

Lanthier M, Miller KL, Nardinelli C, Woodcock J An improved approach to measuring drug innovation finds steady rates of first-in-class pharmaceuticals, 1987-2011. Health Aff (Millwood). 2013;32(8).

Appendix Exhibit A

List of Approved New Molecular Entities (1987 – 2011) and Corresponding Innovation Categories

Approval Year	Trade Name	Active Ingredient(s)	Drug Class	Innovation Category	Top 25 Company
1987	Activase	Alteplase	tissue plasminogen activator (TPA)	First in Class	
1987	Iopidine	Apraclonidine Hydrochloride	ophthalmic alpha adrenergic agonist	First in Class	
1987	Rimadyl	Carprofen	Nonsteroidal anti-inflammatory drug - propionic acid derivative	Addition to Class	Y
1987	Cefmax	Cefmenoxime Hydrochloride	cephalosporin antibacterial	Addition to Class	Y
1987	Cipro	Ciprofloxacin Hydrochloride	fluoroquinolone antimicrobial	Advance in Class	
1987	Prozac	Fluoxetine Hydrochloride	selective serotonin reuptake inhibitor (SSRI)	First in Class	Y
1987	Prinivil	Lisinopril	angiotensin converting enzyme inhibitor	Addition to Class	Y
1987	Mevacor	Lovastatin	HMG CoA-reductase inhibitor	First in Class	Y
1987	Rowasa	Mesalamine	aminosalicylate	Advance in Class	
1987	Primacor	Milrinone Lactate	phosphodiesterase-3 inhibitor	Addition to Class	Y
1987	Novantrone	Mitoxantrone Hydrochloride	topoisomerase II inhibitor	Addition to Class	Y
1987	Elocon	Mometasone Furoate	corticosteroid	Addition to Class	Y
1987	Bactroban	Mupirocin	RNA synthetase inhibitor antibacterial	Addition to Class	
1987	Levatol	Penbutolol Sulfate	beta adrenergic blocker	Addition to Class	Y
1987	Ucephan	Sodium Phenylacetate, Sodium Benzoate	nitrogen binding agent	Advance in Class	
1987	Hytrin	Terazosin Hydrochloride	alpha adrenergic blocker	Addition to Class	Y
1987	Terazol 7	Terconazole	Azole Antifungal - topical	Addition to Class	Y
1987	Actigall	Ursodiol	bile acid	First in Class	
1987	Retrovir	Zidovudine	HIV nucleoside analog reverse transcriptase inhibitor (HIV-1 NRTI)	First in Class	Y
1988	Hismanal	Astemizole	histamine-1 (H1) receptor antagonist	Addition to Class	Y
1988	Photoplex	Avobenzone, Padimate O	sunscreen	Addition to Class	Y
1988	Cartrol	Carteolol Hydrochloride	beta adrenergic blocker	Addition to Class	Y
1988	Ceradon	Cefotiam Hydrochloride	cephalosporin antibacterial	Addition to Class	
1988	Voltaren	Diclofenac Sodium	Nonsteroidal anti-inflammatory drug - acetic acid derivative	Addition to Class	Y
1988	Ethamolin	Ethanolamine Oleate	sclerosing agent	Advance in Class	Y
1988	Ifex	Ifosfamide	alkylating drug	Advance in Class	Y
1988	Mesnex	Mesna	cytoprotective agent - ifosfamide-induced hemorrhagic cystitis	First in Class	
1988	Cytotec	Misoprostol	prostaglandin-1 (PGE1) analog	First in Class	

