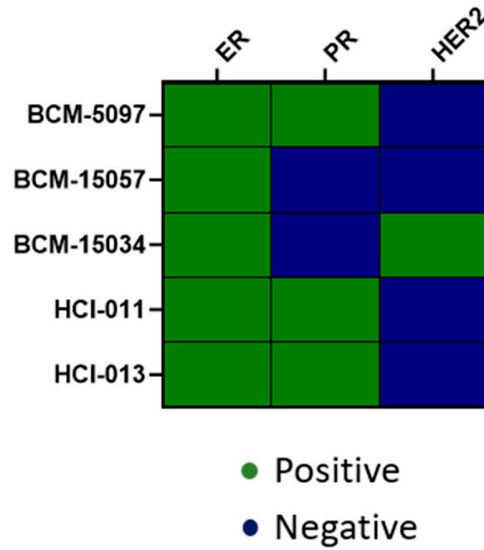


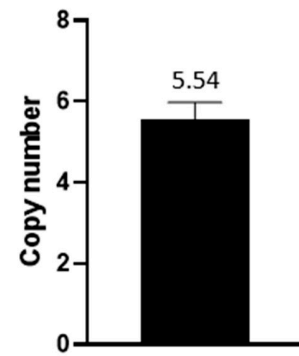
Supplemental Figure S1. Representative histograms of signal intensity of IHC images corresponding to Figure 1A. High positive and positive scores are listed as a percentage of pixels.

A

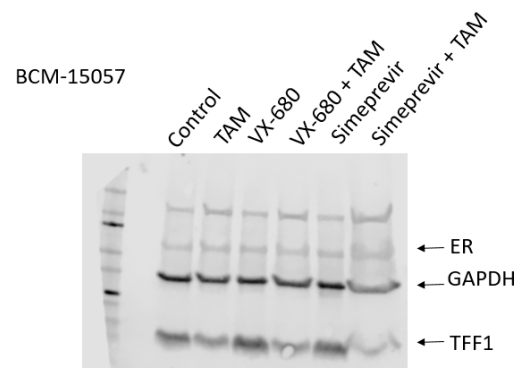
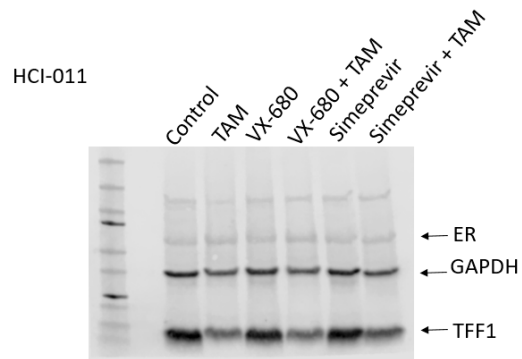
Patient biomarker status



