10
Casopufungin Acetate	B2083	N/A	39.07	78.31	115.30	73.32	69.54	65.50	122.67	116.89	120.28	91.37	77.73	115.49	84.44	83.95	92.04	26.89	77.31	77.31	77.31	77.31
Cathartanthine	N1382	TUBB	78.20	98.22	123.79	98.86	102.17	75.32	95.63	94.71	99.26	108.66	90.43	122.49	92.06	95.67	92.32	116.13	28.71	28.71	28.71	28.71
Cediranib (AZD217)	A1882	CSF1R	61.99	76.70	70.12	51.03	50.66	32.92	43.54	71.15	65.36	30.23	57.37	54.02	61.46	68.71	46.76	76.14	88.63	88.63	88.63	88.63
Cefazolin (sodium salt)	C4183	N/A	110.35	119.68	125.85	110.02	127.29	99.76	108.18	134.71	122.38	104.05	90.80	131.14	85.88	138.21	112.55	134.43	100.17	100.17	100.17	100.17
Cefepime	A8391	N/A	103.68	88.73	121.14	88.38	104.87	82.72	113.47	119.76	108.43	111.00	102.05	137.85	120.06	133.10	126.33	165.63	126.88	126.88	126.88	126.88
Cefoperazone	A8392	N/A	110.52	109.75	130.78	117.71	143.90	92.56	122.96	327.80	204.26	131.62	108.62	157.84	132.21	166.82	180.40	165.93	122.03	122.03	122.03	122.03
Cefotaxime (sodium salt)	C4588	N/A	85.15	104.36	106.54	116.25	116.74	98.42	99.82	136.22	136.46	107.89	102.65	120.75	74.94	163.84	145.66	119.31	89.74	89.74	89.74	89.74
Cefepodoxime Proxetil	B4973	N/A	103.01	98.22	133.45	107.99	90.33	108.74	104.20	113.34	96.97	109.52	94.21	175.50	103.44	121.34	86.04	115.11	27.89	27.89	27.89	27.89
Cefprozil	B4974	N/A	95.26	99.84	115.20	113.28	101.09	74.90	111.82	120.40	109.72	118.97	108.52	87.60	173.80	97.01	84.33	86.43	115.21	115.21	115.21	115.21
Ceftazidime	B3539	N/A	88.38	112.76	148.61	130.17	109.24	117.17	122.28	93.93	105.47	97.12	98.27	98.61	81.64	112.57	124.49	112.67	95.41	95.41	95.41	95.41

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)			ER-positive (luminal)				HER2-enriched			
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	WHM12	WHM2	WHM30	WHM30	WHM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108	
Ceftriaxone	B1907	N/A	81.63	98.67	102.94	111.44	94.96	96.45	111.13	121.02	101.58	101.92	89.84	131.61	100.50	58.54	55.27	137.30	93.38			
Ceftriaxone Sodium Trihydrate	B1691	N/A	116.00	179.38	124.58	105.49	107.39	120.74	139.20	107.31	110.34	116.98	80.30	110.66	101.41	78.95	76.20	147.39	99.73			
Celecoxib	A1664	PTGS2	121.98	155.94	112.10	72.80	67.41	84.67	102.01	99.80	101.21	89.44	99.97	110.37	94.37	96.01	91.94	94.61	85.85			
CEP-18770	A4009	PSMB8	69.61	83.92	82.75	66.51	65.42	40.44	45.12	90.80	95.77	14.42	17.22	93.43	171.27	47.78	33.16	49.35	64.84			
Cephalexin	B1692	N/A	107.78	162.11	112.70	114.13	115.46	109.36	126.53	107.41	115.36	101.53	71.62	121.64	100.87	74.32	78.34	121.48	100.18			
Cepharanthine	N2771	N/A	65.81	48.29	170.50	34.92	37.47	70.38	58.96	101.21	87.34	22.44	30.84	64.29	73.53	185.13	132.62	61.78	83.52			
Cetirizine	A3298	HRH1	103.97	111.24	74.62	89.90	95.24	91.49	98.16	134.57	120.52	95.74	98.69	95.22	93.55	109.54	106.03	106.86	111.34			
Cetirizine DihCl	B1547	HRH1	107.46	115.47	115.76	83.39	73.86	91.40	88.72	114.97	103.74	99.09	97.71	118.25	103.23	142.87	151.67	130.25	87.66			
Cetrimonium Bromide (CTAB)	B1693	N/A	33.91	54.74	69.11	36.12	38.84	36.69	48.14	36.79	34.39	26.88	16.57	56.47	71.97	28.29	25.47	30.19	22.61			
Cetorelix	B4975	GNRHR	99.03	122.01	150.90	101.12	91.16	78.61	164.44	126.18	137.20	110.32	83.15	130.79	102.28	224.40	155.80	129.43	25.82			
Cetylpyridinium Chloride	B1694	N/A	24.72	40.99	42.07	22.90	25.53	27.27	46.11	27.45	28.73	19.16	14.59	44.38	53.06	28.19	21.77	22.48	19.83			
Chenodeoxycholic Acid	B1908	NR1H4	86.93	140.08	102.16	96.75	97.51	98.78	130.89	144.24	148.76	73.11	58.87	104.17	103.10	38.46	44.50	148.28	77.55			
Chlorambucil	B3716	N/A	98.46	119.66	131.36	111.66	104.97	90.07	103.25	120.01	131.71	99.01	100.62	179.12	91.98	113.68	112.71	105.45	42.06			
Chloramphenicol	A2512	N/A	99.09	119.67	90.87	95.39	90.40	124.55	86.60	113.16	87.36	93.88	110.88	127.70	86.06	86.04	76.48	108.89	72.21			
Chlorhexidine digluconate	B3525	N/A	69.69	86.13	112.18	115.18	81.90	47.69	49.87	107.21	98.67	46.36	73.84	117.88	75.96	67.21	69.98	108.62	92.08			
Chlorhexidine HCl	B1695	N/A	97.30	101.53	123.70	87.44	98.19	105.44	111.18	79.61	84.99	91.81	87.49	88.32	75.95	96.14	96.74	107.18	86.06			
Chlormezanone	B1909	TSPO	82.21	97.70	122.29	111.27	97.16	103.80	121.47	171.66	172.72	97.60	87.02	118.20	104.99	76.26	66.03	161.42	98.90			
Chlorocresol	B1696	N/A	84.88	143.05	106.55	88.88	85.33	81.10	116.06	90.95	92.80	100.39	76.78	119.89	85.89	83.54	71.61	118.56	86.72			
Chlorogenic acid	N1769	N/A	102.12	106.76	116.35	114.82	110.92	90.92	111.08	85.16	68.86	150.46	86.99	153.17	95.76	102.88	111.88	119.77	32.13			
Chloroquine diphosphate	A8628	MRGPRX1	72.32	78.50	102.36	72.06	73.28	59.43	82.88	74.64	74.28	108.21	82.75	93.08	88.40	155.65	128.04	113.26	88.36			
Chlorothiazide	A8397	SLC12A3	103.51	97.66	90.01	84.38	103.27	70.61	108.24	144.26	103.25	110.64	92.99	149.14	120.97	123.48	145.48	152.86	126.33			
Chlorotrianisene	B5912	ESR1	81.71	88.67	95.53	98.78	80.87	96.06	93.86	96.36	96.81	102.13	70.20	124.51	101.07	86.81	65.75	80.32	15.70			
Chloroxine	B1910	N/A	39.03	33.99	130.01	182.10	57.63	40.99	118.38	45.50	52.26	26.81	30.59	56.74	69.71	54.28	75.66	86.07	62.64			
Chlorpheniramine Maleate	B1566	HRH1	128.80	185.16	125.76	77.92	81.53	74.76	90.80	135.59	119.23	117.44	99.46	115.31	97.02	204.77	151.25	198.69	97.22			
Chlorpromazine HCl	B1480	HTR1A	108.11	165.15	121.96	47.44	55.28	42.29	53.38	102.15	105.18	62.58	73.56	98.91	76.48	86.90	82.55	81.43	89.49			
Chlorpropamide	B1697	ABCC8	101.27	140.25	105.48	96.69	88.33	89.54	109.54	107.50	100.94	86.72	61.17	112.54	82.88	99.51	64.18	116.69	93.25			
Chlorprothixene	A8398	DRD2	76.17	95.44	83.84	82.66	56.13	35.43	64.27	133.62	115.04	62.42	81.38	87.11	93.87	106.95	103.27	105.09				
Chlorquinaldol	B1698	N/A	83.22	121.19	105.06	57.88	81.25	72.33	116.00	90.05	98.03	20.89	42.31	108.57	52.67	117.31	93.51	79.20	89.47			
Chlorzoxazone	B1701	Kcmm2	104.19	146.09	106.07	90.05	92.78	101.71	112.30	96.77	100.02	73.56	69.55	113.44	79.63	93.86	72.66	131.29	91.28			
Cholic acid	N1680	N/A	90.19	101.79	98.73	100.66	101.65	88.90	104.42	92.22	107.52	94.65	84.63	142.32	87.24	115.99	102.56	124.91	47.08			
Choline Chloride	B1703	CHAT	105.19	164.85	116.39	78.30	92.96	93.23	116.81	103.77	98.76	97.01	81.36	120.35	78.76	74.27	73.28	132.52	84.06			
Chromocarb	B1704	N/A	108.00	140.85	111.00	92.74	92.45	95.32	111.11	87.83	83.92	97.34	95.12	119.29	78.66	75.33	67.91	108.86	87.28			
Ciclesonide	B3477	NR3C1	51.41	83.62	121.99	63.48	29.99	37.34	34.70	110.99	88.95	33.86	67.35	76.29	90.08	50.51	47.36	38.89	39.82			
Ciclopirox	B2087	ATP1A1	51.41	134.51	117.01	90.13	95.23	213.16	323.33	102.70	86.21	24.44	29.18	67.73	51.65	76.56	71.34	44.76	26.41			
Ciclopirox ethanalamine	B1384	ATP1A1	75.60	149.86	123.29	57.58	69.22	278.78	327.34	81.43	91.40	38.36	25.09	60.33	69.36	61.57	57.06	53.11	36.35			
Cidofovir dihydrate	B1238	N/A	127.29	113.32	96.75	87.35	88.68	79.78	114.14	82.26	79.65	138.62	78.51	136.09	94.68	160.01	143.39	122.43	90.61			
Cilgintide	A8660	ITGAV/ITGB3	120.49	107.61	90.98	88.26	80.45	89.24	98.93	153.33	132.84	159.62	89.93	76.66	97.42	132.47	115.63	143.78	82.02			
Cilmiplast	A1447	Caenaf1b	111.34	76.18	54.89	88.84	79.17	30.09	52.20	67.79	69.58	66.84	95.90	90.13	81.66	39.96	93.23	42.89	66.21			
A4329	A4329	PDE4a	126.88	113.16	145.64	94.36	110.85	123.50	114.31	114.31	114.31	73.21	104.72	114.33	88.38	111.18	97.28	111.87	80.77			
A4337	A4337	PDE3A	127.39	138.11	93.67	85.97	75.67	172.13	210.84	142.35	107.28	86.78	69.64	125.04	105.94	142.69	108.92	100.68	88.72			
Cimetidine	B1557	HRH2	120.24	151.26	114.74	84.31	91.85	74.30	113.50	123.14	93.25	94.44	124.10	100.65	113.59	90.80	158.96	97.47				
Cinacalcet	A3313	CASR	35.04	31.27	33.48	16.80	17.74	28.50	40.81	36.92	34.59	14.08	20.05	34.18	121.60	45.53	41.24	11.30	104.19			
Cinacalcet HCl	B1423	CASR	36.92	40.64	43.63	27.93	31.34	39.15	47.18	28.49	26.63	24.96	18.29	46.77	64.80	41.36	45.33	32.20	24.36			
Cinchophen	B1705	ADORA2A	155.79	159.13	123.58	116.68	122.87	142.33	133.24	119.91	158.98	108.98	98.96	124.51	107.23	109.92	111.75	129.18	136.62			
Cinpezide maleate	N1911	ADORA2A	86.62	94.61	106.42	127.01	114.43	98.49	122.59	96.33	108.15	100.72	88.11	129.77	94.42	90.22	73.50	142.29	86.52			
Cinnamic acid	N1877	HCAR2	75.95	121.39	121.01	89.55	107.23	93.94	115.41	117.83	117.98	117.98	99.07	92.86	107.64	94.27	96.60	118.16	151.05	38.39		
Ciprofibrate	A4306	PPARA	106.31	85.78	113.71	98.31	94.16	122.26	116.76	116.65	138.21	102.27	86.29	126.47	79.44	118.48	102.20	106.89	89.86			
Cisatracurium Besylate	B1355	CHRNA2	125.74	228.67	129.18	123.87	115.00	59.90	70.22	125.29	115.36	113.95	89.96	128.74	109.14	83.17	77.66	105.74	136.42			
Cisplatin	A8321	N/A	113.28	114.68	117.14	91.83	107.95	103.74	129.91	122.88	142.30	17.01	110.90	124.22	119.07	85.47	47.79	149.50	128.38			
Citalopram hydrobromide	B6736	SLC6A2	85.32	120.60	128.88	112.30	99.53	77.02	111.47	94.11	81.76	103.50	83.96	137.64	107.87	107.31	97.78	106.47	32.52			

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)			ER-positive (luminal)			HER2-enriched					
Item Name	Catalog#	TARGET	HC101	HC101	HC116	UCD52	UCD52	UCD52	WHM12	WHM12	WHM30	WHM30	WHM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108	
Cleardibine	A2187	N/A	101.00	90.53	58.29	98.76	120.49	82.43	130.15	85.14	72.55	76.13	113.12	117.76	103.68	152.25	104.01	108.98	120.47				
Clarithromycin	A4322	N/A	108.20	115.38	101.69	89.27	110.82	96.69	128.44	96.72	108.01	81.30	136.92	116.31	136.92	117.88	132.85	122.59	92.41				
Clemastine Fumarate	B1588	HRH1	74.70	116.77	74.42	34.11	38.95	35.71	39.97	111.47	96.87	78.03	79.34	69.21	152.56	119.20	58.26	75.20					
Clevipidine Butyrate	B1415	CACNA1B	106.11	106.92	88.07	93.23	91.15	95.92	104.85	92.67	89.33	117.32	89.83	125.88	111.84	109.96	100.62	128.03	98.87				
Climbazole	B1706	N/A	125.83	178.78	131.42	88.83	103.17	116.54	125.46	113.47	125.62	100.98	78.47	114.89	98.79	92.30	80.52	179.91	109.40				
Clindamycin	B1707	N/A	112.31	171.82	122.06	88.45	105.18	107.87	126.59	110.77	120.79	99.38	66.54	124.12	105.72	84.83	67.99	134.93	96.08				
Clindamycin HCl	B1913	N/A	95.75	106.29	142.31	118.14	114.95	82.24	128.78	123.67	119.96	99.33	99.58	122.17	104.07	101.60	74.88	136.07	101.75				
Clindamycin Phosphate	B1708	N/A	88.41	191.77	89.11	61.96	84.36	78.54	106.84	82.52	84.44	93.11	58.11	111.70	96.61	107.49	64.96	127.95	102.70				
Clofazimine	B1915	NR3C1	100.16	132.03	195.76	149.50	135.21	73.58	108.44	197.77	207.48	77.20	154.33	125.30	132.05	226.36	176.21	115.08	95.86				
Clofibrate	A1412	RRM1	162.59	161.92	92.86	159.84	125.94	208.92	231.87	128.56	128.37	91.16	190.33	175.02	126.03	188.22	172.74	103.20	142.56				
Clofazimine	B1710	N/A	34.86	74.80	77.61	45.42	42.97	42.43	63.77	64.47	73.08	29.54	48.04	83.90	88.85	49.96	37.17	26.49	44.78				
Clofibric Acid	B1711	PPARA	93.87	124.89	97.78	70.87	91.36	79.51	107.09	109.93	108.98	95.52	63.71	118.53	99.27	101.53	88.02	122.20	98.74				
Clomiphene citrate	B1504	ESR1	84.04	424.05	134.44	62.04	69.83	26.67	43.43	156.15	135.48	37.62	32.18	51.48	95.83	38.28	40.24	151.49	35.52				
Clomipramine HCl	B2234	SLC6A3	86.41	116.90	88.43	62.24	59.88	57.22	58.84	103.60	85.20	72.32	76.00	108.50	69.69	81.14	95.56	122.89	70.24				
Clonidine HCl	B1333	Adra1d	136.40	126.69	134.89	97.24	92.61	93.71	114.38	124.75	124.44	105.37	92.63	127.12	113.55	106.32	115.96	114.60	92.44				
Clopidogrel	A5183	P2RY12	103.99	99.76	100.58	65.13	88.21	80.01	80.01	140.55	131.27	100.35	81.62	115.06	118.86	106.09	99.34	118.95	83.58				
Clopropranolol HCL	B1713	ADRB2	90.78	116.97	103.51	79.31	101.82	78.86	97.81	101.34	104.73	94.04	52.11	120.80	93.89	90.65	75.46	124.82	98.50				
Cloresulon	B1917	TUBB	95.44	118.94	168.51	123.81	108.07	101.90	122.33	147.12	157.62	91.84	158.87	107.69	105.96	202.04	186.47	130.27	115.53				
Clozantel	B1714	TUBB	24.78	33.95	105.34	59.68	63.41	28.71	46.54	90.39	84.78	18.95	16.38	104.39	85.74	42.55	31.54	29.25	26.13				
Clozantel Sodium	B1715	TUBB	33.05	35.74	96.33	62.64	73.49	37.38	51.88	52.16	53.14	17.97	17.98	113.90	93.16	37.42	33.33	32.52	26.12				
Clotrimazole	A8401	NR113	67.57	97.49	79.81	73.79	85.42	62.38	84.99	124.26	125.71	27.47	82.83	70.84	95.12	100.25	70.70	128.90	102.64				
Cloxacillin Sodium	B1918	N/A	118.38	163.33	237.09	180.75	106.18	158.14	184.78	213.58	94.27	228.16	175.54	133.64	189.76	193.19	126.47	115.62	102.62				
Clozapine	B2235	HTR1A	85.84	105.04	122.71	76.15	91.08	85.24	85.35	132.45	111.08	108.55	92.64	130.37	87.16	106.96	104.69	134.79	77.91				
CO-1686 (AVL-301)	A3320	EGFR	106.27	99.76	73.30	76.88	52.54	64.85	68.57	88.40	110.80	64.42	63.10	99.90	94.04	85.84	90.66	51.40	63.59				
Cobicistat (GS-9350)	A4313	CYP3A4	85.86	80.78	128.27	63.86	70.05	80.43	75.84	94.00	99.20	41.05	65.51	74.21	52.32	71.96	56.87	72.23	65.65				
Cobimetinib	A3321	MAP2K1	61.93	91.76	63.20	42.82	42.49	46.61	51.22	80.21	76.27	47.97	81.50	80.57	82.84	75.00	74.60	42.96	75.34				
Colchicine	A3324	TUBB	127.56	154.58	108.16	165.78	125.98	102.31	89.63	139.78	150.82	122.89	116.60	108.79	102.47	45.97	42.67	126.83	143.75				
Colistin Sulfate	B1716	N/A	85.28	76.25	99.32	80.07	72.65	125.62	105.27	90.47	90.34	66.45	40.62	83.40	76.48	129.95	71.95	73.83	137.31				
Colistin HCl	A8402	AVPR1A	98.20	123.33	105.58	69.88	73.48	88.51	120.05	139.49	142.30	55.43	65.47	83.27	85.34	87.49	111.61	150.43	87.36				
Cortisone acetate	B1919	NR3C1	107.25	131.00	140.09	127.94	83.81	98.73	125.22	123.30	114.60	85.97	151.96	129.59	104.95	105.48	86.73	118.41	96.14				
Curcumin	N1707	VKORC1	99.87	120.89	128.07	103.35	83.30	110.28	116.45	115.80	112.32	104.73	95.15	145.45	95.00	97.08	107.29	111.27	39.40				
CU-945598 HCl	A1435	CNR1_CNR2	92.91	73.14	92.15	64.53	62.23	85.92	93.23	85.92	102.14	28.31	50.24	86.02	75.05	71.86	90.07	59.19	44.15				
Crenolanib (CP-868596)	A8307	CSF1R	56.29	25.87	401.60	40.93	27.10	25.94	44.12	62.72	57.90	11.00	14.39	729.32	275.28	43.72	9.41	38.58	125.30				
Cromoglycol sodium	B3300	N/A	101.98	170.63	115.74	116.20	109.12	123.54	145.18	124.26	117.85	94.45	99.82	135.04	71.85	111.37	92.40	157.28	108.15				
Crystal Violet	B1920	N/A	25.86	31.67	56.69	31.94	27.33	35.85	57.63	38.39	35.28	23.54	30.36	48.90	28.07	24.62	24.84	40.67	21.37				
CUDC-101	A4092	EGFR	2233.87	2514.98	1346.14	1165.41	912.55	40.84	47.91	483.39	502.51	29.17	15.05	105.05	4.55	77.87	77.17	1068.84	408.47				
Curcumin	A3335	EP300	56.21	132.71	110.45	142.49	111.55	182.42	107.88	204.22	190.64	41.38	97.28	134.94	50.97	129.74	66.97	87.59	97.85				
CX-4945 (Silmiteceritinib)	A8330	CSNK2A1	70.99	158.82	106.09	83.76	72.30	99.16	99.80	69.79	90.02	19.41	37.56	110.88	136.69	176.44	208.14	82.65	103.38				
Cyclamic acid	B1921	N/A	81.16	101.70	120.88	101.38	76.00	95.23	113.11	102.22	109.60	92.96	95.86	118.13	91.90	58.94	57.16	135.50	95.04				
Cyclandelate	B1718	CACNA2D1	103.15	117.03	113.39	71.03	90.57	86.14	100.51	95.56	96.26	91.08	84.19	122.33	89.14	83.59	63.40	122.87	90.73				
Cyclobenzaprine HCl	B5994	HTR2A	86.26	109.89	92.32	77.01	75.70	79.57	99.62	88.86	90.96	74.11	72.97	95.09	84.46	134.00	127.83	116.51	31.79				
Cyclophosphamide	A2343	N/A	103.86	110.49	80.30	99.24	98.95	79.69	80.04	124.29	104.84	104.59	105.22	97.98	88.53	108.10	116.39	115.31	90.33				
Cyclophosphamide monohydrate	A4232	N/A	120.82	145.23	125.37	100.15	96.83	107.18	104.00	135.59	123.59	102.29	78.28	146.67	125.31	135.81	143.39	124.05	111.52				
Cyclosporin A	B1922	ABCG2	90.14	70.07	100.84	65.34	47.47	41.86	59.45	66.22	73.60	23.52	36.38	65.66	95.18	34.76	34.58	50.58	49.85				
Cyclosporine	A5938	PPIA	71.77	58.38	74.13	41.22	47.65	39.77	47.01	93.54	65.95	18.60	25.75	55.28	96.12	41.48	33.81	40.25	59.20				
Cyproheptadine hydrochloride	B3309	HTR6	79.48	102.49	90.07	88.68	70.82	71.09	91.14	123.63	108.72	89.70	76.91	114.59	95.83	88.76	90.38	114.80	91.23				
Cyproterone Acetate	A8404	AR	79.82	97.32	110.49	84.05	94.40	85.28	140.50	122.70	133.56	61.27	84.97	111.99	87.07	150.16	138.89	107.23	72.49				
Cyromazine	B3681	N/A	102.02	120.89	133.80	101.60	98.38	85.13	124.58	162.96	145.09	108.49	105.88	181.61	97.77	93.72	124.59	104.99	33.64				
Cysteamine HCl	B1719	N/A	108.50	114.58	107.72	80.03	105.49	101.95	103.39	106.94	97.04	96.46	90.29	111.63	95.83	83.31	75.73	119.26	94.26				
Cytarabine	A8405	N/A	64.15	65.88	83.29	79.61	103.17	52.30	64.50	85.96	86.18	94.96	93.48	100.97	136.09	68.89	83.92	115.38	107.57				
Cytarabine hydrochloride	B1100	N/A	67.74	82.67	73.86	100.92	109.02	52.11	63.91	88.82	73.34	146.95	96.20	104.68	147.37	63.91	59.04	123.11	88.11				
Cytidine	B1923	N/A	75.39	126.67	122.02	105.99	78.99	95.43	120.35	125.23	166.62	92.30	105.40	131.29	104.61	92.12	82.14	144.69	98.07				

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)			ER-positive (luminal)			HER2-enriched						
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	UCD52	WHM12	WHM12	WHM30	WHM30	WHM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108	HC108	
Cytisine	N1738	CHRNA4	84.79	101.85	128.11	94.29	87.58	74.74	101.13	83.99	78.91	83.99	78.91	108.49	87.20	112.31	95.00	115.72	95.99	111.55	111.55	28.30	28.30	28.30
Dabigatran etexilate mesylate	A3345	F2	92.85	104.83	94.62	92.00	104.72	60.51	65.85	108.54	100.39	108.54	100.39	87.25	75.70	125.82	99.42	89.99	122.92	122.92	40.04	40.04	76.51	76.51
Dabrafenib (GSK2118436)	B1407	BRAF	109.84	126.46	73.61	114.20	130.54	119.57	113.31	102.28	80.52	102.28	80.52	99.80	98.03	124.53	118.62	225.03	148.72	138.82	148.72	138.82	149.07	149.07
Dacarbazine	A2197	N/A	115.51	128.67	82.74	101.60	112.84	63.64	96.94	135.08	99.99	135.08	99.99	110.79	110.06	92.93	93.55	131.78	108.58	145.06	145.06	96.37	96.37	96.37
Daclatasvir (BMS-790052)	A5618	N/A	77.71	81.84	87.18	63.10	61.45	54.00	63.56	110.05	94.54	110.05	94.54	17.74	67.58	99.57	72.62	211.14	51.79	91.44	91.44	103.77	103.77	103.77
Dacortin (PF299804, PF299)	A8319	EGFR	36.94	32.01	55.06	27.65	31.78	37.37	50.47	48.59	46.29	48.59	46.29	21.33	23.24	49.83	57.00	34.95	14.24	39.15	39.15	106.56	106.56	106.56
Daidzein	N1862	ESRR1	119.86	171.93	179.55	139.75	157.65	114.04	124.15	266.32	217.81	266.32	217.81	436.29	148.36	155.35	114.46	295.90	277.54	260.95	260.95	76.58	76.58	76.58
Dantrolene, sodium salt	B6329	RYR1	88.30	109.05	110.11	95.75	89.13	100.89	106.58	134.81	124.31	106.58	134.81	89.02	77.96	174.17	99.14	112.45	98.50	132.74	132.74	40.75	40.75	40.75
Dapagliflozin	A5854	SGLT2	105.99	118.34	128.40	82.18	75.43	79.09	88.91	119.74	85.85	119.74	85.85	96.04	83.15	112.60	109.73	94.53	120.32	136.34	136.34	123.05	123.05	123.05
Dapoxetine HCl	B2264	SLC6A4	76.49	98.30	69.99	51.63	44.09	57.11	73.31	97.42	99.36	97.42	99.36	104.54	89.30	79.37	74.17	85.83	104.34	113.39	113.39	66.17	66.17	66.17
Dapsone	B3448	N/A	101.16	126.66	157.62	113.28	119.41	121.18	109.52	110.23	124.38	110.23	124.38	113.60	109.21	145.68	115.73	102.23	133.27	114.02	132.09	132.09	132.09	132.09
DAPT (GS1-IX)	A8200	PSEN1	101.65	120.81	130.15	58.62	61.60	73.99	74.36	141.43	105.49	141.43	105.49	68.56	59.67	115.00	104.46	122.64	108.99	115.36	115.36	109.36	109.36	109.36
Daptomycin	A1206	N/A	138.95	145.89	111.19	131.04	105.51	83.30	123.19	190.17	133.14	190.17	133.14	121.17	135.18	141.33	113.39	226.16	100.09	141.62	141.62	123.94	123.94	123.94
Darifenacin HBr	B1600	CHRM1	104.32	148.78	159.64	50.30	52.68	69.52	91.25	120.47	113.70	120.47	113.70	99.86	103.56	93.28	83.15	94.88	82.83	115.85	115.85	64.76	64.76	64.76
Darunavir	A8206	N/A	197.90	210.92	191.61	95.71	79.12	104.13	114.79	162.67	162.37	162.67	162.37	102.01	117.48	111.84	133.70	96.25	99.51	129.84	129.84	181.85	181.85	181.85
Darunavir Ethanolate	B4950	N/A	87.31	112.24	126.49	93.01	96.21	83.93	86.55	126.30	118.65	126.30	118.65	88.78	86.40	117.17	66.27	82.15	75.76	115.19	115.19	81.25	81.25	81.25
Dasatinib (BMS-354825)	A3017	ABL1	45.07	74.36	40.48	36.77	41.76	41.74	36.96	56.93	58.62	56.93	58.62	55.08	51.33	53.71	60.35	42.74	37.72	54.89	54.89	73.38	73.38	73.38
Daunorubicin HCl	B2285	N/A	28.80	35.58	49.94	32.20	28.58	41.79	42.34	51.75	37.41	51.75	37.41	38.80	26.84	141.15	31.22	38.58	44.05	44.18	44.18	47.08	47.08	47.08
Decamethonium Bromide	B1601	CHRNA2	113.20	106.70	104.78	83.27	74.49	95.91	83.60	108.28	93.71	108.28	93.71	104.99	95.20	120.27	101.51	103.65	106.36	128.42	128.42	75.14	75.14	75.14
Decitabine (NSC127716, 5AZA-CdR)	A1906	N/A	124.79	165.70	122.60	157.30	114.28	93.43	116.03	193.96	183.44	193.96	183.44	104.89	87.11	140.22	107.95	118.06	134.63	105.98	105.98	163.18	163.18	163.18
Deferasirox	A8639	N/A	58.95	72.10	100.93	54.35	101.01	77.31	113.17	71.18	69.11	71.18	69.11	34.52	89.41	129.17	106.79	51.87	73.83	99.05	99.05	75.44	75.44	75.44
Defeniprone	B1723	N/A	83.47	78.57	102.44	84.64	86.92	152.89	135.27	86.90	91.60	86.90	91.60	93.57	73.67	101.97	77.14	97.11	88.86	86.57	86.57	100.40	100.40	100.40
Deflazacort	B1924	NR3C1	79.48	133.54	218.03	270.63	151.12	109.64	129.11	142.43	146.96	142.43	146.96	114.63	159.64	140.93	132.59	246.35	144.06	144.06	131.98	131.98	131.98	131.98
Dehydroepiandrosterone (DHEA)	B1375	GLRA1	118.06	130.49	102.16	91.47	104.90	79.23	107.30	113.45	107.76	113.45	107.76	101.56	72.46	106.90	111.89	119.58	102.66	113.04	113.04	97.49	97.49	97.49
Deoxybutin	B1925	TYR	87.41	118.46	145.01	132.43	126.28	107.74	156.56	109.09	125.03	109.09	125.03	119.53	135.12	138.31	112.33	88.79	80.97	124.86	124.86	62.01	62.01	62.01
Deoxycholic acid	N1669	N/A	101.28	136.13	87.06	115.00	109.63	90.28	117.01	92.02	90.99	92.02	90.99	123.03	90.84	143.27	103.36	106.96	107.25	171.12	171.12	29.83	29.83	29.83
Deoxyflucortone acetate	B1724	NR3C1	159.93	249.53	134.90	152.76	125.44	133.05	147.79	155.18	172.33	155.18	172.33	62.89	128.55	132.25	112.37	157.63	124.82	109.07	109.07	160.60	160.60	160.60
Desloratadine	B1571	HRH1	124.77	202.52	128.06	60.74	73.59	58.02	81.01	107.36	96.41	107.36	96.41	98.56	100.67	143.25	77.54	140.81	114.56	115.35	115.35	75.73	75.73	75.73
Desogestrel	B4976	PGR	96.68	93.08	97.45	72.92	75.81	36.89	91.48	34.20	109.37	34.20	109.37	89.02	72.97	145.82	87.20	45.20	37.87	92.27	92.27	26.12	26.12	26.12
Desonide	B2158	NR3C1	40.20	129.39	211.13	149.93	137.78	85.26	106.94	114.81	139.26	114.81	139.26	86.54	147.35	176.04	124.96	368.17	342.21	23.94	23.94	146.39	146.39	146.39
Desvenlafaxine	B2236	SLC6A3	82.28	85.66	125.70	85.65	98.70	74.32	85.52	129.40	118.57	129.40	118.57	104.88	80.06	118.28	80.52	80.77	99.42	151.71	151.71	82.66	82.66	82.66
Desvenlafaxine Succinate	B2246	SLC6A3	86.09	95.89	128.81	99.38	85.46	97.39	111.82	131.90	135.01	131.90	135.01	116.31	98.21	153.04	92.58	103.57	116.82	140.62	140.62	87.76	87.76	87.76
Detomidine HCl	B1356	ADRA2A	120.71	115.08	92.05	81.86	87.91	62.87	108.05	132.94	137.16	132.94	137.16	118.39	75.50	113.60	97.18	84.22	74.66	148.37	148.37	75.13	75.13	75.13
Dexamethasone (DHAP)	A2324	NR3C1	108.18	147.33	219.96	167.40	169.38	69.12	97.69	209.37	168.78	209.37	168.78	109.45	186.14	137.84	113.61	399.49	403.73	130.33	130.33	164.74	164.74	164.74
Dexamethasone acetate	B1926	NR3C1	90.35	137.27	111.79	155.86	141.58	88.86	149.06	133.77	164.41	133.77	164.41	99.18	162.20	159.99	138.34	274.45	245.63	122.13	122.13	130.15	130.15	130.15
Dexamethasone acetate	B1725	ATP4A	155.74	220.65	169.55	149.42	137.41	183.75	161.33	179.82	193.06	179.82	193.06	58.79	131.06	148.72	133.51	227.92	147.73	301.89	301.89	173.13	173.13	173.13
Dexametomidine	B1334	ADRA2A	125.33	133.42	148.23	93.32	91.99	98.88	112.31	123.46	116.31	123.46	116.31	97.61	83.09	106.04	104.53	114.20	91.66	115.32	115.32	92.86	92.86	92.86
Dexametomidine HCl	B1357	ADRA2A	109.50	111.17	89.87	85.86	87.50	60.37	84.31	112.81	112.81	112.81	112.81	109.66	72.64	103.10	102.62	90.64	74.75	128.84	128.84	76.50	76.50	76.50
Dexrazoxane	B3407	TOP2A	78.59	87.33	102.58	100.20	101.30	79.65	131.07	131.07	131.07	131.07	131.07	115.84	87.66	147.56	92.35	101.10	119.31	132.72	132.72	80.18	80.18	80.18
Dexrazoxane HCl (ICRF-187, ADR-529)	A1602	TOP2A	29.76	99.81	84.20	106.09	86.07	56.61	83.82	115.31	112.55	115.31	112.55	109.28	104.10	133.58	97.88	97.65	94.97	106.94	106.94	99.09	99.09	99.09
Dextrose (D-glucose)	A8406	N/A	123.89	122.94	109.54	89.20	88.34	102.53	107.92	161.06	144.40	161.06	144.40	104.80	106.61	257.34	124.							

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)		ER-positive (luminal)			HER2-enriched				
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	WHIM2	WHIM2	WHIM30	WHIM30	WHIM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108
Dibucaine (Cinchocaine) HCl	A8407	SCN5A	114.82	133.15	100.55	70.34	65.56	92.24	100.61	112.60	106.01	98.89	85.73	154.19	102.88	119.83	112.61	119.83	112.61	144.61	99.78
Diazepam	B1927	N/A	75.75	121.70	122.80	118.25	74.31	100.97	128.12	153.14	168.42	23.74	104.19	119.18	95.30	51.86	66.39	51.86	66.39	73.11	96.97
Diclofenac	B3505	ASIC3	74.71	111.04	127.09	102.07	79.09	86.75	88.08	95.44	88.78	74.40	95.19	123.39	96.76	92.27	135.60	92.27	135.60	123.97	91.16
Diclofenac Diethylamine	B1928	ASIC3	78.59	104.89	112.63	67.12	70.80	102.34	113.57	93.69	94.35	87.36	89.97	77.92	83.10	63.23	77.52	63.23	77.52	99.78	73.00
Diclofenac Potassium	B1929	ASIC3	123.84	110.62	113.77	71.73	75.78	88.71	128.52	89.09	144.88	83.58	116.93	106.09	100.29	67.15	64.71	67.15	64.71	94.50	105.42
Diclofenac Sodium	B1457	ASIC3	81.99	107.84	110.97	67.34	79.89	80.64	99.78	81.40	81.30	85.12	77.44	119.55	73.87	85.99	123.22	85.99	123.22	89.82	69.20
Dicyclomine HCl	A8409	CHRM1	120.65	130.76	140.52	69.92	67.30	102.20	104.93	115.54	119.12	109.27	94.24	122.53	99.69	97.33	82.86	97.33	82.86	146.29	116.55
Dienosine	A8410	N/A	105.51	105.14	130.78	89.95	103.65	83.33	113.70	89.78	91.32	100.37	90.43	138.85	118.38	98.61	99.75	98.61	159.72	105.14	
Dienogest	B1516	PGR	150.41	206.40	164.15	94.56	90.04	110.25	100.58	144.92	132.22	92.31	96.19	123.54	82.16	167.76	172.38	167.76	172.38	188.16	95.81
Diethylstilbestrol	B2088	ESR1	30.59	87.52	107.17	72.40	84.26	80.15	151.83	91.60	76.07	34.04	88.82	95.68	75.48	32.22	49.80	32.22	49.80	10.75	57.48
Difloxacin HCl	A8411	N/A	60.91	59.50	94.82	108.95	122.91	57.00	86.12	146.65	113.74	52.18	54.96	84.67	189.73	121.16	108.94	121.16	108.94	113.08	73.76
Digoxin	B1728	NR3C1	101.30	119.38	284.73	192.05	161.96	132.86	122.57	182.74	167.29	107.50	160.17	137.23	116.16	401.73	375.19	401.73	375.19	113.73	128.62
Diltiazem HCl	B7684	ATP1A1	33.01	37.29	45.80	60.58	72.68	61.11	71.79	42.20	40.62	28.02	52.27	97.92	69.18	402.10	273.43	402.10	273.43	75.28	13.14
Diltiazem HCl	B2089	HTR3A	49.47	113.54	108.17	68.34	76.26	77.11	108.89	119.83	141.29	82.49	88.22	123.39	88.87	90.20	100.73	90.20	100.73	26.25	93.71
Dimesna	A1652	N/A	127.19	94.31	123.63	117.02	104.83	135.34	121.35	133.38	116.40	101.62	92.39	150.38	102.74	133.21	111.68	133.21	111.68	114.29	117.84
Dimethyl Fumarate	B1931	NFE2L2	111.08	141.43	113.44	97.20	92.08	112.99	155.58	115.94	140.72	99.80	107.84	129.12	95.43	81.02	59.83	81.02	59.83	134.88	104.41
Dinaciclib (SCH727965)	A8412	CDK1	35.75	40.53	92.91	37.59	46.67	40.39	57.01	70.46	61.84	37.63	87.32	406.37	72.59	567.81	470.60	567.81	470.60	190.09	234.01
Diosmetin	B5990	N/A	136.35	201.41	180.96	298.62	275.54	434.74	415.56	182.36	643.63	87.62	253.09	245.71	240.15	653.42	443.62	653.42	443.62	774.97	207.98
Diperodon HCl	A8413	SLC6A3	97.56	100.54	138.21	75.22	93.92	79.96	108.61	124.09	155.05	99.54	96.31	124.09	118.94	126.92	196.68	126.92	196.68	138.56	91.67
Diphemanil Methylsulfate	A8414	CHRM3	98.56	102.81	84.72	84.98	103.92	110.38	161.70	162.06	161.70	106.21	89.47	120.88	109.08	115.28	123.52	115.28	123.52	88.99	91.67
Diphenhydramine HCl	B1932	HRH1	96.12	122.19	117.79	88.85	79.59	84.38	129.37	96.53	135.43	88.75	85.23	122.75	90.81	76.29	71.76	76.29	71.76	128.11	95.13
Diphendolol HCl	B4783	CHRM1, CHRM2, CHRM3, CHRM4	103.48	129.96	117.61	83.38	118.12	100.80	114.36	105.37	121.13	115.28	98.97	138.68	82.46	86.19	89.93	86.19	89.93	127.25	94.67
Diphenylpyraline HCl	A8415	HRH1	83.65	88.40	91.74	66.87	84.14	69.80	99.57	116.55	97.39	109.52	85.94	99.88	106.11	88.22	106.13	88.22	106.13	147.37	95.35
Dipyridamole	B1933	SLC29A1	80.43	99.97	150.11	92.02	87.20	88.32	136.48	133.53	151.25	70.83	103.93	116.11	104.78	100.54	100.31	100.54	100.31	99.99	76.92
Dithromycin	B1731	N/A	91.61	193.97	102.65	92.24	71.43	82.27	99.00	89.77	95.11	100.52	78.54	117.48	93.99	84.28	68.23	84.28	68.23	125.41	115.88
Disulfiram	A4015	Aldh2	105.18	174.51	92.32	88.55	76.14	96.44	107.79	105.22	125.36	68.69	74.54	75.84	66.46	93.69	86.41	93.69	86.41	146.40	95.81
Divalproex Sodium	B1391	GABBR1, HDAC1	110.79	112.96	94.53	84.12	88.17	69.17	91.07	100.52	80.20	112.83	79.99	116.41	110.80	142.77	84.73	142.77	84.73	127.76	96.37
DL-Carnitine HCl	B1934	N/A	85.88	135.76	146.51	110.93	92.79	96.64	132.20	123.91	139.34	93.93	146.32	111.81	100.76	116.95	109.34	116.95	109.34	118.66	
DL-α-Difluoromethylornithine (hydrochloride hydrate)	C3328	ODC1	85.33	103.07	99.19	82.48	88.02	88.03	95.83	99.40	94.89	99.47	85.09	94.03	65.94	84.59	77.31	84.59	77.31	111.95	83.40
D-Mannitol	B2090	N/A	56.31	93.00	114.19	75.76	72.19	86.33	108.69	119.40	110.63	82.09	104.02	95.65	83.23	93.43	84.03	93.43	84.03	31.30	88.09
Docetaxel	A4394	TUBB	136.07	172.66	208.54	74.55	89.45	91.02	101.54	138.05	130.51	87.22	112.48	105.90	123.51	100.31	132.13	100.31	132.13	104.72	140.64
Docetaxel Trihydrate	A3370	TUBB	114.67	96.78	154.84	91.56	90.48	67.94	76.72	111.22	103.58	76.42	68.79	96.66	86.09	98.94	103.95	98.94	103.95	84.15	81.09
Docosanol (Abreva)	A8416	N/A	81.06	84.62	84.47	68.83	84.12	68.05	95.48	103.79	99.48	88.19	76.88	93.43	95.55	116.48	78.14	116.48	78.14	151.18	98.05
Dofetilide	A8417	KCNH1	101.50	101.93	89.31	72.53	90.76	83.16	97.30	109.12	101.92	98.46	91.12	113.51	94.17	109.82	85.68	109.82	85.68	131.99	94.43
Domiphen Bromide	B1733	DRD2	25.64	44.20	46.38	28.88	26.30	34.44	53.50	25.14	31.73	25.11	23.03	48.73	50.10	48.58	34.01	48.58	34.01	28.24	29.82
Dompipenone	B1481	N/A	138.93	251.43	357.79	123.72	131.58	80.55	87.10	168.67	182.55	66.71	158.72	103.31	84.87	243.73	225.93	243.73	225.93	162.09	127.83
Donepezil HCl	B1602	ACHE	130.60	143.02	147.42	61.19	70.95	89.01	83.28	96.94	117.46	109.42	116.55	89.93	105.80	152.20	153.06	152.20	153.06	99.54	79.74
Dopamine HCl	B1482	DRD1	94.37	129.77	125.14	93.24	93.95	54.44	57.47	132.02	122.98	86.53	139.35	103.42	84.41	60.97	57.12	60.97	57.12	120.35	96.56
Doripenem	B1076	N/A	88.65	94.15	85.24	87.93	77.37	80.02	106.63	101.17	79.50	194.46	90.98	102.55	106.04	112.75	85.56	112.75	85.56	128.26	89.60
Doripenem Hydrate	A2036	N/A	102.50	104.41	95.33	85.18	92.93	98.87	88.24	112.76	105.54	100.91	90.95	91.10	84.34	80.55	88.96	80.55	88.96	114.05	95.83
Dorzolamide HCl	A4357	CA1	96.94	103.31	98.19	75.46	68.19	111.32	99.48	93.99	84.52	111.38	82.18	110.67	130.40	117.73	125.02	117.73	125.02	99.46	107.74
Dovitinib (TKI-258, CHIR-258)	A2168	CSF1R	105.10	79.94	216.36	147.91	102.18	84.23	55.45	104.82	102.30	33.26	66.44	229.90	79.03	339.05	199.88	339.05	199.88	246.49	485.61
Dovitinib Dilactate acid	A8418	CSF1R	47.16	39.13	44.42	23.94	19.90	43.59	60.73	334.04	274.22	20.02	19.70	1240.56	65.96	80.62	77.34	80.62	77.34	58.52	74.30
Doxapram HCl	A8419	KCNK3	102.56	103.26	104.80	77.50	69.61	79.84	85.85	124.35	109.32	91.58	72.25	197.73	100.64	92.56	89.80	92.56	89.80	106.06	106.68
Doxazosin Mesylate	A2884	ADRA1A	116.59	117.20	122.96	102.16	82.54	55.50	69.62	126.04	107.74	49.30	97.16	94.67	83.26	113.99	92.99	113.99	92.99	132.08	132.78
Doxercalciferol	B2091	VDR	29.17	49.67	105.50	50.17	59.37	42.15	59.54	168.62	192.24	20.33	32.55	136.99	75.32	50.69	54.90	50.69	54.90	8.24	136.38
Doxifluridine	B2092	TYMP, TYMS	42.65	91.59	147.55	79.28	106.62	88.56	115.99	174.73	176.01	98.50	81.07	151.69	109.60	109.25	98.82	109.25	98.82	33.42	95.18
Doxofylline	B1734	PDE5A	91.50	129.47	105.06	98.96	93.90	94.49	109.73	93.97	106.73	103.86	87.33	117.43	100.34	86.11	79.39	86.11	79.39	123.67	102.10