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Approval Year	Trade Name	Active Ingredient(s)	Drug Class	Innovation Category	Top 25 Company
1988	Naftin	Naftifine Hydrochloride	allylamine antifungal	First in Class	Y
1988	Cardene	Nicardipine Hydrochloride	dihydropyridine calcium channel blocker	Addition to Class	Y
1988	Nimotop	Nimodipine	dihydropyridine calcium channel blocker - vasospasm after subarachnol hemorrhage	First in Class	
1988	Axid	Nizatidine	histamine-2 (H2) receptor antagonist	Addition to Class	Y
1988	Sandostatin	Octreotide Acetate	somatostatin analog	First in Class	Y
1988	Oxistat	Oxiconazole Nitrate	Azole Antifungal - topical	Addition to Class	Y
1988	Permax	Pergolide Mesylate	ergot-derived dopamine receptor agonist	Advance in Class	Y
1988	Thiola	Tiopronin	reducing and complexing thiol	First in Class	
1989	Adenocard	Adenosine	antiarrhythmic - Class V (other) - adenosine receptor agonist	First in Class	
1989	Eminase	Anistreplase	tissue plasminogen activator (TPA)	Addition to Class	Y
1989	Paraplatin	Carboplatin	platinum-based drug	Advance in Class	Y
1989	Suprax	Cefixime	cephalosporin antibacterial	Addition to Class	Y
1989	Zefazone	Cefmetazole Sodium	cephalosporin antibacterial	Addition to Class	Y
1989	Cefpiramide	Cefpiramide Sodium	cephalosporin antibacterial	Addition to Class	Y
1989	Anafranil	Clomipramine Hydrochloride	tricyclic antidepressant (TCA)	Advance in Class	Y
1989	Clozaril	Clozapine	atypical antipsychotic	First in Class	Y
1989	Dalgan	Dezocine	opioid agonist/antagonist	Addition to Class	Y
1989	Epogen	Epoetin alfa	erythropoiesis-stimulating agent (ESA)	First in Class	
1989	Eulexin	Flutamide	androgen receptor inhibitor	First in Class	Y
1989	Cytovene	Ganciclovir Sodium	nucleoside analog CMV DNA polymerase inhibitor	First in Class	Y
1989	Zoladex	Goserelin Acetate	gonadotropin releasing hormone (GnRH) agonist	Addition to Class	Y
1989	Decabid	Indecainide Hydrochloride	antiarrhythmic - Class I	Addition to Class	Y
1989	Alferon N Injection	Interferon alfa-n3 (Human Leukocyte Derived)	interferon alpha	Addition to Class	
1989	Toradol	Ketorolac Tromethamine	Nonsteroidal anti-inflammatory drug - acetic acid derivative	Advance in Class	Y
1989	Mefloquine Hydrochloride	Mefloquine Hydrochloride	antimalarial - Aryl amino alcohol	Advance in Class	
1989	Optipranolol	Metipranolol Hydrochloride	beta adrenergic blocker	Addition to Class	
1989	Ortho Cyclen	Norgestimate, Ethinyl Estradiol	estrogen/progestin COC	Addition to Class	Y
1989	Prilosec	Omeprazole	proton pump inhibitor	First in Class	Y
1989	Pindac	Pinacidil	potassium channel opener	Addition to Class	Y
1989	Rythmol	Propafenone Hydrochloride	antiarrhythmic - Class I	Addition to Class	
1989	Diprivan	Propofol	general anesthetic	Addition to class	Y