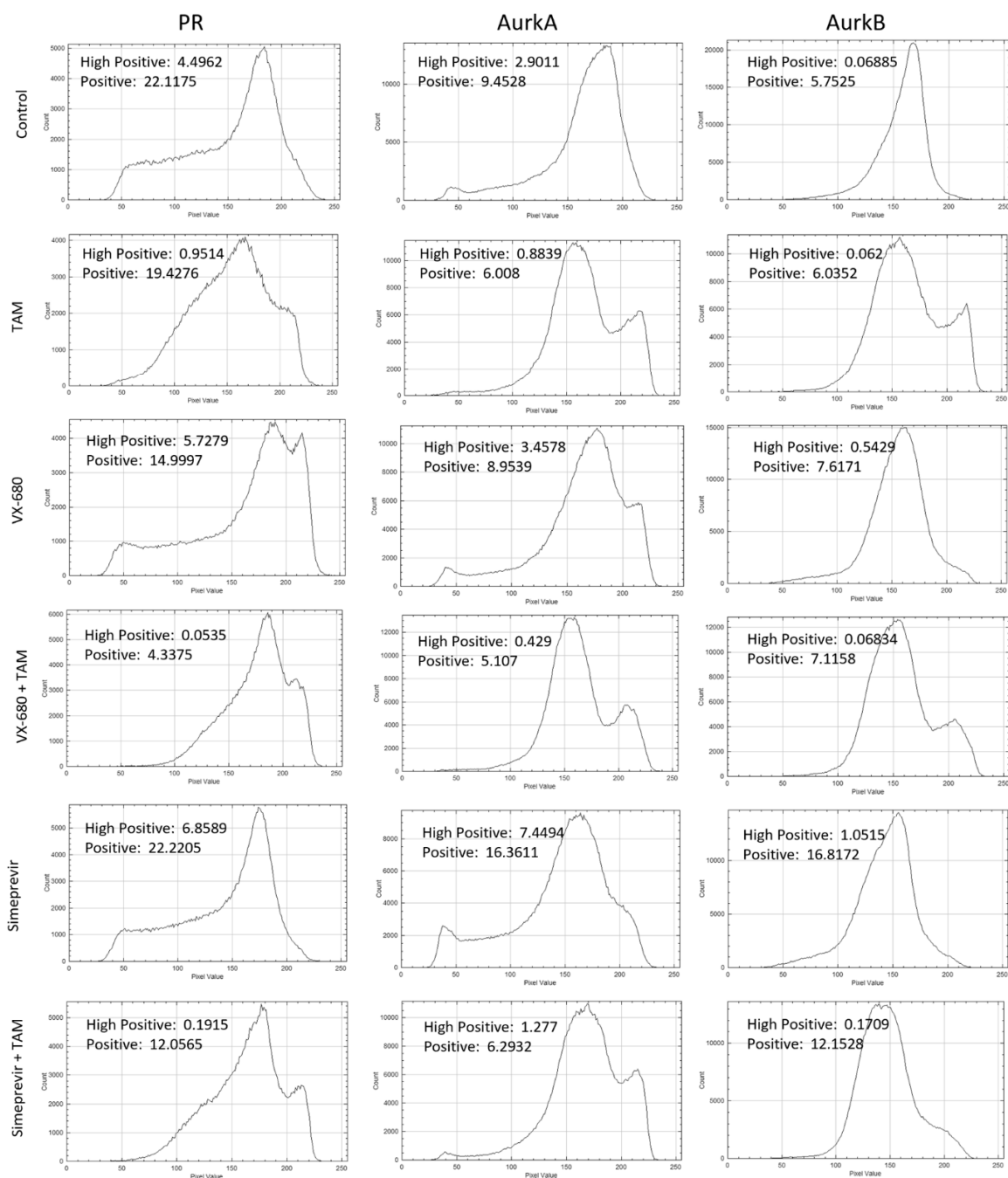
B



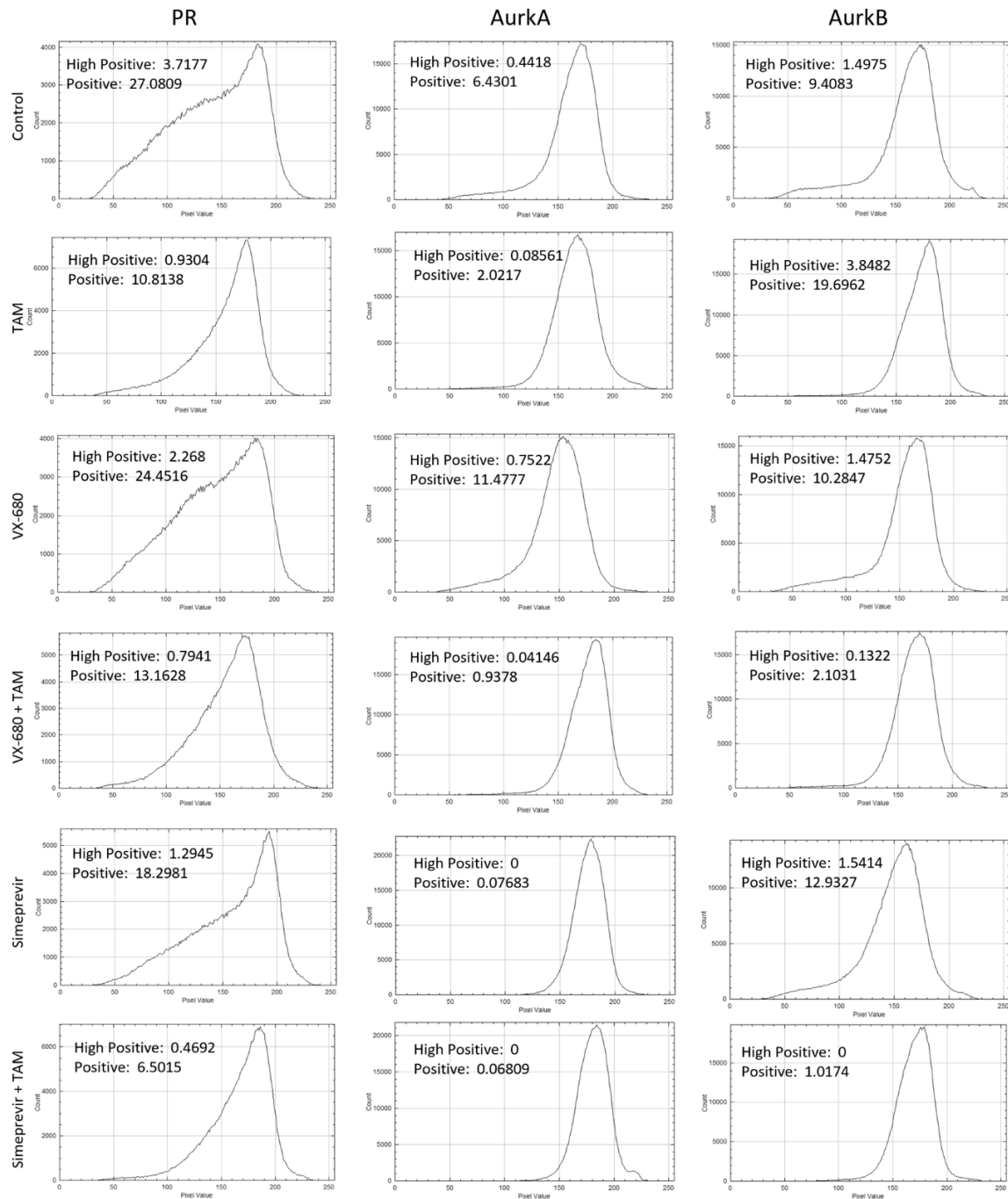
Supplemental Figure S2. (A) Heatmap representing patient ER, PR and HER2 status from which PDX models were generated, as reported by the Baylor College of