Appendix A: PDX 1,363 drug screening dataset

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)			ER-positive (luminal)				HER2-enriched				
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	WHM2	WHM2	WHM30	WHM30	WHM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108	HC108	
Doxorubicin	A3966	TOP2A	45.41	67.15	60.36	24.28	24.31	54.53	46.67	84.39	76.92	26.35	31.18	187.84	49.57	217.44	134.50	100.28	146.47				
Doxorubicin	A1832	TOP2A	53.91	86.90	66.12	34.03	32.11	30.99	40.27	91.70	62.32	23.85	35.51	195.58	41.44	248.98	185.02	100.55	231.41				
Doxycycline HCl	A8420	MMP7	94.48	88.68	103.66	91.86	88.01	127.59	108.04	105.10	92.22	102.39	78.77	106.22	83.75	93.89	74.19	109.72	96.77				
Doxycycline hyclate	A4052	MMP7	143.08	173.97	134.16	113.55	108.83	84.36	97.52	157.34	188.23	103.08	86.58	109.03	113.81	110.59	103.37	208.29	106.08				
Doxylamine Succinate	B1735	HRH1	108.55	134.53	107.86	94.05	94.51	81.85	112.86	103.58	104.27	110.80	90.35	123.56	101.12	95.29	85.81	130.60	109.31				
Dronedarsone HCl	A3374	KCNA5	31.02	33.87	32.73	27.63	31.71	37.46	45.15	36.72	40.58	23.10	21.22	40.72	90.54	35.95	35.17	26.81	34.39				
Dronedarsone HCl	B1935	KCNA5	20.93	37.67	46.61	35.09	26.73	30.90	50.99	29.67	36.90	16.22	32.61	48.05	66.07	34.10	35.63	22.39	24.25				
Droperidol	B1736	DRD2	91.67	123.58	106.62	89.33	96.88	82.69	110.48	98.36	101.58	77.45	81.37	105.75	97.53	126.94	98.49	110.68	100.17				
Dropropizine	B1737	N/A	87.14	107.20	94.25	100.43	96.93	84.83	113.68	101.43	102.00	97.47	81.87	129.04	90.25	73.45	58.54	117.01	105.91				
Drosiprone	B1520	NR3C2	2754.14	9399.09	2294.42	1454.05	1366.13	80.86	48.13	1855.69	1589.98	312.97	43.29	150.02	822.92	101.43	68.10	426.188	1130.26				
D-Sorbitol	B3324	N/A	88.44	103.56	119.93	101.93	90.60	100.79	104.50	134.74	105.66	121.35	92.24	118.20	91.49	112.49	106.12	121.09	88.18				
Duloxetine HCl	A8421	HTR2A	91.78	82.85	66.63	32.15	29.60	37.99	38.99	73.96	87.89	32.05	79.79	106.43	70.78	103.90	119.20	74.91	84.03				
Dutasteride	A1659	SRD5A1	120.27	138.29	111.17	103.24	96.85	75.04	105.64	149.89	133.40	104.17	124.80	107.20	92.37	124.56	122.20	117.82	122.24				
Dyclonine HCl	B1936	SCN10A	66.04	116.67	88.59	99.28	81.94	28.75	51.28	108.03	150.83	85.24	111.23	110.09	109.94	62.33	58.63	112.79	91.13				
Dyphylline	A4343	PDE4A	93.08	103.65	85.87	92.76	87.55	103.21	104.78	136.28	102.22	108.87	87.19	122.33	114.30	127.18	107.51	119.98	102.46				
E 64d	A1903	CTSD	112.74	103.07	70.30	99.72	95.13	131.47	77.95	108.36	90.80	98.94	96.20	118.11	91.90	159.81	169.81	110.79	96.61				
Ebastine	B1740	HRH1	43.27	124.41	77.47	48.92	55.36	47.15	57.44	85.10	71.32	25.75	80.61	70.19	81.23	34.42	29.39	30.99	71.44				
Econazole nitrate	B1937	TRPM2	35.08	32.28	105.34	52.48	55.42	35.09	55.57	73.54	107.74	19.48	35.16	88.11	116.48	37.46	35.06	51.13	24.27				
Edaravone	A5059	N/A	88.84	72.74	112.78	76.65	99.07	66.19	100.07	137.50	123.39	101.07	82.43	107.82	100.40	100.00	98.75	93.83	77.32				
Edoxaban tosylate monohydrate	A3383	F10	103.65	100.06	81.10	77.79	99.75	90.20	102.69	123.55	117.27	95.01	79.49	92.15	91.24	103.09	115.33	106.13	89.39				
Efavirenz	B1119	N/A	102.50	125.87	107.67	68.08	70.84	37.29	101.94	94.13	70.40	74.15	63.67	85.91	99.76	77.74	88.03	97.74	70.33				
Eflornithine	B4834	N/A	102.96	134.29	165.48	81.73	89.04	100.09	91.78	143.05	178.76	96.58	70.00	147.57	91.50	132.59	120.05	93.04	26.78				
Eflornithine	A3384	ABCB1	112.10	111.34	97.69	59.80	67.68	32.60	63.85	90.52	89.26	48.13	95.20	71.72	100.61	138.44	88.37	96.46	102.58				
Eletriptan HBr	B2237	HTR1A	79.48	103.23	112.56	94.06	80.00	80.06	86.50	179.94	146.24	80.65	79.60	107.61	86.08	78.55	88.91	147.92	81.95				
Eliagic acid	A2306	N/A	113.17	91.73	125.33	103.00	104.00	125.62	109.59	107.09	122.75	102.46	98.27	144.13	104.88	207.68	146.36	108.59	120.74				
Eltrombopag	B2159	MPL	17.47	39.15	124.53	59.06	54.99	27.92	47.71	239.78	196.54	17.19	23.90	94.85	60.91	52.74	56.99	11.55	67.92				
Eltrombopag	A3387	MPL	132.75	32.69	119.35	81.50	72.16	37.43	36.15	91.68	116.36	29.26	23.53	79.35	70.98	44.54	43.04	32.27	61.90				
Elvitegravir (GS-9137)	A4070	N/A	74.31	154.19	123.88	82.16	73.51	68.58	79.06	144.51	173.60	66.94	15.39	86.70	108.99	52.44	42.36	104.94	55.54				
Embelin	A8235	XIAP	88.72	62.56	92.74	76.17	68.48	75.02	79.12	79.44	60.83	23.68	21.89	97.06	54.12	84.81	87.83	54.03	59.93				
EMD-1214063	A3388	MET	120.02	54.77	206.45	24.11	31.97	35.83	32.84	62.76	68.80	12.52	18.48	45.72	57.62	47.78	96.94	30.99	103.67				
Empagliflozin (BI 10773)	A4601	SLC5A1	105.65	84.20	112.78	95.22	92.80	117.14	107.19	120.90	106.91	100.29	81.18	132.07	84.07	97.05	77.95	111.89	94.67				
Emtricitabine	A8422	N/A	112.11	98.88	94.60	80.34	79.28	83.77	96.21	99.02	97.13	112.12	95.62	152.75	106.58	120.43	104.97	154.96	115.91				
Enalapril Maleate	B2205	ACE	105.95	149.71	120.13	123.07	116.84	105.02	126.04	105.72	101.50	98.98	103.13	126.09	72.34	108.03	95.85	114.09	98.28				
Enoxacin (Penetrex)	A8423	ATP6V1B2	96.85	104.92	91.00	80.20	79.05	76.60	94.34	100.76	96.90	110.96	92.58	143.65	109.29	112.36	95.38	165.66	109.58				
Enrofloxacin	B1742	N/A	94.91	115.38	110.70	127.56	120.17	117.58	142.82	76.15	84.88	112.62	87.14	105.66	91.83	126.84	114.82	123.48	110.34				
Entacapone	A4168	COMT	126.80	114.32	104.87	108.97	88.51	201.74	182.56	99.30	109.22	106.66	103.31	158.56	80.83	98.48	99.07	130.33	105.34				
Entecavir Hydrate	A1767	N/A	106.02	113.40	107.67	112.71	94.02	73.20	89.34	114.40	100.57	94.46	87.82	103.55	99.49	78.92	86.57	107.45	106.78				
Enitostat (MS-275, SNDX 275)	A8171	HDAC1	2631.98	2996.64	1778.21	476.95	478.37	63.64	87.84	1724.78	1725.75	209.93	28.81	108.60	375.11	53.46	63.90	2365.41	1524.82				
Entrectinib	B5859	ALK	26.46	30.03	58.45	36.94	37.01	39.74	45.48	50.47	33.15	23.24	22.32	59.77	48.87	44.93	37.14	37.36	8.86				
Enzastaurin (LY317615)	A1670	PRKCA	72.74	115.32	99.53	54.26	43.69	94.44	120.47	112.75	114.82	41.31	104.16	95.79	82.34	65.34	78.87	72.62	84.56				
Epalrestat	B1743	AKR1B1	144.03	339.13	102.31	109.21	94.05	398.06	421.61	112.88	154.28	325.53	137.91	112.08	96.38	177.13	162.78	506.84	317.72				
Epinephrine HCl	B1744	HRH1	100.44	102.55	118.36	78.00	80.06	90.52	102.39	94.25	84.34	79.10	85.95	94.79	95.49	78.08	80.71	108.22	87.94				
Epinephrine Bitartrate	B1358	ADRB1, ADRB2, ADRA1A, ADRA1B	108.55	71.62	96.71	94.45	106.38	48.85	86.00	109.36	110.99	105.02	73.07	96.27	90.81	74.05	69.44	106.49	59.56				
Epinephrine HCl	B1327	ADRA1A, ADRA1B	105.10	99.68	119.22	126.34	110.41	144.48	139.82	99.44	101.05	101.93	81.33	112.33	76.57	129.39	105.91	83.92	57.75				
Epiprubicin HCl	A2451	TOP2A	43.03	69.38	35.43	19.84	25.49	18.83	39.46	59.27	42.43	17.36	35.11	220.90	50.53	295.40	198.34	105.98	168.11				
Eplerenone	A8424	NR3C2	94.05	86.68	116.48	105.65	94.91	110.78	104.29	116.66	111.82	117.32	82.96	104.73	90.15	101.19	88.24	117.49	96.25				
Epatiflone B (EPO906, Patupilone)	A1630	TUBB	165.60	142.93	202.47	84.57	71.74	67.00	84.86	146.09	127.40	87.94	94.78	118.64	99.21	112.62	108.88	93.77	139.57				

Appendix A: PDX 1,363 drug screening dataset

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)			ER-positive (luminal)				HER2-enriched		
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	WHIM2	WHIM2	WHIM30	WHIM30	WHIM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108
Eprosartan Mesylate	B1746	AGTR1	137.64	175.21	134.28	130.40	116.69	115.94	129.10	182.34	213.02	94.21	117.80	128.67	119.98	115.70	99.42	121.75	151.89		
Epifibatid	B3490	ITGA2B/ITGB3	82.85	118.48	193.70	133.38	111.71	109.81	91.73	145.82	207.48	64.27	175.78	148.45	93.40	367.00	311.80	120.39	100.36		
Erdosteine	B1938	N/A	96.07	113.21	133.97	99.90	88.21	95.82	142.28	135.80	201.48	89.06	126.98	125.30	107.84	83.19	91.34	120.15	92.37		
Erlotinib	A3397	EGFR	61.24	97.57	81.13	67.41	68.23	54.21	41.55	110.48	103.58	69.47	57.85	73.65	74.16	70.25	75.12	66.75	72.29		
Erlotinib Hydrochloride	A8234	EGFR	50.05	100.14	100.20	51.14	53.65	53.85	42.10	88.18	80.77	50.67	67.40	50.03	104.23	65.69	73.92	87.19	94.21		
Erythromycin	B1939	N/A	97.22	115.05	113.44	107.03	83.01	92.31	143.40	167.33	167.87	87.86	105.53	100.67	92.74	84.09	70.32	121.97	89.67		
Ethylsuccinate	B1940	N/A	101.37	109.05	132.50	84.02	90.58	90.80	119.69	96.32	118.94	82.42	112.45	97.47	96.10	70.51	68.64	111.54	96.87		
Escitalopram Oxalate	B2238	SLC6A4	92.77	106.81	128.22	87.18	94.53	83.29	91.61	172.10	141.90	105.71	88.90	113.81	86.19	81.14	106.01	134.76	100.50		
Escitalopram acetate	B3487	SN5A	93.40	109.64	105.65	94.62	96.43	82.96	121.39	105.09	83.18	115.74	106.20	116.18	85.71	94.37	110.02	132.78	91.86		
Esmolol HCl	B1748	ADRB1	100.94	165.26	121.81	117.31	92.05	95.56	119.76	111.89	114.98	97.56	94.81	120.63	95.30	105.24	88.34	134.80	103.87		
Esomeprazole	B2200	ATP4A	34.51	119.51	112.22	100.16	98.94	87.66	100.77	160.87	201.67	62.45	106.82	142.66	92.61	177.16	151.99	9.81	88.17		
Magnesium	A8425	ESR1	96.55	103.15	91.41	89.27	82.48	87.86	127.87	69.29	79.08	94.49	88.29	111.13	92.97	200.49	271.41	159.81	138.99		
Estradiol Benzoate	B1941	ESR1	123.18	123.76	125.81	73.53	93.59	152.68	111.43	128.99	147.09	80.67	78.65	131.24	84.67	200.45	182.04	92.36	122.82		
Estradiol Cypionate	B1501	ESR1	169.99	166.91	147.28	96.60	87.42	103.08	117.50	138.78	121.13	99.80	93.38	100.69	93.12	190.90	168.63	146.74	96.89		
Estradiol valerate	B1506	ESR1	124.03	190.34	137.44	85.28	95.98	82.67	95.20	142.80	127.12	101.51	94.67	121.81	91.34	156.42	206.75	177.41	82.84		
Estrone	B1507	ESR1	117.83	145.78	151.82	93.56	115.61	92.05	104.67	142.80	157.80	99.15	150.59	117.76	134.16	169.00	143.14	103.71	102.90		
Estrone	A8426	ESR1	95.14	103.81	89.46	82.62	91.98	97.87	128.59	162.62	143.42	104.12	90.43	111.77	102.49	205.39	264.62	158.67	123.25		
Estrone	B7438	ESR1	84.48	95.09	104.38	104.06	104.00	72.09	110.48	98.52	98.01	89.69	73.51	173.06	95.28	173.01	144.40	129.28	36.72		
Ethacridine lactate monohydrate	B1749	N/A	46.98	68.31	296.71	181.16	135.70	43.67	55.62	78.33	74.10	21.30	27.50	41.57	36.27	69.69	45.08	38.91	93.94		
Ethambutol HCl	A8427	N/A	96.91	100.32	102.01	84.62	88.83	78.46	108.29	157.85	147.62	107.29	96.31	122.11	103.44	156.77	135.48	157.20	104.81		
Ethamsylate	B1750	SELP	98.34	225.77	126.37	118.08	99.61	83.85	100.63	106.47	99.90	104.37	94.49	124.25	98.01	104.87	90.71	132.28	112.18		
Ethinyl Estradiol	A8428	ESR1	101.62	112.63	93.28	81.60	86.48	89.32	124.82	124.07	99.40	113.42	92.51	118.59	101.84	335.23	312.01	172.52	105.65		
Ethionamide	A8429	N/A	97.44	113.13	100.18	75.26	89.25	86.61	98.89	105.17	91.87	102.82	97.76	110.64	103.87	126.06	146.83	167.31	102.90		
Ethinolol diacetate	B1508	PGR	120.19	151.26	136.23	80.96	88.84	95.22	119.64	100.84	122.84	82.40	90.11	117.87	73.38	131.17	153.06	136.42	54.19		
Ethronate	B1752	N/A	83.71	104.79	92.32	78.80	71.24	151.87	148.07	102.90	119.00	105.10	84.66	96.82	85.22	106.49	107.75	99.55	109.86		
Etidolac	B1444	PTGS2	100.67	132.67	96.78	72.74	85.76	79.23	105.98	80.02	91.93	117.71	79.99	103.94	97.23	102.95	91.66	109.02	69.60		
Etiomidate	A1958	GABRA1	116.06	112.26	77.48	87.02	67.86	95.75	121.09	112.32	98.73	94.37	89.75	90.07	112.81	92.78	112.84	90.31			
Etiomidate hydrochloride	B1246	GABRA1	115.66	158.45	116.99	90.43	104.08	124.19	166.13	80.11	72.64	150.72	98.29	154.91	117.27	481.72	290.10	117.96	101.23		
Etonogestrel	B3470	PGR	75.41	142.09	144.86	125.56	106.41	90.65	132.37	157.07	134.52	92.81	111.77	134.98	86.30	243.05	270.44	123.73	127.49		
Etoposide	A1971	TOP2A	108.48	97.47	69.72	122.53	116.49	87.59	96.10	110.22	80.46	93.17	86.82	94.22	89.39	86.09	81.85	139.79	91.54		
Etoricoxib	A3405	PTGS2	103.53	109.64	140.89	79.67	74.89	131.62	153.83	124.97	106.57	96.24	73.95	117.98	79.93	98.18	95.26	92.50	90.97		
Etravirine (TMC125)	B2224	N/A	111.84	102.72	109.15	86.92	111.73	94.88	89.74	138.44	137.08	88.67	95.13	126.79	93.36	86.54	86.58	152.01	97.32		
Evacetrapib (LY2484595)	A4377	CETP	30.07	52.37	138.55	117.84	120.81	88.32	95.31	114.73	105.86	24.63	99.19	134.64	98.46	45.27	57.56	116.75	22.54		
Everolimus (RAD001)	A8169	MTOR	189.69	302.84	179.27	48.24	62.20	38.49	45.32	184.57	135.21	30.25	24.67	69.85	101.59	55.18	54.63	232.54	238.16		
EX 527 (SEN014196)	A4181	SIRT1	135.11	154.07	120.94	136.09	119.62	135.43	145.89	177.82	144.20	100.87	104.08	182.27	128.29	141.35	154.15	128.48	109.55		
Exemestane	A1296	CYP19A1	154.01	177.62	124.39	170.60	146.53	107.64	147.60	161.73	140.67	90.99	110.12	103.09	123.81	154.61	145.36	116.66	158.90		
Ezetimibe	A8430	NPC1L1	104.62	113.24	97.28	83.64	79.15	92.16	99.80	96.73	104.16	72.37	100.80	101.65	92.54	118.84	123.62	115.32	95.69		
Famciclovir	B1942	N/A	99.71	123.97	135.75	79.37	91.25	111.56	101.40	115.62	112.60	90.48	96.26	114.23	96.30	117.18	127.90	134.42	127.62		
Famotidine	B1560	HRH2	108.57	131.54	98.63	74.05	82.88	81.61	90.28	167.94	162.16	108.88	96.57	126.74	98.87	162.81	134.99	145.50	85.16		
Famprofazone	A8431	TAAR1	103.92	137.97	120.81	95.62	79.85	86.40	108.74	129.76	118.00	82.78	75.57	128.53	110.54	95.22	75.38	107.20	136.54		
Fasudil (HA-1077) HCl	A5734	ROCK1	68.63	94.55	121.71	67.40	83.33	85.31	89.35	100.70	83.52	62.85	75.83	93.41	76.21	83.50	75.77	96.39	90.87		
Felbamostat	A5926	XDH	2394.56	443.08	190.88	1206.10	840.28	1647.38	2024.37	1074.71	798.18	783.27	1248.60	3472.50	589.22	2289.43	2456.07	722.47	312.15		
Felbamostat	B2093	GRIN2B	41.70	100.75	101.01	75.76	86.65	91.81	107.20	655.27	631.61	97.79	83.63	136.72	95.30	108.59	96.86	34.12	92.94		
Felodipine	B1416	CFTR	119.56	112.44	97.90	86.89	90.10	94.42	108.86	122.06	125.94	122.83	113.46	116.66	114.32	101.71	123.03	142.54	97.27		
Fenendazole	A2610	N/A	159.43	227.00	153.20	121.34	121.45	155.94	127.61	225.30	213.08	163.91	199.51	129.32	129.30	132.24	177.78	164.80	114.56		
Fenofibrate	B1943	Fabp1	95.24	120.82	135.21	79.42	98.86	107.97	110.27	130.63	143.74	96.54	90.65	106.30	92.06	112.51	62.57	134.29	95.78		
Fenoldopam	B1483	DRD1	113.25	136.48	124.12	110.17	110.85	87.49	106.09	119.41	132.90	113.01	101.51	101.10	100.59	88.70	92.05	89.22	79.45		
Fenopropfen Calcium	B1944	PTGS1	87.54	135.72	105.45	80.52	85.42	93.44	103.95	161.32	177.32	106.31	95.58	100.26	94.34	132.08	109.82	125.29	99.46		
Fenopropfen calcium hydrate	B1945	PTGS1	85.19	112.05	119.56	82.43	87.49	103.99	105.76	121.65	157.25	103.74	84.62	103.96	88.98	96.69	106.00	110.67	89.93		
Fenspiride HCl	B1754	HTR2A																			

Appendix A: PDX 1,363 drug screening dataset

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)			ER-positive (luminal)			HER2-enriched				
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	WHIM2	WHIM2	WHIM30	WHIM30	WHIM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108	HC108
Fenticonazole Nitrate	A8432	N/A	41.42	40.12	104.62	58.89	59.35	32.79	48.56	97.74	85.95	17.49	20.95	96.94	74.79	44.97	44.51	78.99	29.46			
Fexofenadine HCl	B1573	HRH1	104.41	149.37	120.07	80.98	94.74	74.25	94.75	117.72	97.72	115.84	113.52	128.87	96.36	126.48	135.22	154.13	88.33			
FG-4592 (ASP15.17)	A4187	EGLN1	119.67	123.49	88.24	117.24	96.38	154.56	166.17	125.99	106.24	96.16	81.14	189.02	139.79	109.46	115.68	105.55	101.17			
Fidaxomicin	B1755	N/A	31.05	48.75	56.33	49.32	39.96	34.38	46.98	29.77	28.83	23.23	33.90	65.47	72.70	46.24	46.37	59.63	57.61			
Finasteride	A5143	SRD5A2	121.26	150.02	99.79	81.93	80.34	92.91	95.09	143.28	168.16	108.75	96.69	115.15	124.86	99.64	92.68	146.98	139.55			
Finlolidom (FTY720)	A8548	Kcnj5	33.01	24.84	49.06	24.72	26.53	75.61	80.15	92.87	72.08	16.59	21.02	53.95	33.83	59.31	45.37	19.51	21.00			
Flavoxate hydrochloride	B3433	CHRM1, CHRM2	72.29	101.65	119.25	100.94	98.03	71.54	105.48	113.39	100.35	115.24	116.29	122.70	90.90	109.05	146.61	105.22	101.00			
Flufenicol	B1758	N/A	100.11	135.13	115.81	103.39	99.68	74.29	100.51	94.25	104.03	90.95	88.02	117.95	101.41	107.67	119.57	126.16	104.77			
Fluorouridine	A2402	N/A	126.00	117.66	161.05	175.86	158.87	95.63	114.64	172.87	124.82	88.77	117.43	102.91	130.80	88.40	80.41	91.02	112.97			
Fluobenzazole	B1759	N/A	101.22	106.27	139.61	82.51	78.17	165.25	113.66	106.22	106.02	104.72	101.18	102.64	81.82	108.22	95.89	110.35	99.44			
Fluonazole	B2094	N/A	41.30	101.62	118.68	70.38	82.67	79.88	181.83	178.52	115.02	83.51	152.52	94.24	115.89	109.11	36.39	99.34				
Fluonazole hydrate	B1226	N/A	121.19	110.49	100.93	89.57	97.49	92.05	106.12	141.74	112.63	117.30	81.51	108.98	89.68	143.19	132.70	135.95	92.65			
Fluorouridine	A8433	N/A	104.80	107.14	94.75	82.43	80.27	93.37	94.07	81.17	82.98	103.11	86.22	136.90	93.10	138.60	132.26	141.71	103.73			
Fludarabine	A5424	RRM1	112.12	149.70	170.51	107.80	107.65	104.88	127.26	115.68	115.68	110.45	96.29	134.27	116.39	158.04	172.18	163.15	136.63			
Fludarabine Phosphate (Fludara)	A8317	RRM1	112.81	89.73	105.80	95.07	101.39	104.11	149.94	106.36	124.25	110.39	85.80	133.87	124.07	91.61	105.98	132.56	129.96			
Flumazenil	A2917	GABRA1	118.52	109.65	92.47	105.86	130.29	97.92	108.45	152.81	132.15	102.16	77.10	106.44	96.76	95.94	91.90	100.88	119.39			
Flumequine	B2292	N/A	85.39	100.30	137.61	103.22	111.44	101.34	95.39	145.52	124.28	98.49	87.72	155.89	118.42	111.90	121.49	99.18	135.35			
Flumethasone	B1761	NR3C1	109.11	178.19	235.65	149.67	181.39	85.06	101.39	159.48	166.89	99.97	179.38	179.75	145.30	328.57	287.06	130.65	141.27			
Flunarizine 2HCl	B1412	DRD2, HRH1, CACNA1H, CACNA1G, CACNA1I																				
Flunixin Meglumine	B1445	PTGS1, PTGS2	91.64	119.51	105.59	44.95	30.04	47.79	93.37	81.30	81.30	52.44	112.00	82.37	96.50	68.90	81.82	115.65	60.27			
Fluocinolone Acetonide	B2095	NR3C1	42.28	125.81	272.15	118.84	142.31	84.52	132.90	218.82	250.12	112.79	151.11	154.34	119.97	324.20	326.60	32.86	129.37			
Fluocinonide	B2144	NR3C1	38.70	113.06	251.74	157.44	153.80	72.59	116.61	176.26	174.94	98.87	154.62	178.69	129.20	378.52	345.95	25.44	136.14			
Fluorouracil (Adrucil)	A4071	N/A	123.01	148.73	150.83	139.18	139.51	91.74	119.90	194.96	207.51	80.21	70.08	111.98	166.77	85.37	76.92	138.71	87.81			
Fluoxetine HCl	A2436	Htr2a	94.52	101.59	58.64	49.07	46.44	40.64	49.12	73.00	58.84	63.91	105.28	98.42	75.18	112.77	95.86	46.15	79.50			
Flutamide	B1376	AR	130.97	141.24	78.37	75.28	82.44	88.30	135.17	120.23	110.88	77.46	66.15	138.76	125.20	103.81	91.94	120.91	88.87			
Fluticasone propionate	B2096	NR3C1	40.28	113.21	271.75	117.76	137.54	70.51	132.96	213.04	236.03	104.03	150.99	166.18	132.75	368.08	317.45	31.30	111.81			
Fluvastatin	A3419	HMGCR	82.15	100.30	108.53	51.19	67.49	47.14	50.75	148.66	129.44	53.22	78.26	129.62	162.18	198.99	184.58	59.60	80.00			
Fluvastatin Sodium	A4363	HMGCR	80.82	101.75	135.26	58.23	51.64	60.02	59.15	120.80	105.54	53.63	68.71	135.19	252.31	231.50	208.00	90.94	64.97			
Fluvoxamine maleate	A2553	Slc6a4	123.24	117.14	67.66	78.88	90.89	56.14	82.48	104.21	110.05	90.53	90.89	111.42	92.98	99.62	89.50	78.58	75.61			
Folic acid	N2075	FOLR1	88.62	118.21	116.69	75.98	108.73	93.14	99.10	95.09	106.92	106.33	88.61	117.66	85.30	99.43	103.38	98.18	33.76			
Foretinib (GSK1363089)	A2974	FLT1	32.24	38.48	48.00	26.49	29.46	57.80	42.33	54.25	75.32	88.14	43.34	54.97	52.68	55.75	64.58	20.47	111.24			
Fosaprepitant dimesylate salt	B2145	TACR1	31.20	103.66	91.74	62.41	52.07	48.69	110.69	107.71	111.13	33.38	71.35	102.72	85.08	80.71	71.74	15.71	68.87			
Fosbretabulin (Combrelistatin A4 Phosphate (CA4P))	B1634	TUBA1A																				
Foscarnet Sodium	B1946	N/A	151.43	217.59	131.55	74.39	97.57	119.49	103.05	107.93	99.81	134.37	84.95	115.09	114.92	45.68	37.80	203.23	19.76			
Fostamatinib (R78B)	B2284	SYK	89.66	117.78	132.74	84.25	88.48	110.53	95.04	124.17	127.26	100.73	95.46	96.72	89.60	90.35	99.85	119.01	116.82			
FT-207 (NSC 148958)	B1474	N/A	82.25	94.39	64.98	53.04	58.32	55.20	61.08	91.26	81.97	82.25	92.14	101.83	60.99	73.80	75.24	98.15	74.34			
Fudosteine	B1763	MUC5AC	151.01	165.09	142.69	101.62	130.55	139.63	121.26	130.58	129.41	105.23	112.60	110.08	112.34	83.75	94.69	96.65	117.10			
Fulvestrant	A1428	ESR1	84.45	97.63	96.07	80.67	73.93	121.96	120.18	85.06	97.12	92.46	81.75	102.66	94.54	115.06	99.56	53.49	89.36			
Furiladone HCl	B1764	MAOA, MAOB	131.47	142.07	95.71	81.63	76.21	52.25	102.71	120.74	137.58	60.40	70.60	89.12	85.63	48.44	57.60	73.82	82.94			
Furosemide	A8435	SLC12A2	59.49	92.13	96.98	144.27	125.52	35.63	49.81	92.64	99.43	31.16	62.27	152.58	63.72	104.32	84.02	146.11	132.80			
Fusidic Acid (sodium salt)	C5167	N/A	103.27	113.74	94.53	83.45	83.68	97.30	99.34	83.31	74.51	104.44	92.30	125.65	104.51	101.11	77.19	168.75	132.41			
Gabapentin	A8436	GABBR1	75.86	118.39	121.41	108.89	113.37	77.39	99.20	162.81	135.72	97.36	126.95	115.77	81.63	127.17	130.63	109.81	106.51			
Gabapentin HCl	B1529	CACNA2D1, CACNA2D2	91.37	102.26	76.02	78.43	77.27	82.27	93.98	84.82	69.07	104.55	91.12	118.71	103.69	86.37	89.90	186.88	102.72			
Gabexate mesylate	A4012	TPSAB1	112.55	171.56	119.87	80.98	79.92	80.37	91.12	115.14	115.76	96.50	91.94	120.52	90.15	119.37	99.18	171.85	89.66			
			163.42	176.35	158.61	146.79	138.09	103.94	118.71	161.26	199.06	100.24	95.77	121.62	147.43	97.64	95.95	152.66	124.68			

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)			ER-positive (luminal)			HER2-enriched		
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	WHM12	WHM12	WHM30	WHM30	WHM30	HC109	HC109	HC103	HC111	HC113	HC113	HC108	HC108
Cadodiamide	B1765	N/A	80.30	118.63	111.70	108.83	98.33	72.05	112.92	98.17	90.79	88.33	109.70	111.33	90.06	89.96	77.33	119.66	106.44	106.44
Gallanthamine HBr	B1745	CHRNA1	108.03	117.47	73.83	99.67	95.98	71.22	88.19	135.19	101.09	97.14	96.90	101.51	98.15	88.15	86.19	74.64	107.74	134.52
Gallamine Triethiodide	B1610	CHRM2	98.07	113.59	92.63	93.51	102.49	122.11	113.33	75.16	83.74	108.54	80.69	118.26	93.14	112.51	100.77	144.04	117.61	117.61
Galic acid	N1830	CA1	76.78	78.15	125.97	84.98	97.46	49.06	66.85	78.25	90.81	97.42	84.14	107.23	54.34	110.66	99.92	106.18	82.29	82.29
Ganciclovir	B2097	N/A	39.20	86.31	126.01	83.25	91.39	61.24	125.71	141.44	143.32	96.19	93.35	123.92	97.91	123.97	99.37	31.45	91.94	91.94
Ganetespib (STA-9090)	A4385	HSP90AA1	39.29	78.88	68.24	41.66	55.54	89.44	100.65	97.97	95.26	23.93	26.72	53.92	36.49	477.10	396.78	46.21	181.24	181.24
Gatifloxacin	A1313	N/A	77.36	121.16	92.21	145.12	135.69	43.05	76.06	140.29	106.94	67.68	82.34	81.10	123.71	88.02	77.28	66.53	57.14	57.14
GDC-0449 (Vismodegib)	A3021	SMO	80.65	137.93	83.37	88.38	65.83	114.70	106.93	131.60	135.04	55.45	83.58	94.37	103.55	99.44	110.29	82.89	114.26	114.26
GDC-0941	A8210	PIK3CA	144.07	236.90	217.44	99.02	78.07	61.40	65.91	1962.30	2322.84	88.70	89.76	94.79	114.08	93.02	88.34	141.35	150.23	150.23
Gefitinib (ZD1839)	A8219	EGFR	59.62	131.61	94.75	51.29	53.16	46.27	49.37	129.11	127.52	62.43	93.39	55.28	110.00	64.45	62.22	80.33	97.56	97.56
Gemcitabine	A8437	RRM1	62.56	78.14	64.72	101.01	100.13	63.19	94.53	110.86	128.12	68.40	81.79	95.87	111.66	113.95	121.46	142.84	114.81	114.81
Gemcitabine HCl	A1402	RRM1	80.57	111.63	107.16	149.65	115.62	70.68	80.74	114.45	94.88	76.97	109.11	109.04	103.29	78.15	100.98	135.00	125.93	125.93
Gemfibrozil	B1947	SLCO1B1	82.54	117.26	224.43	111.88	136.02	89.46	107.06	203.29	203.59	93.14	169.85	117.77	112.06	277.99	293.21	110.18	108.26	108.26
Genipin	N2408	UCP2	153.75	181.99	197.89	105.93	113.37	116.19	131.80	162.28	148.67	99.52	91.11	137.64	98.60	120.92	117.14	105.32	120.85	120.85
Geniposide	N1360	UCP2	87.67	121.28	116.26	115.45	117.32	87.04	80.23	95.98	97.09	119.04	89.69	157.60	98.30	89.87	100.72	126.38	43.00	43.00
Geniposidic acid	N1272	UCP2	92.65	106.32	110.28	107.17	92.50	90.01	98.53	142.80	143.65	105.69	81.67	149.73	95.64	99.34	115.56	127.02	41.61	41.61
Genistein	A2198	CATR	243.46	258.20	182.68	164.69	121.60	117.52	124.88	506.89	174.83	402.59	153.94	159.81	128.72	322.99	288.53	1065.24	205.08	205.08
Gentamycin Sulfate	A2514	N/A	112.44	125.03	97.04	109.06	80.45	73.81	70.99	100.82	100.82	82.24	118.25	90.69	101.00	87.78	100.98	93.09	102.41	102.41
Gestodene	B1517	PGR	201.00	387.09	184.11	144.09	142.16	102.57	109.66	250.68	248.61	82.99	111.77	149.15	122.12	197.29	161.54	260.68	132.90	132.90
Gimeracil	A4342	DPYD	97.67	95.23	91.03	90.52	85.07	112.44	91.30	113.16	89.49	107.30	80.64	130.77	112.32	132.98	112.81	119.03	91.36	91.36
Ginkgolide A	N1900	PTAFR	89.19	108.55	116.18	84.18	99.09	91.71	109.35	84.87	88.11	101.67	93.00	111.85	96.49	110.14	118.70	116.13	38.69	38.69
glatiramer acetate	B4978	N/A	84.95	103.75	124.82	125.03	110.71	69.38	122.38	140.51	150.22	100.80	115.79	135.77	108.23	182.52	159.61	130.68	29.73	29.73
Glibenclamide	B1296	ABCC8	112.15	93.36	110.35	116.45	121.45	135.34	134.01	409.20	444.35	105.14	82.32	150.66	93.22	108.78	107.57	109.79	88.19	88.19
Gliclazide	B2195	ABCC8	42.15	144.27	122.46	103.85	87.39	118.92	130.39	131.73	118.14	75.78	105.74	122.96	90.15	101.64	107.43	33.66	119.97	119.97
Glimepiride	A4033	ABCC8	146.42	170.02	158.49	126.12	131.01	99.91	109.44	164.98	163.89	96.43	76.85	122.66	147.27	101.03	85.45	128.07	85.47	85.47
Glipizide	A8438	ABCC8	92.96	116.01	99.08	87.55	79.63	79.36	95.12	145.82	129.50	117.60	94.79	127.62	107.74	94.36	91.86	160.05	128.55	128.55
Glutathione	B2196	ABCC8	30.77	147.61	142.37	101.43	85.59	115.67	143.96	150.50	123.86	54.76	82.08	108.95	91.40	78.13	111.07	26.51	105.42	105.42
GLPG0634	B1130	JAK2	525.60	1082.51	652.32	536.55	499.92	914.77	1711.87	153.65	139.74	149.57	221.50	1484.42	619.70	6573.00	5610.49	207.88	373.61	373.61
Glycopyrrolate	B1286	CHRM1	106.44	113.91	94.76	91.96	99.23	103.89	96.56	88.21	79.07	159.24	87.13	152.50	99.28	125.98	108.37	113.29	93.97	93.97
GM 6001	A4050	MMP9	138.65	144.02	139.94	137.38	115.37	94.54	114.83	183.01	239.44	95.34	82.40	116.42	129.49	96.31	88.63	201.52	122.46	122.46
Granisetron	A3443	HTR3A	113.71	111.19	89.31	101.85	108.40	130.08	90.92	155.29	111.17	114.89	101.56	118.71	81.83	99.49	116.89	99.19	102.58	102.58
Granisetron HCl	A1295	HTR3A	120.73	112.16	89.64	115.94	110.71	72.73	103.55	126.19	103.42	114.89	89.18	110.81	97.63	107.71	84.73	87.45	102.71	102.71
Griseofulvin	B3680	TUBA1A	132.16	121.00	127.85	152.68	118.99	95.53	146.65	200.88	179.95	120.07	162.52	214.78	98.66	124.35	132.51	114.22	34.21	34.21
GS-7340	B8021	N/A	96.31	98.16	182.67	104.29	103.11	117.54	116.67	138.36	149.98	95.61	80.25	108.56	112.01	60.07	71.35	77.09	37.82	37.82
GS-2973	B3553	SYK	340.54	131.44	86.16	425.63	84.07	115.95	391.11	683.29	569.24	131.92	464.64	812.57	124.72	300.64	229.42	177.91	32.00	32.00
GSK2126458	A8556	MTOR	63.87	64.35	147.09	44.16	42.68	44.33	55.05	44.51	41.29	26.79	26.50	65.60	70.32	270.32	222.24	138.39	69.05	69.05
Guafenesin	A8442	N/A	104.68	111.41	117.43	90.97	92.41	82.15	107.84	133.98	148.61	126.32	97.14	130.67	102.32	246.24	217.04	157.38	109.27	109.27
Guafenesin Acetate	B1335	ADRA2A	116.97	151.53	157.59	78.92	74.95	97.85	120.70	123.46	95.93	79.76	87.34	121.73	107.54	109.64	92.77	101.84	95.70	95.70
Guanfacine hydrochloride	A3451	ADRA2A	106.22	127.94	94.42	88.93	97.49	109.13	95.06	145.46	118.02	88.75	75.51	97.58	86.23	101.99	111.18	99.55	97.18	97.18
Guandine HCl	B1949	N/A	69.79	84.52	125.65	84.81	73.39	93.67	101.63	136.77	133.46	89.73	103.22	96.30	85.55	121.62	127.43	97.89	94.18	94.18
Halobetasol Propionate	B1766	NR3C1	108.44	137.99	246.15	185.27	151.48	106.75	104.15	174.31	180.23	94.97	197.41	143.63	132.93	277.97	254.19	117.07	127.91	127.91
Halobetasol	B1767	NR3C1	153.81	163.54	303.59	204.09	178.87	106.19	119.76	200.63	229.21	65.09	201.37	152.37	132.88	279.53	281.66	113.54	224.08	224.08
Haloperidol	B2099	HTR1A	37.36	89.27	116.91	59.79	63.40	65.18	116.50	115.25	127.56	93.52	78.68	101.65	90.00	96.62	82.57	22.16	75.86	75.86
Haloperidol hydrochloride	B1242	HTR1A	103.71	123.79	126.71	59.91	66.83	109.59	118.73	66.40	53.93	124.98	81.51	99.56	106.35	225.57	206.60	102.45	69.54	69.54
Heparin sodium	A5066	SERPINC1	95.98	92.91	104.08	73.00	81.28	68.28	81.13	131.29	118.15	89.57	77.24	95.26	97.24	88.34	84.76	109.37	91.19	91.19
Histamine 2HCl	B1561	HRH1, HRH2, HRH3, HRH4	107.88	128.30	110.74	84.59	91.07	77.10	85.48	125.60	118.28	110.89	99.23	128.71	104.81	135.09	113.08	151.60	80.77	80.77
Histamine Phosphate	B1770	HRH1, HRH2, HRH3, HRH4	104.25	129.35	131.21	111.94	87.77	95.74	101.76	138.57	158.47	84.60	105.80	116.55	98.45	359.63	216.62	126.61	128.86	128.86
Homatropine Bromide	B1603	CHRM1, CHRM2, CHRM3, CHRM4	125.65	139.72	109.69	60.89	79.82	95.59	94.75	109.07	102.19	118.85	103.18	129.39	99.79	150.39	129.25	146.07	80.67	80.67
Homatropine Methylbromide	B1604	CHRM1, CHRM2, CHRM3, CHRM4	95.30	97.05	114.40	105.12	102.54	106.39	117.74	52.73	48.89	102.65	76.93	97.64	85.88	108.84	101.75	115.00	109.73	109.73
Hydralazine HCl	B2101	N/A	126.70	157.46	179.56	164.43	159.86	151.72	143.96	142.53	158.65	105.84	119.29	131.14	79.77	126.01	115.99	144.14	110.20	110.20

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)			ER-positive (luminal)				HER2-enriched					
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	UCD52	WHM12	WHM12	WHM30	WHM30	WHM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108	HC108	
Hydrochlorothiazide	B1950	SLC12A3	73.50	116.59	177.13	103.23	107.44	103.36	98.01	146.74	131.60	82.97	184.82	92.72	184.82	105.72	92.72	248.89	255.14	248.89	255.14	99.01	123.22	123.22
Hydrocortisone	B1951	NR3C1	93.41	112.16	263.52	121.02	127.38	99.07	92.21	207.13	189.09	91.63	172.01	126.43	172.01	126.43	113.25	286.73	307.09	286.73	307.09	102.44	110.98	110.98
Hydroxychloroquine Sulfate	B4874	TLR7	68.57	75.10	86.46	68.77	74.12	68.80	72.83	102.15	101.18	71.05	73.30	96.60	73.30	96.60	81.85	90.13	78.74	90.13	78.74	89.48	24.67	24.67
Hydroxyurea	B2102	RRM1	37.43	88.20	109.51	75.84	81.59	74.82	118.10	122.45	127.92	83.98	94.36	111.44	94.36	111.44	90.04	120.70	105.06	120.70	105.06	22.94	101.03	101.03
Hydroxyzine 2HCl	B1549	HRH1	166.84	171.44	128.06	76.03	76.94	95.59	98.83	156.44	123.48	108.12	116.02	99.89	117.49	99.89	117.49	84.99	85.84	84.99	85.84	109.29	103.55	103.55
Hygromycin B	A2515	N/A	81.32	51.20	94.27	71.60	103.14	98.12	96.35	104.52	72.00	68.64	174.93	70.16	174.93	70.16	110.31	115.27	113.65	115.27	113.65	93.49	105.71	105.71
Hyoscyamine	B1605	CHRM1, CHRM2, CHRM3, CHRM4	124.96	144.37	118.00	68.95	79.50	90.94	96.63	111.08	105.72	120.68	98.02	132.49	98.02	132.49	94.31	149.10	140.92	149.10	140.92	159.91	81.34	81.34
Ibandronate sodium	B1772	N/A	91.28	134.12	137.63	119.27	111.42	119.62	140.01	112.07	143.05	93.87	121.01	93.20	121.01	93.20	101.41	139.83	112.26	139.83	112.26	127.76	141.87	141.87
Ibuprofen	A8446	ASIC1	104.09	144.13	90.16	85.88	91.92	92.68	110.79	106.82	100.63	126.46	92.58	114.57	92.58	114.57	103.82	128.42	138.44	128.42	138.44	150.49	95.75	95.75
Ibuprofen Lysine	A5791	ASIC1	142.07	274.83	162.08	111.80	153.02	82.30	87.35	186.21	153.99	114.39	98.06	130.30	98.06	130.30	138.08	126.18	134.95	126.18	134.95	156.29	247.75	247.75
Ibutilide Fumarate	B2278	KCNH2	82.66	104.30	116.73	98.18	95.38	120.23	124.54	142.80	112.95	118.14	92.05	102.71	92.05	102.71	102.71	137.05	122.41	137.05	122.41	133.05	86.55	86.55
Ictarubicin HCl	A2476	TOP2A	33.73	41.26	32.05	26.92	35.95	22.30	36.37	54.48	34.87	27.52	29.22	67.60	27.52	67.60	27.78	49.40	44.84	49.40	44.84	61.24	29.82	29.82
Idebenone	B2103	N/A	32.04	36.04	104.06	82.89	73.59	57.25	99.54	37.71	66.04	26.69	51.58	107.10	51.58	107.10	87.24	49.25	135.15	49.25	135.15	15.22	74.99	74.99
Idoxuridine	B1773	N/A	110.65	219.46	129.07	115.87	107.29	178.99	221.21	115.53	117.05	100.10	112.28	214.19	112.28	214.19	106.35	340.64	336.23	340.64	336.23	165.73	163.59	163.59
Ifosfamide	A2097	N/A	116.21	95.84	74.41	103.67	104.59	114.31	77.06	107.30	110.48	96.72	95.84	107.00	95.84	107.00	84.77	145.03	160.02	145.03	160.02	108.42	88.38	88.38
Iloperidone	A5399	Htr1a	136.07	170.85	172.11	89.41	86.92	110.45	101.98	122.79	122.84	130.62	103.22	101.25	103.22	101.25	102.71	110.26	130.83	110.26	130.83	148.21	132.84	132.84
Imatinib (STI571)	B2171	ABL1	57.76	116.40	98.90	90.36	88.00	78.39	104.94	95.56	113.15	86.84	85.78	156.40	85.78	156.40	89.40	104.44	112.39	104.44	112.39	18.87	82.78	82.78
Imatinib Mesylate (STI571)	A1805	ABL1	139.70	174.17	98.96	66.50	69.02	84.56	93.26	126.66	101.21	59.52	75.97	86.73	75.97	86.73	69.73	99.28	83.24	99.28	83.24	105.32	106.25	106.25
Imidapril HCl	A8447	ACE	99.26	111.02	94.23	75.29	80.70	102.49	107.11	110.68	96.58	104.77	94.79	113.10	94.79	113.10	102.01	125.07	127.04	125.07	127.04	168.45	107.28	107.28
Imipramine (hydrochloride)	C4117	Kcnj6	94.80	113.90	118.73	85.24	95.47	73.66	91.24	73.67	85.63	88.62	81.23	88.05	81.23	88.05	60.04	93.77	96.36	93.77	96.36	121.71	115.65	115.65
Imiquimod	A5161	TLR7	101.65	84.15	210.68	75.68	77.70	124.45	104.76	110.23	121.56	73.10	72.32	108.92	72.32	108.92	42.71	105.32	76.60	105.32	76.60	121.45	102.57	102.57
INCB-024360	B6036	IDO1	100.55	110.23	112.16	54.95	60.00	95.80	82.09	100.41	91.98	91.98	28.94	99.97	28.94	99.97	96.37	65.52	67.49	65.52	67.49	59.28	25.28	25.28
Indapamide	B1953	KCNQ1, KCNE1	91.01	104.99	128.06	81.35	79.14	119.24	90.23	102.13	106.97	97.92	91.27	99.97	91.27	99.97	88.75	100.34	119.74	100.34	119.74	117.17	94.58	94.58
Indomethacin	A8449	PTGS1	91.31	119.84	91.99	81.69	63.16	89.08	95.21	96.73	89.18	97.45	95.89	88.67	95.89	88.67	79.18	108.06	101.11	108.06	101.11	133.70	74.49	74.49
Iniparib (BSI-201)	A4157	PARP1	136.12	106.27	106.26	118.20	110.54	165.98	196.63	112.96	144.59	108.65	137.48	198.05	137.48	198.05	82.60	145.51	101.53	145.51	101.53	119.13	84.61	84.61
Iohexol	B3538	N/A	93.72	140.51	122.03	96.59	106.01	97.28	101.05	89.64	102.22	94.48	98.60	115.92	98.60	115.92	83.17	125.71	139.36	125.71	139.36	163.25	95.83	95.83
IPI-145 (INK1197)	A1720	PIK3CD, PIK3CG	92.51	90.44	81.81	66.11	68.53	40.75	61.40	96.78	93.74	90.03	53.71	53.07	53.71	53.07	66.44	49.26	42.30	49.26	42.30	67.42	68.76	68.76
Ipratropium Bromide	A8451	CHRM1, CHRM2, CHRM3, CHRM4	106.39	169.80	239.34	151.31	143.97	91.95	113.29	163.90	196.55	102.21	213.84	151.21	213.84	151.21	107.79	330.98	340.90	330.98	340.90	47.78	119.24	119.24
Iribesartan	A5970	AGTR1	87.78	84.91	107.12	99.25	107.02	108.52	101.54	99.95	65.40	97.36	91.86	104.67	91.86	104.67	91.80	112.18	115.55	112.18	115.55	117.81	144.16	144.16
Irinotecan	A5133	TOP1	114.72	106.17	140.36	111.10	102.42	62.72	72.14	118.87	106.48	117.23	231.09	132.52	231.09	132.52	222.69	122.33	119.23	122.33	119.23	138.95	236.48	236.48
Irinotecan HCl Trihydrate	B2293	TOP1	55.52	86.13	104.77	115.77	91.83	70.65	65.31	120.25	92.93	101.93	137.38	164.86	137.38	164.86	220.71	124.25	103.12	124.25	103.12	161.09	189.32	189.32
Irsogladine	B1593	PDE4D	96.91	88.57	107.96	103.68	109.89	117.28	111.09	79.28	73.48	102.88	80.97	112.94	80.97	112.94	89.74	114.34	89.45	114.34	89.45	121.96	96.15	96.15
Isoconazole nitrate	B1956	N/A	78.02	37.81	139.96	40.05	48.22	47.15	56.97	98.43	101.61	23.36	28.17	119.34	28.17	119.34	101.39	59.95	48.41	59.95	48.41	40.49	93.05	93.05
Isoniazid	B1957	N/A	92.35	102.46	127.48	63.26	81.89	92.81	98.47	116.49	111.86	100.06	85.17	108.63	85.17	108.63	87.21	128.33	110.01	128.33	110.01	122.39	91.69	91.69
Isoprenaline HCl	B1336	ADRB1	106.51	84.85	121.55	85.46	98.34	73.16	81.30	107.63	117.64	78.05	96.39	108.06	96.39	108.06	90.34	77.65	74.84	77.65	74.84	74.47	101.51	101.51
Isonorbide	B1774	NPR1	98.62	131.32	116.39	102.53	97.31	107.68	107.53	100.69	122.42	101.24	105.36	146.74	105.36	146.74	101.89	287.05	233.50	287.05	233.50	126.10	118.71	118.71
Isotretinoin	A4330	RARA	137.50	140.37	104.96	191.51	188.08	98.90	84.18	142.94	142.93	91.90	91.48	108.80	91.48	108.80	121.98	117.23	140.05	117.23	140.05	98.30	98.30	98.30
Isovaleramide	B1775	GABRA1	87.31	118.51	94.60	98.51	101.34	89.17	107.85	101.71	90.54	95.19	99.96	132.38	99.96	132.38	98.50	95.01	113.66	95.01	113.66	130.01	109.77	109.77
Ispinesib (SB-715992)	A5343	KIF11	34.02	35.09	45.54	116.38	128.14	34.14	35.52	42.57	36.98	20.53	24.29	41.17	24.29	41.17	56.79	41.16	35.53	41.16	35.53	32.52	25.31	25.31
Istradipine (Dyncirc)	A8453	Ca α 1c	98.56	123.67	116.95	69.62	82.86	84.62	100.48	86.16	91.21	19.71	77.64	118.26	77.64	118.26	91.93	113.56	104.77	113.56	104.77	62.71	87.89	87.89
Itraconazole	B2104	NCA	67.02	119.99	128.68	77.38	95.78	118.49	102.67	95.49	94.00	55.80	57.50	81.15	57.50	81.15	78.54	87.18	81.39	87.18	81.39	25.82		