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1989	Eldepryl	Selegiline Hydrochloride	monoamine oxidase inhibitor (MAOI)	First in Class	
1990	Hexalen	Altretamine	alkylating drug	Advance in Class	
1990	Vascor	Bepidil Hydrochloride	dihydropyridine calcium channel blocker	Advance in Class	Y
1990	Exosurf	Colfosceril Palmitate, Cetyl Alcohol, Tyloxapol	surfactant	First in Class	Y
1990	Rev-Eyes	Dapiprazole Hydrochloride	ophthalmic alpha adrenergic blocker	First in Class	
1990	Cardura	Doxazosin Mesylate	alpha adrenergic blocker	Addition to Class	Y
1990	Ornidyl	Eflornithine Hydrochloride	decarboxylase inhibitor	First in Class	Y
1990	ProSom	Estazolam	benzodiazepine	Addition to Class	Y
1990	Diflucan	Fluconazole	Azole antifungal - Triazole	First in Class	Y
1990	Cutivate	Fluticasone Propionate	corticosteroid	Addition to Class	Y
1990	Ultravate	Halobetasol Propionate	corticosteroid	Addition to Class	Y
1990	Idamycin	Idarubicin Hydrochloride	anthracycline topoisomerase inhibitor	Advance in Class	
1990	Actimune	Interferon gamma-1b	interferon gamma	First in Class	
1990	Dynacirc	Isradipine	dihydropyridine calcium channel blocker	Addition to Class	Y
1990	Ergamisol	Levamisole Hydrochloride	Immunomodulator	Advance in Class	Y
1990	Ethmozine	Moricizine Hydrochloride	antiarrhythmic - Class I	Advance in Class	
1990	Synarel	Nafarelin Acetate	gonadotropin releasing hormone (GnRH) agonist	Addition to Class	Y
1990	Floxin	Ofloxacin	fluoroquinolone antimicrobial	Addition to Class	Y
1990	Dipentum	Olsalazine Sodium	aminosalicylate	Advance in Class	
1990	Adagen	Pegademase Bovine	bovine intestinal adenosine deaminase	First in Class	
1990	Arduan	Pipecuronium Bromide	nondepolarizing neuromuscular blocker	Addition to Class	
1991	Ceredase	Alglucerase	hydrolytic lysosomal glucocerebrosidase-specific enzyme	First in Class	
1991	Zithromax	Azithromycin	macrolide antimicrobial	Advance in Class	Y
1991	Lotensin	Benazepril Hydrochloride	angiotensin converting enzyme inhibitor	Addition to Class	Y
1991	Survanta	Beractant	surfactant	Addition to Class	Y
1991	BOTOX	Botulinum Toxin Type A	acetylcholine release inhibitor	First in Class	
1991	Cefzil	Cefprozil	cephalosporin antibacterial	Addition to Class	Y
1991	Biaxin	Clarithromycin	macrolide antimicrobial	Advance in Class	Y
1991	Videx	Didanosine	HIV nucleoside analog reverse transcriptase inhibitor (HIV-1 NRTI)	Advance in Class	Y
1991	Nuromax	Doxacurium Chloride	nondepolarizing neuromuscular blocker	Addition to Class	Y
1991	Penetrex	Enoxacin	fluoroquinolone antimicrobial	Addition to Class	Y
1991	Lodine	Etodolac	Nonsteroidal anti-inflammatory drug - acetic acid derivative	Addition to Class	Y

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1991	Plendil	Felodipine	dihydropyridine calcium channel blocker	Addition to Class	Y
1991	Neupogen	Filgrastim	leukocyte growth factor - Granulocyte colony-stimulating factor (G-CSF)	First in Class	
1991	Fludara	Fludarabine Phosphate	nucleoside Metabolic Inhibitor - purine analog	First in Class	
1991	Romazicon	Flumazenil	benzodiazepine antagonist	First in Class	Y
1991	Foscavir	Foscarnet Sodium	pyrophosphate analog CMV DNA polymerase inhibitor	Advance in Class	
1991	Monopril	Fosinopril Sodium	angiotensin converting enzyme inhibitor	Addition to Class	Y
1991	Ganite	Gallium Nitrate	calcium regulator	First in Class	
1991	Supprelin	Histrelin Acetate	gonadotropin releasing hormone (GnRH) agonist	Advance in Class	Y
1991	Ismo	Isosorbide Mononitrate	nitrate vasodilator	Addition to Class	Y
1991	Lorabid	Loracarbef	cephalosporin antibacterial	Addition to Class	Y
1991	Relafen	Nabumetone	Nonsteroidal anti-inflammatory drug - acetic acid derivative	Addition to Class	Y
1991	Zofran	Ondansetron Hydrochloride	serotonin-3 (5-HT3) receptor antagonist	First in Class	Y
1991	Aredia	Pamidronate Disodium	bisphosphonate	Advance in Class	Y
1991	Nipent	Pentostatin	nucleoside Metabolic Inhibitor - purine analog	Advance in Class	Y
1991	Pravachol	Pravastatin Sodium	HMG CoA-reductase inhibitor	Addition to Class	Y
1991	Accupril	Quinapril Hydrochloride	angiotensin converting enzyme inhibitor	Addition to Class	Y
1991	Altace	Ramipril	angiotensin converting enzyme inhibitor	Addition to Class	
1991	Leukine	Sargramostim	leukocyte growth factor - Granulocyte-macrophage colony stimulating factor (GM-CSF)	First in Class	
1991	Zoloft	Sertraline Hydrochloride	selective serotonin reuptake inhibitor (SSRI)	Addition to Class	Y
1991	Zocor	Simvastatin	HMG CoA-reductase inhibitor	Addition to Class	Y
1991	Chemet	Succimer	lead chelator	Advance in Class	Y
1991	Ticlid	Ticlopidine Hydrochloride	P2Y12 platelet inhibitor	First in Class	Y
1992	Proleukin	Aldesleukin	lymphocyte growth factor	First in Class	
1992	Norvasc	Amlodipine Besylate	dihydropyridine calcium channel blocker	Addition to Class	Y
1992	Mepron	Atovaquone	antiprotozoal - Naphthoquinone	First in Class	Y
1992	Zebeta	Bisoprolol Fumarate	beta adrenergic blocker	Addition to Class	Y
1992	Vantin	Cefpodoxime Proxetil	cephalosporin antibacterial	Addition to Class	Y
1992	Suprane	Desflurane	general anesthetic	Addition to Class	
1992	Desogen	Desogestrel, Ethinyl Estradiol	estrogen/progestin COC	Addition to Class	
1992	Proscar	Finasteride	5-alpha reductase inhibitor	First in Class	Y
1992	Manoplax	Flosequinan	vasodilator	Addition to Class	