Medicine PDX Portal. (B) Copy number of HER2 in PDX model BCM-15034 as established by Oncomine.



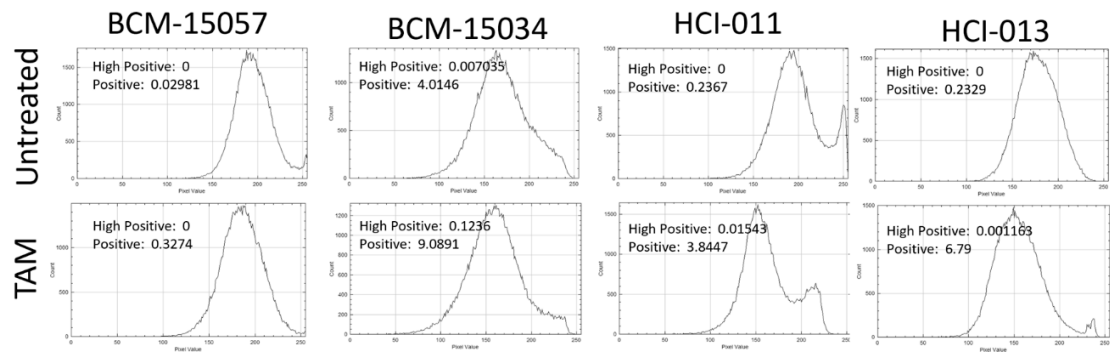
Supplemental Figure S3. Complete western blot images of in vivo experiments included in Figure 8