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)			ER-positive (luminal)				HER2-enriched				
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	WHM2	WHM2	WHM30	WHM30	WHM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108	HC108	
Ketoprofen	B1446	PTGS1	102.98	113.01	88.82	80.42	88.53	85.44	109.05	87.42	81.29	123.90	84.06	113.60	102.05	99.98	108.39	121.75	86.02				
Ketorolac tromethamine salt	B1447	PTGS1, PTGS2	133.14	112.01	131.11	146.28	144.96	140.10	118.96	118.91	112.98	196.03	96.92	174.23	101.68	140.35	103.27	200.00	147.39				
Ketotifen Fumarate	B1562	HRH1	104.22	136.48	173.14	92.25	98.50	87.17	81.66	150.17	158.02	113.37	157.43	124.83	101.71	144.47	125.82	146.03	100.72				
Kinetin	A3528	N/A	112.21	105.92	86.79	87.68	115.48	96.56	90.87	124.62	118.19	111.17	94.96	123.43	100.40	125.19	114.71	113.38	106.51				
KPT-330	B1464	XPO1	59.07	24.76	73.22	78.85	81.35	70.87	71.01	47.00	46.32	41.13	21.95	41.02	92.73	37.15	33.60	61.94	26.89				
Labetalol HCl	B4795	ADRA1D	92.80	109.67	111.60	80.77	90.59	99.09	120.34	101.75	120.61	89.25	102.37	105.67	103.97	99.61	109.95	92.78	31.99				
Lacidipine	B1417	CACNA1B	107.19	108.18	85.72	72.80	81.44	100.67	98.97	130.46	135.96	79.61	93.48	98.11	109.97	90.78	86.63	117.10	67.13				
L-Adrenaline	B1337	ADRB1, ADRB2, ADRA1A, ADRA1B	171.59	90.31	137.85	101.50	122.14	96.30	106.98	156.29	168.36	115.90	167.64	137.29	109.51	144.28	98.54	93.30	123.25				
Lafutidine	B1575	HRH2	114.13	159.79	118.70	86.45	91.83	75.31	101.81	112.75	115.60	108.77	104.32	136.43	107.79	222.55	156.91	168.85	93.98				
Lamivudine	A8458	N/A	93.55	117.84	95.22	82.88	92.43	86.49	102.02	75.73	93.03	100.08	89.81	130.40	107.23	117.99	129.10	89.87	117.24				
Lamotrigine	B2249	Scn2a	86.79	103.14	127.89	122.88	101.75	86.91	105.31	171.66	177.45	110.99	156.71	155.09	89.85	238.53	251.00	170.19	105.11				
Lansoprazole	A1229	ATP4A	152.80	187.04	144.03	185.39	193.73	206.22	195.08	344.44	244.49	74.63	120.08	159.78	128.15	158.41	124.69	375.60	148.91				
Lansoprazole sodium	B1290	ATP4A	182.05	180.04	152.25	138.42	137.98	150.14	136.11	302.58	259.71	117.76	130.53	145.06	162.70	139.22	131.12	373.40	146.89				
Lapatinib	A8218	EGFR	67.70	156.66	167.67	53.68	48.64	36.90	44.47	683.37	1067.44	27.35	51.24	45.43	98.82	42.49	41.83	103.71	103.82				
Lapatinib Ditosylate	A3967	EGFR	49.58	49.44	61.77	26.69	29.41	39.80	35.64	50.21	44.49	23.27	49.36	45.44	67.83	42.18	42.60	60.45	83.71				
L-Carnitine inner salt	N1935	N/A	91.39	153.84	113.66	100.22	105.63	87.52	106.37	110.43	95.91	106.96	92.73	118.52	95.68	110.85	112.46	116.56	33.51				
LCZ696	B4815	AGTR1, AGTR2	86.10	110.11	111.82	101.20	89.01	87.52	99.18	122.92	139.11	108.19	83.08	141.02	92.87	91.95	83.91	122.69	32.94				
LDE225 (NVP-)	B2266	SMO	85.96	110.62	94.79	79.49	82.09	87.92	107.14	91.44	80.74	65.10	68.46	118.97	80.74	66.54	72.82	93.05	64.55				
LDE225, Erisomodegib	A8328	ALK	29.03	39.74	44.56	24.77	24.95	42.33	48.60	30.10	28.46	16.62	18.44	37.78	29.26	39.61	15.51	26.32	131.51				
Ledipasvir	A3546	N/A	101.67	104.03	72.30	70.68	76.50	71.61	58.13	104.67	103.18	58.31	52.90	94.37	80.60	104.99	92.99	102.23	74.46				
LEE011	A8641	CDK4	106.12	112.26	91.71	141.83	153.27	98.75	116.55	137.04	123.57	135.61	92.94	134.83	137.73	134.67	116.84	131.15	131.64				
Leflunomide	A2852	DHODH	328.87	288.98	279.46	347.53	332.01	436.00	303.58	984.01	866.57	497.88	359.71	1016.56	193.77	303.78	270.77	614.76	364.31				
Lenalidomide (CC-5013)	A4211	CRBN	107.78	113.57	101.49	88.92	71.99	76.13	81.03	138.24	128.96	92.54	78.39	106.96	101.89	79.82	81.11	117.09	85.70				
Levatinib (E7080)	A2174	FLT4	113.95	74.36	61.36	62.29	53.36	49.26	78.70	46.61	49.52	84.92	74.61	70.52	48.64	42.47	47.20	72.31	50.56				
Levetiracetam	A1307	CYP19A1	106.12	116.85	99.08	136.98	115.97	58.60	88.79	131.76	119.91	101.16	95.61	99.10	101.75	92.16	84.28	97.88	103.23				
Leucovorin Calcium	A2489	TYMS	88.45	118.86	127.48	119.99	123.57	52.29	83.42	177.26	135.70	91.70	169.68	101.82	83.88	99.24	117.53	98.74	126.19				
Levobupivacaine HCl	B1778	ADRB1	136.49	146.18	120.28	137.68	113.74	84.31	99.13	146.45	139.46	103.63	127.51	165.61	97.95	117.48	97.35	100.24	155.79				
Levobupivacaine HCl	B1784	SCN10A	93.60	124.35	141.23	110.04	104.29	98.36	94.05	159.76	167.15	96.71	138.22	101.11	106.40	131.39	110.97	112.95	96.02				
Levofloxacin	B1959	N/A	84.03	120.56	123.25	89.67	87.68	96.04	112.45	130.74	134.07	99.98	76.12	108.82	89.56	159.37	88.11	128.60	80.81				
Levonorgestrel	B1960	PGR	71.19	106.23	121.07	78.69	88.50	84.61	98.29	156.17	152.91	91.99	108.82	127.38	88.48	230.71	207.01	131.90	151.70				
Levosimendan	B1961	TNNC1	28.34	72.81	82.20	52.86	49.38	40.93	54.65	84.83	88.65	30.33	73.53	183.03	138.64	164.69	125.20	172.61	93.45				
Levosulpride	B1484	DRD2	120.24	133.07	133.59	92.77	94.95	113.84	103.50	105.24	94.72	99.21	99.46	125.67	98.21	73.86	81.86	118.52	92.32				
L-Glutamine	A8461	GPRC6A	91.78	79.46	97.35	85.48	80.36	106.61	101.05	75.66	65.60	109.80	74.52	92.76	87.44	101.64	100.54	105.68	92.22				
L-Glutathione Reduced	B7775	N/A	98.59	106.58	112.62	95.87	103.70	102.09	95.07	129.26	132.66	104.43	110.12	115.29	85.31	99.10	108.53	117.80	99.80				
Licofelone	B1448	PTGS1, PTGS2, ALOX5	57.15	34.99	89.55	83.46	79.13	52.24	42.40	80.73	95.99	29.96	33.10	99.41	90.23	85.27	83.99	53.22	66.24				
Lidocaine	A1450	Scn2a	110.89	102.69	93.87	101.88	79.99	61.34	87.50	137.21	106.96	100.95	108.64	94.43	100.43	102.75	97.65	98.95	102.88				
Linagliptin (BI-1356)	A4034	DPP4	145.07	175.42	179.23	137.51	134.24	110.48	112.27	161.95	172.33	100.46	90.27	107.76	142.09	109.15	100.54	129.41	109.25				
Linezolid	A5181	N/A	97.45	101.51	110.05	72.36	89.54	79.81	81.61	146.76	126.77	97.51	90.08	108.34	103.17	96.04	100.21	135.42	109.42				
Linifanib (ABT-869)	A2949	CSF1R, PDGFRB, KDR, FLT1, FLT3	85.28	148.34	120.12	92.41	91.94	192.74	126.74	171.11	107.36	54.92	53.56	165.30	68.73	73.80	70.12	104.81	128.15				
Linsitinib	A8334	IGF1R	111.22	112.91	127.20	73.59	69.62	94.47	110.29	117.83	134.22	46.02	100.60	108.63	76.30	41.38	35.72	169.88	113.58				
Lisinopril dihydrate	B3290	ACE	83.68	112.71	130.29	104.64	105.39	78.72	109.22	155.87	144.37	119.21	92.31	137.23	113.49	110.52	115.40	133.80	86.41				
Lithocholic Acid	A8463	N/A	100.62	30.32	91.30	82.22	91.38	30.37	45.18	94.62	85.64	111.94	78.33	131.80	102.53	79.89	89.75	92.78	103.03				
Lomefloxacin HCl	B1781	N/A	83.83	111.25	107.38	93.50	89.42	83.85	83.64	143.05	157.56	89.05	100.02	95.22	96.12	85.74	66.20	124.74	102.10				

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)		ER-positive (luminal)			HER2-enriched				
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	WHIM2	WHIM2	WHIM30	WHIM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108	
Lomerizine HCl	B1782	CACNA1B, CACNA1C, CACNA1A, CACNA1D, CACNA1H, CACNA1E	68.43	103.21	87.80	50.88	52.06	38.40	57.77	80.69	79.25	44.74	72.94	73.55	78.52	32.67	32.55	32.67	32.55	111.58	57.05
	B4885	MTTP	29.51	40.00	47.29	30.83	35.11	43.94	38.11	112.58	104.74	28.21	24.81	49.28	43.68	31.54	36.08	31.54	36.08	35.73	8.64
Lomitapide	B1963	N/A	67.58	121.28	146.40	72.11	88.38	82.37	100.15	131.73	117.64	102.24	84.25	115.01	95.22	89.24	77.11	89.24	77.11	102.93	76.80
Lonafamilin	A4379	HRAS	120.39	24.51	170.30	269.89	296.73	134.88	117.86	119.85	109.64	11.02	14.53	120.53	163.49	54.92	31.45	54.92	31.45	37.45	19.84
Londamidine HCl	B1964	HK1, HK2, HK3	76.29	101.43	124.31	81.44	83.79	57.59	102.79	139.73	138.16	97.29	88.44	112.07	82.94	91.09	79.11	91.09	79.11	100.32	65.43
Loperamide HCl	B1392	OPRM1	88.10	115.66	95.08	50.04	48.09	53.89	65.64	108.72	94.95	43.02	63.96	84.75	98.73	83.90	74.52	83.90	74.52	63.99	78.79
Lopinavir	A8204	N/A	84.24	81.78	116.36	50.78	45.16	64.56	82.59	107.86	85.01	42.99	71.65	101.86	88.41	98.13	89.21	98.13	89.21	70.21	77.29
Loratadine	A2960	SLC6A15	74.34	125.16	142.24	87.12	93.82	88.51	81.20	126.15	107.28	90.93	51.25	85.25	86.06	73.90	81.82	73.90	81.82	68.61	65.40
Lorcaserin HCl	B2239	HTR2A	92.45	100.72	105.74	87.53	93.06	83.40	82.37	111.21	111.47	104.01	95.91	109.63	81.30	86.50	103.32	86.50	103.32	151.65	90.66
Loroxicam	B1441	PTGS1, PTGS2	101.42	88.89	98.35	90.13	82.34	114.21	110.48	103.76	94.53	102.04	67.32	111.31	85.63	89.15	75.57	89.15	75.57	101.05	116.68
Losartan Potassium (Dup 753)	A1425	AGTR1	120.32	132.30	82.26	103.36	92.38	75.22	98.68	116.12	119.09	100.07	112.06	123.70	79.01	82.00	83.39	82.00	83.39	111.63	100.48
Losmapimod	B4620	MAPK14	72.65	95.43	81.63	56.79	59.32	64.82	88.19	104.90	96.13	98.91	69.80	91.43	60.05	69.42	72.51	69.42	72.51	96.39	31.73
Loteprednol etabonate	B2106	N/A	48.89	132.69	272.29	134.92	181.85	96.71	112.49	189.25	206.20	100.20	199.93	196.24	122.73	305.68	316.63	305.68	316.63	24.47	196.90
Loxapine	A4365	Hmgcr	99.23	137.96	142.34	54.48	47.00	76.13	66.82	92.51	93.82	96.91	79.54	114.84	180.60	120.45	140.97	120.45	140.97	116.53	83.88
Loxapine Succinate	B1783	HTR2A	88.74	145.31	137.77	112.89	103.30	87.21	120.45	107.69	99.84	72.58	96.51	88.39	84.38	68.95	60.91	68.95	60.91	90.09	85.15
L-Thyroxine	B2107	TPO	35.28	97.65	136.45	83.25	86.74	74.72	112.39	172.66	181.50	103.58	123.81	150.82	93.29	190.18	110.48	190.18	110.48	35.56	100.03
Luliconazole	A3564	N/A	110.71	151.70	72.44	85.51	91.59	99.49	94.63	124.50	135.30	83.77	62.73	107.62	90.64	66.30	74.19	66.30	74.19	105.89	76.85
LY2157290	A8348	TGFBF1	118.65	115.62	89.79	70.79	75.43	117.68	175.70	113.24	109.07	154.72	75.15	90.07	98.74	60.86	51.76	60.86	51.76	202.50	90.99
LY2228920	A5566	MAPK14	55.19	61.61	72.29	37.80	35.58	36.75	42.28	71.02	57.32	25.99	47.69	54.16	80.96	59.45	58.04	59.45	58.04	118.62	89.15
LY2784544	A4147	JAK2	102.62	181.81	199.29	116.52	89.21	231.76	249.29	288.23	293.18	53.59	75.03	116.15	196.05	147.47	361.24	147.47	361.24	154.80	144.36
LY2835219	A1794	CDK4, CDK6	49.80	125.89	116.51	26.25	26.07	20.82	39.94	84.55	76.71	73.50	92.54	135.84	135.49	65.39	77.87	65.39	77.87	99.53	99.53
Macitentan	A1929	EDNRA	115.15	36.73	91.83	75.40	75.36	50.99	103.26	101.66	101.08	53.95	76.14	109.45	91.36	71.79	31.65	71.79	31.65	123.35	99.36
Malcoliate	A2486	ALOX5	100.35	116.66	75.46	87.75	91.19	63.46	87.80	95.04	100.68	80.74	99.68	84.27	90.90	92.01	87.61	92.01	87.61	88.81	66.97
Meprotiline HCl	B1338	Kcnj6	93.27	86.36	80.15	33.46	37.37	73.78	59.34	23.39	66.30	41.86	71.68	75.54	78.41	106.74	107.39	106.74	107.39	47.20	53.98
Maraviroc	A8311	CCR5	118.76	101.82	163.13	89.74	87.96	72.71	110.06	109.94	135.75	98.39	93.34	208.46	128.94	84.05	63.32	84.05	63.32	136.76	194.02
Marbofloxacin	A5346	N/A	98.65	99.60	113.75	123.06	148.42	73.69	77.06	168.99	126.15	63.57	76.24	99.35	137.52	140.86	117.12	140.86	117.12	102.73	94.02
Marimastat	A4049	MMP9, MMP2	131.35	145.11	126.91	112.16	89.82	97.95	112.13	107.67	125.64	80.36	76.19	110.98	117.64	78.84	66.27	78.84	66.27	181.90	101.17
Masitinib (AB1010)	A2942	KIT	57.87	49.28	93.58	58.97	40.83	40.60	51.84	189.05	102.33	21.83	18.11	68.71	37.78	64.20	47.41	64.20	47.41	93.98	42.49
MDV3100 (Enzalutamide)	A3003	AR	107.34	122.42	107.10	112.40	120.84	100.45	95.40	158.14	155.42	104.63	104.43	137.70	96.13	109.79	78.86	109.79	78.86	122.52	109.73
Mebendazole	C4087	TUBA1A	101.94	165.77	176.72	103.15	103.46	79.47	105.68	110.09	110.48	150.58	86.51	109.76	68.58	99.42	78.34	99.42	78.34	188.18	174.26
Mecarbamate	B2109	N/A	41.99	102.25	114.86	84.60	90.02	83.88	115.32	354.81	382.09	108.07	114.09	151.52	90.91	144.78	124.81	144.78	124.81	44.56	106.19
Mechlorethamine HCl	B1785	N/A	55.24	43.33	62.48	28.93	27.59	46.13	58.14	86.73	64.57	28.45	35.35	56.17	63.72	62.48	62.48	62.48	62.48	157.34	155.23
Mecizline 2HCl	B1786	Nr13	80.89	90.94	91.80	48.38	39.58	80.87	62.34	50.25	40.56	65.53	82.46	57.90	67.42	59.77	45.60	59.77	45.60	41.04	41.04
Meclofenamate Sodium	B4796	PTGS1, PTGS2, ALOX5	118.45	104.03	120.67	88.83	95.30	104.76	90.74	142.80	145.92	103.60	96.43	158.46	103.44	126.04	118.94	126.04	118.94	92.53	44.50
Medetomidine HCl	B1361	ADRA2A	113.78	102.95	95.35	89.45	85.31	73.87	104.79	116.68	108.54	108.15	78.23	102.06	102.72	100.17	101.64	102.72	101.64	121.90	67.63
Medroxyprogesterone acetate	B1510	PGR	113.39	130.19	176.74	97.49	92.46	83.68	91.83	190.23	176.86	61.28	135.70	114.23	78.40	163.38	140.37	163.38	140.37	130.78	114.86
Mefenamic Acid	B1449	PTGS1	86.41	119.51	90.89	90.42	98.34	105.14	113.69	111.30	113.42	148.24	86.98	102.47	98.06	107.91	117.35	107.91	117.35	130.16	72.45
Mefloquine hydrochloride	A3593	N/A	30.93	32.83	29.95	26.63	34.03	36.26	39.08	51.00	46.92	27.78	19.96	40.49	51.39	40.13	49.14	40.13	49.14	23.57	27.20
Megestrol Acetate	B1377	PGR	116.09	106.98	101.95	115.03	91.94	84.17	103.29	128.41	127.42	113.17	98.58	121.19	91.84	222.80	214.88	222.80	214.88	124.67	111.54
Meglumine	B1965	N/A	66.62	93.80	110.19	77.15	79.36	68.30	103.49	129.76	137.17	98.67	96.51	93.38	74.42	149.70	133.77	149.70	133.77	109.19	80.33
MEK162 (ARRY-162, ARRY-438162)	A1947	MAP2K1, MAP2K2	75.95	92.25	79.57	53.83	65.80	40.71	69.65	95.92	116.17	56.13	75.08	90.67	76.39	75.88	65.85	75.88	65.85	72.03	90.92
Melatonin	A2842	HTR2B	104.40	119.04	109.36	123.08	130.72	102.42	139.28	169.98	145.78	104.38	107.55	134.32	97.81	110.44	105.77	110.44	105.77	91.13	110.33
Meloxicam (Mobic)	A8466	PTGS1	96.85	111.19	88.84	85.04	75.88	85.68	102.38	72.11	90.55	109.09	83.10	124.64	101.71	127.61	120.55	127.61	120.55	105.01	129.19
Melphalan	A4473	N/A	65.89	86.06	63.09	67.81	82.74	52.37	64.67	126.39	121.82	86.69	95.56	115.86	106.63	75.22	80.27	75.22	80.27	133.07	109.48

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)			ER-positive (luminal)				HER2-enriched						
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	UCD52	WHM12	WHM12	WHM30	WHM30	WHM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108	HC108		
Memantine hydrochloride	B3308	GRIN2A	79.03	98.54	98.20	92.28	92.47	77.83	98.42	170.35	141.21	113.20	94.93	145.62	99.30	30.47	60.83	53.86	24.15	53.71					
Menadione	B1966	GDCX	22.84	100.40	57.60	29.05	32.03	36.90	51.26	128.77	147.83	25.69	36.88	51.90	30.47										
Mepenzolate Bromide	A8467	CHRM1, CHRM2, CHRM3, CHRM4	103.80	113.52	108.25	93.50	81.53	92.76	103.34	130.04	126.16	106.96	98.66	133.49	107.61										
Mepiroxol	A8468	N/A	108.34	126.55	97.02	84.71	97.07	80.67	102.70	120.68	157.44	105.92	104.54	119.49	102.62	99.09	114.03	151.71	103.51	103.48	111.27				
Mepivacaine HCl	B1967	SCN10A	86.58	88.59	117.89	67.87	72.99	80.04	99.45	168.77	162.45	97.41	98.41	89.15	96.22	125.18	122.07	98.73	80.09						
Mepizastrol HCl	B2110	OPRM1	40.49	99.30	111.72	81.41	89.93	68.59	114.91	181.83	180.78	105.29	90.96	141.00	94.01	114.62	107.52	32.39	91.02						
Mepyramine maleate	B6396	HRH1	81.03	106.54	106.69	117.86	100.36	88.45	115.56	107.01	96.64	96.64	80.38	133.22	93.91	91.82	79.47	126.79	34.44						
Mequinol	B1968	TYR	83.84	98.13	117.76	76.03	65.94	82.52	110.41	98.29	102.25	110.86	91.89	108.48	70.38	146.51	101.85	104.52	82.09						
Meraptopurine (6-MP)	A2355	N/A	111.44	104.46	74.93	94.58	88.63	116.47	82.13	140.64	95.47	112.09	120.50	103.53	81.59	83.44	101.13	103.61	79.89						
Meropenem	A5124	N/A	107.79	97.84	103.40	78.01	68.46	80.11	86.60	115.38	108.21	82.75	91.37	105.53	95.10	100.26	96.96	106.32	89.77						
Meropenem trihydrate	B1217	N/A	97.80	110.07	96.19	93.24	86.02	94.04	104.68	78.26	78.26	149.70	104.88	81.82	92.38	95.68	94.32	105.67	83.76						
Mesalazine	B1969	PTGS2	111.98	108.86	103.63	106.89	93.44	90.49	135.45	173.85	110.74	122.19	125.36	103.35	119.31	140.24	126.44	129.14							
Mesna	A8469	N/A	112.46	112.30	97.21	86.59	91.96	91.39	109.24	101.31	110.60	103.22	93.61	117.89	103.00	121.51	161.46	113.47	115.02						
Mesoridazine Besylate	A8701	HTR1A	121.57	108.36	106.01	89.64	102.16	70.89	100.64	108.41	97.84	174.67	89.93	77.89	98.22	129.37	115.21	101.59	78.54						
Mestranol	A8470	ESR1	123.24	139.53	103.92	86.29	56.08	150.41	167.02	121.32	121.11	94.71	94.65	136.41	105.59	463.87	346.88	137.72	122.41						
Metaxalone	B3455	N/A	89.14	111.13	137.40	109.87	100.87	114.33	107.69	104.43	100.15	108.38	108.10	154.97	100.23	126.38	113.12	135.42	102.77						
Metformin HCl	B1970	PRKAA1	90.62	110.04	116.83	78.88	85.46	93.95	89.51	126.25	145.85	102.00	83.08	122.86	86.21	97.47	107.26	150.39	101.54						
Methacycline HCl	B1971	N/A	110.88	116.85	157.78	106.86	114.58	95.73	92.87	119.32	122.71	99.84	108.23	128.10	81.75	148.04	131.43	95.39	97.41						
Methazolamide	A4364	CA1	97.09	108.02	122.50	105.19	82.71	97.17	92.13	98.56	96.80	107.41	77.56	114.49	119.42	126.05	112.86	104.72	79.35						
Methanamine	B1972	N/A	79.17	99.37	103.91	93.36	86.95	90.09	93.46	145.54	138.91	111.37	91.09	127.01	90.79	197.58	156.51	133.36	91.13						
Methimazole	A8472	TPO	150.29	134.85	125.98	99.85	100.27	105.31	108.71	141.31	136.01	146.56	113.69	119.15	112.32	97.01	67.05	121.71	99.01						
Methotrexate	A4347	DHFR	107.42	95.32	93.35	95.24	83.01	99.35	102.31	103.85	86.04	100.39	81.80	114.76	113.26	98.36	108.97	109.64	77.09						
Methscopolamine	B1611	CHRM1, CHRM2, CHRM3, CHRM4	100.43	112.41	97.87	72.35	88.87	82.02	93.39	138.36	139.35	113.49	99.84	128.20	93.19	225.54	252.66	152.48	84.08						
Methylcobalamin	B3404	MTR	72.17	90.96	106.16	118.06	105.20	74.82	107.82	106.59	106.55	121.32	102.01	131.72	91.12	109.77	113.27	124.15	79.11						
Methyldopa	B1787	DDC	102.28	88.26	127.44	89.16	93.12	113.34	111.46	93.67	98.82	100.59	90.47	96.81	63.11	134.13	118.80	95.41	83.85						
Methylprednisolone	A4233	NR3C1	127.60	161.79	210.69	146.14	162.11	113.33	124.83	202.41	184.71	99.64	147.09	155.64	136.06	446.30	410.20	115.97	146.70						
Methylthiouracil	B1974	TPO	76.82	117.67	114.56	87.17	98.30	74.88	86.26	135.13	142.87	106.27	83.20	119.08	93.84	120.46	116.90	146.78	90.49						
Methycarbamol	A8473	CA1, CA2	140.88	155.51	110.52	110.29	98.41	85.25	123.55	135.62	132.39	174.99	112.32	131.93	108.43	111.07	106.08	187.66	124.19						
Metricrane	A8471	N/A	102.56	115.07	110.49	103.69	88.92	102.28	91.66	82.36	78.42	97.56	106.54	117.20	88.96	110.08	96.48	111.10	102.81						
Metoclopramide	A3599	HTR3A	107.93	117.05	72.61	98.08	97.94	86.82	89.92	131.84	94.04	102.49	79.06	107.08	94.63	114.34	128.58	105.20	92.88						
Metolazone	B1975	SLC12A3	108.02	134.02	197.54	108.66	105.99	98.85	107.62	117.81	136.06	92.67	104.36	128.61	57.89	142.65	120.58	111.77	104.42						
Metoprolol Tartrate	B1339	ADRB1	135.93	115.14	111.99	78.95	97.22	85.15	103.73	105.07	108.88	120.98	102.41	111.27	95.00	91.01	71.89	126.62	102.25						
Metronidazole	B1976	N/A	69.60	114.22	133.25	72.25	82.38	69.57	92.44	127.78	134.45	110.74	70.95	134.73	89.60	110.66	97.98	142.43	89.53						
Mevastatin	B1788	Hmgcr	115.51	143.29	132.00	61.40	46.91	76.53	97.12	139.60	133.07	72.12	103.42	118.90	119.54	109.87	75.46	139.47	156.31						
Mexiletine HCl	B1789	SCN4A	107.67	145.43	188.02	124.73	114.85	119.76	139.20	147.72	145.38	87.44	152.23	110.45	123.04	139.92	103.12	150.38	143.18						
Mezlocillin Sodium	B1790	N/A	99.06	187.12	123.27	105.64	103.96	92.62	120.89	96.58	109.90	96.37	111.14	142.45	101.55	92.26	87.13	128.08	111.27						
Mianserin HCl	A1796	Htr1b	107.47	141.35	92.41	70.91	77.79	56.22	90.03	111.20	106.36	92.58	86.23	98.30	95.91	105.11	74.99	109.75	106.26						
Miconazole	A3606	N/A	109.59	98.47	93.30	83.97	67.52	40.97	37.92	107.81	90.27	89.67	81.75	96.40	92.60	110.39	116.06	99.95	79.33						
Miconazole Nitrate	B1977	TRPM2	80.71	138.15	120.04	72.25	76.53	83.00	116.16	125.70	130.98	87.83	36.76	87.55	82.05	54.45	40.15	102.95	71.04						
Mifepristone	B1978	TRPM2	25.69	38.25	113.37	44.43	52.71	30.21	43.87	129.21	126.39	22.24	32.31	93.07	79.89	62.41	51.39	28.46	23.76						
Miglitol	B1511	AR	104.18	122.36	89.28	78.17	68.36	91.17	88.20	95.45	91.23	59.69	85.48	99.16	73.51	47.06	47.95	84.81	56.86						
Milnacipran HCl	B2111	GAA	38.57	99.20	116.44	80.66	91.80	60.34	131.05	229.74	232.57	105.33	92.99	135.93	92.42	112.92	113.16	31.43	95.64						
Milrinone	B2112	SLC6A2	37.80	99.49	105.23	85.14	87.59	60.50	127.10	229.30	221.48	89.88	102.88	137.32	98.06	136.25	117.03	28.26	95.87						
Miltefosine	B1366	PDE2A	123.77	124.16	94.02	87.30	93.80	93.95	108.42	118.40	93.06	119.02	74.10	116.69	102.25	107.23	88.75	132.00	116.52						
Minoxidil	B1371	N/A	105.36	92.43	82.08	84.43	70.77	28.55	47.78	58.25	58.86	108.73	66.63	107.58	106.60	33.44	32.91	104.42	87.39						
Mintocycline HCl	B1791	N/A	74.23	62.15	96.47	67.69	73.79	92.43	73.08	73.88	89.62	97.20	14.48	59.16	52.										

Appendix A: PDX 1,363 drug screening dataset

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)			ER-positive (luminal)				HER2-enriched				
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	UCD52	WHIM2	WHIM2	WHIM30	WHIM30	WHIM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108	HC108
Mitotane (Lisdren)	A8475	CYP11A1	124.36	129.45	120.68	97.85	97.90	97.90	79.50	113.07	149.39	134.31	189.20	105.92	112.28	107.23	107.23	93.62	88.82	88.82	164.62	164.62	94.36
Mitoxantroline HCl	B2114	TOP2A	28.12	82.53	117.01	27.23	27.76	28.75	53.78	56.66	74.22	26.45	25.28	111.24	55.69	80.93	65.91	7.99	7.99	7.99	55.40	55.40	112.79
Mizoribine	B1472	IMPDH1	85.16	79.62	87.74	84.88	92.02	104.85	89.06	87.14	81.56	113.96	72.25	89.37	88.75	90.17	89.94	114.31	89.94	114.31	114.31	114.31	112.79
MK-4305	A3616	HCRTR1, HCRTR2	143.23	129.63	100.96	84.58	99.22	133.92	102.54	133.14	137.93	20.46	58.45	88.05	93.51	77.25	125.72	11.83	11.83	11.83	86.23	86.23	86.23
MLN2238	A4008	PSMB5	47.55	59.29	84.61	56.15	61.54	34.26	34.17	63.44	97.17	15.39	14.36	116.04	173.83	36.90	29.24	45.80	29.24	45.80	118.77	118.77	118.77
MLN8237 (Alisertib)	A4110	AURKA	69.09	90.92	87.94	72.88	56.24	86.09	74.13	147.64	164.17	128.57	82.62	118.11	100.40	104.68	85.20	122.61	85.20	122.61	95.13	95.13	95.13
Mocetinostat (MGCD0103, MG0103)	A4089	HDAC1	3181.33	2033.40	1416.10	1723.05	1228.00	118.37	99.39	1882.18	1979.36	130.14	26.73	87.02	5.73	260.47	40.26	2092.88	40.26	2092.88	1146.88	1146.88	1146.88
Moclobemide (Ro 111163)	A4370	MAOA	129.93	128.92	110.17	103.09	115.62	100.00	122.31	140.88	135.24	129.68	98.95	170.52	113.16	100.26	103.30	141.89	103.30	141.89	180.64	180.64	180.64
Moguisteine	B2115	N/A	41.83	94.60	126.84	86.29	80.19	73.49	103.91	127.80	134.01	96.42	108.01	114.39	89.55	108.81	121.49	22.50	121.49	22.50	92.94	92.94	92.94
Molidustat (BAY85-3934)	B5861	EGLN3	138.60	145.40	262.12	165.70	160.73	109.43	99.05	240.95	321.58	25.98	28.45	121.19	121.42	337.38	165.27	248.49	165.27	248.49	19.29	19.29	19.29
Mometasone furoate	B1979	NR3C1	74.03	115.66	240.14	139.39	139.64	78.31	88.63	197.81	218.21	97.25	139.37	151.06	115.18	464.93	379.92	118.96	379.92	118.96	118.74	118.74	118.74
Monobenzone	A8478	TYR	178.95	194.23	152.79	176.35	157.15	128.56	160.75	237.48	330.84	130.27	179.61	157.31	177.33	184.28	351.90	106.41	184.28	351.90	106.41	106.41	106.41
Montelukast Sodium	B1792	CYSLTR1	27.71	55.34	165.33	193.19	217.97	41.93	59.62	156.65	230.7	143.50	23.07	168.73	102.67	49.96	41.04	43.08	41.04	43.08	18.22	18.22	18.22
Moroxyline HCl	B1980	N/A	66.19	116.90	138.38	88.30	87.66	69.84	70.66	164.71	164.68	90.01	94.97	113.52	89.21	214.01	198.21	101.18	198.21	101.18	83.77	83.77	83.77
Mesapride Citrate	A1334	HTR4	128.31	148.48	118.24	108.06	104.07	71.22	94.01	131.76	139.46	76.30	89.83	109.57	115.75	119.55	87.12	136.07	87.12	136.07	117.26	117.26	117.26
Motolimod (VTX-2337)	B5996	TLR8	70.92	129.27	104.76	63.30	68.71	60.42	81.53	91.75	108.76	31.48	32.74	97.46	63.99	71.72	81.55	55.93	71.72	81.55	55.93	55.93	55.93
Moxalactam (sodium salt)	C4121	N/A	95.20	137.53	148.47	149.11	139.16	97.75	87.92	127.79	123.64	104.97	110.03	120.08	66.44	202.44	200.36	118.21	200.36	118.21	111.20	111.20	111.20
Moxifloxacin HCl	A5323	N/A	128.00	136.05	114.11	125.01	141.11	85.98	98.60	145.02	122.31	94.71	99.43	123.64	119.65	103.23	122.65	131.80	122.65	131.80	118.15	118.15	118.15
Moxonidine	A4080	NISCH	106.74	96.53	95.28	91.96	73.79	107.63	125.01	112.28	124.59	113.69	92.53	116.27	114.56	102.73	94.99	24.00	94.99	24.00	114.84	114.84	114.84
Mubritinib (TAK 165)	B1543	ERBB2	108.00	113.64	123.87	56.48	56.37	141.85	98.34	67.39	58.78	23.88	28.26	89.90	62.16	65.89	65.19	28.55	65.19	28.55	30.43	30.43	30.43
Mupirocin	B4872	N/A	85.37	109.61	100.91	86.60	81.81	73.41	90.40	113.07	113.50	102.57	70.47	129.31	90.61	96.60	82.61	110.05	82.61	110.05	25.77	25.77	25.77
Mycophenolate Mofetil	A4336	IMPDH1	119.20	163.53	86.24	106.97	75.86	117.36	107.25	151.27	109.45	70.38	103.47	106.32	103.19	89.43	74.15	107.13	89.43	74.15	107.13	80.71	80.71
Mycophenolate acid	B1981	IMPDH1	80.13	118.81	103.75	98.29	60.47	71.17	151.89	150.18	150.18	65.88	89.79	93.28	75.12	108.90	95.42	93.11	95.42	93.11	69.75	69.75	69.75
Nabumetone	B1490	PTGS2	193.39	147.50	135.51	168.38	124.93	109.30	398.37	536.15	243.95	536.15	243.95	171.58	140.74	206.39	192.24	259.37	192.24	259.37	95.00	95.00	95.00
Nadifloxacin	B1982	N/A	95.53	72.09	120.26	72.99	82.30	71.81	76.65	118.03	126.76	80.55	77.54	121.58	93.80	105.94	101.01	107.59	101.01	107.59	92.33	92.33	92.33
Nafamostat Mesylate(FUT-175)	A2586	ASIC1	119.87	100.92	98.40	114.94	96.09	76.08	124.04	114.32	96.14	41.05	46.82	81.97	82.09	81.23	109.83	71.20	81.23	109.83	71.20	59.75	59.75
Nafarelin Sodium	B1983	N/A	101.15	113.08	105.48	102.15	90.07	98.01	103.44	132.60	147.83	105.04	113.56	139.14	109.78	123.80	109.73	128.74	123.80	109.73	128.74	128.74	128.74
Nafopidil	B1362	ADRA1A, ADRA1B, ADRA1D	121.66	109.79	108.42	69.41	65.47	73.16	106.48	112.16	95.94	97.32	77.02	84.27	106.60	116.12	89.30	107.72	89.30	107.72	70.13	70.13	70.13
Nalidixic acid	B1985	N/A	72.73	99.37	102.91	83.47	74.52	82.68	92.81	103.61	120.59	103.98	89.18	114.41	92.06	110.94	115.18	136.63	115.18	136.63	99.94	99.94	99.94
Naloxone HCl	B1647	Opr1	110.15	138.49	111.73	65.24	83.05	75.31	96.63	89.32	93.44	114.13	87.99	125.26	93.52	145.96	113.64	147.09	113.64	147.09	80.09	80.09	80.09
Naltrexone	A3639	Opr1	117.50	104.93	93.41	102.98	85.93	102.48	82.29	146.29	114.40	104.75	90.13	121.27	103.20	99.39	100.79	101.26	99.39	100.79	92.22	92.22	92.22
Naltrexone HCl	B1648	Opr1	105.33	134.37	151.48	66.06	94.61	84.60	93.13	87.76	97.94	108.83	108.12	143.28	107.85	169.26	165.34	140.43	165.34	140.43	95.31	95.31	95.31
Napabucasin	B6029	N/A	38.45	71.32	58.71	35.03	45.61	63.76	80.98	39.93	50.21	22.67	35.52	54.21	21.81	53.40	40.37	73.06	40.37	73.06	43.84	43.84	43.84
Naphazoline HCl	B1340	Taar4	133.82	108.36	93.31	75.07	88.19	73.63	110.99	136.49	106.75	118.15	89.53	105.38	100.91	98.52	78.86	142.93	78.86	142.93	97.23	97.23	97.23
Naproxen Sodium	B5984	PTGS1	79.09	88.17	100.02	102.11	97.74	93.89	110.95	105.27	136.85	95.51	76.07	111.08	105.70	144.67	103.04	141.82	103.04	141.82	27.99	27.99	27.99
Naratriptan	B2251	HTR1A	92.42	111.38	105.03	102.04	103.56	85.89	97.21	103.70	114.00	99.63	93.80	127.02	72.55	86.51	85.92	115.17	85.92	115.17	93.58	93.58	93.58
Natamycin	A5786	N/A	181.56	271.82	215.67	122.59	190.07	96.48	109.46	223.36	175.32	134.48	107.97	137.08	146.02	145.55	143.51	210.88	143.51	210.88	287.62	287.62	287.62
Nateglinide	B2198	ABCC8	40.28	127.99	110.18	97.17	90.91	103.16	129.92	133.91	110.45	71.65	80.95	130.85	87.39	125.37	99.46	24.71	99.46	24.71	123.05	123.05	123.05
Nebivolol	B1341	ADRB1	73.57	77.09	64.89	38.19	38.67	34.00	47.02	79.42	82.67	92.54	81.15	87.23	87.18	106.59	81.77	70.74	81.77	70.74	67.78	67.78	67.78
Nedaplatin	B1986	N/A	41.00	64.10	51.12	33.12	33.00	52.23	60.26	68.30	63.78	83.68	91.82	89.05	96.84	105.24	88.71	107.62	88.71	107.62	95.46	95.46	95.46
Nefiracetam	B1532	GABRA1	109.50	138.66	112.92	74.29	75.59	78.85	92.35	169.11	161.21	104.52	95.28	127.80	91.87	172.66	126.15	167.34	126.15	167.34	79.38	79.38	79.38
Nelarabine	A1379	N/A	113.10	141.06	98.38	126.22	96.77	82.03	111.41	127.25	102.80	112.42	113.65	116.62	95.88	82.48	90.05	138.85	90.05	138.85	104.34	104.34	104.34
Nefinavir	B1122	N/A	88.97	144.19	101.23	71.52	65.93	78.02	100.46	56.86	66.05	24.73	81.06	93.43	97.15	89.71	88.8						

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)			ER-positive (luminal)				HER2-enriched		
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	WHIM2	WHIM2	WHIM30	WHIM30	WHIM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108
Neftimicin Sulfate	B1796	N/A	74.94	123.70	138.12	107.40	132.67	116.45	114.93	118.79	158.21	93.07	157.64	125.26	111.30	96.62	100.08	100.08	162.10	146.64	146.64
Nevirapine	A8481	N/A	110.06	113.54	95.96	101.67	91.89	77.12	109.18	125.90	133.86	156.61	87.71	105.18	113.11	99.28	93.70	143.16	84.33	84.33	84.33
Nicardipine HCl	B1798	ADORA3	67.49	64.43	126.09	55.18	55.56	54.77	42.84	76.09	83.86	38.55	32.44	90.94	65.36	61.50	49.28	79.73	147.92	147.92	147.92
Nicorandil	B2197	Kcnj8	40.17	123.62	112.66	88.33	76.94	113.54	126.94	122.78	131.02	86.06	100.08	134.63	89.28	130.49	170.65	27.91	107.88	107.88	107.88
Nicotinamide	N1651	N/A	87.41	103.30	106.69	98.94	100.19	78.19	95.55	90.93	98.56	105.10	85.98	114.09	99.86	113.46	106.43	128.65	31.52	31.52	31.52
Nicotine Difarrate	A8482	Kcmd3	120.49	110.12	98.68	108.36	91.85	92.71	106.58	122.73	118.94	154.31	98.16	107.20	113.60	96.41	101.95	142.75	100.87	100.87	100.87
Nicotinic Acid	B1987	HICAR1	86.82	107.52	98.46	90.84	94.83	76.89	91.74	143.23	143.86	113.83	86.10	118.90	87.33	125.23	99.10	129.33	93.61	93.61	93.61
Nifedipine	B1988	Caenat1s	69.41	94.93	111.38	92.00	92.49	80.56	104.00	111.12	110.17	71.34	62.45	130.32	71.19	102.98	83.68	110.62	71.74	71.74	71.74
Nifenazone	A8483	N/A	123.79	106.70	122.04	93.57	99.86	82.49	105.28	132.02	123.46	145.86	86.15	95.90	113.91	95.51	109.60	132.97	93.36	93.36	93.36
Niflumic acid	B1530	ANO1	101.26	169.68	129.87	71.48	79.04	94.99	114.78	123.72	120.84	44.17	73.56	149.45	68.82	122.97	126.70	115.04	79.04	79.04	79.04
Nifuroxazide	B1799	N/A	30.12	96.96	91.73	42.42	81.94	105.35	84.52	83.77	75.10	25.17	48.91	127.94	82.01	73.31	52.28	141.80	89.04	89.04	89.04
Nilotinib(AMN-107)	A8232	ABL1	61.54	148.32	92.09	47.68	47.99	74.55	63.65	73.33	76.59	104.66	75.58	79.77	76.60	81.88	100.75	132.04	133.19	133.19	133.19
Nilvadipine	A8455	CACNA1C	117.64	106.20	101.21	69.40	70.90	107.51	124.28	76.21	90.68	80.22	80.24	124.93	85.69	158.66	117.94	60.08	74.90	74.90	74.90
Nimesulide	B1452	Slc6a19	162.55	129.51	143.84	71.18	91.89	97.43	115.69	94.54	90.39	80.88	80.24	116.51	104.48	106.50	112.31	80.27	108.12	108.12	108.12
Nimodipine	A8484	CACNA1S	135.67	136.40	121.44	110.61	117.84	126.42	137.61	176.60	137.36	145.60	110.30	106.78	115.06	83.60	91.62	210.01	71.08	71.08	71.08
Nintedanib (BIBF 1120)	A8252	FGFR1	56.90	84.19	85.46	33.22	36.55	75.83	54.62	54.95	39.10	83.89	18.84	63.62	59.00	79.33	63.14	98.57	79.83	79.83	79.83
Nisoldipine	B1989	CACNA1C	75.90	120.61	179.82	80.45	87.84	76.66	100.52	134.25	111.34	26.22	28.52	108.92	74.04	120.56	65.70	105.43	78.34	78.34	78.34
Nitazoxanide	A8485	N/A	180.73	293.89	127.68	148.08	160.22	252.85	151.20	665.33	402.71	59.38	262.56	234.88	167.52	164.90	240.12	681.49	23.87	23.87	23.87
Nitrofurantoin	B1800	N/A	100.22	123.04	133.14	113.47	104.82	107.50	125.65	89.84	92.71	101.24	110.08	158.73	105.38	71.15	63.83	124.45	91.60	91.60	91.60
Nitrosine	B3527	HPD	83.29	126.70	136.60	110.31	95.60	83.01	76.12	135.50	162.78	89.30	97.09	110.47	87.76	91.56	126.41	101.16	54.65	54.65	54.65
Nitrendipine	B1933	Caenat1s	118.33	103.70	90.25	80.64	79.65	79.75	111.37	100.87	93.43	105.56	81.69	123.14	111.78	104.27	103.81	138.82	82.07	82.07	82.07
Nitrofurazone	A8486	N/A	127.86	122.51	147.58	147.61	126.92	100.23	110.71	130.27	105.04	49.31	27.75	148.51	92.29	167.38	150.82	144.09	103.07	103.07	103.07
Nizatidine	B1552	HRH2	143.56	156.67	132.88	74.82	92.31	97.89	95.27	134.54	110.78	119.09	97.79	120.27	92.66	100.24	92.14	144.13	84.17	84.17	84.17
Noradrenaline bitartrate monohydrate	B1990	ADRB1	71.67	101.90	160.32	144.95	138.17	63.26	82.64	199.13	204.95	108.84	156.98	151.53	123.88	338.31	253.23	91.63	117.46	117.46	117.46
Norethindrone	B1991	PGR	73.35	109.37	128.35	85.47	101.08	78.31	107.81	202.41	199.75	88.98	98.29	133.92	97.77	312.77	220.20	124.16	113.38	113.38	113.38
Norflouxacin	B1801	N/A	96.43	111.44	165.73	124.54	135.96	92.55	68.48	151.82	168.38	96.50	134.60	142.77	100.58	125.88	200.19	108.14	132.43	132.43	132.43
Noscapine HCl	A8479	SIGMAR1	131.35	121.92	117.26	97.23	90.09	97.80	123.83	139.88	139.06	161.80	92.28	114.17	116.74	105.66	96.80	175.47	97.78	97.78	97.78
Novobiocin Sodium	B1992	N/A	83.04	169.03	130.12	108.45	130.70	133.93	126.35	126.57	105.30	96.66	89.50	152.65	75.64	141.81	138.20	105.72	103.35	103.35	103.35
Nystatin (Fungicidin)	B1993	N/A	88.02	153.98	150.15	118.62	117.29	97.77	95.18	151.78	142.50	129.54	125.88	138.80	98.46	181.44	152.36	166.93	118.58	118.58	118.58
Obeticholic Acid	B4888	NR1H4	99.61	175.00	145.13	91.53	106.26	118.29	100.91	152.69	149.26	77.31	77.82	149.02	111.73	91.77	71.79	112.32	27.20	27.20	27.20
Ocrotic acid	B4979	Snr12	82.18	90.96	90.10	77.31	91.20	72.88	100.87	112.41	90.73	90.73	78.09	134.78	95.44	90.49	85.36	107.92	24.99	24.99	24.99
Ofloxacin	A5511	N/A	139.18	106.79	133.09	139.35	137.90	269.08	191.84	151.63	167.29	121.67	147.83	173.11	86.62	177.84	193.39	139.19	94.70	94.70	94.70
Olanzapine	B2240	HTR1A	90.80	89.57	111.72	84.51	90.89	84.96	96.93	118.29	96.16	106.91	102.99	107.47	88.73	78.38	98.86	131.09	88.32	88.32	88.32
Oleparib (AZD2281, Ku-0059436)	A4154	PARP1	130.88	201.50	165.92	128.55	105.17	109.47	100.58	214.07	234.79	79.16	65.19	111.96	129.23	99.49	106.85	148.54	127.83	127.83	127.83
Omesartan	A3681	AGTR1	114.29	119.94	135.76	110.87	131.45	93.75	88.58	171.29	135.94	116.71	142.83	120.88	112.58	198.89	219.75	105.75	132.48	132.48	132.48
Omesartan medoxomil	A4082	AGTR1	208.16	236.84	181.56	187.64	147.54	91.46	119.12	156.07	198.78	108.83	110.51	150.47	162.40	129.75	126.28	170.14	183.24	183.24	183.24
Olopatadine HCl	B1576	HRH1	108.80	135.01	99.14	71.86	91.41	78.02	96.24	111.11	104.20	107.23	94.37	130.25	97.61	208.32	155.15	137.19	83.16	83.16	83.16
Olsalazine Sodium	A8490	N/A	124.30	120.85	88.23	96.89	86.67	81.26	92.43	117.48	107.08	160.33	94.11	107.54	102.41	141.51	99.47	162.18	90.64	90.64	90.64
Ollipraz	B5958	N/A	85.55	92.92	104.23	88.27	101.40	80.94	101.14	70.74	74.83	91.37	85.72	112.54	66.06	95.95	83.68	134.17	92.72	92.72	92.72
Omeprazole	A2845	ATPA4	106.32	148.02	121.04	126.85	149.63	83.44	116.22	195.45	188.26	90.24	98.20	149.47	101.63	96.54	91.49	93.34	98.47	98.47	98.47
Ondansetron HCl	A5166	HTR3A	113.59	138.40	103.84	79.59	81.00	68.59	99.23	134.23	121.26	100.50	86.70	123.06	111.31	94.79	98.64	128.58	107.00	107.00	107.00
Ondansetron hydrochloride dihydrate	B1204	HTR3A	92.78	109.00	105.61	83.49	84.19	80.16	96.42	77.85	58.50	151.62	82.10	82.07	106.75	146.75	138.27	107.87	80.51	80.51	80.51
Onitast	A8492	DAGLA	126.40	127.00	81.29	75.36	76.78	64.47	93.78	128.19	118.60	152.00	93.33	121.93	110.06	106.61	88.69	164.31	92.52	92.52	92.52
Ornidazole	B1996	N/A	85.38	104.47	104.84	88.18	82.05	82.13	94.02	101.06	115.19	101.52	90.41	115.25	83.20	123.01	98.22	124.89	107.70	107.70	107.70
Orotic acid	B1147	N/A	99.06	81.36	120.26	86.71	100.41	101.93	102.27	80.28	72.84	104.33	72.60	100.22	93.22	83.03	88.46	111.20	85.41	85.41	85.41
Orphenadrine Citrate	B1606	CHRM1, CHRM2, CHRM3, CHRM4, HRH1	121.44	168.21	137.50	63.90	72.76	71.17	95.35	105.28	94.72	105.11	103.33	129.68	90.94	118.80	98.03	151.07	79.58	79.58	79.58
Osetamivir	A3688	N/A	103.54	118.89	90.97	95.68	96.38	92.62	91.35	131.25	121.44	110.65	81.69	124.45	97.36	93.99	104.42	101.68	102.38	102.38	102.38
Osetamivir phosphate	B1803	N/A	89.24	132.33	123.68	116.47	94.11	90.38	107.34	112.26	114.54	89.30	97.64	126.43	95.44	99.51	86.78	107.23	94.79	94.79	94.79
Ospemifene	B4871	ESR1	93.80	140.43	146.15	87.34	85.27	74.31	82.65	155.10	140.55	121.00	78.16	139.21	105.90	89.38	92.66	136.94	25.04	25.04	25.04