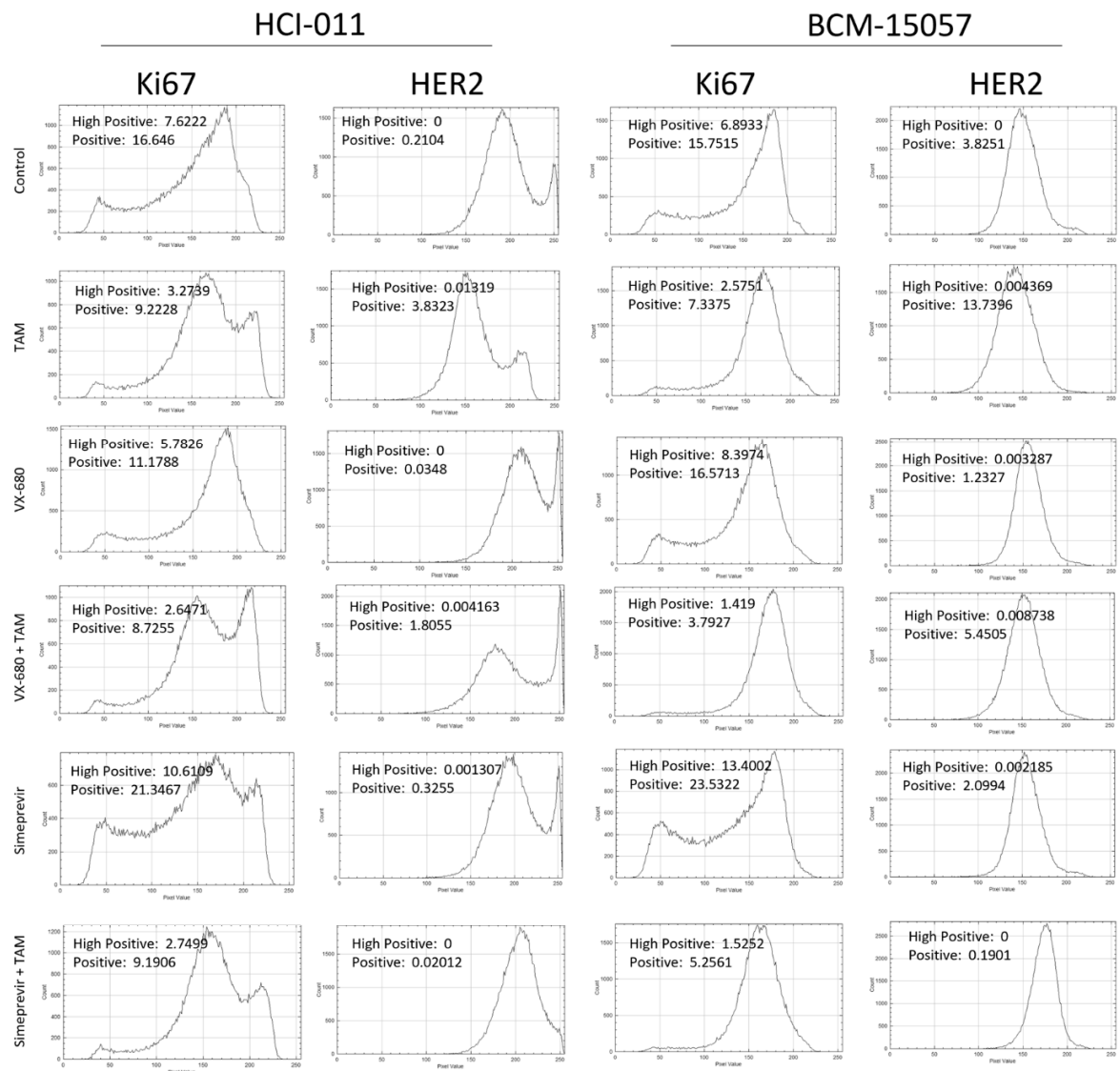
Supplemental Figure S4. Representative histograms of signal intensity of IHC images corresponding to Figure 8C. High positive and positive scores are listed as a percentage of pixels.



Supplemental Figure S5. Representative histograms of signal intensity of IHC images corresponding to Figure 8D. High positive and positive scores are listed as a percentage of pixels.



Supplemental Figure S6. Representative histograms of signal intensity of IHC images corresponding to Figure 9A. High positive and positive scores are listed as a percentage of pixels.



Supplemental Figure S7. Representative histograms of signal intensity of IHC images corresponding to Figure 9B-C. High positive and positive scores are listed as a percentage of pixels.

Supplemental information

| GSE | Samples (bulk) | | GSE | Samples (single cell) |
|-------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| GSE118942 | HCI01.MGT.101020 HCI01.MGT.101021 HCI01.MGT.101022 HCI02.MGT.100945 HCI02.MGT.100946 HCI02.MGT.100948 HCI03.MGT.102031 HCI04.MGT.100763 HCI08.MGT.100879 HCI09.MGT.100241 HCI09.MGT.100508 HCI09.MGT.100511 HCI09.MGT.100512 HCI10.MGT.100276 HCI10.MGT.100277 | HCI13.MGT.100822 PT52.MGT.100302 PT52.MGT.100303 PT52.MGT.100304 PT52.MGT.100775 PT52.MGT.100916 PT52.MGT.100917 WHIM2.MGT.100000 WHIM2.MGT.100027 WHIM2.MGT.100076 WHIM30.MGT.100431 WHIM30.MGT.175278A WHIM30.MGT.181040A WHIM30.MGT.182696A WHIM30.MGT.NSG21A | In progress | BCM-15034_107352 BCM-15034_107244 BCM-15034TamR_107634 BCM-15057_107684 BCM-5097_107348 HCI-011_107322 HCI-011_107409 HCI-013_106662 HCI-013_106663 HCI-013_107785 |
| GSE189325 | WHIM2.107647 WHIM2.107647b | WHIM2.107668 WHIM2.107672 | | |
| In progress | BCM.0132.107564 BCM.15034.107894 BCM.15057.107957 BCM.15057.107968 BCM.2147.107741 BCM.2147.107744 BCM.2147.107745 BCM.2147CR2.107841 BCM.2147CR2.107842 BCM.2277.107573 BCM.3887.107696 BCM.5097.107568 BCM.5097.107931 HCI.001.107935 HCI.011.107898 HCI.013.107857 HCI.013.107939 UCD52CR21.107961 UCD52CR21.107964 UCD52CR21.107966 UCD52CR21.107967 WHIM30.107947 | WHIM30CR6.107919 WHIM30CR6.107920 WHIM30CR7.107949 WHIM30CR7.107950 WHIM30CR7.107951 BCM.15034.107510 BCM.15057.107336 BCM.5097.107567 BCM.7482.107504 HCI.001.100097 HCI.011.107518 HCI.011.107522 HCI.013.102249 UCD52.100398 UCD52.100916 UCD52.107627 UCD52CR.107532 UCD52CR.107591 UCD52CR.107592 WHIM30.107661 WHIM30.107662 WHIM30CR.107502 | | |
| In progress | HCI.013.107415 BCM.15034TamR3.107922 BCM.15034TamR3.107924 | BCM.15057EI3.107630 BCM.15057EI3.107640 | | |

Supplemental Table S1. Bulk and scRNA samples used in this study.