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)			ER-positive (luminal)			HER2-enriched					
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	UCD52	WHIM2	WHIM2	WHIM30	WHIM30	WHIM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108	HC108
Otilonium Bromide	B1607	CHRNA1, CACNA11	53.04	50.83	81.68	63.03	63.91	30.98	44.36	105.49	91.07	30.82	44.03	109.97	77.93	44.78	41.06	59.38	31.74				
Oxacillin sodium monohydrate	B1997	N/A	106.11	122.68	127.38	108.72	101.63	81.78	100.15	162.41	174.59	98.87	133.58	150.32	110.48	253.10	273.83	126.17	146.10				
Oxaliplatin	A8648	N/A	99.77	95.16	118.08	130.87	143.97	117.36	97.82	155.27	152.37	54.42	97.07	107.75	113.58	97.51	80.59	71.67	126.41				
Oxandrolone	B3486	AR	87.17	110.67	116.81	99.57	92.09	94.32	126.58	119.16	100.94	108.25	107.38	107.64	89.07	134.75	159.91	136.77	143.43				
Oxaprolin	B1804	PTGS1	103.42	139.12	121.64	99.55	99.02	93.09	108.79	162.93	138.38	87.14	91.04	106.50	106.80	108.99	95.49	93.60					
Oxcarbazepine	B2279	SCN5A	79.99	103.04	123.63	99.89	99.29	89.76	92.67	161.42	155.99	118.91	95.59	133.45	98.89	93.36	113.98	144.77	96.04				
Oxeladin Citrate	A8493	N/A	110.32	111.94	121.54	81.70	88.04	65.18	99.58	133.55	103.71	194.58	91.17	92.65	99.36	114.67	82.82	165.17	94.70				
Oxethazine	A8494	SLC6A2, SLC6A3, SLC6A4	93.54	99.65	83.15	35.93	42.68	36.58	49.81	103.01	89.73	97.84	40.99	55.88	87.87	53.86	37.53	101.79	56.33				
Oxendazole	B1998	N/A	84.42	119.43	146.85	89.64	100.91	81.82	92.25	145.21	133.33	111.85	114.36	132.21	93.14	202.67	154.60	149.53	104.50				
Oxiracetam	B4748	N/A	99.52	122.39	125.69	119.47	114.62	140.31	122.37	140.31	128.06	91.26	105.30	114.93	70.98	114.07	131.37	115.09	105.13				
Oxybenzone	B4737	N/A	138.18	102.02	127.60	109.35	124.97	119.67	129.34	152.43	121.32	101.07	121.86	141.24	108.87	96.91	109.42	126.48	47.12				
Oxybuprocaine HCl	B1805	SCN10A	138.85	185.75	148.93	112.21	87.81	109.22	143.52	191.30	186.71	75.93	91.92	99.58	88.80	119.55	71.38	143.94	135.79				
Oxybutynin	A8495	Chrm1	133.32	147.82	133.65	78.80	81.00	75.98	118.31	152.67	143.58	183.70	80.60	130.42	117.88	128.81	104.55	164.04	81.23				
Oxybutynin chloride	B1134	Chrm1	139.30	211.48	178.14	102.21	116.61	151.24	179.86	95.39	76.35	180.82	96.92	169.89	139.54	287.63	313.95	139.66	96.33				
Oxymetholone	B1806	AR	93.05	134.83	123.58	83.22	77.89	72.24	109.54	136.61	133.98	57.81	112.21	97.83	86.71	58.86	50.64	139.82	169.55				
Oxytetracycline (Tetracycline)	B2000	N/A	76.00	89.98	122.38	101.30	98.39	59.80	84.41	124.39	117.76	124.55	91.89	126.25	85.32	119.59	110.80	111.86	81.93				
Oxytetracycline Dihydrate	B2001	N/A	70.76	91.94	115.97	94.05	96.51	61.45	82.87	124.06	123.60	127.16	95.33	128.56	83.09	123.89	122.54	124.49	83.53				
Oxytocin	B4723	OXTR	106.48	125.04	128.12	113.78	116.14	124.52	127.27	128.01	139.44	98.17	101.24	110.46	69.16	162.56	104.97	122.46	105.50				
Ozagrel	A4344	TBXAS1	90.42	99.69	98.42	90.32	85.76	96.16	99.53	101.01	73.34	102.37	79.38	145.25	105.72	120.19	110.84	102.43	90.30				
Ozagrel HCl	B2116	TBXAS1	44.60	100.51	122.16	88.65	86.70	72.21	114.45	141.23	137.95	93.15	107.83	134.70	99.50	133.06	118.81	22.75	87.02				
Paclitaxel (Taxol)	A4393	NR112	118.73	128.92	156.45	62.84	69.53	101.17	84.64	118.98	108.57	97.93	92.10	92.41	96.48	94.01	106.44	107.06	97.99				
Paclitaxel HCl	B1023	FLT3	34.26	23.63	132.88	33.94	36.17	53.16	46.59	62.63	38.70	28.05	23.67	384.67	130.73	55.64	45.68	90.76	168.59				
Palbociclib (PD0332991) isethionate	A8335	CDK4	99.46	208.11	179.93	99.79	110.69	112.53	94.26	147.42	143.44	57.36	98.56	200.89	154.20	232.51	126.09	76.18	125.83				
Paliperidone	A8496	DRD2, HTR2A	113.05	98.00	113.12	118.07	107.33	151.65	117.88	129.92	123.97	106.66	82.53	171.53	86.29	120.16	114.55	120.66	92.20				
Palonosetron HCl	B2229	HTR3A	96.33	75.67	110.87	79.40	73.15	78.56	86.59	110.23	98.67	106.87	145.05	87.77	94.82	91.98	108.65	114.32	98.17				
Pamidronate	B1807	N/A	160.60	172.59	210.61	150.03	123.56	208.74	337.14	143.24	144.60	42.32	69.61	112.30	144.37	251.96	204.17	546.29	114.44				
Pamidronate Disodium	A2456	N/A	91.51	78.71	59.90	65.75	81.03	60.15	89.88	101.51	83.23	85.42	88.47	82.89	80.26	105.16	85.23	93.06	93.18				
Pancuronium dibromide	B1612	CHRNA1	93.58	105.23	95.54	76.90	81.83	90.94	97.73	105.72	99.73	106.05	103.11	105.52	93.26	264.76	239.04	146.03	79.13				
Panobinostat (LBH589)	A8178	HDAC1	360.98	827.13	1235.48	574.04	499.55	34.42	38.68	1850.08	2321.31	92.10	44.45	129.54	954.59	51.15	38.79	938.33	854.02				
Pantoprazole	B4720	ATP4A	111.96	133.45	108.48	126.77	133.98	94.58	105.72	134.81	124.43	100.27	103.99	133.25	102.68	95.58	98.55	129.69	34.09				
Paromomycin Sulfate	B1808	N/A	102.21	147.40	129.38	92.26	91.38	97.14	165.66	116.93	105.65	81.05	95.63	132.98	94.96	96.62	76.98	127.50	106.56				
Paroxetine HCl	B2252	P2RX4	50.49	76.88	77.40	42.01	35.18	37.61	48.46	80.92	80.50	78.37	102.27	127.60	74.80	124.04	115.05	81.81	66.88				
Pasinazid	A8497	N/A	102.57	87.21	83.71	97.32	92.94	57.48	103.61	129.28	136.46	169.87	83.41	111.00	121.60	188.50	175.48	147.87	95.56				
Pazopanib (GW-786034)	A3022	CSF1R	144.62	186.74	91.98	92.50	88.44	155.72	147.72	147.83	139.42	51.57	70.56	77.24	85.36	105.34	114.09	80.32	86.43				
Pazopanib Hydrochloride	A8347	CSF1R	108.28	136.92	134.36	85.47	104.31	105.20	149.72	80.61	72.89	76.58	77.43	100.99	96.84	84.57	66.63	237.39	130.74				
PCI-24781 (CRA-024781)	A4098	HDAC1	3844.09	4004.67	1500.73	1850.63	1116.75	74.57	86.55	2222.00	2305.73	105.77	35.87	127.53	9.68	67.85	44.35	1161.36	712.59				
PCI-32765 (Ibrutinib)	A3001	BLK	63.06	97.42	55.60	73.67	79.74	75.49	65.38	96.56	110.34	41.66	70.80	69.01	83.79	93.99	81.88	39.85	53.39				
PD 0332991 (Palbociclib) HCl	A8316	CDK4	81.89	185.39	113.69	83.25	82.48	83.33	94.21	136.37	127.74	79.14	93.13	141.19	152.25	132.25	88.04	114.87	142.34				
Peifloxacin Mesylate	B2003	N/A	68.69	115.77	152.88	114.99	111.37	69.45	91.65	135.89	151.17	104.97	105.74	136.88	103.04	156.27	163.59	127.56	96.18				
Pelitinib (EKB-569)	A1835	EGFR	24.59	36.42	37.87	33.55	32.85	19.01	43.24	65.81	49.37	18.75	24.57	60.70	37.71	33.82	34.49	28.26	41.44				
Pemetrexed	A4390	DHFR	96.65	91.65	104.85	83.98	102.55	88.37	101.94	123.01	137.27	95.81	81.54	102.42	92.86	103.80	101.40	106.98	122.56				
Pemetrexed disodium hemipenta hydrate	A3707	DHFR	97.61	96.87	69.26	96.64	94.11	90.65	90.30	144.75	94.04	110.89	76.80	95.80	91.34	95.54	84.52	97.53	96.64				
Pemirolast potassium	B1563	HRH1	98.67	97.31	107.92	93.03	91.29	119.04	107.80	105.24	81.49	81.54	86.43	98.69	90.15	118.07	77.54	82.02	149.12				
Penciclovir	B1809	N/A	95.70	134.65	130.03	113.77	105.92	99.29	146.78	105.63	93.67	87.69	97.07	140.03	95.30	90.84	77.91	109.07	99.83				
Penicillin G Sodium	B1678	N/A	114.74	225.65	111.14	113.95	85.40	97.52	117.69	104.70	112.66	105.94	77.66	105.21	105.00	77.39	63.99	121.75	110.37				
Pentamidine isethionate	B4980	N/A	100.29	95.82	87.74	89.60	92.90	71.87	98.45	118.09	107.39	27.49	27.50	104.01	74.69	222.72	136.57	72.08	16.65				

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)			ER-positive (luminal)				HER2-enriched		
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	WHM2	WHM2	WHM30	WHM30	WHM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108
Pentobarbital sodium salt	B5646	GABRA1	84.22	88.50	87.02	85.09	88.10	81.53	110.91	91.35	107.51	87.59	76.14	105.21	85.18	108.51	84.15	106.34	84.15	106.34	24.47
Peramivir	A3709	N/A	118.79	105.72	78.92	71.45	91.81	102.20	92.73	152.81	119.24	103.74	78.57	109.88	98.04	116.49	88.32	104.30	88.32	104.30	93.47
Piraracetam	A3710	GRIA1	94.29	109.20	70.43	71.04	87.37	89.75	88.53	99.88	94.12	108.18	62.00	89.86	94.02	80.14	86.50	107.86	86.50	107.86	85.66
Pergolide mesylate	B1485	HTR1A	106.77	107.47	124.46	77.35	75.57	90.71	110.89	118.38	101.39	99.45	111.84	92.39	87.58	94.32	102.19	113.49	102.19	113.49	82.10
Perindopril	B1214	ACE	109.62	110.65	94.20	104.43	100.62	98.28	105.75	102.79	99.33	155.72	105.79	110.53	111.03	130.62	136.55	134.75	136.55	134.75	91.00
Perindopril Erbumine	A8019	ACE	93.78	76.03	107.89	72.15	72.73	97.09	99.23	134.13	94.54	87.18	103.06	101.34	93.51	132.54	124.60	120.91	132.54	120.91	118.26
Pexidartinib (PLX3397)	B5854	CSF1R	99.14	101.12	116.09	108.86	86.00	90.49	92.43	93.67	78.42	76.38	70.81	138.93	91.34	91.90	101.93	127.12	91.90	101.93	31.14
Phenacetin	B1453	PTGS1, PTGS2	143.74	135.20	121.96	73.16	90.77	91.55	105.79	86.67	102.20	108.83	84.97	135.54	96.71	99.34	104.92	109.23	99.34	104.92	127.92
Phenazopyridine HCl	B1812	SCR1A	187.91	204.93	199.66	278.66	235.10	223.85	158.01	360.39	457.00	333.34	253.07	296.93	136.23	318.75	194.29	626.51	194.29	626.51	191.03
Phenformin HCl	B1373	PKKA1	122.07	111.06	94.57	76.14	81.18	84.92	105.86	97.80	82.80	56.98	49.42	113.98	109.61	62.57	54.98	92.28	62.57	54.98	78.87
Phenindione	B1813	VKORC1	103.92	150.97	14.39	109.16	98.77	114.68	133.18	133.91	183.86	108.14	100.09	141.87	94.67	110.70	74.45	133.65	74.45	133.65	106.31
Pheniramine Maleate	B1814	HRH1	103.75	117.98	131.62	136.08	97.29	81.19	114.49	133.82	113.65	83.97	132.82	122.89	101.12	94.00	94.01	107.33	94.01	107.33	86.27
Phenoxylbenzamine HCl	B1343	ADRA2B	119.42	124.05	194.55	105.23	104.21	86.85	100.97	197.52	184.16	113.61	152.94	130.96	114.06	136.55	143.77	133.92	143.77	133.92	118.38
Phentolamine Mesylate	B1363	Adria1a	121.59	101.57	101.41	104.02	94.97	85.44	101.66	145.96	128.85	112.73	122.88	116.03	112.30	132.57	116.42	121.60	116.42	121.60	88.00
Phenylbutazone	B2004	PTGS1	72.53	106.18	120.42	87.90	89.85	72.87	105.21	121.43	116.00	94.28	79.14	128.51	97.15	127.13	127.52	121.13	127.52	121.13	100.66
Phenylephrine HCl	B1344	ADRA1A	108.55	111.58	97.22	84.54	90.39	80.64	91.64	114.42	103.71	118.29	87.89	125.78	104.69	74.55	81.40	123.44	74.55	81.40	96.56
Phenylephrine Mesylate	B2271	SCN2A	99.63	112.29	129.36	94.81	103.09	129.09	106.41	177.22	142.49	104.94	106.20	150.96	107.70	102.19	124.13	117.24	107.70	102.19	129.76
Phenylephrine sodium	B2272	SCN2A	89.78	104.53	114.03	97.39	85.75	110.20	99.14	124.50	112.26	106.88	86.35	142.31	100.91	110.39	97.03	131.97	100.91	110.39	94.06
Phloridzin	N1876	SLSA1	82.07	126.42	115.45	107.96	101.30	89.75	102.56	102.48	92.02	105.43	90.84	122.79	97.73	109.88	101.26	192.84	101.26	192.84	37.56
Pidotimod	B2005	N/A	71.48	114.63	107.63	91.55	105.42	74.69	105.30	120.77	124.04	99.78	92.56	137.41	96.69	134.07	129.30	118.85	134.07	129.30	94.26
Pimasentib (AS-703026)	A5573	MAP2K1, MAP2K2	70.04	75.59	115.62	70.88	70.26	35.88	88.62	139.46	119.54	35.75	74.78	72.92	83.07	68.35	60.43	60.43	68.35	60.43	84.25
Pimavanserin	B8019	HTR2A	97.04	99.11	87.27	44.14	48.57	41.80	45.61	86.16	80.88	44.00	69.32	111.05	80.96	178.85	164.06	178.85	164.06	178.85	27.42
Pimecrolimus	B1817	Fkbp1a	50.65	92.19	71.11	49.53	38.23	52.05	72.86	97.98	77.47	25.74	33.09	65.25	76.87	60.33	52.67	52.67	60.33	52.67	84.36
Pimobendan	A4340	PDE3A, PDE3B	138.70	128.55	120.78	115.06	123.35	167.54	169.36	124.13	114.23	162.13	95.00	132.06	131.56	138.38	154.50	304.34	154.50	304.34	92.57
Pimozide	C3837	HTR1A	88.11	117.71	102.95	74.99	98.37	86.01	120.69	93.42	93.97	26.20	70.05	104.26	70.44	69.69	69.10	26.60	69.10	26.60	92.30
Pioglitazone	B2117	PPARG	62.05	123.96	133.37	111.35	99.90	91.17	120.62	172.00	169.33	101.84	144.79	117.98	104.42	145.82	123.58	29.14	145.82	123.58	29.14
Proglitazone HCl	A4324	PPARG	113.62	123.43	102.07	107.73	123.85	125.53	106.56	210.05	153.06	107.38	80.09	128.64	124.63	125.07	127.85	132.62	125.07	127.85	103.82
Piperacillin Sodium	B1818	N/A	103.42	113.99	111.38	120.02	96.50	92.71	117.69	162.28	140.97	94.59	57.62	91.77	92.63	89.28	87.48	95.27	89.28	87.48	71.94
Pipiperine	N1674	TRPV1	155.46	161.04	131.15	213.39	244.24	117.38	116.58	111.80	111.87	326.50	256.06	239.44	133.85	260.97	250.72	748.01	250.72	748.01	57.17
Pipifenidone	B2288	FUR1	94.48	90.26	91.29	89.14	81.95	86.30	107.61	118.07	103.10	121.62	84.84	99.77	89.37	109.43	103.12	123.19	89.37	109.43	88.89
Pitromidic Acid	A8502	N/A	187.83	114.43	124.56	148.02	141.73	281.36	285.31	937.24	854.53	135.38	128.33	254.74	110.46	152.29	190.17	124.28	110.46	152.29	90.03
Piroxicam	A8503	PTGS1	110.06	96.18	90.55	88.68	87.86	79.26	103.80	126.12	107.25	33.35	74.34	102.13	132.69	100.18	105.27	137.19	100.18	105.27	76.98
Pitavastatin	B1124	Hmgcr	105.87	131.38	170.58	81.38	68.32	60.48	126.71	99.89	84.56	88.62	115.12	125.39	263.75	482.76	324.87	115.73	482.76	324.87	100.77
Pivavastatin Calcium	A8504	Hmgcr	91.19	76.53	113.14	49.27	51.14	83.97	51.57	96.77	89.86	34.96	72.83	78.38	256.06	167.00	129.02	93.73	167.00	129.02	65.55
Pizotifen Maleate	B2007	HTR1A	71.67	129.23	111.22	80.97	84.49	61.33	76.47	173.26	174.47	77.39	71.99	105.25	97.88	181.30	152.22	106.97	181.30	152.22	77.24
Plerixafor (AMD3100)	A2025	ACKR3	91.51	107.33	87.85	85.50	99.19	65.45	80.49	118.29	101.75	99.24	86.05	86.78	84.70	82.14	87.96	99.15	84.70	82.14	123.96
PMSF	A2587	PRTN3	148.64	113.21	100.14	106.66	105.57	125.95	81.53	127.25	95.44	88.77	89.77	126.92	92.55	73.57	100.78	96.20	73.57	100.78	82.11
Polydatin	N1783	N/A	167.55	141.50	194.86	299.11	249.42	83.97	133.20	241.46	268.20	123.50	101.90	559.24	142.50	99.12	100.63	146.47	99.12	100.63	37.79
Pomalidomide (CC-4047)	A4212	CRBN	121.03	123.88	102.55	106.93	101.50	70.26	77.51	134.42	133.31	89.96	85.87	125.64	107.92	98.11	85.65	140.68	107.92	98.11	96.57
Ponatinib (AP24534)	A5467	ABL1	69.18	70.83	65.31	49.28	46.19	96.44	97.82	47.87	47.87	29.26	51.95	77.75	41.93	49.45	45.46	32.98	41.93	49.45	64.91
Posaconazole	A1718	N/A	125.09	121.35	94.52	79.42	70.11	77.49	96.05	118.33	92.38	46.08	72.19	78.01	64.11	82.34	77.53	60.88	64.11	82.34	81.25
Potassium Iodide	B2008	TPO	72.34	124.64	126.81	106.74	98.06	78.15	85.85	115.40	126.02	102.83	91.21	134.02	97.38	166.26	170.76	117.06	97.38	166.26	89.61
Pozotinib	B5827	EGFR	29.84	49.02	66.14	40.97	47.33	46.48	54.45	28.69	42.89	48.82	45.32	48.68	48.02	37.14	31.31	39.94	48.02	37.14	22.47
Pracinostat (SB939)	A4095	HDAC1	3905.10	4912.36	1750.28	1580.00	1150.86	68.30	61.43	1961.40	2437.97	91.12	21.38	212.99	6.31	103.14	72.98	1234.65	6.31	103.14	101.77
Pralatrexate	A4350	HDHR	144.28	123.46	103.19	103.81	116.32	113.39	128.12	119.62	113.61	109.99	94.12	116.55	114.69	176.08	138.50	96.63	114.69	176.08	98.46
Pramipexole	B1488	DRD2	104.73	139.54	151.34	127.80	99.43	101.24	101.81	92.04	108.26	108.59	116.71	111.02	109.77	164.62	161.07	98.41	109.77	164.62	82.40
Pramipexole 2HCl Monohydrate	B1487	DRD2	123.15	128.01	138.07	113.88	91.39	86.71	101.81	106.48	99.51	107.53	106.90	130.68	109.77	96.02	98.72	122.04	109.77	96.02	76.52
Praniracetam	B2118	N/A	44.33	125.90	128.72	105.93	110.07	111.30	126.27	214.89	222.55	94.23	107.59	154.77	110.39	121.35	118.08	32.95	110.39	121.35	154.09
Pranixone HCl	B1819	N/A	137.44	138.35	116.29	83.79	75.34	157.23	174.01	116.48	149.03	98.33	86.51	103.24	111.58	66.34	100.70	140.94	111.58	66.34	150.55
Pranlukast	B2009	CYSLTR1	89.47	103.13	146.53	103.24	100.21	57.79	72.89	159.56	143.62	60.26	67.74	97.53	100.85	238.76	196.02	64.84	100.85	238.76	75.73
Pranoprofen	B2010	PTGER2	103.96	122.45	124.81	85.11	112.39	107.89	112.52	95.53	126.32	104.65	82.60	128.07	78.62	111.95	134.53	111.95	78.62	111.95	125.24
Prasugrel	A1607	P2RY12	29.17	123.98	121.																

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)			ER-positive (luminal)				HER2-enriched		
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	WHM12	WHM12	WHM30	WHM30	WHM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108
Prasugrel hydrochloride	B1283	P2RY12	148.42	130.72	149.19	95.81	124.28	109.42	110.80	126.15	140.48	118.63	99.31	136.76	119.66	70.32	78.12	139.36	118.80	139.36	118.80
Prazosin HCl	A4369	HMGCR	132.93	151.83	152.31	97.43	102.82	90.41	119.29	157.44	154.91	145.72	105.72	183.76	112.57	142.22	142.38	151.69	143.72	151.69	143.72
Praziquantel	B2011	N/A	88.26	110.09	112.41	99.70	93.83	80.08	107.99	120.11	108.88	98.60	90.65	131.95	93.10	145.86	121.65	134.89	108.34	134.89	108.34
Prednisolone	B2012	Adra1a	154.14	150.02	155.60	134.64	144.77	49.20	55.77	115.28	112.93	35.80	38.06	129.28	131.42	97.19	119.34	203.61	203.61	203.61	203.61
Prednisolone Acetate	B2013	NR3C1	107.12	162.49	305.47	169.24	175.95	116.13	112.26	193.43	218.09	107.97	223.86	175.03	132.24	336.37	317.48	120.31	189.55	120.31	189.55
Prednisolone	B2148	NR3C1	85.95	152.58	274.91	152.90	151.99	98.05	96.34	197.48	166.04	107.58	159.51	184.61	122.80	500.09	382.43	120.38	122.02	120.38	122.02
Pregabalin	A3734	CACNA2D1, CACNA2D2	90.49	105.13	70.78	72.76	83.65	74.76	88.11	126.39	96.20	97.19	84.50	103.64	95.57	150.49	124.94	98.17	101.87	98.17	101.87
Pregnenolone	B1512	GLRA1	127.36	155.55	110.96	77.13	73.76	101.70	96.37	130.23	102.73	80.99	71.09	125.72	84.54	206.11	143.61	121.76	56.89	121.76	56.89
Pridinol Methanesulfonate	A8507	CHRM1, CHRM2, CHRM3, CHRM4, CHRM5																			
Phlocaine	B2119	SCN5A	115.78	110.60	111.62	81.78	90.46	226.89	100.46	136.17	121.31	156.81	90.91	103.97	118.64	100.92	84.19	142.20	83.21	142.20	83.21
Phlocaine hydrochloride	B1280	SCN5A	41.86	112.62	107.87	78.87	80.46	85.31	112.13	278.30	251.19	100.72	103.00	144.82	92.01	119.17	120.31	37.06	100.03	37.06	100.03
Phlocaine Diphosphate	B1820	SCN5A	160.45	134.45	122.10	90.86	113.90	106.36	97.59	131.43	138.49	112.34	112.25	117.20	112.67	79.20	87.04	98.35	112.99	98.35	112.99
Primidone	B2120	GABRA1	63.26	49.39	116.23	82.98	68.39	62.92	78.08	111.21	113.69	36.33	22.33	95.20	49.04	76.20	60.13	100.20	72.93	100.20	72.93
Probenecid	B2014	SLCO1C1	40.01	116.11	120.62	78.82	91.42	77.17	123.75	2879.09	2286.36	103.25	107.35	161.67	90.57	134.24	135.24	35.33	104.42	35.33	104.42
Procabrol	B2015	ABCA1	75.57	128.50	145.38	108.87	117.87	87.84	97.59	160.88	148.57	120.12	129.02	142.08	94.61	237.37	189.26	113.72	104.26	113.72	104.26
Procainamide HCl	B4798	SCN5A	67.53	98.75	102.82	93.48	93.88	74.33	106.60	114.41	112.32	121.74	110.30	128.59	89.71	94.33	95.38	99.72	206.29	99.72	206.29
Procaine	B3435	RYR1	112.85	107.32	116.31	105.63	94.64	102.43	116.62	204.41	190.34	104.80	110.60	233.72	95.76	96.38	99.71	123.89	29.89	123.89	29.89
Procabazine HCl	B1470	N/A	96.46	102.25	102.03	90.57	85.65	80.79	113.73	111.75	78.55	121.15	88.58	122.44	86.98	96.75	96.78	133.44	88.04	96.78	133.44
Prochlorperazine	A8508	DRD1	90.41	96.63	87.59	88.88	70.48	87.03	108.93	84.43	83.38	105.07	87.16	90.52	99.72	89.27	119.24	109.20	99.68	109.20	99.68
Progesterone	B1821	N/A	115.02	110.81	92.14	58.23	69.12	78.16	71.15	362.72	206.78	92.59	104.94	117.51	91.14	140.19	116.77	180.89	52.64	180.89	52.64
Promethazine HCl	A8509	CATSPER1	43.91	121.38	165.00	65.56	43.63	40.77	59.75	86.73	83.62	20.70	25.83	143.70	41.59	771.93	229.23	31.87	332.35	31.87	332.35
Propafenone HCl	B2281	ADRB1	151.94	168.81	112.55	91.72	86.18	119.24	176.85	134.09	112.22	107.06	48.60	107.97	90.61	149.40	159.19	111.30	103.92	111.30	103.92
Proparacaine HCl	B2274	SCN5A	95.47	116.65	107.41	68.98	72.67	97.28	119.11	108.22	119.11	108.22	71.98	90.06	92.87	98.68	93.53	73.76	81.24	73.76	81.24
Propofolol HCl	B1346	ADRB2	85.52	95.00	100.81	82.40	71.36	82.40	101.01	119.92	110.59	105.78	86.28	119.26	87.24	90.35	100.23	117.00	88.89	117.00	88.89
Propylthiouracil	B2121	TPO	91.11	108.11	109.02	109.68	94.21	91.71	102.41	123.84	104.98	103.24	78.68	164.81	91.94	115.58	107.38	177.14	88.99	177.14	88.99
Protonamide	B2016	N/A	109.77	109.68	96.64	86.40	80.13	71.94	94.58	113.99	102.90	110.63	89.35	104.19	84.49	114.61	81.08	113.52	98.22	113.52	98.22
Prucalopride	B2253	HTR4	39.54	101.24	119.92	93.88	88.58	73.23	126.84	289.87	243.67	108.59	91.74	152.91	97.80	164.05	122.36	31.48	86.17	31.48	86.17
PSI-7977	A3738	N/A	67.77	112.41	111.77	99.44	100.79	65.07	102.88	106.68	117.61	99.62	95.46	116.67	89.18	124.35	109.49	110.76	93.53	110.76	93.53
Puromycin dihydrochloride	B7587	N/A	80.24	92.08	121.99	97.24	81.36	84.91	97.86	121.12	124.28	114.27	85.50	133.74	94.22	110.98	129.16	156.01	88.18	156.01	88.18
Pyrazinamide	B2149	N/A	90.84	79.78	140.75	84.04	108.66	98.80	116.22	123.30	87.34	71.26	102.62	79.48	78.62	86.34	78.62	99.33	60.54	78.62	99.33
Pyrazinamide	B2122	N/A	26.96	30.31	52.04	34.91	34.07	39.08	45.00	31.72	34.93	26.94	26.83	58.60	33.42	61.18	40.97	38.71	8.59	40.97	38.71
Pyridoxine HCl	B2017	N/A	50.97	113.69	109.44	108.19	90.77	84.09	107.61	128.24	132.46	106.11	122.79	117.35	101.16	155.53	137.24	20.84	72.85	137.24	20.84
Pyrimethamine	A4353	Slc47a2	36.96	95.95	98.94	86.54	85.15	68.75	111.62	199.40	209.07	101.17	80.47	126.31	93.79	100.73	98.73	29.16	98.41	29.16	98.41
Quercetin	N1841	MAPK1	96.59	112.35	105.21	73.90	70.19	92.09	101.43	98.60	103.14	105.35	100.37	119.89	92.07	126.43	145.00	143.32	72.52	143.32	72.52
Quetiapine Fumarate	B1490	HTR1A	67.58	110.87	107.34	96.14	103.66	84.89	88.31	97.75	102.61	93.29	86.96	120.89	91.91	129.95	103.90	120.93	97.14	120.93	97.14
Quinapril HCl	B2207	ACE	106.84	115.92	108.90	73.52	76.95	115.46	122.09	102.28	105.03	87.90	75.31	129.35	120.74	113.52	96.30	103.48	80.86	103.48	80.86
Quinidine	B7590	Kcnk10	91.97	156.74	150.64	101.14	102.99	106.67	107.58	139.63	116.09	144.10	137.44	122.73	99.18	224.05	226.43	87.19	27.38	226.43	87.19
Quinazolinib (AC220)	A5793	CSF1R	113.22	131.52	94.10	98.50	104.15	107.89	100.11	140.01	122.24	111.17	78.69	108.90	94.14	110.49	121.88	116.11	89.01	116.11	89.01
R788 disodium	A8332	SYK	176.28	195.93	162.82	77.35	80.21	122.53	132.47	149.30	158.52	77.62	85.55	91.61	123.31	83.60	82.41	99.36	79.12	99.36	79.12
Rabeprazole	B3467	ATP4A	35.20	87.72	96.86	87.62	79.71	97.83	92.99	94.73	114.44	80.16	65.33	111.47	94.81	107.67	99.64	22.61	101.03	99.64	22.61
Racemadrolil	B1649	MME	81.60	96.32	123.36	96.03	99.81	93.83	108.88	96.61	105.38	116.48	87.60	134.97	102.40	115.94	128.45	122.34	27.39	122.34	27.39
Radiolimb(Y-5511)	B5846	BCL2	148.47	187.19	126.63	125.69	166.17	71.60	76.90	217.37	168.77	82.41	80.58	112.36	111.12	105.88	82.11	156.75	195.09	156.75	195.09
Raloxifene HCl	B1515	ESR1	94.83	77.88	64.52	60.85	55.23	91.11	67.73	94.12	89.61	87.72	103.02	76.77	86.78	94.25	78.48	95.02	82.38	95.02	82.38
Raltegravir (MK-0518)	A4073	N/A	128.56	184.43	161.07	147.24	108.66	119.84	141.26	144.21	132.65	113.73	118.71	159.27	123.05	153.46	151.13	323.98	117.50	323.98	117.50
Ramelteon	A1748	MTNR1A	113.88	219.57	204.15	182.22	174.07	124.35	145.47	301.28	274.06	62.60	102.27	196.85	114.84	406.30	394.67	452.01	184.22	452.01	184.22
			92.47	119.71	104.36	54.55	76.69	91.82	93.84	85.73	72.96	99.74	85.93	111.48	93.26	108.08	120.63	122.40	79.66	122.40	79.66
			91.76	87.16	106.60	94.91	109.44	108.79	91.44	122.48	84.73	102.07	83.15	142.13	92.95	73.97	87.73	141.31	35.56	87.73	141.31
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continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)			ER-positive (luminal)			HER2-enriched						
Item Name	Catalog#	TARGET	HC101	HC101	HC116	UCD52	UCD52	UCD52	WHM12	WHM12	WHM30	WHM30	WHM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108	HC108	
Ramipril	B2208	ACE	43.33	112.04	106.37	91.75	83.44	84.20	97.43	99.80	99.75	83.39	90.01	128.96	91.63	104.97	124.27	124.27	104.97	124.27	124.27	4.28	100.64	100.64
Ranitidine	B1564	H1n2	106.21	113.30	122.28	96.77	83.00	87.63	87.63	105.35	120.88	110.71	113.44	124.94	102.63	126.99	117.95	126.99	126.99	126.99	126.99	158.60	83.83	83.83
Ranolazine	A8510	SCN5A	134.15	138.10	120.11	102.66	76.10	96.14	122.53	141.96	117.47	186.52	80.60	96.26	103.08	144.59	95.33	120.34	95.33	144.59	95.33	120.34	86.83	86.83
Ranolazine 2HCl	A5300	SCN5A	102.45	88.74	137.72	75.80	95.56	114.99	112.57	172.37	144.20	107.73	96.93	124.29	109.24	109.47	100.91	100.91	109.47	100.91	115.47	106.81	106.81	
Rapamycin (Sildenafil)	A8167	FKBP1A	35.08	45.71	57.14	27.59	23.43	40.50	43.52	89.49	48.24	36.65	24.50	69.61	51.59	35.83	43.26	111.11	35.83	43.26	111.11	45.68	45.68	
Resagiline Mesylate	A4366	MAOB	152.94	161.48	141.13	101.22	113.14	118.46	109.41	127.91	150.26	110.72	122.80	117.22	127.37	122.54	129.37	122.54	129.37	122.54	86.19	142.70	142.70	
Rebamipide	B2018	Cckar	70.76	114.01	102.27	104.65	95.60	78.74	93.60	120.99	108.44	89.14	88.13	128.87	96.96	112.83	120.77	116.02	112.83	120.77	116.02	102.74	102.74	
Regorafenib	A8236	BRAF	19.57	25.51	39.65	114.30	120.66	25.28	35.88	43.91	45.85	10.46	15.88	48.02	43.48	79.02	87.09	21.92	79.02	87.09	21.92	63.63	63.63	
Regorafenib hydrochloride	A3750	BRAF	55.68	56.71	62.66	101.41	86.17	100.90	94.44	83.52	37.77	89.35	75.08	114.33	65.45	37.57	35.85	30.68	37.57	35.85	30.68	80.17	80.17	
Regorafenib monohydrate	A5316	ABCC8	87.18	88.74	118.31	80.72	80.62	92.91	100.69	139.35	113.32	128.24	106.60	130.53	111.22	88.91	71.59	128.88	88.91	71.59	128.88	99.20	99.20	
Reserpine	N1867	SLC18A1	102.22	143.62	132.39	106.06	104.21	88.00	88.71	113.89	103.90	89.35	96.16	112.12	88.96	136.17	121.40	91.31	136.17	121.40	91.31	44.65	44.65	
Reserpine hydrochloride	B1270	SLC18A1	114.89	102.32	87.89	80.94	78.81	105.74	79.45	73.94	82.90	64.28	69.11	113.69	97.60	111.74	135.54	83.43	111.74	135.54	83.43	75.56	75.56	
Resveratrol	A4182	PTGS2	248.42	160.31	174.06	387.40	261.94	228.52	152.74	720.68	432.73	117.21	274.22	683.16	205.93	494.18	441.39	122.22	494.18	441.39	122.22	481.10	481.10	
Retapamulin	B2019	N/A	58.83	88.23	108.66	78.36	85.17	76.50	84.03	134.91	156.75	85.50	80.99	112.68	93.30	117.97	103.86	102.04	117.97	103.86	102.04	75.30	75.30	
Retinyl (Vitamin A)	N/A	N/A	87.30	117.70	103.90	97.82	90.84	93.43	131.08	116.32	134.49	90.64	86.06	100.42	88.13	91.21	66.84	142.14	91.21	66.84	142.14	94.76	94.76	
Palmitate	B1869	N/A	85.04	42.73	97.08	96.23	104.79	38.79	50.99	91.73	111.29	43.69	30.48	142.95	117.58	66.25	55.48	27.14	66.25	55.48	27.14	109.73	109.73	
RG7388	A3763	MDM2	38.30	107.05	109.98	101.34	91.54	66.89	131.26	223.74	177.20	94.26	91.14	148.33	93.71	125.50	111.48	26.37	125.50	111.48	26.37	92.10	92.10	
Ribavirin	B2125	IMPDH1	38.30	107.05	109.98	101.34	91.54	66.89	131.26	223.74	177.20	94.26	91.14	148.33	93.71	125.50	111.48	26.37	125.50	111.48	26.37	92.10	92.10	
Rifabutin	B2126	N/A	32.14	80.06	121.25	82.47	79.95	60.34	97.94	148.87	137.95	38.28	76.36	115.59	83.16	124.11	101.55	24.53	124.11	101.55	24.53	77.77	77.77	
Rifampin	B2021	N/A	65.70	107.31	144.86	83.26	82.55	63.50	64.58	94.35	95.41	84.04	87.51	132.52	94.53	119.17	96.45	98.90	119.17	96.45	98.90	80.57	80.57	
Rifampine	B2127	N/A	28.17	67.22	121.56	80.66	74.09	36.55	71.21	118.09	117.54	22.70	31.03	120.43	104.30	145.78	120.53	15.90	145.78	120.53	15.90	73.39	73.39	
Rifaximin (Xifaxan)	A8512	N/A	130.34	112.47	97.62	97.48	86.34	59.15	78.01	136.61	119.73	145.15	83.80	114.99	98.79	121.97	75.56	133.17	121.97	75.56	133.17	80.21	80.21	
Rigoserib (ON-01910.Estybon)	A1404	PIK3CA, PLK1	126.30	126.85	114.54	131.39	102.84	63.64	84.17	122.99	100.43	104.34	119.61	111.05	99.60	36.84	43.44	127.25	36.84	43.44	127.25	150.47	150.47	
Rilpivirine	A3765	N/A	128.31	115.07	83.89	91.67	79.39	101.63	85.72	130.42	90.10	93.43	99.60	110.91	96.27	122.54	121.36	98.21	122.54	121.36	98.21	100.97	100.97	
Riluzole	A8513	KCNK2	219.49	211.32	138.73	185.43	163.94	150.15	139.79	247.53	195.47	414.46	144.95	158.18	161.69	180.05	141.44	431.89	180.05	141.44	431.89	151.39	151.39	
Rimonabant	B1429	CNR1	45.10	99.33	96.71	69.43	55.16	28.50	43.39	79.08	57.65	26.48	17.87	113.68	87.28	60.75	87.73	28.57	60.75	87.73	28.57	40.15	40.15	
Riociguat	A3767	GUCY1B1 GUCY1A1	124.67	118.60	91.63	102.29	106.45	96.39	97.97	134.45	114.03	100.46	108.41	105.50	113.84	95.19	94.55	102.94	113.84	95.19	94.55	94.80	94.80	
Risperidone	A8514	HTR1A	127.48	138.58	106.61	91.70	75.84	68.42	103.52	138.14	117.01	150.66	64.24	82.76	104.76	145.53	91.29	161.77	145.53	91.29	161.77	96.49	96.49	
Ritodrine HCl	B1347	ADRB2	118.26	102.84	110.56	83.09	89.46	71.75	123.90	107.26	113.99	115.90	85.64	115.50	105.98	322.92	280.57	118.36	322.92	280.57	118.36	89.33	89.33	
Ritonavir	A8203	CYP3A4	69.37	74.66	96.06	41.07	41.84	60.73	64.54	94.40	70.54	48.59	47.78	98.01	83.56	60.07	55.44	77.59	60.07	55.44	77.59	77.59	77.59	
Rivastigmine	A4338	F10	106.64	122.22	94.75	94.56	75.94	115.68	103.00	127.27	105.83	92.35	87.52	118.80	105.00	140.12	119.37	128.14	140.12	119.37	128.14	99.29	99.29	
Rivastigmine Tartrate	A3768	ACHE	114.88	99.86	96.34	95.31	106.05	114.08	91.68	124.50	110.83	111.54	105.66	111.93	106.17	97.09	99.49	109.41	97.09	99.49	109.41	96.08	96.08	
Rivastigmine Tartrate	A8515	ACHE	115.85	115.67	150.80	122.10	100.25	69.94	113.63	140.10	121.54	170.44	83.34	116.39	119.03	168.67	96.57	149.34	168.67	96.57	149.34	94.08	94.08	
Rizatriptan Benzoate	A8516	HTR1A	115.97	100.24	106.08	109.04	94.99	71.60	101.01	128.41	119.27	187.48	85.69	117.53	121.42	124.51	95.20	118.69	124.51	95.20	118.69	80.95	80.95	
Rocilinosat (ACY-1215)	A4083	HDAC6	1127.88	702.02	637.17	891.68	561.58	57.45	44.93	271.38	255.47	64.81	25.43	108.38	208.36	54.81	43.79	887.46	54.81	43.79	887.46	646.90	646.90	
Rocuronium Bromide	A1366	CHRNA1, CHRNA2	94.47	106.27	80.37	112.64	123.92	115.10	84.56	124.41	113.57	105.97	100.50	133.44	102.22	110.17	120.41	100.57	110.17	120.41	100.57	92.32	92.32	
Rofecoxib	B1454	PTGS2	120.64	132.44	96.75	71.62	85.85	94.13	103.91	80.55	88.71	96.93	71.61	119.22	99.66	127.10	155.46	92.64	127.10	155.46	92.64	100.33	100.33	
Roflumilast	A4319	PDE4B	156.33	144.42	196.36	126.26	111.96	114.06	93.04	155.38	147.29	79.72	157.05	145.07	123.76	441.37	428.97	128.99	441.37	428.97	128.99	110.99	110.99	
Rolipram	A4328	PDE4A	133.28	126.08	111.88	113.98	89.21	109.81	91.58	135.79	109.41	78.22	93.35	139.87	105.75	202.27	148.44	108.25	202.27	148.44	108.25	93.40	93.40	
Romidepsin (FK228, depsipeptide)	A8173	HDAC1	2670.00	4740.80	1399.39	553.41	505.18	31.45	37.32	627.48	577.13	97.89	57.12	176.70	1060.40	70.85	61.41	717.08	70.85	61.41	717.08	1078.79	1078.79	
Ronidazole	B2022	N/A	80.90	109.73	107.53	92.78	89.62	76.89	103.81	99.97	103.55	96.02	92.99	133.68	88.10	111.26	93.09	111.55	111.26	93.09	111.55	89.93	89.93	
Ropinivole HCl	B2129	DRD2	34.30	89.02	101.95	73.88	83.93	64.81	118.46	134.02	111.46	89.73	86.01	93.76	86.30	90.06	101.74	21.57	90.06	101.74	21.57	91.71	91.71	
Ropivacaine HCl	B2023	SCN5A	88.22	108.60	121.26	91.38	90.57	86.78	98.75	94.21	100.79	99.94	92.07	128.14	85.98	98.40	93.93	112.15	98.40	93.93	112.15	93.78	93.78	
Ropivacaine hydrochloride monohydrate	B3377	SCN5A	75.28	98.58	117.36	104.55	87.95	81.06	100.63	106.41	93.53	116.34	93.82	115.63	96.09	110.77	109.87	146.48	110.77	109.87	146.48	98.52	98.52	
Roscovitine	A1723	CDK2	46.94	113.79	137.71	162.51	127.22	89.50	91.32	125.95	119.97	39.70	70.48	205.44	176.42	75.59	79.21	80.11	75.59	79.21	80.11	88.51	88.51	
Rosiglitazone	A4304	FFAR1	151.32	200.51	142.21	130.94	116.28	185.78	161.55	200.94	196.53	105.62	152.49	161.95	153.33	170.27	207.19	138.71	170.27	207.19	138.71	127.75	127.75	
Rosiglitazone maleate	A4302	FFAR1	117.64	146.22	99.61	100.35	110.60	173.86	138.76	154.01	118.80	104.95	83.06	115.49	90.14	107.87	107.15	140.65	107.87	107.15	140.65	90.15		