| Drugs included in high throughput screening | | |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Gatifloxacin Gemcitabine HCl Rigosertib (ON-01910, Estybon) Fulvestrant Cilnidipine Lidocaine Dexrazoxane HCl (ICRF-187, ADR-529) Epothilone B (EPO906, Patupilone) Celecoxib Enzastaurin (LY317615) Aprepitant Posaconazole IPI-145 (INK1197) Ramelteon Tenofovir Disoproxil Fumarate Vincristine Entecavir Hydrate Vatalanib (PTK787) 2HCl LY2835219 Mianserin HCl Imatinib Mesylate (STI571) Doxorubicin (Adriamycin) HCl Pelitinib (EKB-569) Cediranib (AZD217) 5-Azacytidine Macitentan Carfilzomib (PR-171) MEK162 (ARRY-162, ARRY-438162) Etoposide Bendamustine HCl Plerixafor (AMD3100) Saracatinib (AZD0530) Bosutinib (SKI-606) Carboplatin Lenvatinib (E7080) Cladribine Tivozanib (AV-951) Mercaptopurine (6-MP) Floxuridine Acitretin Fluoxetine HCl | Salmeterol xinafoate Saquinavir mesylate Simeprevir Tamibarotene Teneligliptin hydrobromide TH-302 Vinblastine sulfate Vinorelbine ditartrate Ziprasidone Ziprasidone hydrochloride monohydrate Doxorubicin Lapatinib Ditosylate MLN2238 CEP-18770 Disulfiram Marimastat 17-AAG (KOS953) AT13387 (Onalespib) Elvitegravir (GS-9137) Rocilinostat (ACY-1215) Vorinostat (SAHA, MK0683) CUDC-101 Pracinostat (SB939) Belinostat (PXD101) PCI-24781 (CRA-024781) MLN8237 (Alisertib) VX-680 (MK-0457, Tozasertib) Barasertib (AZD1152-HQPA) Birinapant (TL32711) YM155 Amuvatinib (MP-470, HPK 56) Ketoconazole Sildenafil Citrate Mycophenolate Mofetil | CX-4945 (Silmeltasertib) Bleomycin Sulfate Linsitinib BYL-719 (Alpelisib) Pazopanib Hydrochloride LY2157299 VX-809 Alendronate sodium Arbidol HCl Chlorprothixene Clotrimazole Conivaptan HCl Cytarabine Dinaciclib (SCH727965) Diphenylpyraline HCl Docosanol (Abreua) Dovitinib Dilactic acid Duloxetine HCl Emtricitabine Enoxacin (Penetrex) Estradiol Fenticonazole Nitrate Furosemide Gabapentin Gemcitabine Indomethacin Lamivudine Lithocholic Acid Meloxicam (Mobic) Oxethazaine Pitavastatin Calcium Prochlorperazine Rosuvastatin Calcium Simvastatin (Zocor) Terfenadine Thioridazine HCl Vitamin D2 (Ergocalciferol) GSK2126458 (Omipalisib) BI6727 (Volasertib) Chloroquine diphosphate Deferasirox |

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|----------------------------------|----------------------------------|---------------------------|
| Epirubicin HCl | Aminophylline | Sunitinib |
| Pamidronate Disodium | Methotrexate | Ulipristal acetate |
| Idarubicin HCl | Pralatrexate | Doripenem |
| Malotilate | Pyrimethamine | Cytarabine hydrochloride |
| Ampicillin | Fluvastatin Sodium | AZD-9291 (Osimertinib) |
| Kanamycin Sulfate | Lovastatin | Efavirenz |
| Tetracycline Hydrochloride | Atorvastatin Calcium | Nelfinavir |
| Vortioxetine (Lu AA21004) HBr | Evacetrapib (LY2484595) | Pitavastatin |
| Carmofur | Lonafarnib | Ondansetron |
| Fluvoxamine maleate | Tolcapone | hydrochloride dihydrate |
| Aprotinin | Ganetespib (STA- 9090) | Meropenem trihydrate |
| Nafamostat Mesylate(FUT-175) | Pemetrexed | (+)-Ketoconazole |
| Amonafide | Paclitaxel (Taxol) | Haloperidol hydrochloride |
| Ivermectin | Docetaxel | Valproic acid |
| Doxazosin Mesylate | 10-DAB (10- Deacetylbaecatin) | Glycopyrrolate |
| Nepafenac | Mitomycin C | Reserpine hydrochloride |
| Masitinib (AB1010) | Streptozocin | Carvedilol |
| Loratadine | Melphalan | Nebivolol |
| Foretinib (GSK1363089) | Asenapine | Epinephrine Bitartrate |
| Cabozantinib (XL184, BMS-907351) | Ivacaftor (VX-770) | Miltefosine |
| PCI-32765 (Ibrutinib) | Heparin sodium | Phenformin HCl |
| CAL-101 (Idelalisib, GS-1101) | Ondansetron HCl | Spirolactone |
| ABT-263 (Navitoclax) | Alfuzosin HCl | Ciclopirox ethanolamine |
| Sorafenib | Linezolid | Amiodarone HCl |
| Dasatinib (BMS-354825) | Clopidogrel | Loperamide HCl |
| (R)-Crizotinib | Prazosin HCl | Tamoxifen Citrate |
| Pazopanib (GW-786034) | TSU-68 (SU6668,Orantinib) | Trifluoperazine 2HCl |
| Afatinib dimaleate | Ispinesib (SB-715992) | Benidipine HCl |
| Bardoxolone methyl | Ziprasidone HCl | Amlodipine |
| Boceprevir | LY2228820 | Amlodipine Besylate |
| Cariprazine | Abiraterone acetate | Flunarizine 2HCl |
| Cinacalcet | Ritonavir | Cinacalcet HCl |
| CO-1686 (AVL-301) | Lopinavir | Rimonabant |
| Cobimetinib | Atazanavir | Acemetacin |
| Colchicine | AZD6244 (Selumetinib) | Etodolac |
| Dabigatran etexilate mesylate | Lapatinib | Tolfenamic Acid |
| Docetaxel Trihydrate | Gefitinib (ZD1839) | Procarbazine HCl |
| Dronedarone | Nilotinib(AMN-107) | Chlorpromazine HCl |
| Elacridar | | Dopamine HCl |
| Eltrombopag Olamine | | Clomiphene citrate |
| EMD-1214063 | | Mifepristone |
| Erlotinib | | Toremifene Citrate |
| Fluvastatin | | Raloxifene HCl |

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| Ledipasvir Luliconazole Mefloquine hydrochloride Micafungin sodium MK-4305 Nelfinavir Mesylate Pemetrexed disodium hemipenta hydrate Perampanel Pregabalin Regorafenib hydrochloride RG7388 Salirasib Benzydamine HCl Bosentan Broxyquinoline Cetrimonium Bromide (CTAB) Cetylpyridinium Chloride Chlorocresol Chlorquinaldol Chlorzoxazone Clindamycin Phosphate Clofazimine Closantel Closantel Sodium Dirithromycin Domiphen Bromide Ebastine Epinastine HCl Ethacridine lactate monohydrate Fidaxomicin Furaltadone HCl Lomerizine HCl Loxapine Succinate Mechlorethamine HCl Mevastatin Neomycin sulfate Nifuroxazide Oxymetholone Pimecrolimus Piperacillin Sodium Primaquine Diphosphate Proflavine Hemisulfate | Erlotinib Hydrochloride Regorafenib Sorafenib Tosylate Afinatinib (BIBW2992) Nintedanib (BIBF 1120) Sunitinib malate Crenolanib (CP-868596) Quinapril HCl Adefovir Dipivoxil Palonosetron HCl Amitriptyline HCl Clomipramine HCl Clozapine Olanzapine Paroxetine HCl Prucalopride Sertraline HCl Dapoxetine HCl LDE225 (NVP-LDE225,Erismodegib) Propafenone HCl Daunorubicin HCl Irinotecan HCl Trihydrate Topotecan HCl Apatinib Chlorotrianisene Tamoxifen Cyclobenzaprine HCl Motolimod (VTX-2337) INCB-024360 Tacrine hydrochloride Estropipate Puromycin dihydrochloride Digoxin Pimavanserin Brucine Nicotinamide Caffeic acid | Clemastine Fumarate Azelastine HCl Otilonium Bromide Pyridostigmine Bromide Solifenacin succinate Tolterodine tartrate Fosbretabulin (Combretastatin A4 Phosphate (CA4P)) Disodium Racecadotril Alverine Citrate Amfenac Sodium Monohydrate Azithromycin Dihydrate Benzbromarone Benzethonium Chloride Pimasertib (AS-703026) Daclatasvir (BMS-790052) SAR245409 (XL765) BIRB 796 (Doramapimod) Fasudil (HA-1077) HCl Quizartinib (AC220) Dapagliflozin Cyclosporine Irbesartan Rapamycin (Sirolimus) Everolimus (RAD001) DAPT (GSI-IX) Amprenavir (agenerase) Temsilolimus Dacomitinib (PF299804, PF299) Cisplatin Tivantinib (ARQ 197) LDK378 |
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| Sertaconazole nitrate | Cytisine | Eltrombopag |
| Sodium ascorbate | Artemether | Ticlopidine HCl |
| Sodium butyrate | Chlorogenic acid | Ticagrelor |
| Sodium Nitrite | Vinorelbine | Zinc Pyrithione |
| Thiamphenicol | vinblastine | Candesartan Cilexetil |
| Tiratricol | Cepharanthine | Cyproheptadine |
| Valganciclovir HCl | CP-945598 HCl | hydrochloride |
| Valnemulin HCl | Dovitinib (TKI-258, CHIR-258) | Dibucaine |
| Azathioprine | Altretamine | Ciclesonide |
| Bisacodyl | Linifanib (ABT-869) | Tiagabine |
| Bromhexine HCl | PSI-7977 | Bedaquiline fumarate |
| Butoconazole nitrate | Sildenafil | Bedaquiline |
| Chenodeoxycholic Acid | Artemether (SM-224) | Chlorhexidine |
| Chloroxine | Cobicistat (GS-9350) | digluconate |
| Crystal Violet | Imiquimod | Promethazine HCl |
| Cyclamic acid | Ponatinib (AP24534) | Losmapimod |
| Cyclosporin A | ABT-199 | Mupirocin |
| Diclazuril | Embelin | Hydroxychloroquine |
| Diclofenac Diethylamine | Neratinib (HKI-272) | Sulfate |
| Diphenhydramine HCl | Orotic acid | Lomitapide |
| Dronedarone HCl | Anidulafungin | Desogestrel |
| Econazole nitrate | EMPTY | Octreotide acetate |
| Erythromycin Ethylsuccinate | Cabozantinib malate (XL184) | Pentamidine |
| Isoconazole nitrate | Azelnidipine | isethionate |
| Isoniazid | Licofelone | Topotecan |
| Levosimendan | KPT-330 | Pentobarbital sodium salt |
| Menadione | Mizoribine | Radotinib(IY-5511) |
| Mequinol | Benserazide HCl | Pexidartinib (PLX3397) |
| Miconazole | Bazedoxifene HCl | Entrectinib |
| Miconazole Nitrate | Mubritinib (TAK 165) | R788 disodium |
| Mycophenolic acid | Tripelennamine HCl | Doxycycline HCl |
| Nadifloxacin | Rupatadine Fumarate | L-Glutamine |
| Nalidixic acid | Homatropine | Fingolimod (FTY720) |
| Nedaplatin | Methylbromide | Vandetanib (ZD6474) |
| Nifedipine | Amoxapine | TOK-001 |
| Nisoldipine | Bacitracin | Oxaliplatin |
| Oxytetracycline (Terramycin) | Capreomycin Sulfate | Pacritinib |
| Rifampin | Chlorhexidine HCl | VRT752271 |
| Sodium salicylate | Colistin Sulfate | |
| Sorbitol | Diacerein | |
| Streptomycin sulfate | Flubendazole | |
| Sulbactam sodium | | |
| Sulconazole Nitrate | | |