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)			ER-positive (luminal)				HER2-enriched		
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	WHM12	WHM2	WHIM30	WHIM30	WHIM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108
Rosuvastatin Calcium	A8518	HMGCR	110.70	106.70	116.96	47.84	53.74	39.31	48.88	96.02	80.80	142.85	80.86	114.82	238.91	147.03	103.97	134.41	81.97		
Roxithidine Acetate HCl	B1565	HRH2	159.76	190.51	131.04	88.49	102.56	103.40	107.78	138.73	117.30	113.01	128.26	118.38	120.14	156.89	125.50	112.04	105.46		
Roxithromycin	B2024	MLNR	113.71	161.82	153.97	104.77	100.89	90.64	114.82	167.45	208.92	95.43	130.62	146.70	100.58	141.19	124.87	106.00	137.94		
Rucaparib (AG-014699,PF-01367338)	A4156	PARP1	161.65	160.46	207.39	153.10	98.47	191.15	155.07	219.36	205.11	67.27	84.71	104.38	85.86	151.27	138.35	127.38	114.91		
Rufinamide	B2280	N/A	82.15	104.44	106.07	99.03	94.69	80.73	105.78	122.43	124.97	116.37	95.85	137.03	99.08	95.83	110.12	131.21	97.95		
Rupatadine Fumarate	B1566	HRH1	92.72	86.94	109.38	60.69	65.49	83.43	72.65	83.90	78.56	44.11	39.81	87.72	70.25	65.18	51.19	82.16	55.95		
Rutin	N1833	N/A	84.64	129.60	137.99	112.50	92.80	115.37	129.26	91.94	110.55	108.32	94.41	127.56	102.00	112.45	124.44	95.17	40.75		
Ruxolitinib (INC018424)	A3012	JAK1	299.40	355.89	105.61	118.07	117.40	125.46	142.81	188.58	186.18	119.42	92.33	184.87	129.19	86.24	65.87	146.67	116.57		
S-(+)-Rolipram	A4349	PDE4A	137.97	150.75	136.49	107.15	91.79	118.15	117.48	140.98	126.98	71.76	117.00	152.11	121.36	165.75	121.99	101.07	97.17		
S/GSK1349572	A4074	N/A	150.54	115.07	124.32	153.10	124.65	109.20	130.40	161.75	189.49	164.41	114.36	109.56	136.52	74.89	73.89	201.89	156.14		
Safinamide Mesylate	A4368	MAOB	214.64	221.34	256.06	197.02	182.05	215.76	151.84	311.72	289.25	258.67	238.02	288.08	161.32	165.49	217.17	601.42	193.27		
Salbutamol Sulfate	B1348	ADRB2	136.72	98.41	103.99	88.82	81.92	79.23	106.48	118.73	109.92	110.93	83.88	103.96	90.55	120.67	91.01	124.22	95.37		
Salicylanilide	B1827	N/A	106.60	193.50	153.33	126.28	120.15	145.84	174.41	249.50	253.33	166.65	118.40	133.41	111.49	93.76	102.74	244.67	84.02		
Salicylic acid	B1092	ASIC3	101.10	111.46	98.35	108.51	131.61	85.68	104.49	134.09	101.08	182.10	94.24	114.39	115.81	104.06	94.09	149.72	89.78		
Salsalib	A3787	TRPA1	104.99	34.04	102.91	92.25	96.77	38.58	40.46	130.18	109.42	100.83	90.31	112.02	97.92	81.49	87.59	95.93	77.92		
Salmeterol xinafoate	A3789	ADRB2	86.75	85.19	76.11	61.48	62.75	76.17	57.23	120.82	93.05	51.65	62.92	92.49	75.18	95.34	81.77	55.92	41.69		
Saquinavir mesylate	A3791	N/A	115.42	86.54	63.80	50.89	49.88	34.47	38.11	105.25	100.36	21.92	93.49	104.50	95.33	38.75	38.51	41.18	39.88		
SAR245409 (XL765)	A5634	PIK3CD	83.44	89.35	94.90	78.71	90.31	45.56	63.07	105.19	71.77	49.68	49.67	101.81	86.92	78.97	54.85	104.50	56.72		
Saracatinib (AZD0530)	A2133	ABL1	64.15	63.54	69.09	47.66	39.98	32.14	48.20	87.16	82.09	55.54	81.10	48.68	104.65	54.02	52.03	60.14	115.38		
Saxagiprine	B1829	PTGS1, PTGS2	103.10	123.59	121.66	89.35	91.10	105.94	139.64	137.26	147.51	120.27	96.18	109.06	104.40	69.86	78.87	134.88	114.15		
Saxagiprine	A8650	DPP4	100.40	89.63	93.78	93.45	101.34	128.11	117.98	100.03	96.05	86.16	78.14	145.41	89.20	90.63	80.72	96.34	99.05		
Scopolamine	B1364	CHRM2	148.90	119.68	99.03	89.94	115.62	97.66	127.22	141.22	146.85	116.49	104.47	137.75	109.51	138.58	118.78	119.11	121.80		
Scopolamine butylbromide	N2505	CHRM1	109.13	101.53	118.81	101.18	100.28	146.46	127.02	135.90	129.93	102.54	75.16	115.96	97.29	99.20	95.62	103.07	105.66		
Scopolamine hydrobromide	N2570	CHRM1	110.89	105.37	126.75	91.31	90.64	121.38	123.41	132.56	134.13	103.65	79.27	120.05	103.69	83.49	83.85	103.52	108.56		
Secnidazole	B2162	N/A	34.88	80.25	113.73	80.53	78.00	78.50	106.22	163.38	135.32	81.79	83.39	132.54	89.32	95.05	110.29	17.95	93.41		
Semagacestat (LY450139)	A8190	PSEN1	124.00	163.40	179.80	95.41	66.66	69.86	70.10	191.98	176.84	76.36	66.04	105.68	119.32	87.25	117.17	162.00	167.55		
Serotonin HCl	B1830	HTR1A	93.97	112.56	109.09	106.84	93.33	105.16	168.22	143.88	181.31	102.69	97.08	132.21	94.84	56.64	58.96	119.19	100.00		
Sertaconazole nitrate	B1831	N/A	88.77	137.49	103.42	147.50	66.14	125.01	175.59	114.35	130.93	25.99	81.13	85.14	103.19	40.76	48.43	104.64	82.27		
Sertraline HCl	B2257	SLC6A4	25.82	29.52	60.39	29.03	29.62	40.62	45.06	57.52	60.24	35.43	28.89	74.85	79.21	120.10	115.55	56.20	58.72		
Sildenafil	A3817	PDE5A	88.14	79.04	102.89	81.38	84.31	91.69	93.13	105.80	105.83	95.55	70.09	101.36	73.32	76.09	71.37	97.23	67.39		
Sildenafil Citrate	A4321	PDE5A	114.09	118.03	94.41	90.97	85.37	87.15	80.39	61.29	46.59	106.41	85.65	144.09	118.19	113.46	146.27	117.84	89.47		
Sildenafil	A8521	ADRA1A	108.35	97.94	117.36	92.71	72.23	82.92	113.07	98.82	89.63	133.50	78.06	99.50	127.12	108.11	85.17	141.82	88.91		
Silymarin	N1711	ABCB1	88.62	133.40	116.31	107.73	107.86	80.79	106.50	93.16	90.26	115.28	88.75	128.82	89.45	124.75	129.47	131.57	36.48		
Simeprevir	A3820	N/A	27.06	32.48	28.67	32.72	32.56	36.38	41.53	30.02	27.04	22.64	18.91	39.50	72.70	36.08	40.88	27.33	22.10		
Simvastatin (Zocor)	A8522	HMGCR	99.32	126.84	100.20	52.90	43.38	79.26	45.07	112.02	95.19	102.51	93.65	105.59	256.81	54.49	59.43	132.62	79.85		
Sitafloxacin Hydrate	B2150	N/A	49.02	117.62	122.06	95.84	81.80	76.74	114.45	122.67	116.10	101.73	119.51	95.52	90.49	117.24	115.94	44.00	82.32		
Sildenafil phosphate monohydrate	A4036	DPP4	123.32	144.87	134.52	117.84	123.03	115.46	116.24	133.93	153.20	104.91	83.23	153.71	131.11	160.51	108.72	124.20	96.42		
SKF 525A (hydrochloride)	C3560	CYP3A4	79.12	126.33	130.04	57.34	65.70	91.45	106.65	119.96	119.68	92.94	94.62	123.31	66.31	122.61	83.28	110.15	79.17		
Sodium 4-Aminosalicylate	B1643	N/A	123.71	152.90	143.14	66.36	89.01	73.75	102.01	93.06	91.49	121.63	93.99	157.19	95.30	105.81	87.74	152.23	76.93		
Sodium 4-amitriparaty Hyalrate	A8523	N/A	106.63	107.56	106.64	97.69	85.22	91.14	99.67	185.57	156.13	146.56	97.37	109.49	109.93	120.95	103.51	135.89	86.35		
Sodium ascorbate	B1834	N/A	84.62	104.78	92.31	83.57	70.96	93.77	137.21	117.69	121.90	91.18	89.39	87.01	87.00	47.47	56.62	115.62	105.51		
Sodium butyrate	B1835	HDAC1	85.10	113.48	91.89	78.54	68.81	70.71	96.26	111.31	127.07	87.44	92.08	85.51	92.49	43.28	50.92	122.94	99.91		
Sodium																					
Monofluorophosphate	B1837	N/A	88.93	132.51	102.58	97.27	72.79	107.01	133.12	109.45	128.20	99.14	104.57	106.14	93.04	50.11	54.76	135.45	108.73		
Sodium Nitrite	B1838	N/A	99.90	109.00	108.07	88.08	79.82	101.80	126.48	100.83	130.94	87.21	93.81	95.50	91.53	53.78	57.85	110.21	102.20		
Sodium Nitroprusside	B2026	NPR1	108.08	159.91	161.35	84.83	102.42	96.90	107.25	166.69	159.35	99.62	110.85	112.78	87.02	113.53	103.02	127.12	92.01		
Sodium Phenylbutyrate	A4107	HDAC9	116.91	126.14	126.77	114.89	91.49	104.22	103.18	181.35	143.07	114.37	87.85	134.63	117.31	130.57	117.91	143.67	118.39		

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)		ER-positive (luminal)				HER2-enriched			
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	WHM2	WHM2	WHIM30	WHIM30	WHIM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108
Sodium Picosulfate	B2027	N/A	79.56	126.29	117.19	90.80	90.61	77.33	105.07	104.29	96.75	105.72	97.31	118.95	86.75	120.93	112.01	118.28	106.10		
Sodium salicylate	B2018	PTGS1, PTGS2	78.84	113.34	123.50	83.14	88.07	78.70	99.45	96.79	92.02	105.20	94.97	101.26	91.41	115.65	98.54	115.00	94.34		
Solfenacin succinate	B1614	CHRM1	83.17	97.58	104.27	57.71	57.01	78.85	74.72	90.19	85.01	96.73	86.85	107.09	86.91	124.73	111.23	105.21	59.93		
Sorafenib	A3009	BRAF	34.52	51.79	41.14	47.25	44.67	38.77	46.59	35.26	38.68	27.31	23.15	89.24	52.37	37.08	29.26	24.12	29.44		
Sorafenib Tosylate	A8245	BRAF	22.20	21.88	45.93	83.31	81.86	31.86	32.48	54.85	28.99	9.67	19.57	65.51	63.95	77.62	33.44	16.05	21.03		
Sorbitol	B2029	N/A	69.26	109.17	110.93	88.04	87.22	80.52	92.72	82.95	83.70	98.64	86.53	131.50	83.98	100.02	104.55	117.50	101.22		
Sotalol	B1367	ADRB1	127.71	112.32	104.71	86.71	83.75	91.88	110.62	130.35	106.06	130.98	78.96	115.85	102.62	107.14	98.96	138.37	101.50		
Sotalol hydrochloride	B3341	ADRB1	94.04	109.55	143.64	112.30	118.82	113.49	106.33	116.55	120.24	111.26	107.12	150.47	111.21	113.20	138.70	115.32	130.32		
Sotrostatin (AEB071)	A8525	PRKCA	105.68	161.50	110.65	64.93	62.79	187.47	201.75	115.08	106.44	197.46	149.39	101.76	136.10	110.24	107.62	167.16	102.82		
Spiramycin	B1839	N/A	127.15	138.08	137.66	93.36	95.48	127.10	170.26	127.39	119.13	101.42	118.02	124.97	116.23	65.07	92.75	119.55	122.61		
Spironolactone	B1378	NR3C2	107.60	111.29	64.18	89.96	69.48	82.61	94.96	120.23	105.88	80.24	67.36	114.36	109.92	80.21	71.61	88.23	92.26		
Stavudine (d4T)	B2225	N/A	119.98	103.42	117.49	111.30	96.37	102.63	89.27	130.27	123.19	100.00	119.04	115.37	90.97	82.61	81.65	137.28	98.66		
Streptomyacin sulfate	B2034	N/A	60.80	104.32	103.20	81.60	86.64	73.54	90.02	91.80	81.32	88.78	80.49	97.66	82.90	91.23	88.85	101.87	105.14		
Streptozocin	A4457	PARP1	102.18	108.31	112.87	82.77	83.58	73.89	96.07	123.12	124.69	107.96	99.11	122.84	99.51	89.02	89.75	130.30	117.96		
Succinylcholine Chloride Dihydrate	B1595	CHRNA1	103.02	114.30	100.96	60.74	62.46	85.24	93.39	148.43	117.94	103.69	90.11	104.33	97.15	123.18	101.22	134.83	91.57		
Sucralose	B1840	N/A	109.93	113.32	140.06	66.08	75.72	102.73	144.78	115.18	105.18	95.16	87.67	128.02	89.05	73.21	66.84	144.24	100.46		
Sulfabactam	B2131	N/A	45.44	106.18	107.74	94.67	93.66	82.87	104.88	185.10	154.41	99.09	110.51	109.75	101.58	108.46	115.62	26.03	84.40		
Sulfabactam sodium	B2035	N/A	61.23	101.02	97.75	81.66	77.21	61.57	88.03	86.69	90.99	85.02	74.77	97.27	86.33	95.58	91.18	106.05	83.05		
Sulfacetamide Nitrate	B2036	N/A	23.78	32.94	74.05	33.20	37.12	28.89	40.97	118.47	119.44	22.66	26.39	77.29	78.27	42.26	37.96	28.35	21.85		
Sulfacetamide Sodium	B1395	N/A	97.27	99.10	79.66	72.15	73.73	85.76	85.75	106.78	111.23	97.66	76.96	86.12	103.76	92.60	100.99	110.19	92.50		
Sulfadiazine	A8527	N/A	124.55	137.41	100.67	106.84	84.11	85.82	116.00	131.03	105.17	216.48	98.74	126.07	103.03	174.05	132.67	182.54	92.69		
Sulfadimethoxine	B3301	N/A	80.11	103.56	117.65	115.46	108.12	79.39	92.71	191.05	152.54	112.60	92.64	155.11	103.48	117.01	115.30	135.54	85.28		
Sulfaguanidine	B1842	N/A	88.67	110.94	134.90	90.29	80.48	111.82	121.01	119.74	110.31	79.98	97.13	135.49	86.07	112.85	102.68	123.48	98.44		
Sulfamerazine	B2037	N/A	75.18	125.51	111.41	92.77	80.77	67.95	82.36	95.26	103.80	88.94	87.88	130.84	84.24	109.64	97.29	112.26	80.97		
Sulfamerazine	B2038	N/A	80.47	114.99	112.63	95.55	66.34	79.10	105.25	95.32	94.94	87.28	84.99	142.16	83.01	93.63	92.81	127.65	86.65		
Sulfamethazole	B2132	N/A	76.05	95.95	114.06	98.78	88.07	80.52	110.85	130.42	133.17	104.18	98.71	88.91	89.62	107.85	116.48	36.87	82.55		
Sulfamethoxazole	B2039	N/A	89.90	114.48	113.95	83.87	78.43	88.39	94.30	91.84	84.73	94.36	87.94	119.32	86.98	99.00	79.39	97.35	77.18		
Sulfamethoxazole	B2040	N/A	94.42	134.85	153.59	96.62	102.50	117.90	117.00	192.77	198.39	86.25	128.71	127.40	95.38	118.66	120.40	95.16	103.46		
Sulfamylamide	B2041	N/A	88.36	123.55	119.62	100.74	88.38	99.66	110.22	130.63	149.19	84.63	110.67	126.83	83.05	170.43	157.53	111.02	88.01		
Sulfapyridine	B1844	N/A	111.37	111.13	146.79	99.70	126.11	99.58	100.48	111.53	129.21	102.54	99.53	131.27	92.61	149.00	127.76	107.62	121.07		
Sulfasalazine	A5770	SLC46A1	183.89	227.86	179.80	96.94	103.96	111.07	98.78	199.39	162.98	112.87	125.70	123.75	137.19	141.64	179.66	123.39	220.66		
Sulfathiazole	B2042	N/A	80.95	122.88	116.00	88.81	104.26	93.67	102.65	103.52	115.71	87.87	98.97	139.61	84.48	216.87	177.71	108.99	99.54		
Sulfisoxazole	B2043	N/A	69.84	108.75	112.50	97.35	102.27	77.84	90.35	117.92	116.13	88.66	100.08	120.92	86.86	104.50	108.51	103.52	103.62		
Sulfisoxazole Acetyl	B4954	N/A	89.92	91.91	104.33	92.39	93.16	103.12	108.62	102.02	104.69	98.47	83.35	115.94	95.68	92.79	97.68	100.59	28.41		
Sulindac	B2044	PTGS1, PTGS2	75.52	108.60	119.17	95.08	99.52	84.02	93.41	95.09	113.01	78.50	84.43	89.18	76.16	107.65	108.42	63.94	50.57		
Sumatriptan	B4981	HTR1A	91.39	94.09	110.11	103.07	92.85	81.95	109.18	96.36	122.76	89.06	78.90	118.58	90.65	123.51	128.50	123.35	30.81		
Sumatriptan Succinate	A5294	HTR1A	102.36	76.20	120.30	109.95	91.89	118.60	92.95	103.32	109.26	111.29	67.86	110.03	82.84	85.32	77.50	129.04	79.63		
Sunitinib	B1045	FGFR1	78.99	133.62	125.15	64.22	59.37	55.87	152.40	42.92	32.84	47.06	96.52	134.09	133.93	369.67	313.14	118.55	122.95		
Sunitinib malate	A8255	FGFR1	50.46	24.98	128.22	14.53	16.15	22.87	40.43	33.84	49.56	10.94	11.69	73.59	110.89	56.91	59.25	34.77	136.80		
Suprofen	B2133	PTGS1	95.68	136.60	124.65	102.45	102.14	104.47	109.97	89.64	110.71	100.71	95.00	132.96	69.45	119.40	108.24	121.74	93.02		
Tacrine hydrochloride	B6527	ACHE	72.18	91.52	98.31	99.50	93.67	74.21	78.37	86.74	87.37	93.78	87.67	118.95	97.01	92.30	83.19	113.18	31.28		
Tacrolimus (FK506)	B2143	FKBP1A	24.32	87.47	92.01	86.37	80.46	71.84	99.90	179.64	152.62	39.02	62.23	111.61	85.39	103.70	94.68	20.43	80.16		
Tadalafil	A4327	PDE11A	106.84	109.01	88.37	105.14	88.19	114.29	110.03	116.49	94.33	105.40	74.54	150.02	140.63	93.43	98.02	103.40	74.21		
Tamibarotene	A3856	RARA	92.26	123.86	77.12	117.03	131.81	118.25	77.91	127.46	114.65	97.56	33.70	63.13	95.92	52.40	95.18	116.87	92.71		
Tamoxifen	B5965	ESR1	45.11	33.11	88.81	63.94	84.99	69.86	70.93	129.86	117.05	27.35	89.56	138.90	119.77	112.45	52.46	46.65	27.14		
Tamoxifen Citrate	B1394	ESR1	114.39	33.52	59.69	35.21	33.82	37.01	47.79	108.82	98.84	32.39	23.88	78.90	96.50	34.82	40.37	31.12	39.39		
Tasitulum	B1422	N/A	160.86	205.45	216.05	96.98	132.11	155.97	178.20	182.23	161.06	96.00	72.16	125.90	147.58	161.78	153.34	143.53	126.47		
Taurine	B1846	GLRA1	88.14	121.16	114.55	76.11	75.72	95.96	122.66	121.74	108.06	113.86	87.79	119.20	86.62	66.90	55.87	132.41	97.70		
Tazarotene	A5710	RARA	107.59	175.24	97.86	92.23	115.04	121.52	123.78	195.58	181.11	111.40	142.14	108.04	113.49	190.11	177.49	203.80	161.31		
Tebipenempivoxil	A8529	N/A	144.76	115.51	89.65	105.16	89.23	73.84	149.30	145.68	121.20	202.01	82.23	109.94	114.79	125.35	77.41	182.40	102.90		
Tedizolid	A3863	N/A	202.65	214.03	169.73	232.32	236.46	196.96	116.74	362.95	411.29	399.43	182.27	290.57	107.29	303.93	276.43	486.20	174.25		
Telaprevir (VX-950)	A4031	CTSA	123.84	184.40	144.27	127.71	118.70	87.38	105.01	154.50	175.43	88.88	71.62	102.07	218.53	104.94	87.77	133.81	101.02		
Telivudine	A8530	N/A	122.39	127.85	99.44	102.05	89.03	82.49	105.07	140.87	106.73	196.89	86.08	128.02	114.79	210.94	116.05	185.74	101.01		
Telesatant	A8531	AGTR1, AGTR2	90.49	122.94	116.33	121.84	122.72	72.36	97.68	147.21	144.94	155.27	71.40	110.57	101.40	141.99	168.84	184.05	83.36		

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)		ER-positive (luminal)				HER2-enriched					
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	UCD52	WHM2	WHM2	WHM30	WHM30	WHM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108	HC108
Temocapril HCl	B2213	ACE	52.10	109.28	101.18	91.32	86.05	90.75	107.35	105.02	122.91	83.87	127.74	103.35	82.29	108.85	122.72	43.04	88.09				
Temozolomide	B1399	N/A	143.94	127.50	135.54	77.92	117.74	112.90	120.45	118.62	95.51	115.12	94.02	125.27	110.75	133.93	109.63	138.76	112.27				
Temsirolimus	A8314	MTOR	32.77	30.82	45.19	21.51	24.70	31.83	52.92	31.61	29.30	32.77	20.58	57.54	54.28	32.62	16.65	96.44	26.33				
Teneligiptin hydrobromide	A8665	DPP4	112.85	108.41	88.19	81.14	82.92	112.90	85.10	91.22	85.66	91.78	73.19	95.16	71.47	79.55	80.37	96.08	71.58				
Teniposide	A8532	Top2a	102.63	118.09	112.63	110.12	109.99	103.61	93.56	99.67	130.17	130.17	79.49	112.41	110.72	162.04	105.14	153.98	93.75				
Tenofovir	A5275	N/A	95.78	82.44	115.97	85.70	95.49	109.38	89.26	122.14	120.42	113.71	92.10	122.56	106.40	119.36	104.38	124.56	113.43				
Tenofovir Disoproxil Fumarate	A1755	N/A	107.83	104.03	105.05	113.94	97.12	137.49	97.94	142.90	128.37	99.91	89.12	129.62	97.02	45.39	58.39	70.18	85.63				
Tenoxicam	B1849	PTGS1, PTGS2	114.92	128.57	119.14	84.26	90.04	100.00	146.36	163.24	155.54	131.47	97.53	126.37	89.68	59.72	70.14	162.48	18.29				
Tenoxicam HCl	B1365	ADRA1A	142.24	131.01	122.64	75.42	96.09	108.33	116.69	122.60	105.16	123.17	96.88	115.88	101.32	104.95	102.15	124.28	95.40				
Terbinastine	A8533	N/A	109.37	100.99	139.49	103.56	107.87	55.72	90.44	119.45	114.64	186.07	86.87	113.78	107.50	128.81	92.24	159.85	91.91				
Terbutaline HCl	B2047	N/A	72.20	115.04	123.34	65.26	75.70	55.38	70.25	92.37	89.91	85.93	86.10	99.00	81.63	71.80	74.18	101.82	78.82				
Terbutaline Sulfate	B1328	ADRB2	113.85	115.02	126.93	83.58	75.69	93.38	119.57	118.62	127.13	112.93	84.79	110.19	109.19	86.95	89.95	134.52	107.50				
Terfenadine	A8534	CYP2J2	38.04	30.69	45.79	32.27	37.87	40.04	43.97	32.12	27.12	32.50	28.34	38.12	55.34	51.70	44.86	53.63	25.97				
Teriflunomide	B1850	DHODH	463.18	337.74	199.60	292.09	254.20	763.02	622.11	936.87	1094.20	483.92	314.99	458.28	161.91	230.24	161.82	867.44	434.28				
Tetracaine HCl	B1413	RYR1, RYR2	116.97	143.65	98.96	81.53	99.89	80.22	104.10	103.48	103.37	122.68	87.04	134.13	120.64	135.12	108.75	121.69	85.43				
Tetracycline Hydrochloride	A2517	N/A	112.04	97.18	87.52	78.24	76.31	62.85	91.37	129.86	102.46	88.86	90.06	108.45	96.70	89.08	95.17	94.34	83.41				
Thiethylperazine HCl	B1349	ADRA1A	111.40	115.83	108.21	90.93	88.10	85.86	116.00	117.33	113.20	108.83	85.40	116.34	105.88	85.54	88.15	120.82	91.65				
Tigatone (SAR302503)	A4136	JAK2	257.65	200.11	161.15	234.55	156.47	44.47	43.15	316.06	348.74	101.73	164.31	172.99	137.59	69.80	53.30	765.48	339.16				
TH-302	A3872	N/A	89.48	109.50	44.90	79.92	82.82	46.43	42.81	108.88	105.39	99.86	146.87	100.46	119.96	153.59	154.24	84.67	96.38				
Thalidomide	A4216	CRBN	138.86	149.96	114.22	104.93	98.84	116.08	89.20	134.71	155.59	98.11	104.13	128.57	103.09	139.56	118.11	159.47	109.93				
Theophylline	N1442	ADORA1	84.58	111.68	116.85	106.65	98.77	75.25	97.82	84.22	107.48	109.51	78.42	123.21	66.89	91.59	93.15	123.87	88.67				
Theophylline Hydrochloride	A8536	N/A	154.17	141.04	119.08	157.00	177.81	110.69	128.61	102.35	102.77	24.68	140.97	160.03	162.13	156.21	167.73	363.92	121.92				
Thiamine HCl (Vitamin B1)	B1852	N/A	107.25	119.43	103.39	149.70	94.53	131.29	167.03	145.68	140.72	114.28	91.83	142.98	88.59	67.24	52.27	163.86	105.05				
Thiamphenicol	B1853	N/A	91.03	127.59	103.39	93.95	75.44	86.62	127.03	125.95	117.38	88.29	83.31	104.49	82.89	67.28	61.48	131.39	98.71				
Thioridazine HCl	A8537	HTR1A	51.45	38.31	41.38	36.44	37.19	35.09	49.30	64.48	59.34	25.54	27.30	52.11	88.40	58.02	53.17	42.88	90.46				
Thio-TEPA	B3742	N/A	90.66	127.20	120.16	93.09	100.43	67.68	99.92	126.94	111.17	102.80	104.80	142.90	102.72	111.56	111.06	96.24	31.33				
Thioguanine	B3488	SLC6A1	88.13	104.58	114.92	92.77	85.40	84.69	115.82	104.52	87.46	108.12	101.22	81.88	84.18	98.17	95.71	110.21	90.52				
Thiopyridine Hydrochloride	B3443	SLC6A1	98.68	101.28	95.63	107.36	86.96	85.19	133.60	106.06	103.20	100.80	80.85	93.22	86.38	91.65	100.53	126.01	84.07				
Tianeptine sodium	A5322	HTR3A	116.32	147.67	119.97	125.24	118.73	79.70	90.95	141.97	142.51	102.47	87.75	134.25	121.76	96.51	95.39	134.68	127.91				
Ticagrelor	B2166	SLC29A1	14.14	68.14	80.03	64.62	65.28	32.41	50.06	94.06	101.39	26.05	69.15	121.79	80.54	43.55	48.66	4.57	61.95				
Ticlopidine HCl	B2164	CYP2B6	33.91	78.99	97.20	64.12	60.79	65.50	99.49	85.74	93.66	79.97	84.05	108.26	91.63	131.62	83.80	21.01	83.47				
Tidiglusib	B1539	GSK3B	104.82	133.01	94.72	79.71	77.11	85.79	86.65	138.27	124.50	105.94	90.42	113.67	96.29	105.81	85.56	148.78	66.06				
Tigecycline	A5226	N/A	87.31	72.74	119.97	82.03	111.31	86.49	117.06	135.54	123.33	101.75	89.76	121.20	81.94	113.38	145.36	123.36	80.02				
Tilimicosin	B2049	N/A	66.81	111.95	102.47	70.68	84.68	81.30	86.87	89.88	104.09	78.65	85.42	115.59	80.89	104.09	95.00	97.64	88.01				
Timolol Maleate	B1350	ADRB2	115.82	116.06	120.26	95.09	97.79	82.24	103.98	116.90	107.35	109.41	102.16	116.11	107.17	97.66	81.31	112.50	100.88				
Timidazole	B2050	N/A	72.20	111.90	100.67	73.90	92.95	79.93	82.55	164.60	161.96	71.14	88.56	111.05	88.86	103.90	97.71	102.64	87.29				
Tioconazole	B2051	N/A	69.94	159.60	119.05	54.30	66.17	32.14	39.37	101.82	98.54	18.24	63.19	109.55	92.14	52.60	47.57	95.98	66.50				
Tiotropium (Thiola)	A8538	N/A	107.27	101.42	99.31	96.22	91.14	93.05	112.47	118.68	112.24	20.80	88.43	109.36	107.14	117.74	92.95	143.40	81.58				
Tiotropium Bromide	A3874	CHRM1	111.89	135.59	102.91	85.94	91.92	107.38	82.05	133.62	116.12	93.39	119.54	116.33	101.84	124.79	108.01	85.07	92.20				
Toxolone	A4362	CA1	116.03	115.01	171.81	108.49	109.68	148.72	109.30	165.78	123.82	97.04	78.77	226.25	96.79	97.87	73.87	91.89	133.63				
Toracetamol	B1855	THRA	78.38	146.35	97.18	80.70	70.42	88.95	116.67	119.32	109.74	87.55	78.06	99.05	87.16	39.54	45.43	120.78	87.28				
Tirofiban hydrochloride monohydrate	A3877	ITGA2B ITGB3	120.12	117.70	101.13	96.95	86.88	115.72	82.48	128.88	97.76	101.60	113.24	122.76	105.93	128.94	140.94	88.61	94.74				
Tivantinib (ARQ 197)	A8325	MET	146.69	175.07	124.77	85.10	78.51	99.69	114.65	128.85	164.87	48.08	54.95	81.00	110.93	50.34	36.78	62.62	67.65				
Tivozanib (AV-951)	A2251	FLT1	59.23	111.49	69.67	96.48	65.77	49.26	74.12	59.14	57.16	31.47	102.51	80.00	75.14	66.35	55.41	86.05	63.81				
Tizaniptine	B1063	ADRA2A	95.07	100.24	109.63	105.56	95.50	66.66	97.49	105.85	77.99	201.31	96.00	94.56	109.53	127.06	90.74	113.98	85.01				
Tizanidine HCl	B1368	ADRA2A	109.84	120.54	100.39	83.84	84.76	78.57	98.03	102.82	131.54	126.05	65.05	125.37	102.46	142.73	107.65	130.76	81.86				
Tobramycin	B1856	N/A	95.44	127.70	87.99	90.13	80.54	98.98	144.71	126.91	119.45	94.66	102.33	123.67	83.14	64.57	51.34	132.46	99.17				
Tofacitinib (CP-690550)	A4135	JAK3	182.14	193.87	141.29	123.54	93.57	85.76	90.03	270.21	312.87	76.69	78.77	150.98	115.17	110.95	97.26	198.11	186.94				

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)		ER-positive (luminal)			HER2-enriched				
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	WHIM2	WHIM2	WHIM30	WHIM30	WHIM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108
Tofacitinib (CP-690550, Tascocitinib)	A4138	JAK3	164.99	173.85	150.72	152.07	119.67	90.62	101.03	159.79	160.94	80.06	82.24	143.03	109.67	133.60	118.11	236.51	151.46		
TOK-001	A8623	AR	107.96	129.49	96.27	80.31	86.11	130.81	104.99	102.69	84.43	25.35	83.24	58.22	76.24	107.92	97.37	33.99	77.11		
Tolazoline HCl	B1329	ADRA2A	95.54	92.79	114.54	90.64	94.78	100.83	108.27	83.80	90.89	101.05	82.96	100.36	91.42	123.88	111.91	109.78	88.29		
Tolbutamide	B2194	KCNJ8	50.97	110.93	101.18	100.20	92.94	87.13	122.42	107.08	95.12	87.66	95.13	118.04	83.65	86.35	91.40	31.95	78.16		
Tolcapone	A4383	COMT	42.33	98.88	84.25	88.62	84.67	98.73	134.81	124.86	114.22	15.64	13.61	52.47	57.45	63.82	64.49	27.27	66.52		
Toifenamic Acid	B1455	AKR1C3	78.59	121.52	103.04	72.94	68.36	31.56	51.83	75.41	80.08	87.41	73.74	117.98	91.89	47.80	94.43	97.33	57.91		
Tolnaftate	B2053	N/A	93.07	132.53	107.56	72.98	69.40	85.91	97.31	137.21	124.16	51.12	94.23	139.51	95.18	90.35	101.99	106.69	90.25		
Tolperisone HCl	B1857	SCN9A	104.36	132.19	108.64	98.39	86.28	125.11	134.18	112.54	107.01	103.20	98.04	117.95	92.45	41.60	54.07	127.64	96.60		
Tolterodine tartrate	B1620	CHRM1	139.72	85.34	132.54	54.23	66.79	89.75	93.26	91.34	93.71	101.87	91.78	101.04	93.59	109.88	84.41	152.48	75.57		
Toltrazuril	B2054	N/A	76.67	74.93	114.52	76.09	82.96	38.50	44.04	108.69	88.41	74.90	48.89	131.53	84.01	124.91	109.35	91.94	60.54		
Tolvaptan	B2300	Avpr1a	70.70	124.61	159.39	92.42	85.48	79.00	105.95	163.17	151.75	85.42	75.41	137.92	85.89	97.17	104.24	103.23	64.59		
Tolterodine HCl	A4360	CA1	89.64	116.07	115.10	83.12	74.40	115.85	93.63	113.45	105.88	109.47	80.86	128.21	137.52	134.37	131.74	121.20	89.92		
Topotecan	B4982	TOP1	38.47	47.18	73.03	41.74	43.11	42.20	46.74	87.92	78.38	28.81	27.43	128.20	44.36	53.17	44.99	76.40	34.83		
Topotecan HCl	B2296	TOP1	28.56	47.50	69.14	47.20	36.90	41.92	45.48	89.01	75.17	42.58	27.91	204.00	51.95	53.31	56.03	96.83	139.81		
Toremifene Citrate	B1513	ESR1	38.52	35.82	73.23	39.98	36.55	40.38	46.23	57.81	50.96	33.05	35.55	63.80	86.78	44.55	48.23	31.44	24.32		
Torsemide	B2055	SLC12A1	54.15	114.51	127.01	107.10	104.60	107.15	105.04	162.29	180.55	84.20	106.52	140.34	93.52	105.23	135.15	29.38	160.17		
Trametinib																					
Trametinib (GSK1120212)	A3018	MAP2K1	79.48	126.90	120.01	38.49	57.54	67.89	80.43	149.85	115.39	57.75	106.51	94.05	98.34	98.89	121.57	38.69	116.77		
Trandolapril	B3540	ACE	118.87	123.01	130.20	97.78	125.56	99.35	118.66	184.39	163.36	107.03	121.99	148.16	98.66	115.19	132.32	100.97	85.09		
Tranexamic Acid	B1858	PLG	122.90	112.73	102.34	95.76	88.73	111.73	135.43	99.12	122.22	112.04	77.16	115.93	110.57	74.15	75.51	118.88	136.30		
Tranilast	A5375	N/A	245.72	193.11	107.51	110.15	122.76	70.80	343.94	681.52	344.08	293.56	167.60	391.82	87.91	211.66	245.78	203.37	255.66		
Trazodone HCl	B2230	Htr2a	103.70	119.82	147.81	89.21	88.88	121.18	88.97	203.68	180.41	84.49	106.53	122.78	101.32	97.46	111.09	99.90	118.21		
Trelagliptin	A3888	DPP4	115.47	105.57	95.25	88.18	104.22	100.00	93.59	170.60	112.10	108.02	116.60	116.23	111.25	103.19	105.05	94.10	100.63		
Tretinoin (Aberela)	A8539	PPAR	197.57	434.71	174.73	449.42	44.63	44.94	72.12	570.36	431.65	248.05	172.69	143.27	149.00	137.53	154.08	322.96	159.87		
Triamcinolone	B1859	NR3C1	104.36	130.46	215.66	114.84	127.46	108.37	133.39	188.14	180.89	111.62	112.83	175.87	129.78	234.72	191.90	147.94	135.02		
Triamcinolone Acetonide	A8540	NR3C1	146.22	148.09	241.85	210.92	185.59	80.26	98.00	226.77	191.18	197.46	169.49	171.30	110.68	305.09	244.65	171.21	133.50		
Triamterene	B2275	SCNN1B/SCNN1A	87.04	122.15	138.41	142.93	103.30	83.85	105.10	133.97	109.31	128.37	104.50	148.05	109.20	111.73	128.80	190.06	100.50		
Trichloromethiazide	B2056	SLC12A1	63.58	144.71	186.06	135.61	148.77	134.47	146.79	266.30	248.56	98.05	98.06	164.49	89.85	128.87	129.46	38.18	133.53		
Triclabendazole	A8541	AKT1	183.79	88.94	127.80	94.82	119.00	1363.68	758.38	115.35	97.17	101.13	49.92	310.99	48.70	521.23	339.66	80.75	86.10		
Triclosan	C4035	N/A	63.39	83.69	137.20	90.36	103.93	48.75	50.33	108.63	110.08	24.89	58.43	109.21	71.68	52.62	80.18	39.97	111.65		
Trifluoperazine 2HCl	B1397	HTR2A	48.83	36.76	54.14	35.54	32.13	41.09	45.46	102.46	93.09	35.82	24.54	57.45	82.10	40.78	43.59	30.64	68.78		
Trifluridine (Viroptic)	A8542	TYMS	124.30	122.30	97.12	114.90	116.98	62.38	113.27	143.27	121.54	187.22	87.71	131.64	110.72	164.10	130.16	149.82	93.98		
Triflusal	B1461	PTGS1, PTGS2	92.52	124.16	98.45	73.75	78.17	95.03	119.57	82.39	88.35	106.15	87.95	128.51	101.22	108.23	105.61	115.38	93.26		
Triostane	A4348	HSD3B2	148.14	114.02	102.53	120.70	108.76	104.61	126.11	89.52	110.53	86.11	94.01	119.11	114.27	86.81	60.57	90.28	101.85		
Trimebutine	B1650	OPRM1	120.47	110.76	134.84	74.07	95.76	94.30	98.19	111.62	110.87	108.88	97.86	109.22	92.86	262.29	261.56	134.58	77.47		
Trimethoprim	B2057	N/A	51.99	104.53	120.12	90.11	100.60	112.48	122.83	2691.37	2027.42	96.68	85.48	144.35	93.03	132.89	101.14	35.03	113.74		
Trimipramine (maleate)	C5734	SLC6A3	90.26	108.11	104.87	87.94	85.86	66.81	88.33	94.60	91.99	98.28	84.98	101.22	69.04	90.30	94.07	110.64	94.26		
Tripeleminamine HCl	B1553	HRH1	92.29	87.31	99.88	81.44	80.62	110.48	111.69	99.61	88.77	96.16	92.60	62.64	80.59	88.08	90.43	97.89	94.93		
Trometamol	B1861	N/A	81.84	90.83	104.11	90.93	81.02	87.64	110.67	104.98	121.79	109.88	79.92	114.43	91.48	67.80	49.03	139.46	94.48		
Tropicamide	B1608	CHRM3	101.31	122.48	109.77	64.76	84.76	81.84	101.04	99.28	97.94	114.08	97.94	136.10	100.92	152.09	119.71	158.22	86.58		
Tropium chloride	B1616	CHRM1	156.75	159.08	165.40	93.51	107.74	119.91	100.39	118.42	122.92	115.61	107.97	119.38	123.77	184.20	129.53	122.40	109.37		
Troxipride	B1862	N/A	98.12	99.53	106.21	102.38	91.28	92.85	113.57	128.84	144.46	126.29	86.83	110.31	96.31	55.34	60.31	134.51	104.69		
TU-68																					
(SU6668, Oranitinib)	A5331	EGFR	92.38	66.05	110.82	110.59	135.49	64.15	57.55	102.78	120.80	73.33	108.21	115.64	105.84	56.12	65.42	71.52	48.26		
Tylosin tartrate	B2059	N/A	46.49	103.76	125.77	81.08	89.25	110.24	111.36	251.13	264.44	92.07	84.35	164.82	82.32	73.98	120.72	32.45	100.49		
Ulipristal	B2134	PGR	37.15	104.48	118.28	88.96	100.96	80.63	95.01	141.12	142.96	45.52	27.61	146.84	82.85	114.93	110.29	19.74	145.54		
Ulipristal acetate	B1049	PGR	79.24	116.58	116.73	89.31	97.55	103.89	106.81	123.49	89.75	76.13	88.89	116.37	78.94	104.72	80.96	81.40	53.79		
Uracil	B1863	N/A	134.02	105.43	115.87	106.24	96.40	127.10	143.26	213.29	244.46	135.29	96.31	138.93	98.83	64.70	64.24	210.28	105.61		
Urapidil HCl	B2242	HTR1A	90.97	102.45	104.71	92.44	102.79	95.00	102.67	108.57	113.23	89.97	89.12	125.48	80.19	92.49	94.18	112.46	109.82		
Uridine	B1473	N/A	113.44	98.58	103.76	87.59	83.66	86.38	93.02	123.68	137.56	100.88	100.65	114.92	100.28	87.45	117.58	106.07	84.63		
Ursodiol	B2135	N/A	41.01																		

continued

Item Name	Catalog#	TARGET	TNBC (basal-like)										TNBC (luminal AR)			ER-positive (luminal)				HER2-enriched	
			HC101	HC101	HC16	UCD52	UCD52	WHM2	WHM2	WHM30	WHM30	WHM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108
Valdecoxib	B1459	CA12	105.97	146.18	99.84	66.49	81.42	92.54	98.53	79.17	78.67	93.32	77.32	125.72	97.95	108.46	110.05	88.29	75.31		
Valganciclovir HCl	B1864	N/A	92.08	100.18	111.10	146.97	93.27	91.19	131.28	147.24	128.67	106.90	73.19	104.47	90.60	62.79	53.69	56.47	151.92		
Valsartan	B1865	N/A	84.99	95.21	120.46	81.79	74.84	87.45	116.04	111.82	111.82	63.49	68.58	106.76	91.78	62.74	63.70	98.63	72.20		
Valproic acid	B1251	HDAC1	93.10	111.24	106.14	90.97	100.70	90.24	100.92	83.47	83.24	152.96	113.75	121.15	102.68	145.77	141.04	115.60	92.69		
Valproic acid sodium salt																					
(Sodium valproate)	A4099	HDAC9	151.69	227.52	158.93	187.13	127.95	92.08	116.97	199.57	185.27	104.42	79.49	153.60	139.98	120.81	101.60	160.37	106.38		
Valsartan	B2214	AGTR1	107.58	116.06	118.88	100.94	115.59	112.10	89.01	216.54	181.10	101.37	135.03	117.50	97.17	99.18	133.16	108.10	127.21		
Vancomycin hydrochloride	B1223	N/A	126.08	123.68	166.83	116.53	127.37	110.12	104.12	163.49	132.05	119.41	173.01	110.05	92.38	203.89	185.84	111.85	93.14		
Vandetanib (ZD6474)	A8555	EGFR	44.97	73.30	56.37	22.16	28.17	62.33	46.53	27.03	24.29	16.15	45.27	32.17	52.93	98.99	47.88	22.79	44.05		
Vardenafil	B3343	PDE5A	81.51	114.80	126.71	117.85	100.95	97.50	98.03	108.70	106.06	122.76	102.27	169.30	97.28	106.29	98.45	137.47	86.62		
Varenicline Tartrate	A5391	CHRNA4	169.95	168.99	152.87	93.70	106.13	110.05	102.87	175.86	140.76	127.33	135.21	128.35	138.05	128.94	128.72	152.53	198.90		
Vatilanib (PTK787) 2HCl	A1778	FLT1	98.99	173.36	76.55	51.89	58.91	32.60	95.96	91.34	95.04	53.28	56.20	103.67	92.33	39.88	51.63	124.63	91.57		
Vecuronium Bromide	A5220	CHRM2	92.31	77.18	93.90	81.91	93.39	75.73	86.11	157.44	152.62	91.00	90.00	145.51	104.66	100.26	120.64	120.88	101.59		
Vehicle		N/A	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00		
Vemurafenib (PLX4032)	A3004	BRAF	125.95	109.70	102.08	109.74	107.16	101.58	102.78	181.12	188.56	118.69	108.71	195.00	98.34	108.59	102.66	163.99	116.27		
RG7204																					
Venlafaxine	A5355	SLC6A2	106.12	100.14	105.67	107.01	131.61	110.40	124.80	193.83	144.55	99.40	99.11	138.90	103.47	131.49	115.66	121.65	121.21		
Verapamil HCl	B1867	CACNA1S	99.27	119.11	135.41	74.25	81.08	87.54	122.92	112.32	119.35	100.18	80.17	92.45	98.62	65.50	62.38	126.45	89.11		
Vidarabine	B2062	N/A	38.96	90.62	96.09	78.47	82.58	91.12	118.56	158.47	147.97	86.47	93.64	135.50	86.86	101.51	110.16	34.32	107.81		
Vidufolumus	B4669	DHODH	302.25	602.35	203.94	218.83	240.16	634.52	594.50	506.02	522.01	106.48	390.76	215.20	99.51	397.24	221.59	682.20	670.70		
Vilazodone Hydrochloride	A3919	HTR1A	132.26	137.19	165.57	109.08	113.80	123.04	95.49	123.90	99.96	91.09	116.85	102.98	121.60	117.64	108.16	74.24	81.19		
Vildagliptin (LAF-237)	A4037	DPP4	118.73	119.15	113.88	129.39	112.50	111.38	113.46	127.36	154.89	100.13	77.34	125.04	126.19	108.33	83.94	116.28	115.44		
vinblastine	N2256	TUBB	120.45	125.12	163.98	60.86	75.15	96.59	64.82	135.51	111.97	75.77	15.61	91.14	96.22	39.66	35.22	93.79	168.13		
A3920																					
Vinorelbine	A1765	TUBB	143.07	110.00	143.88	81.29	79.39	86.14	67.38	114.96	88.50	78.97	42.95	88.54	101.56	38.65	41.63	88.79	106.00		
Vinorelbine	N2250	TUBB	223.38	189.53	199.52	94.26	75.96	82.14	98.83	164.10	141.75	109.66	72.96	110.82	112.14	40.23	44.12	108.89	174.99		
Vinorelbine dihydrate	A3921	TUBB	89.87	110.78	166.51	41.58	73.51	51.72	69.25	99.27	94.19	87.89	53.15	104.65	78.47	49.32	42.71	85.87	38.39		
Vinorelbine	N2250	TUBB	118.30	104.04	122.39	58.60	52.87	58.70	55.61	106.97	84.00	69.35	61.00	112.30	109.04	44.37	33.55	77.23	104.19		
Vinorelbine	B2276	PDE1A	92.83	121.96	112.43	116.54	103.76	87.86	98.84	132.67	116.79	104.01	84.84	108.10	105.80	96.58	80.44	136.38	80.60		
Vitamin B12	B2063	N/A	44.96	88.73	123.70	83.29	88.91	106.62	119.23	119.73	136.63	87.69	96.92	123.52	85.88	84.08	110.57	31.39	102.80		
Vitamin C	B2064	N/A	55.23	98.57	107.87	77.66	72.26	89.10	137.79	131.73	139.02	85.95	101.21	111.41	84.33	81.72	98.32	30.23	106.50		
Vitamin D2																					
(Ergocalciferol)	A8543	VDR	99.45	135.97	77.87	67.19	63.82	31.20	50.14	96.28	81.97	72.03	51.67	100.69	95.17	70.02	47.50	121.05	85.68		
Voglibose	B1870	GANAB	96.86	115.81	129.47	83.94	76.76	98.10	136.68	103.35	115.81	105.17	80.75	108.91	89.09	58.04	59.38	141.02	98.44		
Vorapaxar	A8809	F2R	106.12	158.66	107.80	78.90	73.97	95.99	133.62	80.02	65.18	105.33	75.77	121.26	104.23	99.49	68.62	126.00	85.57		
Voriconazole	A4320	N/A	127.34	114.71	115.46	121.50	89.85	111.82	98.34	152.74	121.80	106.74	90.82	132.63	120.62	131.65	141.63	134.27	104.12		
Vorinostat (SAHA)																					
MK0683	A4084	HDAC1	5407.38	3745.34	1938.36	2161.22	1361.47	44.63	50.43	1973.16	2972.55	72.39	19.80	277.84	21.71	77.00	44.93	1724.27	1148.39		
Vortioxetine (Lu AA21004) HBr	A2547	HTR1A	30.17	25.90	35.25	20.63	26.49	24.00	43.77	30.18	23.63	14.74	20.33	44.35	76.68	34.61	43.62	23.85	27.75		
VRT752271	B1106	MAPK1, MAPK3	45.32	32.76	105.91	53.68	59.37	49.75	40.83	111.59	97.06	21.97	51.70	135.04	81.74	45.27	41.71	120.18	70.63		
VX-680 (MK-0457, Tozasertib)	A4111	AURKA	113.73	129.82	110.65	73.73	59.37	66.07	69.11	131.77	151.79	54.94	84.99	84.31	132.66	80.28	82.62	75.57	161.05		
VX-809	A8351	CFTR	81.83	125.22	103.45	86.61	87.03	72.55	112.33	148.03	165.99	77.63	78.68	89.54	100.89	67.73	64.17	122.88	91.10		
Xylazine HCl	B1351	ADRA2A	184.36	133.25	123.53	84.41	100.15	125.40	115.44	121.09	132.36	117.80	101.31	120.46	115.26	100.35	109.40	115.23	110.71		
Xylitol	N1725	N/A	86.73	106.88	100.79	106.58	95.67	80.15	100.48	76.88	89.40	111.85	90.90	133.18	95.52	94.74	99.32	125.72	37.86		
Xylometazoline HCl	B2066	Adra1d	40.49	109.33	106.43	82.70	85.11	107.58	112.70	149.19	166.23	74.66	130.96	113.98	89.89	114.97	156.59	26.02	132.68		
Xylose	B2067	N/A	45.54	95.47	107.94	83.74	82.19	91.07	97.84	128.89	129.12	82.87	100.74	96.11	90.91	90.59	116.53	27.19	92.33		
YM155	A4221	BIRC5	64.92	106.09	82.50	59.68	48.15	53.82	43.02	58.71	65.87	25.72	30.86	48.33	60.18	62.66	75.05	49.62	30.69		
Zafirlukast	B2068	CYSLTR1	24.66	23.50	106.50	73.96	83.42	41.70	47.49	109.36	121.72	21.31	23.32	87.79	86.45	112.57	108.61	31.69	32.07		
Zalcitabine	B2223	N/A	87.87	92.31	127.76	96.99	111.76	84.85	85.31	200.96	151.26	97.69	105.54	123.82	93.51	92.52	91.45	133.02	106.45		
Zalcitabine	B1460	PTGS2	101.62	146.70	112.06	70.13	85.74	88.92	107.17	86.77	78.82	114.10	76.90	119.98	102.51	138.40	128.99	107.63	79.00		
Zanamivir	B2136	N/A	41.36	123.48	113.49	91.48	89.42	84.68	128.02	320.87	301.79	104.21	87.74	156.33	90.84	109.73	106.47	33.64	95.02		
Zaniprifin	A5489	EDNRA	111.52	132.92	124.73	98.70	97.12	83.17	88.15	143.50	133.73	112.16	98.54	115.90	116.62	117.07	133.65	162.90	130.64		
Zidovudine	B2221	N/A	106.06	101.28	143.34	112.12	134.69	97.78	98.67	149.44	138.56	115.04	116.75	160.02	100.61	118.55	128.70	202.95	112.05		

Appendix A: PDX 1,363 drug screening dataset

continued

Information from ApexBio		TNBC (basal-like)										TNBC (luminal AR)			ER-positive (luminal)			HER2-enriched						
Item Name	Catalog#	TARGET	HC101	HC101	HC16	UCD52	UCD52	UCD52	WHIM2	WHIM2	WHIM30	WHIM30	WHIM30	HC109	HC109	HC103	HC111	HC113	HC113	HC113	HC108	HC108	HC108	
Zileuton	A5384	ALOX5	109.79	91.54	128.43	109.09	114.74	96.58	126.49	143.60	125.01	112.69	98.22	136.09	101.49	117.07	150.45	119.58	105.32					
Zinc Pyrrithione	B2201	KCNQ1	8.47	23.47	43.06	26.77	24.41	39.26	48.93	42.08	10.80	48.34	45.12	24.75	54.71	232.65	2.78	18.54						
Ziprasidone	A3952	HTR1A	93.38	102.84	67.16	85.30	88.20	100.23	91.06	114.64	85.94	85.15	79.06	101.68	96.06	120.79	69.98	72.53	67.36					
Ziprasidone HCl	A5350	HTR1A	37.38	54.08	46.55	123.08	136.52	34.13	42.15	131.40	115.44	19.09	48.56	78.64	57.78	49.95	41.79	29.99	30.12					
Ziprasidone hydrochloride monohydrate	A3953	HTR1A	23.51	43.24	27.17	25.78	24.20	34.57	36.97	39.90	31.55	18.34	25.29	64.89	36.03	51.50	44.08	21.23	33.63					
Zoledronic Acid	A1352	FDPS	121.93	146.56	94.70	61.61	59.65	58.31	79.10	122.04	92.84	97.65	79.15	135.19	171.70	81.32	69.08	84.34	87.42					
Zolmitriptan	B2261	HTR1A	73.31	100.26	106.87	100.67	88.88	85.08	88.03	123.41	139.05	115.14	99.32	133.60	95.98	103.91	133.52	133.89	84.14					
Zonisamide	A5354	CA1	95.85	96.42	99.08	118.91	141.17	87.81	97.89	132.16	126.61	86.54	93.55	135.76	108.38	103.90	129.15	123.17	113.40					
Zoxazolamine	B1871	Kcnn2	131.77	118.51	114.43	105.69	109.45	115.04	167.82	120.54	138.40	118.95	111.74	133.69	123.99	117.33	99.71	122.99	121.41					

APPENDIX B

Appendix B: Statistical analyses of drug target gene expression between TNBC PDXs

Target genes and associated drugs are listed with statistical comparisons of expression values between the PDXs. Significant p-values (p<0.05) are bolded and italicized.

Gene	Drug(s)	HC109 vs HC101	HC109 vs UCD52	HC109 vs WHIM30	HC109 vs WHIM2	HC101 vs UCD52	HC101 vs WHIM30	HC101 vs WHIM2	UCD52 vs WHIM2	UCD52 vs WHIM30	WHIM30 vs WHIM2
PPIA	Cyclosporine	0.0012	0.006159	0.000604	0.245379	0.000019	0.000025	0.000072	0.012858	0.015311	0.035844
TUBB	Cloasatel	0.00045	0.007929	0.422069	0.177501	<0.000001	<0.000001	0.000841	0.012858	0.012858	0.347584
ATP1A1	Digoxin	0.000017	<0.000001	0.226771	0.341419	0.062575	0.062575	0.007962	0.000234	0.000234	0.167381
MAP2K2	MEK162	0.000298	0.00005	0.000504	0.389217	0.058958	0.058958	0.00453	0.006551	0.006551	0.033125
HSP90AA1	Ganetespib	0.074256	0.000002	0.001275	0.000385	0.000008	0.000324	0.000801	0.000324	0.000324	0.365359
CDK4	Abemaciclib	0.901123	0.325842	0.746366	0.006285	0.101664	0.101664	0.003706	0.009748	0.009748	0.000311
TOP1	Topotecan	0.000233	0.000044	0.001157	0.002489	0.824776	0.824776	0.114377	0.63841	0.63841	0.11214
PSMB5	Bortezomib, Carfilzomib, Ixazomib	0.312958	0.000209	0.001598	0.045661	0.000134	0.000471	0.115023	0.000002	0.000002	0.127831
XPO1	KPT-330	0.003409	0.057372	0.009443	0.103859	0.19315	0.19315	0.01908	0.000085	0.000085	0.010596
CDK1	Dinaciclib	0.01332	0.257244	0.008599	0.031161	0.000087	0.000087	0.00727	0.010361	0.010361	0.002458
MAPK14	LY2228820	0.00091	0.522589	0.000114	0.025899	0.000084	0.000084	0.001075	0.000007	0.000007	0.000735
KIF11	Ispinesib	0.000089	0.002113	0.003079	0.830435	0.007223	0.036246	0.013472	0.535483	0.535483	0.054366
FKBP1A	Pimecrolimus, Sirolimus	0.000162	0.000001	0.000175	0.002069	0.000446	0.005736	0.007142	0.040371	0.040371	0.211476
GGCX	Menadione	0.00183	0.000003	0.022038	0.158108	0.021929	0.444779	0.066878	0.018259	0.018259	0.281805
MAP2K1	Cobimetinib, MEK162	0.001499	0.039067	0.000046	0.00074	0.218785	0.000017	0.000359	0.000006	0.000006	0.475157
MAPK3	VRT752271	0.765419	0.000006	0.000081	0.001712	0.000017	0.000113	0.002833	0.030047	0.030047	0.315579
HMGCR	Rosuvastatin	0.005889	0.000018	0.00362	0.005415	0.000005	0.000005	0.004929	0.126909	0.126909	0.066646
ABL1	Bosutinib, Dasatinib, Nilotinib, Ponatinib, Saracatinib	0.032434	0.000066	0.040035	0.000084	0.001009	0.574063	0.000912	0.000708	0.000708	0.001302
MTOR	GSK2126458, Temsirolimus	0.000346	0.205441	0.000766	0.014849	0.006043	0.817552	0.256651	0.003777	0.003777	0.241489
TOP2A	Doxorubicin, Epirubicin, Idarubicin, Mitoxantrone	0.006002	0.000001	0.002661	0.066769	<0.000001	0.19323	0.077862	0.007655	0.007655	0.042744
BIRC5	YM155	0.000008	<0.000001	0.000022	0.032763	0.000004	0.047056	0.003472	0.021105	0.021105	0.001114
KEAP1	Baroxolone methyl	0.000024	<0.000001	0.002878	0.067414	<0.000001	0.000323	0.000003	<0.000001	<0.000001	0.00061
MDM2	RG7388	0.002511	0.002069	0.035129	0.00103	0.259673	0.3572	0.028395	0.072225	0.130831	0.013735
P2RX4	Ivermectin, Paroxetine	0.000206	0.003551	0.499879	0.00001	0.000428	0.035123	0.002091	0.373219	0.373219	0.002186
VDR	Alfalcaldol, Calcitriol, Doxercalciferol	0.000134	0.727685	0.2351	0.000063	0.00003	0.000473	0.005791	0.128132	0.128132	0.000005
XIAP	Embelin	0.04084	0.123622	0.197648	0.015102	0.110344	0.015751	0.3969	0.010437	0.010437	0.007936
BRAF	Regorafenib, Sorafenib	0.22589	0.007537	0.037574	0.002561	0.063415	0.045006	0.011225	0.001538	0.001538	0.009615
MAPK1	VRT752271	0.000011	0.304405	0.022895	0.004109	0.000033	0.000576	0.000238	0.143707	0.143707	0.00194
BIRC2	Birinapant	0.004109	0.195913	0.000087	0.033437	0.00003	0.001963	0.001132	<0.000001	<0.000001	0.000093
EGFR	Afatinib, AZD-9291, Dacomitinib, Erlotinib, Lapatinib, Neratinib, Pelitinib, Pozotinib, Vandetanib	0.000217	0.011432	0.000306	0.055963	0.000253	0.023246	0.003949	0.000065	0.000065	0.000956
SLC29A1	Ticagrelor	0.000001	0.064723	0.000735	0.000007	<0.000001	0.013498	0.402404	0.000029	0.000029	0.027651
SYK	Fostamatinib	0.022906	0.000004	0.684189	0.217506	0.000003	0.042657	0.457667	0.000004	0.000004	0.000026
XDH	Benzbromarone	0.014277	0.188069	0.004283	0.023593	0.001128	0.19784	0.758483	0.000615	0.000615	0.191041
PSMB8	CEP-18770	0.004772	0.741021	0.01187	0.000005	0.000009	0.000089	0.000005	0.000064	0.000064	<0.000001
NR3C1	Ciclesonide	0.763006	0.195903	0.000249	0.000003	0.131194	0.000856	0.000002	0.00001	0.00001	0.000004
HRH1	Flunarizine, Clemastine, Ebastine	0.028838	0.489356	0.000572	0.000008	0.055405	0.0124	0.000356	0.000092	0.000092	0.000137
PIK3CA	BYL-719	0.000298	0.000006	0.001219	0.158003	0.995108	0.212727	0.00077	0.114565	0.114565	0.001446
CYP2J2	Terfenadine	0.229306	0.723728	0.066266	0.000002	0.656669	0.223401	0.000011	0.085775	0.085775	0.000046
MET	Crizotinib, EMD-1214063	0.000043	0.001089	0.497789	0.000025	0.000399	0.000209	0.000014	0.001097	0.001097	0.000001
CDK6	Abemaciclib	0.001832	0.219741	0.05382	0.002549	0.000243	0.036254	0.000004	0.095024	0.095024	0.000522
CACNA1D	Amlodipine, Lomerizine	0.003727	0.824513	0.859691	0.009289	0.011807	0.000678	0.000761	0.722075	0.722075	0.003788

Appendix B: Statistical analyses of drug target gene expression between TNBC PDXs

continued

Gene	Drug(s)	HC109 vs HC101	HC109 vs UCD52	HC109 vs WHIM30	HC109 vs WHIM2	HC101 vs UCD52	HC101 vs WHIM30	HC101 vs WHIM2	UCD52 vs WHIM30	UCD52 vs WHIM2	WHIM30 vs WHIM2
TRPM2	Econazole, Miconazole	0.111082	<0.000001	0.000016	0.000182	0.000003	0.0001	0.000363	0.000407	0.314873	0.004408
FGFR1	Nintedanib, Sunitinib	0.011394	0.023086	0.000017	0.070314	0.000575	0.000375	0.011187	0.000463	0.457708	0.001647
AKR1C3	Toifenamic acid	0.001152	0.703286	0.003392	0.22176	<0.000001	0.000012	0.000032	0.000007	0.001679	0.004734
CA1	Gallic acid	0.433563	0.768765	0.611714	0.673828	0.411089	0.255824	0.450708	0.862088	0.824132	0.929512
KCNA7	Amiodarone	0.278494	0.571212	0.051737	0.408833	0.826391	0.033652	0.215295	0.030183	0.263834	0.361073
NR1H3	Mecizine	0.19753	0.022521	0.774778	0.247194	0.31278	0.295698	0.031469	0.042812	0.001723	0.168335
KIT	Masitinib	0.000005	<0.000001	0.000033	0.000006	0.36288	0.001802	0.008777	0.001086	0.34379	0.007213
SLC6A4	Oxethazaine, Sertraline	0.000209	0.064516	0.006135	0.155491	0.179164	0.013079	0.432449	0.921453	0.876919	0.816963
CACNA1A	Lomerizine	0.000595	0.000077	0.007859	0.066773	0.834272	0.015939	0.139998	0.003542	0.042129	0.7331
BCL2	Navitoclax	0.19306	0.000002	0.413974	0.445025	0.000021	0.688386	0.671075	0.000007	0.000003	0.986887
	Bazedoxifene, Tamoxifen,										
ESR1	Toremifene	0.00004	0.000486	0.455372	0.014274	0.076732	0.32759	0.000354	0.022574	0.000782	0.273147
DRD2	Flunarizine	0.027354	0.005894	0.010781	0.436588	0.034527	0.215041	0.029314	0.043943	0.014008	0.019546
CSF1R	Cediranib, Crenolanib, Dovitinib	0.325228	0.004391	0.128873	0.638743	0.031434	0.822568	0.491464	0.017224	0.013785	0.25692
MGRPRX3	Chloroquine	N/A	0.170649	0.138771	N/A	0.239527	0.208788	N/A	0.474366	0.239527	0.208788
PPARG	Bexarotene	0.051151	0.002598	0.000652	0.001219	0.001075	0.000183	0.004493	0.834126	0.000153	0.000019
FLT1	Foretinib, Tivozanib	0.714716	0.001328	0.005575	0.329095	0.004203	0.015305	0.378514	0.319018	0.015287	0.065058
PTGS1	Amfenac, Licoferone	0.008748	0.276844	0.000179	0.05451	0.333712	0.010747	0.0014	0.004789	0.083912	0.000151
MTTP	Lomitapide	0.001297	0.048806	0.007639	0.089076	0.9608	0.115325	0.861673	0.06836	0.889288	0.212519
KDR	Cabozantinib	0.005133	0.002516	0.003282	0.005225	0.0501	0.020989	0.591886	0.025855	0.034474	0.01825
	Duloxetine, Fluoxetine,										
HTR2A	Pimavanserin, Trifluoperazine	0.285591	0.004636	0.004546	N/A	0.026477	0.019624	0.373901	0.091905	0.012797	0.013677
CACNA1E	Lomerizine	0.13553	0.161961	0.038521	0.244733	0.147822	0.062093	0.686186	0.087429	0.160575	0.064444
ADRB1	Carvedilol, Nebivolol	0.675495	0.015919	0.00976	0.08896	0.018577	0.02268	0.136655	0.008655	0.004347	0.015727
AGTR1	Candesartan	0.920109	0.001811	0.008522	0.086221	0.00152	0.019807	0.017642	0.025792	0.000043	0.007839
CACNA1G	Lomerizine, Flunarizine	0.254781	0.450682	0.486765	0.254781	0.185327	0.206756	N/A	0.167604	0.185327	0.206756
KCNJ6	Maprotiline	0.167515	0.289671	0.189813	0.171866	0.347224	0.038442	0.929835	0.018675	0.360671	0.039165
CHRNA1	Otilonium bromide	0.436588	0.268446	0.004389	0.436588	0.18184	0.012338	N/A	0.000755	0.18184	0.012338
SLC6A3	Oxethazaine	0.436588	0.241504	0.033413	0.436588	N/A	0.066141	N/A	0.008002	N/A	0.066141
ALK	Entrectinib, LDK378	0.000047	0.054766	0.006802	0.003781	0.000001	0.000336	0.170855	0.004103	0.000481	0.018702
TNNC1	Levosimendan	0.000131	0.084031	0.256804	0.2243	0.00019	0.004344	0.00398	0.931819	0.799139	0.911193
MPL	Eltrombopag	0.0142	0.476951	0.596498	0.503022	0.009362	0.034448	0.07079	0.948756	0.927625	0.903961
CNR1	Rimonabant	0.009801	0.006004	0.026335	0.056177	0.00018	0.002463	0.009277	N/A	N/A	N/A
SLC6A2	Oxethazaine	0.025612	0.099964	0.059352	0.000088	0.00416	0.813412	0.335967	0.015495	<0.000001	0.550727
KCNJ5	Fingolimod	0.000223	0.00058	0.000154	0.023426	0.001098	0.570604	0.015385	0.001497	0.527641	0.013669
FLT3	Pacritinib	0.016727	0.510095	0.058939	0.436588	0.016029	0.827519	0.027343	0.051028	0.319008	0.079202
ADORA3	Nicardipine	0.384494	0.241504	0.540439	0.436588	0.170471	0.695763	0.373901	0.241504	N/A	0.436588
CACNA1C	Lomerizine	<0.000001	0.000129	0.000033	0.000002	0.000404	0.000037	0.016371	0.784768	0.000986	0.000096
KCNQ1	Zinc pyrrithione	0.000258	0.000006	0.003035	0.010344	0.047221	0.070069	0.110335	0.102229	0.128249	0.939954
CACNA1F	Lomerizine	0.000976	0.000605	0.260068	0.003918	0.440062	0.188375	0.336002	0.14943	0.987308	0.301253
CYSLTR1	Toltrazuril	0.000154	0.000096	0.000023	0.000154	0.074777	0.436588	N/A	0.052912	0.074777	0.436588
	Azelinidipine, Benidipine,										
CACNA1B	Cilnidipine, Lomerizine	0.030567	0.00754	0.017818	0.023986	0.269025	0.686445	0.353718	0.456742	0.113303	0.334621
CACNA1H	Lomerizine, Flunarizine	0.00257	0.000032	0.001115	0.002621	N/A	0.01022	0.373901	0.000323	0.170471	0.012483
KCNA5	Dronedarone	0.436588	0.241504	0.355918	0.436588	N/A	N/A	N/A	N/A	N/A	N/A
FLT4	Lenvatinib	0.45822	0.282313	0.000026	<0.000001	0.136952	0.000189	0.00001	<0.000001	<0.000001	0.005976

Appendix B: Statistical analyses of drug target gene expression between TNBC PDXs

continued

Gene	Drug(s)	HC109 vs HC101	HC109 vs UCD52	HC109 vs WHIM30	HC109 vs WHIM2	HC101 vs UCD52	HC101 vs WHIM30	HC101 vs WHIM2	UCD52 vs WHIM30	UCD52 vs WHIM2	WHIM30 vs WHIM2
CACNA11	Lomerizine, Otilonium bromide, Flunarizine	0.33643 0.000014	0.905851 0.001667	0.007228 0.000031	0.012064 0.000004	0.392345 0.000587	0.011447 0.000372	0.025344 0.000359	0.006934 0.897944	0.003183 <0.000001	0.105494 0.000009
PTGS2	Amfenac, Licoferlone	0.94798	0.023615	0.274573	<0.000001	0.048011	0.321329	0.000007	0.035331	0.00004	<0.000001
ABCG2	Cyclosporin A	0.285591	0.113592	N/A	0.285591	0.593651	0.285591	0.618844	0.113592	0.743297	0.285591
CYP3A4	Ritonavir	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
CYP2B6	Ticlopidine	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
HTR1A	Thioridazine, Vortioxetine,	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
CASR	Ziprasidone Cinacalcet	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

APPENDIX C

Adapted from [190]

Appendix C: 176 drugs combined with carfilzomib in basal-like TNBC PDXs

Shown are cell viability data and analyses in response to each drug (1µM) combined with the indicated dose of carfilzomib for each PDX.

Drug	HC101 (n=2)				WHIM30 (n=3)				UCD52 (n=2)				WHIM2 (n=2)			
	Drug (1µM) alone: % viability	Drug (1µM) + Carfilzomib (10nM): % viability	Difference in % inhibition	±	Drug (1µM) alone: % viability	Drug (1µM) + Carfilzomib (10nM): % viability	Difference in % inhibition	±	Drug (1µM) alone: % viability	Drug (1µM) + Carfilzomib (10nM): % viability	Difference in % inhibition	±	Drug (1µM) alone: % viability	Drug (1µM) + Carfilzomib (10nM): % viability	Difference in % inhibition	±
(R)-Crizotinib	154.07	16.77	146.40	45.94	-12.63	55.52	95.67	22.91	27.37	7.36	-6.97	21.59	67.62	7.15	49.15	3.23
5-Azacytidine	91.51	14.03	75.93	4.70	-4.72	11.53	93.90	31.12	20.74	4.01	-2.10	30.07	70.11	15.34	68.16	0.75
ABT-263																
(Navitoclax)	76.17	11.47	47.05	3.27	8.82	7.54	62.18	8.01	13.28	4.58	-26.37	10.61	54.10	7.69	31.80	16.07
Atarab																
(BWM2992)	71.33	13.34	63.07	8.86	-12.04	15.01	49.65	11.59	12.30	0.51	-37.91	16.52	27.16	4.80	26.18	1.68
dimalate	85.23	6.46	86.12	32.06	-21.20	31.32	55.96	14.62	12.95	2.39	-32.24	16.70	32.67	2.89	26.56	0.64
Aflacalcidol	72.26	2.18	55.45	4.45	-3.49	0.56	91.27	13.33	16.57	0.56	-0.57	15.34	58.98	8.12	40.95	8.46
Amrenac Sodium																
Monohydrate	97.65	7.52	76.49	0.85	0.86	1.18	99.46	14.17	23.73	5.37	2.46	11.76	93.04	8.37	66.32	18.33
Amiodarone HCl	96.65	0.21	90.75	3.95	-14.41	3.04	98.39	14.55	20.33	4.23	0.80	8.02	101.47	5.92	63.67	11.76
Amiodipine	102.88	10.91	113.09	58.16	-30.51	40.05	90.16	15.08	15.78	4.00	-0.87	9.08	93.68	2.24	62.47	17.41
Amiodipine																
Bevyolate	93.30	2.00	97.07	30.52	-24.07	25.33	88.52	5.70	16.49	3.84	-3.23	6.20	97.49	3.98	64.83	20.63
Anidulafungin	100.39	9.06	73.75	8.03	6.34	8.22	72.22	2.87	21.69	6.32	-19.73	1.34	82.50	3.85	60.01	15.60
Arbidol HCl	86.49	1.27	76.60	16.15	-10.41	10.22	92.57	11.80	21.98	7.16	-4.67	11.50	78.94	0.65	58.07	0.09
Atazanavir	92.81	10.85	79.81	16.40	-7.31	1.64	84.59	11.39	24.51	3.84	-15.18	12.55	80.16	8.42	63.16	4.67
AZD-9291	57.65	3.16	59.80	15.45	-22.46	11.42	61.79	10.61	14.51	2.72	-30.99	13.06	62.99	5.88	53.66	5.79
Azelidipine	93.56	2.17	112.50	60.48	-39.25	55.46	88.35	10.61	14.55	7.43	-1.46	9.19	73.48	9.59	46.59	17.91
Bardoxolone methyl	144.51	40.06	158.20	90.93	-34.00	123.80	65.28	20.58	14.33	3.71	-24.32	22.55	60.90	26.86	28.10	3.97
Bazedoxifene HCl	120.40	15.19	107.14	25.24	-7.04	33.24	91.56	4.79	11.25	1.71	5.05	8.64	94.23	12.47	64.40	8.70
Bedaquiline fumarate	90.68	15.66	77.10	6.59	-6.72	15.06	99.79	30.72	22.46	9.52	2.06	20.94	108.30	6.56	68.80	14.80
Bendamidone HCl	96.35	1.20	105.74	51.16	-29.69	42.77	93.71	11.67	13.56	2.18	4.89	9.87	88.77	14.84	57.69	24.57
Benzbromarone	88.43	15.47	84.63	2.43	-16.50	10.71	88.32	13.01	20.09	6.75	-7.04	10.64	92.87	4.45	63.07	21.70
Benzofenonium Chloride	91.86	5.50	77.20	1.30	-5.65	0.39	79.59	11.09	12.94	3.38	-8.61	11.68	88.07	3.00	60.36	18.16
Bexarotene	105.68	8.94	71.82	18.32	13.55	16.58	141.60	17.77	25.68	2.69	40.66	18.76	106.56	2.76	79.61	4.47
Birnapant (TL32711)	82.78	0.92	61.89	2.74	0.59	3.53	56.61	7.81	11.42	3.55	-30.08	8.90	68.49	4.91	43.01	13.23
Borizomib	32.78	4.63	28.85	4.49	-16.37	7.05	24.03	2.45	5.02	1.44	-56.25	6.55	21.63	0.81	15.45	2.42
Bosutinib (SKI-606)	61.14	26.38	70.13	7.57	-29.29	26.76	68.38	7.47	20.93	3.32	-27.81	8.62	30.44	13.76	35.26	15.98
BYL-719	73.99	2.16	62.57	9.46	-8.88	0.11	83.31	7.66	19.95	3.39	-11.91	4.31	64.68	7.44	42.29	7.25
Capecitabine (XL164)	92.86	0.07	76.97	8.46	-4.41	1.34	84.43	9.45	16.12	6.02	-6.95	9.65	93.90	2.54	57.17	19.02
Calcitriol	70.83	0.99	53.81	1.08	-3.28	7.28	92.90	11.02	19.06	3.61	-1.42	10.40	50.05	4.42	38.39	0.73
Candesartan																
Cilexetil	88.48	8.50	77.46	1.90	-9.29	3.21	99.68	14.26	18.87	5.91	5.54	11.11	97.25	5.59	61.42	23.77
Carboplatin	87.87	6.21	81.24	18.08	-13.67	4.67	77.00	14.13	22.91	4.67	-21.17	12.02	80.05	15.37	70.61	13.90
Carfilzomib (PR-171)	29.24	5.82	30.96	5.62	-22.02	7.00	22.86	5.00	9.47	4.02	-61.87	6.60	16.64	1.68	14.19	0.25
Carvedilol	92.45	0.54	76.75	4.20	-4.60	2.45	110.86	5.73	20.75	3.98	14.85	4.97	99.91	10.04	61.38	3.56
Cediranib (AZD217)	81.92	29.48	80.63	16.74	-19.01	39.03	47.54	16.03	11.58	2.67	-39.30	19.73	29.20	7.88	31.63	12.42
CEP-18770	55.20	12.94	42.44	14.02	-7.54	8.67	22.49	1.73	8.71	3.81	-61.48	3.60	25.03	2.51	20.15	1.57
Cepharanthine	86.14	3.55	76.16	13.97	-10.32	3.23	60.59	12.01	9.41	1.08	-24.08	13.87	78.15	0.74	56.09	9.69
Cetirizine																
Bromide (CTAB)	87.76	11.68	72.76	2.16	-5.31	2.33	49.18	9.27	12.00	1.80	-38.09	13.13	75.61	7.78	53.09	22.41
Cetylpyridinium Chloride	92.72	9.15	76.97	3.37	-4.55	1.41	52.80	9.16	11.87	1.02	-34.34	13.27	67.60	10.70	48.07	22.13
Chloroquine diphosphate	88.65	15.40	64.04	3.59	4.31	4.62	81.18	13.86	13.49	3.61	-7.57	17.55	68.52	13.88	52.84	12.49
Chloroxine	93.21	13.13	79.38	0.20	-6.47	6.13	71.64	5.92	18.97	4.70	-22.59	6.95	96.68	6.69	62.39	26.39
Ciclesonide	114.92	17.77	108.44	30.09	-13.83	40.66	144.81	18.24	31.18	5.83	8.37	20.70	127.05	10.13	88.59	9.77
Cilnidipine	111.02	0.18	103.60	39.03	-12.88	31.66	103.39	17.96	19.24	6.42	8.90	17.45	95.40	5.40	63.20	18.78
Cinacalcet	102.08	13.91	82.44	0.84	-0.65	5.88	83.89	16.85	19.48	4.28	-10.86	15.24	78.15	0.74	56.09	9.69
Cinacalcet HCl	94.54	8.88	89.62	26.35	-15.38	10.18	81.56	6.58	18.62	0.56	-12.30	5.50	86.72	9.30	59.86	20.30
Clemastine Fumarate	96.52	1.22	77.18	5.70	1.04	2.72	78.77	5.35	15.55	3.22	-12.04	10.97	85.77	6.91	61.08	12.24
Clofazimine	88.13	12.01	71.89	11.40	-4.07	7.81	80.24	8.69	16.71	4.25	-11.74	7.85	84.85	6.80	62.72	17.41

Appendix C: 176 drugs combined with carfilzomib in basal-like TNBC PDXs

continued

Drug	HC101 (n=2)				WHIM30 (n=3)				UCD52 (n=2)				WHIM2 (n=2)												
	Drug (1uM) alone: % viability	Drug (1uM) + Carfilzomib (10nM): % viability	Difference in % inhibition	±	Drug (1uM) alone: % viability	Drug (1uM) + Carfilzomib (10nM): % viability	Difference in % inhibition	±	Drug (1uM) alone: % viability	Drug (1uM) + Carfilzomib (10nM): % viability	Difference in % inhibition	±	Drug (1uM) alone: % viability	Drug (1uM) + Carfilzomib (10nM): % viability	Difference in % inhibition	±									
Cloasentel	86.77	9.42	70.27	2.22	-1.80	0.01	82.72	6.63	16.79	2.83	-9.34	8.35	91.33	7.12	65.72	25.64	-0.88	4.97	105.19	13.38	97.83	44.18	-0.60	7.80	
Cloasentel Sodium	93.12	2.88	68.87	4.03	3.94	14.10	88.20	11.51	17.83	2.15	-4.89	12.76	90.88	8.51	65.87	25.69	-1.49	3.64	106.00	6.44	89.30	41.34	8.73	1.99	
Cobimetinib	74.94	4.39	65.63	6.96	-10.99	4.15	59.79	7.04	24.73	13.59	-40.20	10.14	52.86	10.11	44.71	4.53	-18.34	7.97	58.75	0.76	52.01	18.10	-1.22	32.43	
Crenolanib (CP-868596)	97.62	7.60	101.97	11.74	-24.65	12.14	71.34	24.74	64.33	37.26	-68.25	27.39	137.87	16.37	135.31	0.06	-23.93	29.98	442.93	56.09	384.27	207.94	50.70	102.08	
Cystostatin A	74.70	17.25	67.96	5.75	-13.66	4.31	40.79	6.75	6.00	0.56	-40.46	10.05	61.15	3.52	32.35	18.64	2.31	1.57	51.21	4.34	32.70	6.50	10.55	47.62	
Cyclosporin A	97.08	10.92	92.59	8.57	-15.81	12.30	72.47	6.04	10.01	4.60	-12.81	15.50	59.85	11.03	42.69	21.60	-9.32	2.98	79.33	15.85	73.46	40.35	-2.09	6.43	
Cytosporine	95.59	6.00	80.56	3.06	-3.07	1.87	71.37	11.17	19.88	6.17	-23.77	12.83	61.78	13.11	52.78	13.11	-17.49	13.91	95.95	0.39	86.83	45.17	1.15	4.99	
Cytarabine	75.04	2.26	57.82	6.46	-3.09	11.39	80.86	14.78	19.30	5.25	-13.71	13.78	106.16	22.15	68.26	23.57	11.41	12.13	87.10	4.29	43.65	11.56	35.48	42.50	
Cytarabine hydrochloride	71.52	10.34	65.55	5.57	-14.33	8.72	90.14	3.44	18.76	2.67	-3.88	4.56	114.05	14.17	77.11	14.38	10.45	13.34	86.25	13.10	38.75	8.96	39.53	53.91	
Dactasvir (BMS-790052)	85.12	1.78	70.80	8.16	-5.99	2.75	82.83	9.97	25.32	6.32	-17.75	8.81	82.59	2.26	60.40	5.20	-4.31	10.61	93.69	8.00	87.84	60.83	-2.11	3.06	
Dacomitinib (PF299804, PF299)	70.79	0.57	68.06	12.54	-17.58	5.92	54.64	6.09	14.65	2.60	-35.27	2.14	39.96	8.08	34.06	3.46	-20.59	18.16	43.92	3.68	38.21	10.53	-2.25	42.91	
Dasatinib (BMS-354825)	78.65	5.84	61.30	7.37	-2.96	6.01	55.60	11.08	26.63	9.94	-48.29	6.59	39.75	2.69	32.36	2.92	-19.10	13.31	67.66	4.63	88.48	61.06	-28.78	15.92	
Daurorubicin	127.55	52.95	79.89	31.35	27.36	14.41	47.99	25.89	4.41	0.24	-31.68	30.97	27.80	3.91	17.11	6.28	-15.80	3.36	23.11	4.29	16.36	9.00	-1.22	36.48	
HCI	87.89	6.32	67.80	0.15	-0.21	0.73	98.21	12.56	23.73	4.71	-0.78	4.76	92.02	5.54	61.19	0.30	4.34	8.31	93.17	12.87	80.55	63.66	3.66	1.03	
Deferasirox	50.60	23.10	40.71	17.72	-10.41	12.58	25.72	2.23	4.55	0.35	-54.08	6.73	25.28	3.05	16.91	7.52	-18.12	9.08	137.50	47.92	65.43	3.71	64.10	101.39	
Digoxin																									
Dinacircib (SCH279665)	46.81	8.79	33.57	6.30	-7.06	4.70	34.91	10.00	7.14	1.32	-47.49	14.11	29.21	7.74	23.75	5.84	-21.03	15.45	38.13	15.21	19.67	5.42	10.50	29.13	
Doriphen Bromide	88.48	7.31	71.13	7.94	-2.95	7.83	57.15	5.98	9.06	2.02	-27.18	10.02	80.40	12.25	57.13	24.48	-3.21	1.32	81.71	1.46	65.45	24.50	8.30	23.81	
Dovitinib Dilactate	102.90	14.37	71.24	5.06	11.36	16.51	77.82	18.72	32.05	13.24	-29.49	27.64	89.57	36.71	88.81	36.63	-25.74	86.89	96.95	7.74	72.87	56.88	16.11	0.63	
Doxorubicin	75.30	3.03	66.98	11.71	-11.99	1.49	93.14	9.16	17.02	1.18	0.86	11.84	63.61	6.94	43.97	7.87	-6.84	12.62	61.82	5.18	87.40	67.01	-33.55	22.42	
Doxorubicin	80.15	3.50	55.35	4.35	4.49	15.04	44.16	12.41	8.32	2.13	-39.43	15.77	42.14	3.97	28.33	8.53	-12.68	8.99	30.43	2.88	22.32	12.26	0.15	34.63	
Doxorubicin (Adriamycin) HCl	93.56	11.31	60.94	0.52	12.32	19.03	45.93	17.82	7.61	4.36	-36.94	19.29	38.73	1.71	30.22	0.06	-17.98	11.79	26.75	2.02	17.61	7.86	1.18	39.89	
Dronedarone	96.74	8.87	76.13	0.28	2.30	1.39	79.83	11.86	18.96	0.73	-14.39	10.62	81.42	2.83	59.30	3.28	-4.37	13.10	91.75	4.12	88.06	57.44	-4.27	3.55	
Droxidolone HCl	109.85	11.47	92.26	9.84	-2.71	14.12	76.23	9.88	12.70	2.46	-11.74	7.69	86.45	8.09	59.93	15.68	0.04	5.16	106.30	0.33	91.45	50.63	6.88	1.85	
Duloxetine HCl	85.40	7.77	81.57	23.30	-16.47	23.88	79.74	17.07	16.07	2.27	-11.60	16.94	95.38	0.30	62.37	2.65	6.52	11.99	65.42	9.51	2.65	56.42	4.25	2.85	
Ebastine	94.37	1.04	74.01	0.07	0.06	6.09	83.40	7.54	15.82	2.12	-7.67	12.27	87.53	2.93	59.79	16.71	1.25	0.23	106.54	15.74	91.65	46.27	6.92	12.24	
Econazole nitrate	101.29	8.58	89.14	14.68	-8.16	16.07	92.67	8.85	17.71	3.64	-0.30	9.09	92.02	2.69	59.81	12.07	5.72	4.16	115.34	3.33	93.34	64.20	14.04	17.77	
Eltrombopag	85.76	1.88	74.78	1.27	-9.33	4.05	96.23	21.65	19.83	3.45	1.14	21.40	94.64	6.32	58.81	18.74	9.34	1.13	101.16	3.44	102.00	75.69	-8.80	22.48	
Embelin	92.78	3.57	71.12	6.30	1.36	2.68	85.62	17.19	17.74	4.56	-7.38	15.96	86.81	13.76	55.54	12.06	4.78	12.27	93.47	5.05	85.01	58.73	0.50	3.90	
EMD-1214063	83.23	10.78	80.42	18.79	-17.49	22.38	79.56	17.60	26.89	12.11	-22.59	20.13	79.15	0.10	56.99	2.24	-4.33	11.40	97.76	1.02	86.97	52.32	-7.17	3.57	
Enrectinib	92.33	13.69	90.71	14.88	-18.69	21.38	71.90	17.96	10.13	3.37	-13.49	19.47	72.95	17.20	45.01	20.81	1.05	9.94	81.73	10.61	63.40	41.69	10.37	18.69	
Eprubicin HCl	105.20	8.35	73.93	8.96	10.96	24.50	46.38	19.77	5.02	1.17	-33.90	23.41	35.92	2.68	20.99	5.65	-11.56	5.22	22.24	3.32	15.23	5.32	-0.95	41.13	
Ertroinib	62.63	1.86	66.83	16.64	-24.51	11.32	65.00	9.06	27.38	14.21	-37.64	10.75	59.75	6.71	49.14	2.45	-15.87	9.30	53.71	4.39	69.20	43.37	-23.45	10.79	
Ertroinib Hydrochloride	63.09	3.47	62.64	16.38	-19.84	5.71	80.49	3.98	26.26	4.06	-21.04	5.91	68.33	0.42	57.39	1.91	-15.55	12.05	50.12	0.14	65.20	45.06	-23.05	4.57	
Ethacridine lactate																									
Ethacridine monohydrate	83.71	4.06	74.31	10.51	-10.90	7.38	68.29	5.79	15.19	0.74	-22.16	4.85	95.65	9.50	66.70	20.06	2.46	2.99	58.78	1.10	44.18	23.27	6.64	27.60	
Feniconazole Nitrate	89.62	12.44	83.93	15.09	-14.62	20.33	91.45	17.62	21.14	5.63	-4.95	16.94	92.52	5.81	65.19	3.33	0.84	16.03	107.20	13.16	94.20	72.92	5.04	9.99	
Fidaxomicin	99.29	6.57	92.50	22.82	-13.51	22.20	102.06	11.13	21.16	6.90	5.64	5.91	108.56	6.16	62.72	20.65	20.35	13.27	122.13	15.38	110.40	79.56	3.77	45.17	
Fingolimod (FTY720)	97.68	10.02	77.28	2.71	0.10	5.54	84.30	22.14	16.68	5.09	-7.64	22.07	87.93	0.36	61.50	17.39	-0.08	3.49	92.19	12.86	75.48	47.42	8.74	15.21	
Flunarizine 2HCl	106.11	9.27	103.33	33.21	-17.52	16.75	88.94	7.10	15.04	2.63	-1.36	7.12	94.08	4.23	61.10	26.13	6.49	8.35	100.89	12.71	85.10	61.63	7.82	24.58	
Fluoxetine HCl	91.08	8.89	72.39	4.57	-1.61	6.26	84.10	15.33	16.32	2.87	-7.48	18.44	75.56	8.76	52.64	18.73	-3.57	3.58	99.14	7.35	80.07	50.30	11.10	7.88	
Foretinib (GSK363089)	89.12	10.03	75.85	26.42	-7.02	29.26	70.19	17.64	22.36	6.24	-27.43	20.78	48.20	29.84	32.46	9.15	-10.75	34.23	71.18	9.68	58.61	29.14	4.60	10.95	
Fostatinib (R788)	116.01	7.87	119.12	50.00	-23.41	50.68	112.01	18.07	16.93	3.05	19.81	19.51	92.28	2.11	64.91	10.10	0.88	5.55	79.01	13.89	77.38	62.57	-6.33	1.09	
Gallic acid	96.36	1.23	74.53	1.08	1.53	4.88	102.30	7.30	16.30	5.53	10.75	6.84	97.14	12.81	60.93	13.47	9.72	12.73	82.15	10.94	85.86	65.22	-11.68	4.51	

Appendix C: 176 drugs combined with carfilzomib in basal-like TNBC PDXs

continued

Drug	HC101 (n=2)				WHIM30 (n=3)				UCD52 (n=2)				WHIM2 (n=2)											
	Drug (1uM) alone: % viability	Drug (1uM) + Carfilzomib (10nM): % viability	Difference in % inhibition	Drug (1uM) alone: % viability	Drug (1uM) + Carfilzomib (10nM): % viability	Difference in % inhibition	Drug (1uM) alone: % viability	Drug (1uM) + Carfilzomib (10nM): % viability	Difference in % inhibition	Drug (1uM) alone: % viability	Drug (1uM) + Carfilzomib (10nM): % viability	Difference in % inhibition	Drug (1uM) alone: % viability	Drug (1uM) + Carfilzomib (10nM): % viability	Difference in % inhibition									
Ganetespib (STA-9090)	83.87	11.91	66.07	10.98	-2.50	6.27	138.28	43.86	23.66	7.73	39.36	41.36	48.58	0.37	58.84	34.67	-38.55	47.85	55.22	4.91	55.53	34.41	-8.28	20.27
GSK2126458	52.97	13.67	37.55	6.55	-4.68	0.07	48.03	6.94	8.27	1.27	-35.50	10.02	23.24	2.89	17.95	2.11	-20.80	14.33	31.95	1.86	44.83	46.14	-20.85	5.49
Arbutin HCl	331.11	185.17	187.30	149.44	123.51	28.54	41.22	11.11	5.43	0.99	-39.48	15.29	32.54	1.70	21.10	6.77	-15.05	8.48	28.75	0.85	17.55	6.80	3.24	42.13
Rebunone	91.14	8.67	82.76	5.80	-11.92	7.28	94.45	5.50	17.50	2.74	1.69	8.57	90.23	1.37	62.03	20.45	-1.70	0.47	107.31	2.64	101.33	64.09	-1.99	16.96
Isoconazole	123.17	9.89	92.55	4.10	10.32	6.80	105.37	4.98	16.40	4.04	13.70	11.29	111.88	6.53	61.53	22.65	23.85	2.57	126.16	18.89	93.45	63.55	24.74	32.68
ispinesib (SB-715992)	98.73	6.81	88.56	13.11	-10.14	12.73	78.04	20.14	19.65	1.30	-16.87	21.74	47.70	3.86	42.94	0.10	-21.73	17.30	62.49	27.29	47.48	10.56	7.04	11.92
Ivermectin	90.56	11.20	92.62	37.10	-22.36	41.10	73.32	11.14	20.59	11.58	-22.54	17.42	57.56	22.24	43.02	18.43	-11.95	17.36	86.62	9.48	89.93	64.56	-11.28	24.27
KPT-330	67.37	9.23	57.33	0.81	-10.25	1.23	41.84	4.64	5.58	1.01	-39.00	1.47	59.45	23.51	40.08	35.65	-7.11	1.41	66.08	6.35	36.72	4.13	21.40	51.99
Lapatinib	71.71	8.14	69.47	31.67	-18.05	16.33	61.14	17.79	23.70	2.96	-37.82	14.28	57.12	14.42	47.73	7.37	-17.11	20.60	56.21	1.05	56.95	33.53	-8.71	15.19
Diosquib	76.39	3.13	81.55	31.15	-25.46	20.83	47.86	4.67	7.66	0.14	-35.07	5.28	45.75	3.33	31.37	5.65	-12.10	4.58	63.14	5.99	68.60	50.23	-13.43	5.53
Lenvatinib	89.06	1.40	97.88	38.98	-29.12	33.18	94.08	10.67	21.85	3.38	-3.03	10.28	56.21	17.15	38.19	12.50	-8.47	18.20	82.97	11.50	58.96	33.26	16.05	5.01
Levosimendan	89.15	2.06	74.07	3.30	-5.22	5.95	96.67	11.07	21.47	7.17	-0.06	10.82	95.23	13.51	61.55	19.72	7.20	7.34	113.55	7.98	99.28	62.63	6.30	20.86
Licetolone	124.59	7.43	83.73	6.66	20.56	6.43	97.09	6.72	18.57	5.51	3.26	6.29	102.63	10.23	64.74	17.30	11.40	13.99	90.31	3.69	77.08	55.06	5.27	1.61
Lithocholic Acid	89.20	4.02	67.36	5.69	1.53	2.51	91.49	7.08	21.58	2.84	-5.35	10.10	96.65	2.82	60.50	4.89	9.66	21.26	92.93	12.90	90.34	77.34	-2.47	14.67
Lomerizine HCl	85.24	11.62	91.13	22.69	-26.18	27.12	92.25	8.14	15.64	3.64	1.34	7.48	90.79	1.57	57.70	17.83	6.60	2.71	99.62	2.18	94.05	66.54	-2.40	18.94
Lomitapide	92.15	4.54	84.89	8.50	-13.04	5.84	63.85	4.00	9.93	2.29	-21.34	9.41	56.31	8.76	39.92	16.50	-9.11	5.81	62.68	45.47	58.70	30.16	-3.96	25.87
LY2238200	67.65	7.92	61.86	6.24	-14.51	6.97	61.08	10.74	14.37	2.06	-28.56	12.25	48.38	5.86	28.28	10.32	-9.39	9.09	65.44	2.97	49.20	24.75	8.27	27.99
LY2855219	83.95	12.95	62.75	11.71	0.90	17.47	52.64	29.99	23.59	21.31	-46.22	13.24	46.66	16.71	64.94	37.84	-44.77	34.67	130.29	3.92	71.53	0.14	50.79	45.71
Maprotiline HCl	90.93	3.57	76.48	5.97	-5.85	4.80	83.30	8.91	15.96	7.18	-7.93	9.87	81.06	2.18	55.51	20.42	-0.94	4.69	93.21	14.92	77.60	45.78	7.64	18.91
Mastinit	112.60	14.62	86.34	11.50	5.96	18.93	84.62	14.60	28.66	11.14	-19.30	21.52	85.93	14.95	69.63	10.81	-10.19	17.70	114.16	21.68	103.49	63.91	2.71	35.83
Mechlorethamine HCl	91.46	1.77	80.71	5.94	-9.55	0.51	140.20	16.01	28.20	10.40	36.74	10.64	121.24	7.32	86.45	22.68	8.30	1.81	83.65	6.74	92.91	61.62	-17.22	18.59
Mefloquine	136.42	22.34	105.25	8.42	10.87	23.57	99.51	6.71	11.65	1.81	12.59	11.49	93.38	0.95	57.24	15.10	9.65	2.50	97.98	15.13	67.40	53.40	22.61	11.50
MEK162 (ARRY-162, ARRY-443)	97.49	4.43	82.87	14.97	-5.68	12.20	74.00	12.75	20.28	14.15	-21.55	21.26	65.97	10.95	51.62	12.67	-12.14	11.82	102.56	2.74	83.46	22.05	11.14	24.98
Milofexine	71.63	10.87	67.07	23.79	-15.75	27.47	69.91	14.85	36.10	15.22	-41.45	11.17	59.94	8.65	50.05	1.04	-16.60	23.23	80.70	8.23	64.24	22.15	8.49	19.38
Minoxidil	98.56	1.43	78.18	2.53	0.08	11.15	98.22	14.50	21.39	4.81	1.56	12.06	94.20	8.95	62.01	18.98	5.71	3.51	105.23	5.56	100.55	62.12	-3.29	17.92
Miconazole Nitrate	100.42	17.66	87.13	2.19	-7.01	8.27	95.88	15.18	14.02	1.92	6.60	17.32	96.95	7.59	59.29	20.29	11.17	0.86	110.76	6.23	96.31	61.56	6.48	18.01
Milfetosine	89.62	1.57	75.19	9.11	-5.88	17.88	92.00	8.30	22.68	4.85	-5.35	3.90	101.17	12.63	71.64	4.14	3.03	3.22	85.78	15.27	83.69	62.91	-5.88	2.13
Minoxycline HCl	103.19	6.71	83.93	2.58	-1.05	2.09	102.25	11.57	26.39	9.82	0.60	11.26	100.43	4.50	65.92	21.34	8.22	12.30	91.25	7.42	90.23	76.65	-6.95	19.46
Mitomycin C	59.31	2.66	51.07	5.95	-12.06	3.90	66.89	11.65	23.50	7.48	-31.87	7.19	88.25	7.28	63.98	10.97	-2.22	9.86	75.39	4.77	69.69	44.08	-2.27	0.91
Mitoxantone HCl	105.42	26.05	74.14	11.35	10.98	21.90	37.22	20.68	5.21	1.25	-43.25	25.18	36.22	7.35	30.00	5.38	-20.27	11.58	27.28	3.37	19.89	10.15	-0.57	36.25
MILN2238	51.71	6.55	43.68	13.40	-12.27	13.94	23.06	2.23	9.50	3.26	-61.70	4.75	24.91	0.19	19.76	1.25	-21.35	14.99	129.68	18.44	75.29	33.01	46.42	101.22
Nabapucasin	30.13	7.79	22.63	2.98	-12.60	3.18	33.89	6.31	5.17	0.97	-46.54	11.05	29.98	4.65	15.70	7.55	-12.61	10.64	50.29	6.00	23.60	2.95	18.73	40.81
Nabivolol	91.12	2.87	72.54	3.01	-1.72	7.05	103.01	7.76	21.21	5.76	6.54	3.89	92.33	4.16	64.32	2.34	1.52	11.72	91.49	15.01	72.88	53.25	10.65	11.52
Nedaplatin	85.06	0.14	71.57	1.15	-6.81	8.48	79.37	15.58	16.39	2.73	-12.28	15.30	102.98	16.92	68.80	40.17	7.69	9.70	104.97	0.27	103.02	75.59	-6.02	25.55
Nefinavir Mesylate	90.13	6.98	80.35	19.53	-10.52	19.31	81.37	11.62	26.68	15.54	-20.57	6.84	61.63	13.74	57.22	5.93	-22.09	21.36	100.65	5.45	94.98	52.19	-2.30	7.87
Neratinib (HKI-272)	78.45	17.49	87.80	28.72	-29.65	39.01	68.91	11.92	17.53	9.85	-23.88	19.67	43.87	10.86	48.67	3.05	-31.30	0.36	36.36	3.57	43.45	31.88	-15.06	21.46
Nicardipine HCl	107.83	2.17	114.56	45.88	-27.03	40.86	100.50	9.14	13.78	1.55	11.46	14.16	94.40	0.77	51.96	18.57	15.95	4.25	93.52	15.14	80.33	63.47	5.22	1.43
Nifuroxazide	76.79	0.21	72.19	2.49	-13.70	4.92	77.48	13.73	12.52	1.03	-10.30	17.13	91.13	0.39	57.63	19.62	7.01	5.88	95.31	7.48	106.68	71.14	-19.33	28.85
Nilotinib (AMN-107)	78.20	14.33	69.14	20.13	-11.24	1.39	75.25	4.42	22.16	2.73	-22.17	5.08	77.54	14.63	45.09	34.54	5.35	6.36	88.00	2.61	68.41	5.27	11.63	47.11
Nintedanib (BIBF 1120)	83.06	7.32	76.37	5.46	-13.61	5.59	51.20	18.00	24.89	7.87	-48.96	12.55	46.00	12.43	37.48	1.11	-17.97	27.08	46.61	1.67	38.59	16.70	0.05	34.74
Oflonilium Bromide	91.28	2.45	81.54	14.42	-10.56	9.67	90.70	4.89	17.74	4.47	-2.30	10.88	100.18	2.23	66.96	20.79	6.72	5.02	104.90	17.81	80.98	36.57	15.96	4.61
Oxethazone	87.28	4.51	70.66	4.00	-3.68	1.31	88.40	14.20	20.79	5.14	-7.65	14.48	93.61	5.08	66.90	2.34	0.63	16.28	86.45	8.34	64.66	33.23	15.82	24.87
Pacritinib	70.46	13.73	58.20	19.56	-8.04	1.37	47.30	7.93	11.52	3.44	-39.48	12.56	49.06	0.34	57.94	10.39	-35.37	23.00	77.30	13.80	52.37	25.28	16.97	38.28
Paroxetine HCl	91.57	0.96	90.85	27.78	-19.57	21.54	87.44	15.87	12.86	2.44	-0.69	15.93	79.66	5.18	54.73	12.07	-1.56	6.67	100.43	5.65	81.02	48.36	11.45	7.06
Peflitinib (EKB-568)	98.53	29.33	139.65	81.29	-61.42	103.43	46.05	17.84	5.92	0.63	-35.13	22.83	27.01	4.17	40.85	23.31	-40.32	32.69	31.40	1.95	26.89	7.34	-3.46	56.16
Pinavarserin	93.47	7.49	76.07	8.93	-2.90	9.23	88.00	14.38	15.81	2.16	-3.06	14.61	83.58	10.73	62.38	13.85	-5.29	10.42	102.81	12.59	71.08	18.07	23.77	44.29