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| Sulfamerazine | Fudosteine | |
| Sulfameter | Meclizine 2HCl | |
| Sulfamethizole | Minocycline HCl | |
| Terbinafine HCl | Nicardipine HCl | |
| Tilmicosin | Alendronate | |
| Tioconazole | Naratriptan | |
| Toltrazuril | K-115 | |
| Zafirlukast | DL- α - | |
| Diethylstilbestrol | Difluoromethylornithine | |
| D-Mannitol | (hydrochloride hydrate) | |
| Doxercalciferol | Atovaquone | |
| Doxifluridine | Fostamatinib (R788) | |
| Haloperidol | Darunavir Ethanolate | |
| Idebenone | SKF 525A | |
| Itraconazole | (hydrochloride) | |
| Mitoxantrone HCl | BAF312 (Siponimod) | |
| Rifapentine | Gallic acid | |
| Calcitriol | Maprotiline HCl | |
| Tacrolimus (FK506) | Trimipramine | |
| Fosaprepitant dimeglumine salt | (maleate) | |
| Sitafloxacin Hydrate | Napabucasin | |
| Alfacalcidol | Theophylline | |
| Cabazitaxel | Aminoguanidine | |
| Poziotinib | hydrochloride | |
| Pimozide | Imipramine | |
| Ciclopirox | (hydrochloride) | |
| Oltipraz | | |
| Triclosan | | |