Appendix C: 176 drugs combined with carfilzomib in basal-like TNBC PDXs

continued

Drug	HC101 (n=2)				WHIM30 (n=3)				UCD52 (n=2)				WHIM2 (n=2)											
	Drug (1uM) alone: % viability	Drug (1uM) + Carfilzomib (10nM): % viability	Difference in % inhibition	±	Drug (1uM) alone: % viability	Drug (1uM) + Carfilzomib (10nM): % viability	Difference in % inhibition	±	Drug (1uM) alone: % viability	Drug (1uM) + Carfilzomib (10nM): % viability	Difference in % inhibition	±	Drug (1uM) alone: % viability	Drug (1uM) + Carfilzomib (10nM): % viability	Difference in % inhibition	±								
Pimecrizolimus	101.60	8.30	95.68	25.37	-14.38	26.48	85.96	11.64	11.67	0.40	-0.98	14.69	89.02	14.20	49.18	30.93	13.36	3.19	82.40	1.10	91.14	72.03	-16.70	23.36
Ponatinib (AP24534)	84.54	28.66	72.58	27.89	-8.34	7.96	59.38	24.69	10.98	6.35	-26.87	17.84	36.25	6.43	25.76	7.68	-16.01	12.30	79.09	17.54	46.13	15.99	25.00	16.24
Pozotinib	62.35	6.62	52.82	12.43	-10.77	1.39	50.72	14.12	8.92	0.26	-33.46	19.16	36.50	7.81	28.92	6.28	-18.91	15.08	32.90	2.64	32.34	22.04	-7.40	30.37
Proflavine	91.42	8.15	78.04	1.71	-6.93	0.75	58.76	8.81	11.18	2.36	-27.68	11.59	139.33	18.19	93.97	49.88	18.87	18.14	51.29	2.64	58.76	40.21	-15.44	12.20
Purromycin dihydrochloride	93.78	3.71	76.39	13.25	-2.92	16.73	76.75	30.71	5.17	0.70	-3.68	33.79	22.30	1.60	13.75	6.11	-17.94	9.04	86.86	40.75	20.21	9.40	58.69	81.12
Rapamycin (Stromolis)	78.13	5.95	68.32	7.96	-10.49	6.71	75.42	12.33	25.82	8.09	-25.66	13.23	52.55	2.01	49.06	2.68	-23.00	18.24	68.31	3.56	89.57	76.63	-29.22	23.30
Regorafenib	102.82	5.12	74.61	1.02	7.90	3.10	89.87	16.94	22.43	6.39	-7.82	11.06	80.74	25.92	58.60	18.10	-4.36	21.37	99.60	5.20	89.11	62.21	2.52	17.64
Regorafenib hydrochloride	104.12	5.13	77.74	1.49	6.08	3.56	98.72	13.86	32.77	12.34	-9.31	15.61	71.48	11.09	52.70	11.03	-7.70	13.61	104.19	2.64	77.81	36.01	18.42	11.12
RG7388	95.09	5.65	79.11	5.72	-4.31	4.17	91.30	14.98	23.54	7.18	-7.50	17.05	89.06	1.68	62.65	7.87	-0.08	7.35	99.12	2.08	90.15	56.63	1.01	8.94
Rifampine	93.71	0.92	78.81	4.15	-5.40	2.12	95.82	16.46	21.93	6.31	-1.37	13.97	88.83	5.18	58.59	15.12	3.75	3.60	103.75	3.11	90.62	60.04	5.16	13.39
Rimnabant	87.37	7.02	78.40	7.77	-11.33	7.59	82.57	11.63	16.33	2.45	-9.02	12.70	91.06	9.27	63.04	31.04	1.54	8.23	100.32	21.22	83.28	27.64	9.08	0.91
Ritonavir	88.23	2.36	73.00	4.28	-5.07	5.27	91.13	8.59	27.27	7.41	-11.40	7.43	82.12	7.10	65.57	4.46	-9.94	16.19	88.45	0.59	89.65	59.82	-9.16	10.45
Rosuvastatin	96.17	6.25	80.77	6.57	-4.91	5.63	84.83	12.27	19.64	4.24	-10.08	11.13	83.05	2.31	67.69	2.38	-11.13	8.86	83.43	8.89	99.17	69.29	-23.71	10.63
Saquinavir mesylate	96.90	11.67	79.54	0.63	-2.94	3.84	99.36	23.10	22.86	4.88	1.23	20.68	89.52	9.70	60.21	11.12	2.82	12.13	105.29	2.68	91.15	59.24	6.17	12.16
Saracatinib (AZD0530)	67.94	19.30	66.12	16.93	-18.48	29.04	57.48	9.67	21.10	5.17	-38.89	9.98	39.67	0.18	39.30	8.03	-27.13	21.40	33.87	2.29	45.84	31.26	-19.94	20.79
Sevraline HCl	92.92	4.72	72.15	0.23	0.47	2.71	85.22	5.80	11.02	4.28	-10.67	11.98	78.57	12.83	61.70	16.41	-9.03	9.97	101.25	4.34	80.92	33.30	12.36	20.81
Simeprevir	103.81	1.03	82.74	3.74	0.77	2.42	86.72	11.13	22.14	3.74	-10.69	14.97	90.36	2.23	62.47	11.45	1.40	4.33	106.03	2.83	94.40	59.23	3.66	6.63
Sorafenib	107.20	23.02	68.95	0.04	17.95	15.79	78.01	10.06	17.98	4.47	-15.24	11.98	67.71	1.36	49.02	6.53	-7.80	8.38	92.63	6.90	100.77	54.93	-16.10	12.06
Sorafenib Tosylate	90.63	7.83	70.30	0.70	0.03	0.06	65.17	4.75	19.54	1.84	-29.63	10.50	74.52	16.50	58.58	6.24	-4.56	23.80	81.70	1.97	83.58	53.94	-9.85	2.20
Suiconazole Nitrate	95.23	11.30	93.47	1.25	-18.54	2.86	92.95	13.93	14.16	2.25	3.53	14.42	96.49	16.22	62.09	22.19	7.91	7.56	108.41	1.86	96.10	53.59	4.35	1.97
Sunitinib	81.14	0.26	66.04	8.05	-5.21	0.60	86.75	13.61	33.21	9.68	-21.73	17.74	73.03	14.80	59.33	3.53	-12.79	31.88	66.00	26.48	53.36	40.79	4.68	35.45
Sunitinib malate	73.39	1.23	67.22	12.99	-14.14	7.03	69.19	9.06	33.11	12.60	-39.18	9.94	64.56	6.53	61.51	2.25	-23.43	22.32	96.05	9.93	79.09	50.06	9.00	9.64
Tamoxifen Citrate	110.51	6.89	90.43	16.50	-0.22	17.00	99.90	3.76	23.80	5.09	0.84	2.83	100.86	3.67	71.20	0.08	3.16	9.80	86.20	16.20	86.72	59.98	-8.48	5.99
Temsirolimus	76.22	6.85	72.38	6.26	-16.47	5.91	74.24	11.66	23.94	4.07	-24.96	11.79	55.11	1.76	49.54	1.22	-20.92	16.52	80.02	12.85	102.20	83.75	-30.14	21.13
Terfenadine	89.00	3.88	77.14	9.12	-10.94	8.07	73.07	10.82	15.52	4.91	-17.71	7.32	79.91	7.90	64.91	6.58	-11.49	14.86	81.10	8.35	77.37	38.66	-4.24	2.76
Thioridazine HCl	87.04	11.00	77.68	4.73	-10.44	8.53	84.66	8.30	17.70	5.32	-8.30	10.41	82.53	3.27	64.45	3.78	-8.40	13.04	92.41	8.06	84.35	51.27	0.09	6.57
Ticagrelor	97.79	2.15	95.08	28.08	-17.59	23.04	75.54	7.63	14.40	0.47	-14.12	11.41	90.99	14.29	54.27	22.33	10.23	5.51	89.67	5.49	88.87	65.94	-7.16	10.58
Ticlopidine HCl	95.35	10.81	78.36	4.96	0.69	8.57	91.88	18.34	15.98	3.58	0.64	20.52	97.40	9.92	58.68	16.87	12.23	6.60	99.59	10.06	99.83	71.67	-8.20	11.84
Tivozanib (AV-951)	98.74	8.64	88.44	9.27	-10.00	7.83	90.12	8.05	16.92	1.90	-2.06	11.39	104.04	15.30	62.49	25.42	15.05	3.43	111.09	1.25	100.31	61.12	2.82	10.10
Tofenamide	91.01	10.21	97.49	35.39	-26.78	38.41	85.05	16.21	18.07	4.55	-8.28	15.02	61.39	15.71	48.92	14.72	-14.03	14.54	94.33	1.45	69.26	35.66	17.10	12.66
Tofenamide Acid	95.92	2.08	74.73	3.81	0.90	5.46	92.50	6.46	20.68	2.57	-3.34	10.28	101.55	14.45	69.71	22.37	5.34	5.62	106.42	16.51	89.27	35.09	9.18	1.83
Toltrazuril	90.80	6.28	76.36	0.08	-5.87	0.99	90.84	13.00	19.33	6.45	-3.76	9.06	97.99	2.74	60.99	24.39	10.11	8.11	105.43	3.12	97.06	53.30	0.40	0.41
Topotecan	65.95	5.63	56.94	10.24	-11.30	8.67	37.38	7.48	11.30	8.67	-45.04	12.97	100.61	11.72	57.88	13.02	16.24	11.19	56.51	0.46	82.76	73.93	-34.21	24.63
Topotecan HCl	65.37	3.95	55.90	2.88	-10.84	0.37	41.66	8.93	7.58	1.54	-41.18	12.02	93.37	21.27	54.70	7.04	12.19	14.76	49.57	4.65	62.33	48.35	-20.73	3.22
Toremifene Citrate	127.38	2.46	103.44	4.52	3.64	5.14	102.08	11.06	17.12	3.19	9.70	8.99	98.41	5.67	70.21	19.30	1.71	0.09	118.56	22.56	95.31	31.73	15.28	4.52
Trifluoperazine 2HCl	95.65	7.68	76.21	8.45	-0.86	8.93	84.86	17.24	16.72	6.69	-7.12	11.20	82.13	1.14	59.53	16.62	-3.89	4.21	102.32	26.43	63.28	17.71	31.08	5.63
Vandetanib (ZD6474)	70.04	3.49	64.12	12.92	-14.39	9.21	64.80	9.80	15.07	2.15	-25.54	14.89	46.49	11.70	39.38	7.92	-19.38	17.33	37.51	8.93	35.64	21.39	-6.10	19.45
Vehicle/Anchor drug alone	100.00	0.00	79.70	7.19	0.00	0.00	100.00	0.00	24.74	5.55	0.00	0.00	100.00	0.00	73.51	13.55	0.00	0.00	100.00	0.00	92.04	49.77	0.00	0.00
Vortioxetine (Lu AA21004) HBr	112.59	23.99	96.32	26.28	-6.04	43.08	80.61	20.05	15.65	4.09	-10.30	22.67	71.19	11.35	50.76	8.16	-6.06	16.73	101.61	11.72	80.68	41.44	12.96	3.39
VR152271	84.84	5.49	93.96	40.69	-29.42	38.99	78.38	11.36	21.74	2.84	-18.63	14.08	59.08	2.45	48.95	6.79	-16.36	4.31	72.73	9.64	66.77	42.88	-2.00	16.53
YM155	29.61	1.00	25.48	1.67	-16.17	6.53	27.03	2.32	6.30	2.11	-64.53	5.00	21.27	0.30	17.36	0.49	-22.58	13.36	21.09	0.19	19.19	7.33	-6.06	42.63
Zincifinast	93.59	4.57	83.16	2.47	-9.87	0.15	97.17	12.95	17.92	4.18	3.98	10.17	95.29	6.09	65.00	25.51	3.80	6.87	110.51	0.90	104.36	63.54	-1.82	12.86
Zinc Pyritione	52.05	12.93	68.34	1.02	-36.59	4.71	65.28	28.95	13.39	2.94	-23.37	27.55	67.22	10.50	42.83	13.33	-2.10	10.28	70.16	13.74	36.64	16.93	25.55	46.67
Ziprasidone hydrochloride monohydrate	88.52	2.26	79.55	12.13	-11.33	7.19	94.57	14.78	22.54	1.92	-3.23	15.02	94.74	3.02	64.25	6.95	4.00	9.61	94.55	2.24	71.66	39.30	14.92	8.23

APPENDIX D

Adapted from [190]

Appendix D: 176 drugs combined with afatinib in basal-like TNBC PDXs

Shown are cell viability data and analyses in response to each drug (1uM) combined with the indicated dose of afatinib for each PDX.

Drug	HC101 (n=2)				WHIM30 (n=3)				UCD52 (n=2)				WHIM2 (n=2)									
	Drug (1uM) alone: % viability	Drug (1uM) + Afatinib (10nM): % viability	Difference in % inhibition	Drug (1uM) alone: % viability	Drug (1uM) + Afatinib (10nM): % viability	Difference in % inhibition	Drug (1uM) alone: % viability	Drug (1uM) + Afatinib (10nM): % viability	Difference in % inhibition	Drug (1uM) alone: % viability	Drug (1uM) + Afatinib (10nM): % viability	Difference in % inhibition	Drug (1uM) alone: % viability	Drug (1uM) + Afatinib (10nM): % viability	Difference in % inhibition							
(R)-Crizotinib	154.07	16.77	47.05	14.41	95.67	22.91	71.02	34.32	2.50	19.13	67.62	7.15	48.31	1.77	-3.58	0.77	106.72	0.11	44.38	6.46	14.54	3.97
5-Azacytidine	91.51	14.03	-3.01	16.43	93.90	31.12	76.06	33.83	-4.30	29.52	70.11	15.34	58.54	9.12	-11.32	0.08	91.28	15.81	48.90	12.35	-4.42	1.08
ABT-263 (Navitoclax)	76.17	11.47	2.13	18.05	62.18	8.01	43.87	15.69	-3.84	23.03	54.10	7.69	38.04	1.04	-6.83	0.50	66.79	12.02	29.49	7.13	-9.51	2.51
Afatinib (BIBW2992)	71.33	13.34	-14.26	19.82	49.65	11.59	36.86	12.00	-9.35	28.56	27.16	4.80	21.32	2.71	-17.05	4.05	50.94	1.17	32.44	2.17	-28.31	1.38
Afatinib dimaleate	85.23	6.46	-6.55	9.82	55.96	14.62	44.31	16.75	-10.49	28.50	32.67	2.89	24.45	1.99	-14.68	1.26	57.83	0.65	35.40	2.72	-24.38	4.45
Aflacitadol	72.26	2.18	-10.85	8.60	91.27	13.33	63.47	28.87	5.65	17.13	58.98	8.12	50.00	4.49	-13.91	2.51	51.84	1.89	34.43	0.40	-29.39	0.89
Aminac Sodium Monohydrate	97.65	7.52	1.98	9.97	99.46	14.17	83.57	44.31	-6.26	2.13	93.04	8.37	76.28	0.07	-6.13	14.44	114.90	22.41	47.65	4.52	20.44	15.50
Amiodarone HCl	96.65	0.21	-13.11	26.05	98.39	14.55	75.83	28.83	0.42	14.01	101.47	5.92	66.30	3.63	12.29	8.44	94.69	13.60	57.67	7.54	-9.79	8.44
Amiodipine	102.88	10.91	58.15	1.56	90.16	15.08	80.85	41.35	-12.83	10.32	93.68	2.24	79.60	5.33	-8.81	9.23	100.65	16.63	51.07	5.51	2.77	8.74
Amiodipine Besylate	93.30	2.00	-7.23	6.75	88.52	5.70	68.28	38.09	-1.91	11.14	97.49	3.98	83.59	13.31	-8.99	15.47	106.80	15.25	51.67	5.34	8.32	7.53
Anidulafungin	100.39	9.06	55.51	12.78	72.22	2.87	67.37	30.51	-17.28	4.68	82.50	3.85	68.58	3.97	-8.97	6.03	82.80	10.77	43.05	8.89	-7.05	4.26
Arbidol HCl	86.49	1.27	55.25	17.28	92.57	11.80	67.40	20.46	3.03	26.71	78.94	0.65	53.05	1.79	3.01	5.01	82.90	0.71	45.22	0.99	-9.13	1.70
Atazanavir	92.81	10.85	-48.84	3.89	84.59	11.39	59.63	20.59	2.82	18.42	80.16	8.42	56.93	1.30	0.35	0.98	91.73	4.59	54.00	1.77	-9.07	5.20
AZD-9291	57.65	3.16	-39.96	2.03	-23.32	10.37	61.79	7.10	-47.65	17.54	62.99	5.88	50.19	3.37	-10.09	3.11	52.67	7.50	34.93	2.29	-29.07	7.59
Azeldipine	93.56	2.17	58.73	20.03	-4.18	8.62	88.35	10.61	4.35	15.67	73.48	9.59	52.32	3.71	-1.72	0.26	85.90	11.10	42.98	8.08	-3.89	5.40
Bardoxolone methyl	144.51	40.06	53.53	17.02	65.28	20.58	52.10	21.69	-8.96	30.80	60.90	26.86	47.94	27.39	-9.93	5.62	59.93	0.57	30.37	3.29	-17.24	6.24
Barzoxifene HCl	120.40	15.19	64.59	23.46	14.81	0.97	91.56	4.79	-0.75	5.44	94.23	12.47	69.68	14.80	1.66	8.47	89.67	6.04	49.66	13.63	-6.80	5.21
Bedaquiline fumarate	90.68	15.66	52.93	14.53	-3.26	10.36	99.79	30.72	85.01	48.91	108.30	6.56	91.24	6.29	-5.83	6.70	97.84	4.69	49.00	8.56	2.03	1.49
Benidipine HCl	96.35	1.20	53.36	3.93	1.98	4.11	93.71	11.67	66.91	38.57	4.65	7.11	88.77	14.84	-13.35	0.74	104.83	16.97	51.37	4.05	6.65	10.55
Benzbromarone	88.43	15.47	56.35	8.89	-8.92	15.82	88.32	13.01	-10.53	5.90	92.87	4.45	79.23	9.44	-7.25	12.04	102.23	8.74	48.04	1.12	7.39	7.47
Benzlithonium Chloride	91.86	5.50	-0.71	10.78	79.59	11.09	60.93	35.38	-3.49	15.66	88.07	3.00	68.77	5.54	-3.59	8.68	66.82	2.57	36.59	2.04	-16.58	2.91
Bexarotene	105.68	8.94	51.78	17.37	12.89	0.81	141.60	17.77	14.19	11.05	106.56	2.76	82.38	2.27	1.29	6.63	91.92	1.68	35.67	3.40	9.44	0.65
Birinapant (TL32711)	82.78	0.92	42.34	11.74	-0.56	1.57	56.61	7.81	-12.58	9.71	68.49	4.91	53.47	9.94	-7.87	1.11	36.26	5.47	19.11	2.69	-29.66	5.15
Bortezomib	32.78	4.63	22.49	7.96	-30.71	5.91	24.03	2.45	-16.74	23.94	21.63	0.81	15.13	1.86	-16.39	5.09	24.92	3.40	14.37	4.44	-36.25	1.34
Bosutinib (SKI-606)	61.14	26.38	40.34	7.97	-20.21	27.65	68.38	7.47	61.57	33.90	-15.33	8.59	30.44	13.76	-18.35	10.93	55.39	16.13	37.95	0.09	-29.37	18.42
BYL-719	73.99	2.16	46.90	7.41	-13.92	0.33	83.31	7.66	63.17	20.19	-2.00	16.77	64.68	7.44	-43.42	2.03	43.42	3.52	37.90	2.15	-29.82	3.75
Cabozantinib malate (XL184)	92.86	0.07	50.81	10.11	1.04	0.80	84.43	9.45	67.45	31.46	-5.17	7.81	93.90	2.54	64.75	2.20	64.75	2.20	43.17	9.91	0.85	1.42
Calceitrol	70.83	0.99	42.09	9.54	-12.26	0.70	92.90	11.02	64.42	34.81	6.34	11.15	50.05	4.42	43.34	8.91	43.34	8.91	31.16	0.35	-31.21	1.15
Candesartan	88.48	8.50	55.50	7.05	-8.03	10.69	99.68	14.26	72.36	33.88	5.17	11.28	97.25	5.59	74.45	0.29	106.08	8.33	50.79	10.02	8.48	0.69
Chexetill	87.87	6.21	60.14	4.07	-13.28	1.05	77.00	14.13	65.01	22.35	-10.15	4.56	80.05	15.37	68.58	2.84	68.58	2.84	53.08	14.12	0.02	2.62
Carfilzomib (PR-171)	29.24	5.82	17.53	4.51	-29.30	10.55	22.86	5.00	17.31	7.77	-16.59	28.02	16.64	1.68	13.09	0.05	43.95	6.30	26.67	6.72	-29.53	2.80
Carvedilol	92.45	0.54	48.73	3.57	2.72	6.21	110.86	5.73	77.64	28.62	11.08	6.86	99.91	10.04	59.23	8.18	91.28	21.07	41.09	8.82	3.39	14.63
Cediranib (AZD2175)	81.92	29.48	47.51	3.98	-6.59	34.74	47.54	16.03	48.29	24.77	-22.89	21.71	29.20	7.88	24.46	7.40	25.61	3.63	31.60	11.34	-52.79	17.35
CEP-18770	86.20	12.54	34.14	7.11	-19.95	16.77	22.49	1.73	18.35	7.33	-18.00	24.36	25.03	2.51	18.88	2.51	131.67	12.73	96.96	22.67	-12.10	7.56
Cepharanthine	55.14	3.55	48.50	11.40	-3.36	5.61	60.59	12.01	52.58	27.08	-14.14	16.34	40.06	7.40	-10.02	6.82	80.73	5.61	38.14	9.56	-4.22	1.57
Ceftriaxone	87.76	11.68	50.09	10.55	-3.34	10.37	49.18	9.27	38.77	19.86	-11.73	19.51	75.61	7.78	66.06	2.01	74.24	0.54	38.04	1.80	-10.61	1.12
Ceftriaxone Bromide (CTAB)	92.72	9.15	52.05	11.04	-0.34	7.35	52.80	9.16	38.23	19.98	-7.58	21.25	67.60	10.70	55.26	3.47	63.39	4.04	32.22	4.01	-15.63	2.41
Chloroquine diphosphate	88.65	15.40	44.64	8.31	3.00	16.33	81.18	13.56	66.72	37.20	-7.68	7.97	68.52	13.88	48.47	4.84	77.37	16.82	34.46	10.46	-3.90	8.74
Chloroxine	93.21	13.73	55.11	15.40	-3.91	6.97	71.64	5.92	57.52	31.78	-8.03	21.39	96.68	6.69	75.42	2.47	96.49	8.42	45.94	1.24	3.75	7.28
Ciclesonide	114.92	17.77	67.53	17.20	6.38	9.91	144.81	18.24	105.46	42.57	17.20	7.07	99.54	14.32	81.59	1.56	41.32	4.53	41.32	4.53	-6.54	3.71
Cilnidipine	111.02	0.18	48.93	11.21	21.08	2.14	103.39	17.96	73.73	44.32	7.52	7.16	95.40	5.40	70.60	15.61	192.16	16.89	40.44	8.92	10.44	7.59
Cinacalcet	102.08	13.91	51.59	10.43	9.49	12.71	83.89	16.85	65.88	29.75	-4.13	18.89	78.15	0.74	59.84	0.47	91.86	1.06	46.09	1.26	-1.04	4.70

Appendix D: 176 drugs combined with afatinib in basal-like TNBC PDXs

continued

Drug	HC101 (n=2)				WHIM30 (n=3)				UCD52 (n=2)				WHIM2 (n=2)											
	Drug (1uM) alone: % viability	Drug (1uM) + Afatinib (10nM): % viability	Difference in % inhibition	±	Drug (1uM) alone: % viability	Drug (1uM) + Afatinib (10nM): % viability	Difference in % inhibition	±	Drug (1uM) alone: % viability	Drug (1uM) + Afatinib (10nM): % viability	Difference in % inhibition	±	Drug (1uM) alone: % viability	Drug (1uM) + Afatinib (10nM): % viability	Difference in % inhibition	±								
Cinacalcet HCl	94.54	8.98	58.13	3.96	-4.60	4.22	81.58	6.58	66.35	36.77	-6.91	4.81	85.72	9.30	67.73	9.75	-4.90	6.60	76.67	24.95	43.11	3.54	-13.25	23.79
Clemastine	98.52	1.22	54.64	4.09	2.87	3.93	78.71	5.95	59.67	26.72	-3.05	10.79	85.77	6.91	65.18	0.36	-2.30	1.13	103.27	12.57	53.96	2.92	2.50	7.27
Fumate	88.13	12.01	45.81	3.17	1.31	5.95	80.24	8.69	65.47	30.97	-7.38	8.74	84.85	6.80	69.63	7.96	-7.66	7.30	90.30	9.54	38.89	2.15	4.60	5.00
Clofazimine	88.77	9.42	50.58	10.23	-2.82	8.44	82.72	6.63	70.27	30.46	-9.69	7.40	91.33	7.12	75.77	0.92	-7.33	0.05	105.19	13.38	47.00	3.97	11.39	7.04
Closoanel	93.12	2.88	53.17	2.39	-1.06	3.97	88.20	11.51	69.67	32.34	-3.61	10.21	90.88	8.51	72.70	2.87	-4.71	5.23	106.00	6.44	49.11	2.03	10.08	2.03
Sodium Cobimetinib	74.94	4.39	42.23	5.98	-8.30	7.65	59.79	7.04	44.99	17.21	-7.34	23.14	52.86	10.11	36.55	2.38	-6.57	13.87	58.75	0.76	26.95	1.55	-15.01	1.59
Crenolanib (CP-868596)	97.62	7.60	56.33	7.16	0.28	9.67	71.34	24.74	54.42	25.92	-5.23	29.51	137.87	16.37	108.22	11.43	6.76	1.21	442.93	56.09	240.70	84.09	155.43	25.62
Crystall Violet	74.70	17.25	45.04	13.25	-11.35	13.24	40.79	6.75	31.96	17.64	-13.30	20.64	61.15	3.52	41.01	4.33	-2.75	1.71	51.21	4.34	28.38	3.64	-23.98	3.03
Cyclosporin A	97.08	10.92	57.41	14.38	-1.33	5.79	72.47	6.04	62.41	29.09	-12.08	6.15	59.85	11.03	51.58	2.80	-14.62	7.68	79.33	15.85	46.84	1.29	-14.32	12.18
Cyclosporine	95.59	6.00	51.12	8.62	3.47	6.62	71.37	11.17	60.24	26.36	-11.01	16.67	61.78	13.47	50.01	2.85	-11.12	4.48	95.95	0.39	55.55	7.85	-6.41	5.08
Cytarabine	75.04	2.26	44.33	6.96	-10.30	4.55	80.86	14.78	65.87	37.96	-7.16	10.81	106.16	22.15	65.68	11.36	17.59	4.65	87.10	4.29	38.33	4.50	1.97	2.17
Cytarabine hydrochloride	71.52	10.34	46.58	8.02	-16.07	11.56	90.14	3.44	70.43	33.87	-2.44	0.89	114.05	14.17	72.25	4.88	18.91	3.14	86.25	13.10	40.33	5.28	-0.88	10.20
Dactasvir (BMS-790052)	85.12	1.78	48.34	0.32	-4.23	10.70	82.83	9.97	59.72	28.55	0.97	15.84	82.59	2.26	59.05	3.45	0.64	0.43	93.69	8.00	46.31	4.28	0.57	6.10
Dacomitinib (PF299804, PF299)	70.79	0.57	45.09	3.03	-15.30	6.78	54.64	6.09	39.67	10.15	-7.17	18.56	39.96	8.08	32.96	3.97	-15.89	2.04	43.92	3.68	29.78	0.31	-32.67	5.75
Dasatinib (BMS-354825)	78.65	5.84	41.52	7.54	-3.88	7.54	55.60	11.08	40.99	16.22	-7.53	24.81	39.75	2.69	27.59	2.84	-10.73	6.30	67.66	4.63	30.80	3.40	-9.94	1.14
Dauorubicin	127.55	52.95	70.73	25.14	15.82	37.05	47.99	25.89	27.20	17.85	-1.35	20.86	27.80	3.91	20.85	1.20	-15.94	8.85	23.11	4.29	9.65	0.10	-33.35	2.01
Deferasirox	87.89	6.32	43.21	2.20	3.67	13.36	98.21	12.56	81.34	40.37	-5.27	13.01	92.02	5.54	68.16	5.10	0.97	6.58	92.17	12.87	42.20	9.21	3.17	6.04
Digoxin	50.60	23.10	27.75	7.22	-18.16	6.64	25.72	2.23	21.80	10.05	-18.22	23.29	25.28	3.05	19.50	0.72	-17.11	3.81	137.50	47.92	61.33	33.28	29.36	17.02
Dinaciclib (SCH727965)	46.81	8.79	25.61	3.54	-19.80	14.48	34.91	10.00	29.05	15.05	-16.29	24.47	29.21	7.74	21.39	4.24	-15.07	2.64	38.13	15.21	16.39	4.39	-25.07	8.43
Domiphen Bromide	88.48	7.31	50.97	6.24	-3.49	10.31	57.15	5.98	49.36	21.31	-14.35	15.59	80.40	12.25	65.29	0.33	-7.77	5.78	81.71	1.46	41.61	2.19	-6.71	1.27
Dovitinib Dilactate	102.90	14.37	42.28	1.93	19.61	7.06	77.82	18.72	50.40	20.81	5.27	30.23	89.57	36.71	56.71	17.38	9.97	13.19	96.95	7.74	30.35	1.81	19.79	8.32
Doxercalciferol	75.30	3.03	44.83	7.62	-10.55	1.41	93.14	9.16	71.38	29.68	-0.38	11.98	63.61	6.94	47.62	5.94	-6.90	6.74	61.82	5.18	37.08	2.17	-22.07	4.98
Doxorubicin	80.15	3.50	43.79	3.09	-4.66	2.65	44.16	12.41	35.22	18.46	-13.21	22.46	42.14	3.97	28.51	1.44	-9.26	0.73	30.43	2.88	15.61	0.89	-31.98	1.39
Doxorubicin (Adriamycin) HCl	93.56	11.31	49.50	1.18	3.06	0.89	45.93	17.82	30.98	15.50	-7.19	30.83	38.73	1.71	40.85	20.87	-25.01	13.03	26.75	2.02	13.65	1.15	-33.70	1.50
Dronedarone	98.74	8.87	48.10	9.23	9.64	8.88	79.83	11.86	59.33	24.97	-1.64	18.31	81.42	2.83	57.65	5.43	0.88	8.75	91.75	4.12	44.14	0.69	0.81	5.81
HCl	109.85	11.47	54.38	10.30	14.47	10.41	76.23	9.88	58.15	28.63	-4.06	12.32	86.45	8.09	63.56	0.79	0.01	1.16	106.30	0.33	52.48	8.28	7.01	6.24
Dutoxetine HCl	85.40	7.77	45.29	3.59	-0.90	13.42	79.74	17.07	61.57	32.66	-3.97	13.19	95.38	0.30	59.79	1.71	12.70	7.55	91.07	9.51	41.07	9.01	3.19	2.88
Ebastine	94.37	1.04	48.25	9.98	5.12	0.29	83.40	7.54	65.83	29.73	-4.57	9.01	87.53	2.93	70.12	2.61	-5.48	0.60	106.54	15.74	50.33	4.34	9.40	17.70
Econazole nitrate	101.29	8.58	55.79	10.11	4.49	7.71	92.67	8.85	68.80	30.89	1.73	9.12	92.02	2.69	62.19	3.65	6.94	0.19	115.34	3.33	55.77	5.35	12.76	6.30
Eltrombopag	85.76	1.88	52.92	10.08	-8.17	1.03	96.23	21.65	78.81	34.66	-2.72	18.30	94.64	6.32	77.07	4.69	-5.31	4.52	101.16	3.44	48.50	8.92	5.85	3.10
Embellin	92.78	3.57	52.93	13.78	-1.15	0.97	85.62	17.19	70.21	35.61	-6.73	12.60	86.81	13.76	67.80	0.10	-3.88	19.80	93.47	5.05	42.87	9.89	3.79	2.46
EMD-1214063	83.23	10.78	39.95	5.18	2.28	14.84	79.56	17.60	56.77	28.87	0.65	20.20	79.15	0.10	60.47	1.37	-4.21	4.68	97.76	1.02	50.99	0.02	-0.03	1.34
Entrectinib	92.33	13.69	57.52	22.20	-6.20	0.73	71.90	17.56	52.20	24.71	-2.44	24.01	72.55	17.20	54.30	5.37	-4.64	16.42	81.73	10.61	38.53	8.62	-3.61	4.38
Eprubicin HCl	105.20	8.35	57.99	6.95	6.20	7.84	46.38	19.77	30.68	16.06	-6.44	35.52	35.92	2.68	28.01	2.68	-14.97	5.30	22.24	3.32	10.17	0.95	-34.74	0.01
Ertotibin	62.63	1.86	41.14	5.99	-19.52	5.12	65.00	9.06	63.75	24.86	-20.90	10.10	59.75	6.71	55.04	4.94	-18.17	7.91	53.71	4.39	42.04	4.77	-35.14	11.55
Ertotibin Hydrochloride	63.09	3.47	47.73	9.19	-25.65	3.42	80.49	3.98	54.74	16.66	3.60	18.14	68.33	0.42	54.50	4.05	-9.06	1.68	50.12	0.14	37.46	6.58	-34.15	8.82
Ethacridine lactate	83.71	4.06	52.47	8.71	-9.77	4.60	68.29	5.79	49.71	20.13	-3.56	14.44	95.65	9.50	70.48	6.27	2.28	9.63	58.78	1.10	31.05	4.34	-19.08	0.86
Fenticonazole Nitrate	89.62	12.44	49.15	9.17	-0.54	12.51	91.45	17.62	69.60	32.22	-0.29	16.92	92.52	5.81	59.86	1.55	9.78	1.22	107.20	13.16	49.92	9.76	10.47	5.78
Fidaxomicin	99.29	6.57	56.18	5.13	2.10	10.68	102.06	11.13	87.62	44.99	-7.71	3.52	109.56	6.16	81.86	0.03	4.81	12.34	122.13	15.38	51.89	2.65	23.43	10.35
Fingolimod (FTY720)	97.68	10.02	53.66	15.01	3.01	4.25	84.30	22.14	69.64	36.35	-7.49	14.99	87.93	0.36	69.91	4.33	-4.86	10.12	92.19	12.86	44.50	12.29	0.88	2.95

Appendix D: 176 drugs combined with afatinib in basal-like TNBC PDXs

continued

Drug	HC101 (n=2)				WHIM30 (n=3)				UCD52 (n=2)				WHIM2 (n=2)								
	Drug (1uM) alone: % viability	Drug (1uM) + Afatinib (10nM): % viability	Difference in % inhibition	Drug (1uM) alone: % viability	Drug (1uM) + Afatinib (10nM): % viability	Difference in % inhibition	Drug (1uM) alone: % viability	Drug (1uM) + Afatinib (10nM): % viability	Difference in % inhibition	Drug (1uM) alone: % viability	Drug (1uM) + Afatinib (10nM): % viability	Difference in % inhibition	Drug (1uM) alone: % viability	Drug (1uM) + Afatinib (10nM): % viability	Difference in % inhibition						
Flunarizine 2HCl	106.11	9.27	1.70	1.83	88.94	7.10	75.95	41.63	-9.15	6.70	94.08	4.23	76.98	6.60	100.89	12.71	50.63	4.94	3.45	5.39	
Fluoxetine HCl	91.08	8.89	46.38	3.07	84.10	15.33	65.02	28.27	-3.06	18.41	75.56	8.76	59.06	0.71	99.14	7.35	43.79	2.98	8.55	1.99	
Foretinib (GSK1363089)	89.12	10.03	33.90	4.77	70.19	17.64	44.75	12.90	3.30	36.10	48.20	29.84	28.48	6.31	71.18	9.68	37.74	11.36	-13.37	4.06	
Fosamatinib (R788)	116.01	7.87	64.17	12.86	112.01	18.07	82.06	33.25	7.80	16.18	92.28	2.11	74.85	7.23	79.01	13.89	41.25	13.41	-9.05	2.86	
Gallic acid	96.36	1.23	51.42	11.91	102.30	7.30	83.69	38.88	-3.53	4.54	97.14	12.81	73.64	2.56	82.15	10.94	46.34	13.98	-11.00	0.66	
Ganetespib (STA9090)	83.87	11.91	49.12	13.99	7.16	138.28	43.86	75.99	36.30	40.15	35.80	46.58	0.37	30.87	0.27	55.22	4.91	29.08	3.86	-20.67	3.43
GSK2126458	52.97	13.67	28.69	3.18	-16.73	19.73	48.03	6.54	35.25	13.66	-9.37	25.00	23.24	2.89	15.79	1.86	15.72	0.57	-30.58	3.67	
Idarubicin HCl	331.11	185.17	130.99	45.82	159.12	148.59	41.22	11.11	26.75	12.44	-7.68	30.49	24.33	1.70	28.75	0.85	11.73	0.91	-29.78	2.44	
Idebenone	91.14	8.67	58.79	11.26	-8.67	6.65	73.72	32.19	-1.41	4.58	90.23	7.37	62.69	3.79	107.31	2.64	50.05	8.85	10.45	9.11	
Isoconazole	123.17	9.89	63.77	12.37	18.39	6.76	86.92	49.51	-3.69	26.78	111.88	6.53	78.27	1.93	126.16	18.89	52.15	0.79	27.20	15.72	
Ispinesib (SB-715992)	98.73	6.81	50.53	8.19	7.19	7.86	78.04	20.14	-3.57	19.69	47.70	3.86	35.95	1.10	-11.14	3.38	62.49	27.29	-20.15	22.81	
Ivermectin	90.56	11.20	45.95	1.94	3.61	18.50	73.32	11.14	-3.04	21.76	57.56	22.24	45.82	13.09	-11.14	3.00	86.62	9.48	-4.67	2.69	
KPT-330	67.37	9.23	39.27	13.04	-12.90	5.42	31.30	19.73	-11.60	11.62	59.45	23.51	52.22	27.70	-15.66	10.33	66.08	6.35	-22.57	0.28	
Lapatinib	71.71	8.14	41.59	3.51	-10.88	4.61	61.14	17.79	-20.05	14.55	57.12	14.42	41.52	1.15	-7.30	9.42	36.67	5.75	-27.27	7.08	
Ditosylate LDK378	76.39	3.13	44.39	5.47	-9.01	0.65	47.86	4.67	-10.13	19.78	45.75	3.33	28.70	8.05	-5.83	17.51	36.68	4.20	-20.35	4.17	
Lenvatinib (E7060)	89.06	1.40	39.98	4.28	8.06	6.36	94.08	10.67	16.83	16.56	56.21	17.15	39.79	9.72	-6.47	1.29	82.97	11.50	32.50	2.43	
Levosimendan	89.15	2.06	52.71	10.55	-4.56	3.37	96.67	11.07	7.10	37.53	102.63	13.51	75.01	1.89	-2.66	5.68	113.55	7.99	51.16	3.53	
Licocholine	124.59	7.43	66.14	12.10	17.45	4.57	97.09	6.72	-6.89	17.95	102.63	10.23	72.70	1.18	7.03	15.20	90.31	3.69	46.84	8.26	
Lithocholic Acid	89.20	4.02	45.05	2.04	3.14	11.22	91.49	7.08	5.74	16.67	96.65	2.82	52.61	5.10	21.15	1.78	92.93	12.90	40.51	9.41	
Lomerizine HCl	85.24	11.62	57.74	6.65	-13.50	14.21	92.25	8.14	-5.96	2.23	90.79	1.57	68.68	0.76	-0.98	5.33	98.62	2.18	50.92	2.07	
Lomitapide	92.15	4.54	55.04	12.15	-3.89	1.63	63.85	4.00	-11.24	15.83	56.31	8.76	43.93	1.28	-10.51	1.34	62.68	45.47	27.42	14.20	
LY2228220	67.65	7.92	35.88	8.94	-9.24	8.22	61.08	10.74	-8.25	22.37	46.38	5.86	30.31	1.19	-6.82	0.91	65.44	2.97	35.38	0.69	
LY2835219	83.95	12.95	40.50	5.84	2.44	16.64	52.84	28.99	-5.42	30.94	46.66	16.71	40.55	9.47	-16.78	13.39	130.29	3.92	82.24	13.50	
Maprotiline HCl	90.93	3.57	55.09	13.84	-5.17	8.17	83.30	8.91	-0.27	13.05	81.06	2.18	61.44	2.69	-3.27	1.27	93.21	14.92	45.98	11.38	
Mastlabin (AB1010)	112.60	14.62	47.79	3.76	23.81	20.10	84.62	14.60	0.33	27.33	85.93	14.95	64.52	7.11	-1.48	1.70	114.16	21.68	54.71	22.01	
Mechlorethamine HCl	91.46	1.77	52.27	11.03	-1.82	0.02	140.20	16.01	17.73	21.75	121.24	7.32	99.27	2.30	-0.91	3.48	83.65	6.74	43.21	0.03	
Mecizine 2HCl	136.42	22.34	65.37	30.55	30.04	1.04	99.51	6.71	-11.07	6.96	93.38	0.95	68.60	3.76	1.89	10.86	97.98	15.13	53.14	16.99	
Mefloquine hydrochloride	97.49	4.43	49.27	6.63	7.22	7.04	74.00	12.75	-9.29	25.92	65.97	10.95	50.29	2.71	-7.21	2.09	102.56	2.74	55.93	3.50	
MEK162 (ARRY-162, ARRY-438162)	71.63	10.87	40.47	5.45	-9.85	14.66	69.91	14.85	-9.92	8.54	59.94	8.65	54.00	2.53	-16.95	5.04	80.70	8.23	34.83	6.25	
Menadione	98.56	1.43	55.77	11.32	1.79	3.51	98.22	14.50	1.41	8.05	94.20	8.95	74.61	2.01	-3.30	4.82	106.23	5.56	50.25	5.58	
Miconazole Nitrate	100.42	17.66	63.92	19.14	-4.51	7.76	95.88	15.18	-1.12	10.06	96.95	7.59	76.26	5.61	-2.20	4.16	110.76	6.23	52.15	7.17	
Miltefosine	89.62	1.57	56.74	12.95	-8.13	5.29	92.60	8.30	-2.04	17.54	101.17	12.63	69.48	10.07	8.80	8.70	85.78	15.27	49.31	9.21	
Mitoxycine HCl	103.19	6.71	66.60	25.43	-4.42	9.49	102.25	11.57	-5.37	3.37	100.43	4.50	75.89	3.87	1.85	6.78	91.25	7.42	49.87	14.15	
Mitomycin C	59.31	2.66	36.01	3.84	-17.71	2.74	66.89	11.65	-3.37	18.01	88.25	7.28	58.44	8.42	6.93	7.28	75.39	4.77	35.06	3.11	
Mitoxantrone HCl	105.42	26.05	61.65	1.71	2.76	15.10	37.22	20.68	-11.42	25.82	36.22	7.35	32.23	9.43	-18.90	4.06	27.28	3.37	13.54	2.41	
MLN2238	51.71	6.65	36.98	6.08	-26.27	9.81	23.06	2.23	-16.69	25.91	24.91	0.19	18.12	0.98	-16.10	4.98	129.68	18.44	94.26	16.99	
Nababucasin	30.13	7.79	16.22	1.67	-27.10	15.37	33.89	6.31	24.19	11.23	29.58	4.65	17.35	1.74	-10.66	0.25	50.29	6.00	29.68	3.08	
Nebivolol	91.12	2.87	47.07	3.17	3.04	3.20	103.01	7.76	3.23	11.46	92.33	4.16	64.86	8.23	4.58	2.07	91.49	15.01	44.72	5.42	
Necaplathin	85.06	0.14	49.94	8.97	-5.89	0.14	79.37	15.58	-9.76	11.60	102.98	16.92	82.82	7.81	-2.53	2.97	104.97	0.27	48.47	8.93	
Nelfinavir Mesylate	90.13	6.98	44.53	10.81	4.59	5.41	81.37	11.62	-11.42	9.93	61.63	13.74	47.94	5.56	-9.21	2.04	100.65	5.45	53.61	5.30	
Neratinib (HK1272)	78.45	17.49	60.88	18.60	-23.44	8.12	68.91	11.92	-16.19	19.71	43.87	10.86	50.90	10.04	-29.93	27.04	36.36	3.57	25.54	1.56	
Nicardipine HCl	107.83	2.17	58.68	15.48	8.15	4.07	100.50	9.14	0.49	7.37	94.40	0.77	69.61	1.44	1.91	3.93	93.52	15.14	48.04	13.40	
Nifuroxazide	78.79	0.21	50.83	9.31	-13.05	0.28	77.48	13.73	-13.96	11.87	91.13	0.39	79.36	5.06	-11.12	0.70	95.31	7.48	48.76	1.18	

Appendix D: 176 drugs combined with afatinib in basal-like TNBC PDXs

continued

Drug	HC101 (n=2)				WHIM30 (n=3)				UCD52 (n=2)				WHIM2 (n=2)											
	Drug (1uM) alone: % viability	Drug (1uM) + Afatinib (10nM): % viability	Difference in % inhibition	±	Drug (1uM) alone: % viability	Drug (1uM) + Afatinib (10nM): % viability	Difference in % inhibition	±	Drug (1uM) alone: % viability	Drug (1uM) + Afatinib (10nM): % viability	Difference in % inhibition	±	Drug (1uM) alone: % viability	Drug (1uM) + Afatinib (10nM): % viability	Difference in % inhibition	±								
Nilotinib(AMIN-107)	78.20	14.33	45.86	2.10	-8.67	7.19	75.25	4.42	58.91	20.65	-5.80	8.89	77.54	14.63	56.11	9.46	-1.46	0.98	88.00	2.61	63.21	1.37	-22.01	3.62
Nintedanib (BIBF 1120)	83.06	7.32	45.00	5.46	-2.95	11.10	51.20	18.00	43.00	22.25	-13.95	24.61	46.00	12.43	19.63	5.29	3.48	0.99	46.61	1.67	22.49	2.68	-22.69	1.37
Oflonum Bromide	91.28	2.45	52.91	0.04	-2.64	11.64	90.70	4.89	76.18	38.29	-7.62	13.78	100.18	2.23	78.59	0.77	-1.30	3.15	104.90	17.81	53.94	4.27	4.15	11.16
Oxethazaine	87.28	4.51	49.12	0.51	-2.85	14.26	88.40	14.20	66.48	27.27	-0.23	16.41	93.61	5.08	62.87	4.70	7.86	5.77	88.45	8.34	41.39	9.07	0.26	1.65
Paclitaxel	70.46	13.73	37.80	0.84	-8.35	3.65	47.30	7.93	40.61	16.50	-15.45	22.34	49.06	0.94	47.92	4.02	-21.75	11.70	77.30	13.80	38.83	8.32	-8.33	7.86
Paroxetine HCl	91.57	0.96	52.26	9.29	-1.70	0.91	87.44	15.87	65.49	30.28	-0.19	17.02	79.66	5.18	60.41	0.62	60.41	0.97	100.43	5.65	49.57	11.26	4.06	3.24
Pelitinib (EKB-569)	98.53	29.33	72.13	0.67	-14.61	37.90	46.05	17.84	38.26	18.03	-14.35	26.34	27.01	4.17	28.64	5.89	-24.51	4.42	31.40	1.95	22.09	6.77	-37.49	7.20
Pimavanserin	93.47	7.49	52.83	10.88	-0.37	5.86	88.00	14.38	69.40	32.98	-3.54	12.24	83.58	10.73	65.24	1.83	-4.55	6.41	102.81	12.59	50.81	13.58	5.20	1.39
Pimicrotinolimus	101.60	8.30	51.16	11.29	9.44	6.25	85.96	11.64	66.65	31.59	-2.84	11.12	89.02	14.20	70.72	7.96	-4.58	0.09	82.40	1.10	42.57	6.40	-6.97	5.12
Ponatinib	84.54	28.66	44.49	7.44	-0.96	11.98	59.38	24.69	50.89	32.68	-13.66	20.96	36.25	6.43	29.30	11.28	-15.94	10.99	79.09	17.54	36.05	4.21	-3.76	19.37
Pozotinib	62.35	6.62	42.90	5.83	-21.56	3.21	50.72	14.12	47.25	23.97	-18.67	23.16	36.50	7.81	27.63	2.74	-14.03	1.07	32.90	2.64	22.19	2.79	-36.10	2.24
Profavine	91.42	8.15	59.56	11.81	-9.15	5.57	58.76	8.81	44.08	22.91	-7.46	16.36	139.33	18.19	115.65	7.56	0.79	4.49	51.29	2.64	29.50	3.15	-25.02	1.87
Purromycin dihydrochloride	93.78	3.71	69.52	18.09	-16.75	5.14	76.75	30.71	64.01	42.82	-9.40	22.48	22.30	1.60	18.22	1.14	-18.81	3.40	86.86	40.75	82.56	41.71	-42.51	1.42
Rapamycin (Stromolimus)	78.13	5.95	50.99	5.31	-13.87	9.88	75.42	12.33	60.82	26.18	-7.54	16.55	52.55	2.01	42.53	2.25	-12.87	1.88	68.31	3.56	39.32	2.69	-17.82	3.26
Regorafenib	102.82	5.12	48.79	7.66	15.02	6.70	89.87	16.94	67.54	33.62	0.19	6.36	80.74	25.92	55.93	22.46	1.92	2.69	99.60	5.20	44.21	5.23	8.99	8.05
Regorafenib hydrochloride	104.12	5.13	52.01	16.72	11.10	2.35	98.72	13.86	67.45	29.20	9.13	15.91	71.48	11.09	53.34	16.50	-4.74	11.55	104.19	2.64	43.29	1.45	14.10	1.71
RG7388	95.09	5.65	49.08	14.65	5.00	0.23	91.30	14.98	73.76	39.06	-4.60	8.21	89.06	1.68	60.38	1.23	5.79	3.23	99.12	2.08	44.66	2.34	7.65	2.04
Ritaparitin	93.71	0.92	56.23	15.78	-3.52	5.61	95.82	16.46	74.68	36.29	-1.00	11.61	88.83	5.18	72.18	1.66	-6.24	2.62	100.75	3.11	46.15	5.69	10.79	6.42
Rimnabant	87.37	7.02	56.74	7.94	-10.37	8.32	82.57	11.63	66.57	32.02	-6.14	20.09	91.06	9.27	75.01	15.96	-6.84	12.84	100.32	21.22	48.44	10.42	5.07	8.42
Ritonavir	88.23	2.36	49.12	3.46	-1.89	3.42	91.13	8.59	62.79	22.42	6.20	15.41	82.12	7.10	62.55	0.79	-3.32	0.18	88.45	0.59	49.00	3.13	-7.36	1.35
Rosuvastatin Calcium	96.17	6.25	51.45	8.75	3.71	6.74	84.83	12.27	66.16	24.95	-3.48	18.81	83.05	2.31	55.22	6.78	4.94	15.23	83.43	8.89	44.15	10.35	-7.53	0.92
Saquinavir mesylate	96.90	11.67	48.22	12.20	7.67	8.70	99.36	23.10	78.40	40.29	-1.19	17.27	89.52	9.70	61.15	2.12	5.49	1.44	105.29	2.68	47.86	3.23	10.62	3.54
Saracatinib (AZD0530)	67.94	19.30	41.13	8.67	-14.19	19.87	57.48	9.67	50.75	22.83	-15.41	11.79	38.67	0.18	37.93	9.63	-22.15	3.31	33.87	2.29	24.50	4.61	-37.44	9.27
Setratraline HCl	92.92	4.72	53.41	9.16	-1.50	4.80	85.22	5.80	54.39	29.44	8.68	13.11	78.57	12.83	56.44	6.38	-0.76	0.31	101.25	4.34	49.16	9.43	5.28	2.71
Simeprevir	103.81	1.03	53.88	13.18	8.92	2.91	86.72	11.13	74.53	31.38	-9.95	4.02	90.36	2.23	64.52	6.43	2.95	2.52	106.03	2.83	46.76	2.18	12.46	3.03
Sorafenib	107.20	23.02	49.63	10.79	16.57	21.47	78.01	10.06	55.94	20.36	-0.07	21.91	67.71	1.36	52.16	5.09	-7.34	0.31	92.63	6.90	48.49	11.63	-2.66	7.11
Sorafenib Tosylate	90.63	7.83	46.61	6.78	3.01	10.29	65.17	4.75	53.41	22.51	-10.38	14.18	74.52	16.50	42.27	14.20	9.36	3.84	81.70	1.97	42.39	5.51	-7.50	1.16
Sulectazole Nitrate	95.23	11.30	62.78	16.70	-8.55	3.84	92.95	13.93	75.31	38.90	-4.50	6.15	96.49	16.22	74.14	5.44	-0.54	4.64	108.41	1.86	49.51	5.85	12.10	1.61
Sumitinib	81.14	0.26	38.81	4.81	1.33	4.17	86.75	13.61	62.82	24.26	1.78	11.91	73.03	14.80	50.42	3.99	-0.28	4.67	66.00	26.48	25.66	9.01	-6.47	19.85
Sumitinib malate	73.39	1.23	42.00	2.24	-9.62	8.23	69.19	9.06	50.88	23.77	-3.83	16.55	64.56	6.53	43.62	7.47	-1.94	7.07	96.05	9.93	44.22	13.56	5.02	1.25
Tamoxifen Citrate	110.51	6.89	64.98	20.65	4.52	4.71	99.90	3.76	74.07	29.92	3.69	3.93	100.86	3.67	69.48	1.08	8.49	8.73	86.20	16.20	50.98	2.26	-11.58	16.32
Temsirolimus	76.22	6.85	45.93	8.58	-10.72	7.51	74.24	11.66	60.54	26.27	-8.45	16.36	55.11	1.76	40.43	1.09	-8.20	5.48	80.02	12.85	43.96	8.62	-10.74	6.61
Terfenadine	89.00	3.88	52.79	8.74	-4.80	4.39	73.07	10.82	54.46	23.49	-3.53	17.05	79.91	7.90	59.10	1.31	-2.08	0.44	81.10	8.35	51.10	6.16	-16.80	12.13
Thioridazine HCl	87.04	11.00	61.80	25.36	-15.77	5.11	84.66	8.30	67.56	25.72	-5.05	14.53	82.53	3.27	58.07	1.61	1.57	4.48	92.41	8.08	47.38	6.04	-1.78	4.41
Ticagrelor	97.79	2.15	57.82	16.05	-1.04	4.66	75.54	7.63	55.70	27.72	-2.30	16.66	90.99	14.29	72.18	0.62	-4.08	8.76	89.67	5.49	42.96	6.96	-0.10	0.91
Ticlopidine HCl	99.35	10.81	57.83	10.64	0.52	9.41	91.88	18.34	65.94	31.21	0.80	18.05	97.40	9.92	75.93	1.94	-1.42	5.72	99.59	10.06	47.90	8.28	4.88	4.16
Ticozanole	98.74	8.64	65.42	20.79	-7.69	2.91	90.12	8.05	74.17	34.25	-6.19	4.65	104.04	15.30	81.79	6.92	-0.64	16.08	111.09	1.25	47.48	5.32	16.80	1.69
Tivozanib (AV-951)	91.01	10.21	43.87	2.08	6.13	17.36	85.05	16.21	45.95	12.10	16.96	34.76	104.16	15.71	40.16	7.49	-1.66	2.07	94.33	1.45	39.84	6.08	7.69	7.01
Tofenamic Acid	95.92	2.08	57.26	2.65	-2.34	4.52	92.60	6.46	78.75	36.57	-8.29	8.98	101.55	14.45	78.45	0.21	7.85	10.42	106.42	16.51	50.95	8.47	8.66	5.66
Toltrazuril	90.80	6.28	58.15	10.03	-8.35	5.49	90.84	13.00	70.20	33.76	-1.50	10.14	97.59	2.74	76.12	5.60	-1.41	2.20	105.43	3.12	48.44	3.24	10.18	2.26
Topotecan	65.95	5.93	40.10	7.90	-15.17	6.97	37.38	7.48	30.85	15.15	-15.62	23.15	100.61	11.72	76.38	2.93	1.34	14.93	95.51	0.46	31.41	2.90	-21.71	0.98
Topotecan HCl	65.37	3.65	41.36	8.28	-17.00	4.91	41.66	8.93	31.00	14.72	-11.48	25.29	93.37	21.27	66.51	3.87	3.98	23.55	49.57	4.65	25.23	0.07	-22.46	2.20
Toremifene Citrate	127.38	2.46	70.84	6.96	15.54	0.18	102.08	11.06	85.37	39.14	-5.43	2.05	98.41	5.67	77.40	5.56	-1.88	6.04	118.56	22.56	55.72	4.22	16.02	15.96

Appendix D: 176 drugs combined with afatinib in basal-like TNBC PDXs

continued

Drug	HC101 (n=2)				WHIM30 (n=3)				UCD52 (n=2)				WHIM2 (n=2)											
	Drug (1uM) alone: % viability	±	Drug (1uM) + Afatinib (10nM): % viability	Difference in % inhibition ±	Drug (1uM) alone: % viability	±	Drug (1uM) + Afatinib (10nM): % viability	Difference in % inhibition ±	Drug (1uM) alone: % viability	±	Drug (1uM) + Afatinib (10nM): % viability	Difference in % inhibition ±	Drug (1uM) alone: % viability	±	Drug (1uM) + Afatinib (10nM): % viability	Difference in % inhibition ±								
Trifluoperazine 2HCl	95.65	7.68	56.06	2.29	-1.42	14.62	84.86	17.24	70.60	39.61	-7.88	7.99	82.13	1.14	73.12	0.40	-13.87	6.89	102.32	26.43	43.98	6.05	11.54	17.99
Vandetanib (ZD6474)	70.04	3.49	47.30	11.86	-18.26	0.87	64.80	9.80	52.08	21.69	-9.42	16.25	46.49	11.70	36.24	9.60	-12.63	4.05	37.51	8.93	24.39	1.27	-33.69	5.28
Vehicle/Anchor drug alone	100.00	0.00	58.99	9.24	0.00	0.00	100.00	0.00	77.86	31.03	0.00	0.00	100.00	0.00	77.11	6.14	0.00	0.00	100.00	0.00	53.19	2.38	0.00	0.00
Vortioxetine (LU AA21004) HBr	112.59	23.99	49.67	1.85	21.91	31.38	80.61	20.05	53.29	24.68	5.18	26.06	71.19	11.35	55.40	5.22	-7.10	0.01	101.61	11.72	46.73	6.17	8.07	3.17
VRT752271	84.84	5.49	50.67	20.92	-6.84	6.19	78.38	11.36	59.26	22.82	-3.03	20.39	59.08	2.45	50.51	3.34	-14.32	11.94	72.73	9.64	30.28	7.50	-4.35	4.52
YM155	29.61	1.00	18.27	1.50	-29.66	6.74	27.03	2.32	20.24	7.91	-15.35	22.00	21.27	0.30	15.24	0.19	-16.86	5.66	21.09	0.19	11.78	0.96	-37.49	3.53
Zafitukast	93.59	4.57	61.43	12.12	-8.84	1.69	97.17	12.95	74.27	34.64	0.75	12.71	95.29	6.09	71.58	4.33	0.83	4.28	110.51	0.90	52.15	9.69	11.56	6.41
Zinc Pyrrithione	52.05	12.93	47.43	18.10	-36.39	4.07	65.28	28.95	54.06	44.11	-10.93	25.21	67.22	10.50	55.96	5.18	-11.63	21.82	70.16	13.74	33.87	4.44	-10.52	20.56
Ziprasidone hydrochloride monohydrate	88.52	2.26	46.68	9.71	0.84	1.79	94.57	14.78	72.59	31.17	-0.16	19.85	94.74	3.02	70.26	8.30	1.59	5.17	94.55	2.24	45.21	2.30	2.53	2.17

APPENDIX E

Adapted from [190]

Appendix E: Statistical analyses for 176 drugs combined with carfilzomib in basal-like TNBC PDXs

Significant p-values (p<0.05, unpaired t-test) are bolded and italicized.

Drug	Difference in % inhibition across 4 PDXs		Supra-additive with carfilzomib (mean difference in % inhibition >0)		Sub-additive with carfilzomib (mean difference in % inhibition <0)					
	Lower 95% CI of mean	Upper 95% CI of mean	P-value	Proportion of PDXs (n=4)	Lower 95% CI	Upper 95% CI				
(R)-Crizotinib	-23.26	17.38	0.6764817	0.25	0.699358157	0.012823324	0.987176676	0.75	0.987176676	0.300641843
5-Azacytidine	-25.59	7.875	0.190650006	0	0.489890836	0	1	1	0.489890836	0.510109164
ABT-263 (Navitoclax)	-30.23	25.55	0.80676487	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378	0.088840378
Afatinib (BIBW2992)	-48.73	15.69	0.20108323	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843	0.300641843
Afatinib dimaleate	-42.92	9.137	0.130835398	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843	0.300641843
Alfacaicidol	-41.86	15.72	0.244213295	0	0.489890836	0	1	1	0.489890836	0.510109164
Amitenac Sodium Mor	-6.117	13.23	0.326426824	1	1	0.510109164	0	0	0.489890836	0
Amiodarone HCl	-17.26	16.8	0.9682901	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378	0.088840378
Amiodipine	-32.41	17.83	0.423806696	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843	0.300641843
Amiodipine Besylate	-26.14	15.91	0.495317106	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378	0.088840378
Amidulafungin	-22.61	11.54	0.378255807	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843	0.300641843
Arbidol HCl	-13.05	-2.998	0.014734302	0	0.489890836	0	1	1	0.489890836	0.510109164
Atazanavir	-15.7	-4.925	0.00897281	0	0.489890836	0	1	1	0.489890836	0.510109164
AZD-9291	-39.56	5.434	0.094701316	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843	0.300641843
Azelethidine	-41.82	25.81	0.505987016	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378	0.088840378
Bardoxolone methyl	-43.34	15.62	0.231384088	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843	0.300641843
Bazedoxifene HCl	-7.749	11.46	0.582264909	0.75	0.987176676	0.300641843	0.25	0.699358157	0.012823324	0.012823324
Bedaquiline fumarate	-11.32	15.04	0.683522405	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378	0.088840378
Benidipine HCl	-31.29	24.04	0.704932268	0.75	0.987176676	0.300641843	0.25	0.699358157	0.012823324	0.012823324
Benzbromarone	-19.18	6.795	0.226468791	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843	0.300641843
Benzthionium Chlorid	-10.61	3.828	0.23174137	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843	0.300641843
Bexarotene	-10.4	43.76	0.144777218	1	1	0.510109164	0	0	0.489890836	0
Bitriapant (TL32711)	-31.47	15.17	0.347224764	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843	0.300641843
Bortezomib	-60.23	12.36	0.126718546	0	0.489890836	0	1	1	0.489890836	0.510109164
Bosutinib (SKI-606)	-33.27	-22.66	0.00461077	0	0.489890836	0	1	1	0.489890836	0.510109164
BYL-719	-23.2	0.04904	0.050518652	0	0.489890836	0	1	1	0.489890836	0.510109164
Cabozantinib malate (-12.51	11.61	0.912740288	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843	0.300641843
Calcitriol	-47.4	15.52	0.205278955	0	0.489890836	0	1	1	0.489890836	0.510109164
Candesartan Cilexetil	-11.74	14.17	0.785224949	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378	0.088840378
Carboplatin	-29.36	5.177	0.112157402	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843	0.300641843
Carfilzomib (PR-171)	-67.82	13.81	0.125871073	0	0.489890836	0	1	1	0.489890836	0.510109164
Carvedilol	-5.833	25.54	0.139451656	0.75	0.987176676	0.300641843	0.25	0.699358157	0.012823324	0.012823324
Cediranib (AZD217)	-41.79	-11.99	0.010485471	0	0.489890836	0	1	1	0.489890836	0.510109164
CEP-18770	-84.51	65.22	0.709308408	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843	0.300641843
Cepharanthine	-49.53	41.76	0.804167128	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843	0.300641843
Cetrimonium Bromide	-39.63	13.71	0.219774566	0	0.489890836	0	1	1	0.489890836	0.510109164
Cetylpyridinium Chlorid	-36.03	12.63	0.223363378	0	0.489890836	0	1	1	0.489890836	0.510109164
Chloroquine diphosph	-26.03	34.41	0.688673344	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378	0.088840378
Chloroxine	-26.91	12.61	0.333183697	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843	0.300641843
Ciclesonide	-24.68	44.59	0.427806536	0.75	0.987176676	0.300641843	0.25	0.699358157	0.012823324	0.012823324
Cilindipine	-13.99	17.43	0.750819489	0.75	0.987176676	0.300641843	0.25	0.699358157	0.012823324	0.012823324
Cinacalcet	-11.72	1.99	0.109105886	0	0.489890836	0	1	1	0.489890836	0.510109164
Cinacalcet HCl	-19.04	2.218	0.086301659	0	0.489890836	0	1	1	0.489890836	0.510109164
Clemastine Fumarate	-17.2	18.32	0.926924054	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378	0.088840378
Clofazimine	-12.29	1.102	0.076429481	0	0.489890836	0	1	1	0.489890836	0.510109164
Clozantel	-9.764	3.452	0.225844121	0	0.489890836	0	1	1	0.489890836	0.510109164
Clozantel Sodium	-7.971	11.12	0.635908686	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378	0.088840378
Cobimetinib	-44.04	8.67	0.122364548	0	0.489890836	0	1	1	0.489890836	0.510109164
Crenolanib (CP-86858)	-95.11	62.04	0.551003999	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843	0.300641843

continued

Drug	Difference in % inhibition across 4 PDXs			Supra-additive with carfilzomib (mean difference in % inhibition >0)			Sub-additive with carfilzomib (mean difference in % inhibition <0)		
	Lower 95% CI of mean	Upper 95% CI of mean	P-value	Lower 95% CI	Upper 95% CI	Proportion of PDXs (n=4)	Lower 95% CI	Upper 95% CI	Proportion of PDXs (n=4)
Crystal Violet	-46.04	25.46	0.427142075	0.911159622	0.88840378	0.5	0.911159622	0.88840378	0.5
Cyclosporin A	-19.41	-0.6122	0.042781983	0	0.489890836	0	0.489890836	0	1
Cyclosporine	-29.38	6.682	0.138922978	0.25	0.699358157	0.012823324	0.012823324	0.012823324	0.75
Cytarabine	-26.36	41.41	0.530628078	0.5	0.911159622	0.88840378	0.88840378	0.88840378	0.5
Cytarabine hydrochlor	-29.26	45.15	0.545648962	0.5	0.911159622	0.88840378	0.88840378	0.88840378	0.5
Daciatasvir (BMS-790)	-18.66	3.581	0.119821815	0	0.489890836	0	0.489890836	0	1
Dacomitinib (PF29980)	-40.46	2.617	0.068087061	0	0.489890836	0	0.489890836	0	1
Dasatinib (BMS-35482)	-53.14	4.57	0.075151222	0	0.489890836	0	0.489890836	0	1
Daunorubicin HCl	-45.27	34.6	0.69924896	0.25	0.699358157	0.012823324	0.012823324	0.012823324	0.75
Deferasirox	-2.419	5.922	0.273766946	0.5	0.911159622	0.88840378	0.88840378	0.88840378	0.5
Digoxin	-83.58	74.32	0.863873385	0.25	0.699358157	0.012823324	0.012823324	0.012823324	0.75
Dinaciclib (SCH72796)	-55.23	22.69	0.275884989	0.25	0.699358157	0.012823324	0.012823324	0.012823324	0.75
Domiphen Bromide	-30.04	17.51	0.463485736	0.25	0.699358157	0.012823324	0.012823324	0.012823324	0.75
Dovitinib Dilactic acid	-45.13	31.25	0.603669237	0.5	0.911159622	0.88840378	0.88840378	0.88840378	0.5
Doxercalciferol	-36.36	10.6	0.179171419	0.25	0.699358157	0.012823324	0.012823324	0.012823324	0.75
Doxorubicin	-43.32	19.59	0.316048749	0.5	0.911159622	0.88840378	0.88840378	0.88840378	0.5
Doxorubicin (Adriamycin)	-44.88	24.17	0.410248305	0.5	0.911159622	0.88840378	0.88840378	0.88840378	0.5
Dronedarone	-16.14	5.776	0.229381753	0.25	0.699358157	0.012823324	0.012823324	0.012823324	0.75
Dronedarone HCl	-14.15	10.38	0.658982574	0.5	0.911159622	0.88840378	0.88840378	0.88840378	0.5
Duloxetine HCl	-22.5	13.85	0.503927511	0.5	0.911159622	0.88840378	0.88840378	0.88840378	0.5
Ebastine	-9.418	9.698	0.965773974	0.75	0.987176676	0.300641843	0.300641843	0.300641843	0.25
Econazole nitrate	-12.11	12.27	0.696941266	0.5	0.911159622	0.88840378	0.88840378	0.88840378	0.5
Eltrombopag	-8.365	7.997	0.94733489	0.75	0.987176676	0.300641843	0.300641843	0.300641843	0.25
EMD-1214063	-26.56	0.7719	0.057544946	0	0.489890836	0	0.489890836	0	1
Entrectinib	-26.38	16	0.492475697	0.5	0.911159622	0.88840378	0.88840378	0.88840378	0.5
Epirubicin HCl	-39.19	21.46	0.42100471	0.25	0.699358157	0.012823324	0.012823324	0.012823324	0.75
Erlotinib	-39.75	-10.98	0.01182477	0	0.489890836	0	0.489890836	0	1
Erlotinib Hydrochloride	-24.91	-14.83	0.001091624	0	0.489890836	0	0.489890836	0	1
Ethacridine lactate mc	-26.87	14.89	0.428552359	0.5	0.911159622	0.88840378	0.88840378	0.88840378	0.5
Fenticonazole Nitrate	-16.97	10.13	0.48034402	0.5	0.911159622	0.88840378	0.88840378	0.88840378	0.5
Fidaxomicin	-18	26.13	0.599013807	0.75	0.987176676	0.300641843	0.300641843	0.300641843	0.25
Fingolimod (FTY720)	-10.37	10.93	0.938874248	0.5	0.911159622	0.88840378	0.88840378	0.88840378	0.5
Flunarizine 2HCl	-19.67	17.39	0.856942852	0.5	0.911159622	0.88840378	0.88840378	0.88840378	0.5
Fluoxetine HCl	-13.18	12.4	0.929005917	0.25	0.699358157	0.012823324	0.012823324	0.012823324	0.75
Foretinib (GSK136308)	-31.23	10.93	0.222917132	0.25	0.699358157	0.012823324	0.012823324	0.012823324	0.75
Fostamatinib (R788)	-30.74	26.21	0.816673105	0.5	0.911159622	0.88840378	0.88840378	0.88840378	0.5
Galic acid	-13.91	19.07	0.652631954	0.75	0.987176676	0.300641843	0.300641843	0.300641843	0.25
Ganetespib (STA-909)	-53.52	48.53	0.886329228	0.25	0.699358157	0.012823324	0.012823324	0.012823324	0.75
GSK2126458	-40.41	-0.6084	0.046435135	0	0.489890836	0	0.489890836	0	1
Idarubicin HCl	-97.23	133.3	0.652408465	0.5	0.911159622	0.88840378	0.88840378	0.88840378	0.5
Isoconazole nitrate	6.64	29.67	0.015245339	1	1	0.510109164	0.510109164	0.510109164	0
Ispinesib (SB-715992)	-30.43	9.589	0.196007484	0.25	0.699358157	0.012823324	0.012823324	0.012823324	0.75
Ivermectin	-26.99	-7.069	0.012189782	0	0.489890836	0	0.489890836	0	1
KPT-330	-48.04	30.55	0.529917348	0.25	0.699358157	0.012823324	0.012823324	0.012823324	0.75
Lapatinib Ditosylate	-40.05	-0.7946	0.04534865	0	0.489890836	0	0.489890836	0	1
LDK378	-38.78	-4.246	0.028667064	0	0.489890836	0	0.489890836	0	1
Lenvatinib (E7080)	-35.71	23.42	0.555592584	0.25	0.699358157	0.012823324	0.012823324	0.012823324	0.75

Appendix E: Statistical analyses for 176 drugs combined with carfilzomib in basal-like TNBC PDXs

continued

Drug	Difference in % inhibition across 4 PDXs			Supra-additive with carfilzomib (mean difference in % inhibition >0)			Sub-additive with carfilzomib (mean difference in % inhibition <0)		
	Lower 95% CI of mean	Upper 95% CI of mean	P-value	Proportion of PDXs (n=4)	Upper 95% CI	Lower 95% CI	Proportion of PDXs (n=4)	Upper 95% CI	Lower 95% CI
Levosimendan	-7.217	11.32	0.53159362	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378
Licofelone	-2.246	22.49	0.080067461	1	1	0.510109164	0	0.489890836	0
Lithocholic Acid	-11.25	11.48	0.975958457	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378
Lomerizine HCl	-28.22	17.9	0.527879356	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378
Lomitapide	-23.52	-0.209	0.047869275	0	0.489890836	0	1	1	0.510109164
LY2228820	-35.26	13.17	0.242424301	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
LY2835219	-82.95	63.3	0.697744714	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378
Maprotiline HCl	-12.78	9.249	0.644808969	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Masitinib (AB1010)	-23.83	13.42	0.439198042	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378
Mechlorethamine HCl	-33.57	42.7	0.728536019	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378
Mecizine 2HCl	4.524	23.34	0.018084542	1	1	0.510109164	0	0.489890836	0
Mefloquine hydrochlor	-28.97	14.85	0.380715376	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
MEK162 (ARRY-162)	-48.77	16.12	0.207673471	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Menadiione	-4.918	6.947	0.624162449	0.75	0.987176676	0.300641843	0.25	0.699358157	0.012823324
Miconazole Nitrate	-8.193	16.81	0.352790876	0.75	0.987176676	0.300641843	0.25	0.699358157	0.012823324
Miltefosine	-10.48	3.441	0.205966777	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Minocycline HCl	-9.646	9.959	0.962719598	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378
Mitomycin C	-34.33	10.12	0.181464591	0	0.489890836	0	1	1	0.510109164
Mitoxantrone HCl	-51.13	24.57	0.345490943	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
MLN2238	-83.21	58.76	0.621807472	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Napabucasin	-55.72	29.11	0.391764943	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Nebivolol	-4.437	12.93	0.217514852	0.75	0.987176676	0.300641843	0.25	0.699358157	0.012823324
Nedaplatin	-17.87	9.17	0.381084895	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Neflavinir Mesylate	-28.61	0.8736	0.057952016	0	0.489890836	0	1	1	0.510109164
Neratinib (HKI-272)	-36.64	-13.3	0.006482712	0	0.489890836	0	1	1	0.510109164
Nicardipine HCl	-29.56	32.36	0.894609633	0.75	0.987176676	0.300641843	0.25	0.699358157	0.012823324
Nifuroxazide	-27.15	8.982	0.207870345	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Nilotinib (AMN-107)	-28.66	20.44	0.631276483	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Nintedanib (BIBF 1120)	-53.06	12.82	0.147126347	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Olitumum Bromide	-15.75	20.66	0.696629418	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378
Oxethazaine	-15.06	17.62	0.819089791	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378
Pacritinib	-58.34	25.38	0.298968033	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Paroxetine HCl	-22.93	17.75	0.712089214	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Pelitinib (EKB-569)	-73.2	3.034	0.061044572	0	0.489890836	0	1	1	0.510109164
Pimavanserin	-18.84	25.09	0.681054886	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Pimecrolimus	-26.75	17.4	0.548665707	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Ponatinib (AP24534)	-42.14	29.04	0.599007982	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Pozotinib	-36.1	0.8258	0.055862485	0	0.489890836	0	1	1	0.510109164
Proflavine Hemisulfate	-39.16	23.57	0.486833664	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Puromycin dihydrochlor	-45.78	62.86	0.651337597	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Rapamycin (Stromlimus)	-35.05	-9.138	0.012276028	0	0.489890836	0	1	1	0.510109164
Regorafenib	-11.62	10.75	0.908706923	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378
Regorafenib hydrochlor	-18.84	22.58	0.792507718	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378
RG7388	-8.971	3.524	0.259428963	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Rifapentine	-7.184	8.253	0.839723499	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378
Rimonabant	-17.55	12.68	0.643696848	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378
Ritonavir	-13.21	-4.576	0.00722976	0	0.489890836	0	1	1	0.510109164
Rosuvastatin Calcium	-25.16	0.2414	0.052391707	0	0.489890836	0	1	1	0.510109164
Saquinavir mesylate	-4.197	7.836	0.406749435	0.75	0.987176676	0.300641843	0.25	0.699358157	0.012823324

Appendix E: Statistical analyses for 176 drugs combined with carfilzomib in basal-like TNBC PDXs

continued

Drug	Difference in % inhibition across 4 PDXs		P-value	Supra-additive with carfilzomib (mean difference in % inhibition >0)		Sub-additive with carfilzomib (mean difference in % inhibition <0)		
	Lower 95% CI of mean	Upper 95% CI of mean		Proportion of PDXs (n=4)	Upper 95% CI	Lower 95% CI	Upper 95% CI	Lower 95% CI
Saracatinib (AZD0530)	-40.94	-11.28	0.01123678	0	0.489890836	0	1	0.510109164
Sertraline HCl	-13.36	14.73	0.886761116	0.5	0.911159622	0.088840378	0.5	0.911159622
Simeprevir	-11.46	9.028	0.730967169	0.75	0.987176676	0.300641843	0.25	0.699358157
Sorafenib	-30.66	20.06	0.563772009	0.25	0.699358157	0.012823324	0.75	0.987176676
Sorafenib Tosylate	-31.78	9.779	0.190603949	0.25	0.699358157	0.012823324	0.75	0.987176676
Sulconazole Nitrate	-19.86	18.49	0.91644473	0.75	0.987176676	0.300641843	0.25	0.699358157
Sunitinib	-26.61	9.089	0.216192966	0.25	0.699358157	0.012823324	0.75	0.987176676
Sunitinib malate	-48.99	15.11	0.191206679	0.25	0.699358157	0.012823324	0.75	0.987176676
Tamoxifen Citrate	9.247	6.898	0.674910986	0.5	0.911159622	0.088840378	0.5	0.911159622
Temozolimus	-32.39	-13.85	0.004166255	0	0.489890836	0	1	0.510109164
Terfenadine	-19.49	-1.447	0.034447447	0	0.489890836	0	1	0.510109164
Thioridazine HCl	-14.54	0.7625	0.064295402	0.25	0.699358157	0.012823324	0.75	0.987176676
Ticagrelor	-26.86	12.54	0.331097614	0.25	0.699358157	0.012823324	0.75	0.987176676
Ticlopidine HCl	-11.99	14.67	0.769899438	0.75	0.987176676	0.300641843	0.25	0.699358157
Ticoconazole	-15.24	18.15	0.799567488	0.5	0.911159622	0.088840378	0.5	0.911159622
Tivozanib (AV-951)	-37.33	21.33	0.449443322	0.25	0.699358157	0.012823324	0.75	0.987176676
Toifenamic Acid	-5.615	11.65	0.346970651	0.75	0.987176676	0.300641843	0.25	0.699358157
Toltrazuril	-11.05	11.5	0.963997844	0.5	0.911159622	0.088840378	0.5	0.911159622
Topotecan	-61.76	24.61	0.264462303	0.25	0.699358157	0.012823324	0.75	0.987176676
Topotecan HCl	-50.41	20.14	0.265418008	0.25	0.699358157	0.012823324	0.75	0.987176676
Toremifene Citrate	-2.213	17.38	0.090573043	1	1	0.510109164	0	0.489890836
Trifluoperazine 2HCl	-23.36	32.97	0.625100149	0.25	0.699358157	0.012823324	0.75	0.987176676
Vandetanib (ZD6474)	-29.43	-3.273	0.028396171	0	0.489890836	0	1	0.510109164
Vehicle/Anchor drug a	0	0	N/A	0	0.489890836	0	1	0.510109164
Vortioxetine (Lu AA21)	-18.92	14.2	0.680993721	0.25	0.699358157	0.012823324	0.75	0.987176676
VRT752271	-34.55	1.347	0.060331403	0	0.489890836	0	1	0.510109164
YM155	-58.15	8.473	0.098246948	0	0.489890836	0	1	0.510109164
Zafirlukast	-11.34	9.387	0.78410438	0.5	0.911159622	0.088840378	0.5	0.911159622
Zinc Pyrrithione	-52.31	34.05	0.549259448	0.25	0.699358157	0.012823324	0.75	0.987176676
Ziprasidone hydrochlorid	-16.65	18.83	0.857370134	0.5	0.911159622	0.088840378	0.5	0.911159622

APPENDIX F

Adapted from [190]

Appendix F: Statistical analyses for 176 drugs combined with afatinib in basal-like TNBC PDXs

Significant p-values (p<0.05, unpaired t-test) are bolded and italicized.

Drug	Difference in % inhibition across 4 PDXs		Supra-additive with afatinib (mean difference in % inhibition >0)		Sub-additive with afatinib (mean difference in % inhibition <0)	
	Lower 95% CI of mean	Upper 95% CI of mean	P-value	Proportion of PDXs (n=4)	Upper 95% CI	Lower 95% CI
(R)-Crizotinib	-20.79	51.05	0.272601539	0.75	0.987176676	0.300641843
5-Azacytidine	-11.74	0.2154	0.054658521	0	0.489890836	0
ABT-263 (Navitoclax)	-12.46	3.436	0.168594026	0.25	0.699358157	0.012823324
Afatinib (BIBW2992)	-30.02	4.456	0.023260155	0	0.489890836	0
Afatinib dimaleate	-26.22	-1.836	0.035203931	0	0.489890836	0
Alfalcicloid	-34.98	10.73	0.190010051	0.25	0.699358157	0.012823324
Amfenac Sodium Mor	-17.48	22.5	0.71616726	0.5	0.911159622	0.08840378
Amiodarone HCl	-20.76	15.66	0.686253931	0.5	0.911159622	0.08840378
Amiodipine	-16.98	9.406	0.428246407	0.5	0.911159622	0.08840378
Amiodipine Besylate	-14.84	9.94	0.57374973	0.25	0.699358157	0.012823324
Anidulafungin	-21.21	6.493	0.189467297	0.25	0.699358157	0.012823324
Arbidol HCl	-14.67	8.242	0.437647004	0.5	0.911159622	0.08840378
Atazanavir	-9.783	8.312	0.812604611	0.75	0.987176676	0.300641843
AZD-9291	-33.86	-1.369	0.040917492	0	0.489890836	0
Azelinidipine	-7.669	4.948	0.541743201	0.25	0.699358157	0.012823324
Bardoxolone methyl	-46.23	53.15	0.838827185	0.25	0.699358157	0.012823324
Bazedoxifene HCl	-12.26	16.73	0.657857194	0.5	0.911159622	0.08840378
Bedaquiline fumarate	-10.16	2.957	0.178770714	0.25	0.699358157	0.012823324
Benidipine HCl	-14.49	14.45	0.996971812	0.75	0.987176676	0.300641843
Benzbromarone	-17.96	8.304	0.326518561	0.25	0.699358157	0.012823324
Benzethonium Chlorid	-17.41	5.234	0.185503806	0	0.489890836	0
Bexarotene	0.2289	18.68	0.047081469	1	1	0.510109164
Birinapant (TL32711)	-32.33	7	0.132794324	0	0.489890836	0
Bortezomib	-40.98	-9.064	0.015471713	0	0.489890836	0
Bosutinib (SKI-606)	-30.44	-11.19	0.00627938	0	0.489890836	0
BYL-719	-32.96	9.282	0.172428208	0	0.489890836	0
Cabozantinib malate	-6.693	8.19	0.769919995	0.75	0.987176676	0.300641843
Calcectol	-37.91	11.25	0.182927766	0.25	0.699358157	0.012823324
Candesartan Cilexetil	-10.07	12.84	0.726236246	0.5	0.911159622	0.08840378
Carboplatin	-18.19	0.7769	0.06140988	0.25	0.699358157	0.012823324
Carfilzomib (PR-171)	-34.36	-13.02	0.005823069	0	0.489890836	0
Carvedilol	-2.593	20.08	0.091312967	1	1	0.510109164
Cediranib (AZD217)	-56.43	6.217	0.083885561	0	0.489890836	0
CEP-18770	-22.01	-11.38	0.002128954	0	0.489890836	0
Cepharanthine	-16.03	0.1603	0.052494479	0	0.489890836	0
Cetrimonium Bromide	-16.79	-2.723	0.021571985	0	0.489890836	0
Cetylpyridinium Chlor	-18.69	1.645	0.075845443	0	0.489890836	0
Chloropyridine diphosph	-9.889	4.179	0.286941946	0.25	0.699358157	0.012823324
Chloroxine	-10.27	5.363	0.391540945	0.25	0.699358157	0.012823324
Ciclesonide	-10.05	20.88	0.346194813	0.75	0.987176676	0.300641843
Cilindipine	-2.567	23.05	0.084341958	1	1	0.510109164
Cinacalcet	-10.57	10.39	0.979682063	0.25	0.699358157	0.012823324
Cinacalcet HCl	-13.82	-1.011	0.034635536	0	0.489890836	0
Clemastine Fumarate	-4.95	4.964	0.99671587	0.5	0.911159622	0.08840378
Clofazimine	-12.14	7.581	0.515195814	0.5	0.911159622	0.08840378
Closetel	-17.14	12.91	0.684380206	0.25	0.699358157	0.012823324
Clozantel Sodium	-10.61	10.96	0.961999433	0.25	0.699358157	0.012823324
Cobimetinib	-15.46	-3.154	0.017069623	0	0.489890836	0
Crenolanib (CP-8685)	-84.11	162.7	0.38539195	0.75	0.987176676	0.300641843

Appendix F: Statistical analyses for 176 drugs combined with afatinib in basal-like TNBC PDXs

continued

Drug	Difference in % inhibition across 4 PDXs		Supra-additive with afatinib (mean difference in % inhibition >0)		Sub-additive with afatinib (mean difference in % inhibition <0)	
	Lower 95% CI of mean	Upper 95% CI of mean	P-value	Proportion of PDXs (n=4)	Upper 95% CI	Lower 95% CI
Crystal Violet	-26.73	1.035	0.060258651	0	0.489890836	0
Cyclosporin A	-20.57	-0.6074	0.043214157	0	0.489890836	0
Cyclosporine	-17.16	4.633	0.164738573	0.25	0.699358157	0.012823324
Cytarabine	-19.38	20.43	0.938480269	0.5	0.911159622	0.088840378
Cytarabine hydrochloride	-23.04	22.8	0.987768481	0.25	0.699358157	0.012823324
Daclatasvir (BMS-790)	-4.463	3.441	0.708403433	0.75	0.987176676	0.300641843
Dacomitinib (PF2998)	-34.8	-0.7247	0.045126871	0	0.489890836	0
Dasatinib (BMS-3548)	-12.92	-3.121	0.013750945	0	0.489890836	0
Daurorubicin HCl	-42.02	24.61	0.466634159	0.25	0.699358157	0.012823324
Deferasirox	-5.9	7.172	0.776974608	0.75	0.987176676	0.300641843
Digoxin	-43.59	31.52	0.644491695	0.25	0.699358157	0.012823324
Dinaciclib (SCH72796)	-26.19	-11.93	0.003414766	0	0.489890836	0
Domiphen Bromide	-15.34	-0.8266	0.038225502	0	0.489890836	0
Dovitinib Diolactate acid	2.152	25.17	0.032503139	1	1	0.510109164
Doxercalciferol	-24.44	4.495	0.115859734	0	0.489890836	0
Doxorubicin	-33.86	4.306	0.090523055	0	0.489890836	0
Doxorubicin (Adriamyl)	-42.25	10.83	0.156140806	0.25	0.699358157	0.012823324
Dronedarone	-5.463	10.3	0.400714853	0.75	0.987176676	0.300641843
Dronedarone HCl	-8.604	17.32	0.363225599	0.75	0.987176676	0.300641843
Duloxetine HCl	-8.776	14.29	0.502310544	0.5	0.911159622	0.088840378
Ebastine	-10.52	12.76	0.779946406	0.5	0.911159622	0.088840378
Econazole nitrate	-0.9959	13.95	0.070242103	1	1	0.510109164
Eltrombopag	-12.22	7.039	0.455050797	0.25	0.699358157	0.012823324
Embelin	-9.121	5.137	0.439355955	0.25	0.699358157	0.012823324
EMD-1214063	-4.722	4.065	0.827270096	0.5	0.911159622	0.088840378
Entrectinib	-6.761	-1.683	0.013167023	0	0.489890836	0
Epirubicin HCl	-39.85	14.87	0.242289463	0.25	0.699358157	0.012823324
Erlotinib	-35.97	-10.89	0.009510337	0	0.489890836	0
Erlotinib Hydrochloride	-43.17	10.54	0.148695596	0.25	0.699358157	0.012823324
Ethacridine lactate monohydrate	-22.07	7.007	0.197785964	0.25	0.699358157	0.012823324
Fenticonazole Nitrate	-4.84	14.55	0.209253553	0.5	0.911159622	0.088840378
Fidaxomicin	-15.05	26.37	0.448303515	0.75	0.987176676	0.300641843
Fingolimod (FTY720)	-9.893	5.665	0.450679881	0.5	0.911159622	0.088840378
Flunarizine 2HCl	-12.02	7.186	0.481666661	0.5	0.911159622	0.088840378
Fluoxetine HCl	-9.976	11.37	0.848810076	0.5	0.911159622	0.088840378
Foretinib (GSK136308)	-18.16	18.65	0.968955891	0.5	0.911159622	0.088840378
Fostamatinib (R788)	-14.49	16.55	0.846155162	0.5	0.911159622	0.088840378
Gallic acid	-12.74	7.746	0.494348101	0.5	0.911159622	0.088840378
Ganetespib (STA-909)	-40.8	43.82	0.916766805	0.25	0.699358157	0.012823324
GSK2126458	-32.29	-3.771	0.027573156	0	0.489890836	0
Idarubicin HCl	-114.4	167.9	0.589123622	0.25	0.699358157	0.012823324
Idebenone	-11.79	14.3	0.779318215	0.5	0.911159622	0.088840378
Isoconazole nitrate	-7.686	33.99	0.13815509	0.75	0.987176676	0.300641843
Ispinesib (SB-715992)	-25.36	11.53	0.318364034	0.25	0.699358157	0.012823324
Ivermectin	-13.45	5.828	0.297255565	0.25	0.699358157	0.012823324
KPT-330	-23.47	-7.896	0.007697223	0	0.489890836	0
Lapatinib Ditosylate	-30.75	-2	0.0366110149	0	0.489890836	0
LDK378	-21.33	-1.335	0.036672368	0	0.489890836	0
Lenvatinib (E7080)	-9.892	20.94	0.336977185	0.75	0.987176676	0.300641843

Appendix F: Statistical analyses for 176 drugs combined with afatinib in basal-like TNBC PDXs

continued

Drug	Difference in % inhibition across 4 PDXs		Supra-additive with afatinib (mean difference in % inhibition >0)		Sub-additive with afatinib (mean difference in % inhibition <0)	
	Lower 95% CI of mean	Upper 95% CI of mean	P-value	Proportion of PDXs (n=4)	Upper 95% CI	Lower 95% CI
Levosimendan	-11.51	17.4	0.563014973	0.5	0.911159622	0.088840378
Licoflone	-13.91	21.03	0.562432375	0.5	0.911159622	0.088840378
Lithocholic Acid	-4.213	22.04	0.119484727	1	0.510109164	0
Lomerizine HCl	-15.37	6.095	0.262886589	0.25	0.699358157	0.012823324
Lomitapide	-15.07	-3.522	0.014393346	0	0.489890836	0
LY228820	-17.32	-3.209	0.018982176	0	0.489890836	0
LY2835219	-18.64	9.384	0.370370085	0.5	0.911159622	0.088840378
Maprotiline HCl	-6.234	2.088	0.211083687	0.25	0.699358157	0.012823324
Masitinib (AB1010)	-9.941	27.59	0.231377399	0.75	0.987176676	0.300641843
Mechlorethamine HCl	-14.79	19.11	0.712402011	0.25	0.699358157	0.012823324
Mecizine 2HCl	-23.49	32.94	0.63095008	0.5	0.911159622	0.088840378
Mefloquine hydrochlor	-14.27	9.547	0.572637358	0.25	0.699358157	0.012823324
MEK162 (ARRY-162)	-19.85	1.019	0.063960037	0	0.489890836	0
Menadione	-5.476	9.515	0.454193823	0.75	0.987176676	0.300641843
Miconazole Nitrate	-10.69	12.67	0.804754191	0.25	0.699358157	0.012823324
Miltefosine	-16.56	10.71	0.543759703	0.25	0.699358157	0.012823324
Minocycline HCl	-8.792	2.009	0.139531645	0.25	0.699358157	0.012823324
Mitomycin C	-21.29	10.98	0.383898167	0.25	0.699358157	0.012823324
Mitoxantrone HCl	-38.93	8.621	0.135533788	0.25	0.699358157	0.012823324
MLN2238	-27.54	-7.678	0.010150175	0	0.489890836	0
Napabucasin	-33.03	-5.167	0.022264154	0	0.489890836	0
Nebivolol	-0.3984	5.802	0.069367445	0.75	0.987176676	0.300641843
Nedaplatin	-15.5	11.26	0.649021505	0.25	0.699358157	0.012823324
Neftinavir Mesylate	-16.07	8.163	0.37552563	0.5	0.911159622	0.088840378
Neratinib (HKI-272)	-39.92	-12.84	0.008447886	0	0.489890836	0
Nicardipine HCl	-4.241	8.85	0.344201108	0.75	0.987176676	0.300641843
Nifuroxazide	-19.69	0.4896	0.056400408	0	0.489890836	0
Nilotinib (AMN-107)	-23.59	4.617	0.121792833	0	0.489890836	0
Nintedanib (BIBF-112)	-27.5	9.451	0.21788901	0.25	0.699358157	0.012823324
Olitonium Bromide	-9.557	5.85	0.499510423	0.25	0.699358157	0.012823324
Oxethazaine	-6.066	8.586	0.62228411	0.5	0.911159622	0.088840378
Pacritinib	-23.74	-3.196	0.025061164	0	0.489890836	0
Paroxetine HCl	-5.577	4.84	0.836480192	0.25	0.699358157	0.012823324
Pelitinib (EKB-569)	-40.11	-5.377	0.025137544	0	0.489890836	0
Pimavanserin	-7.796	6.166	0.734965933	0.25	0.699358157	0.012823324
Pimecrolimus	-12.88	10.4	0.757075888	0.25	0.699358157	0.012823324
Ponatinib (AP-24534)	-20.24	3.081	0.101067904	0	0.489890836	0
Pozotinib	-37.75	-7.433	0.01774862	0	0.489890836	0
Profavine Hemisulfat	-27.37	6.954	0.154703023	0.25	0.699358157	0.012823324
Puromycin dihydrochl	-44.69	0.9546	0.055457806	0	0.489890836	0
Rapamycin (Sirolimus)	-19.76	-6.29	0.008632844	0	0.489890836	0
Regorafenib	-4.353	17.21	0.15400402	1	0.510109164	0
Regorafenib hydrochl	-5.884	20.68	0.174408762	0.75	0.987176676	0.300641843
RG7388	-5.272	12.2	0.296339877	0.75	0.987176676	0.300641843
Rifapentine	-11.93	11.94	0.998735236	0.25	0.699358157	0.012823324
Rimonabant	-15.21	6.073	0.26515596	0.25	0.699358157	0.012823324
Ritonavir	-10.64	7.455	0.614446866	0.25	0.699358157	0.012823324
Rosuvastatin Calcium	-10.03	8.853	0.855060359	0.5	0.911159622	0.088840378
Saquinavir mesylate	-2.341	13.63	0.109969259	0.75	0.987176676	0.300641843

Appendix F: Statistical analyses for 176 drugs combined with afatinib in basal-like TNBC PDXs

continued

Drug	Difference in % inhibition across 4 PDXs		Supra-additive with afatinib (mean difference in % inhibition >0)		Sub-additive with afatinib (mean difference in % inhibition <0)				
	Lower 95% CI of mean	Upper 95% CI of mean	P-value	Proportion of PDXs (n=4)	Upper 95% CI	Lower 95% CI			
Saracatinib (AZD0536)	-39.3	-5.3	0.025072799	0	0.489890836	0	1	0.510109164	
Sertraline HCl	-4.866	10.71	0.318314431	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378
Simeprevir	-12.07	19.27	0.51801613	0.75	0.987176676	0.300641843	0.25	0.699358157	0.012823324
Sorafenib	-14.94	18.19	0.77538535	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Sorafenib Tosylate	-15.99	13.24	0.783956135	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378
Sulconazole Nitrate	-14.59	13.85	0.938684917	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Sunitinib	-6.975	5.154	0.665413455	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378
Sunitinib malate	-12.2	7.011	0.453155857	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Tamoxifen Citrate	-12.77	15.32	0.791128802	0.75	0.987176676	0.300641843	0.25	0.699358157	0.012823324
Temozolimus	-11.74	-7.312	0.000843637	0	0.489890836	0	1	0.510109164	
Terfenadine	-17.56	3.954	0.137637755	0	0.489890836	0	1	0.510109164	
Thioridazine HCl	-17.21	6.695	0.256091805	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Ticagrelor	-4.618	0.8595	0.116940997	0	0.489890836	0	1	0.510109164	
Ticlopidine HCl	-3.017	5.408	0.433089277	0.75	0.987176676	0.300641843	0.25	0.699358157	0.012823324
Tioconazole	-17.31	18.45	0.925744962	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Tivozanib (AV-951)	-4.874	19.43	0.152702617	0.75	0.987176676	0.300641843	0.25	0.699358157	0.012823324
Tolfenamic Acid	-11.63	10.75	0.907989037	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378
Toltrazuril	-12.51	11.97	0.948095464	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Topotecan	-28.51	2.934	0.081177598	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Topotecan HCl	-29.88	6.397	0.131493468	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Toremifene Citrate	-11.94	24.07	0.362444609	0.5	0.911159622	0.088840378	0.5	0.911159622	0.088840378
Trifluoperazine 2HCl	-20.24	14.43	0.630576527	0.25	0.699358157	0.012823324	0.75	0.987176676	0.300641843
Vandetanib (ZD6474)	-35.63	-1.375	0.041296454	0	0.489890836	0	1	0.510109164	
Vehicle/Anchor drug	0	0	N/A	0	0.489890836	0	1	0.510109164	
Vortioxetine (Lu AA21)	-11.94	25.97	0.323731024	0.75	0.987176676	0.300641843	0.25	0.699358157	0.012823324
VRT752271	-15.16	0.8887	0.066193026	0	0.489890836	0	1	0.510109164	
YM155	-41.71	-7.976	0.018352147	0	0.489890836	0	1	0.510109164	
Zafirlukast	-12.19	14.33	0.813523933	0.75	0.987176676	0.300641843	0.25	0.699358157	0.012823324
Zinc Pyrrithione	-37.56	2.825	0.071507917	0	0.489890836	0	1	0.510109164	
Ziprasidone hydrochlorid	-0.614	3.015	0.125903319	0.75	0.987176676	0.300641843	0.25	0.699358157	0.012823324