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1992	Halfan	Halofantrine Hydrochloride	antimalarial - Aryl amino alcohol	Advance in Class	Y
1992	Sporanox	Itraconazole	Azole antifungal - Triazole	Advance in Class	Y
1992	Maxaquin	Lomefloxacin Hydrochloride	fluoroquinolone antimicrobial	Addition to Class	Y
1992	Actinex	Masoprocol	topical keratolytic agent	Addition to Class	
1992	Mivacron	Mivacurium Chloride	nondepolarizing neuromuscular blocker	Advance in Class	Y
1992	Tilade	Nedocromil Sodium	mast cell stabilizer	Addition to Class	
1992	Daypro	Oxaprozin	Nonsteroidal anti-inflammatory drug - propionic acid derivative	Addition to Class	Y
1992	Taxol	Paclitaxel	Microtubule Inhibitor - taxane	First in Class	Y
1992	Paxil	Paroxetine Hydrochloride	selective serotonin reuptake inhibitor (SSRI)	Addition to Class	Y
1992	Mycobutin	Rifabutin	rifamycin antimycobacterial	Advance in Class	
1992	Betapace	Sotalol Hydrochloride	antiarrhythmic - Class II / III	Advance in Class	Y
1992	Imitrex	Sumatriptan Succinate	serotonin (5-HT) 1b/1d receptor agonist	First in Class	Y
1992	Omniflox	Temafloxacin Hydrochloride	fluoroquinolone antimicrobial	Addition to Class	Y
1992	Vumon	Teniposide	topoisomerase II inhibitor	Advance in Class	Y
1992	Lamisil	Terbinafine Hydrochloride	allylamine antifungal	Addition to Class	Y
1992	HIVID	Zalcitabine	HIV nucleoside analog reverse transcriptase inhibitor (HIV-1 NRTI)	Advance in Class	Y
1992	Ambien	Zolpidem Tartrate	non-benzodiazepine hypnotic	Addition to Class	
1993	Trasylol	Aprotinin	antifibrinolytic	Advance in Class	Y
1993	Dovonex	Calcipotriene	vitamin D analog	First in Class	Y
1993	Propulsid	Cisapride Monohydrate	prokinetic	Addition to Class	Y
1993	Leustatin	Cladribine	nucleoside Metabolic Inhibitor - purine analog	Advance in Class	Y
1993	Pulmozyme	Dornase alfa	recombinant human deoxyribonuclease 1 (rhDNase) enzyme	First in Class	
1993	Lovenox	Enoxaparin Sodium	low molecular weight heparin (LMWH)	First in Class	Y
1993	Felbatol	Felbamate	antiepileptic	Advance in Class	
1993	Tricor	Fenofibrate	peroxisome proliferator-activated receptor (PPAR) alpha agonist	Addition to Class	
1993	Lescol	Fluvastatin Sodium	HMG CoA-reductase inhibitor	Addition to Class	Y
1993	Neurontin	Gabapentin	antiepileptic	Advance in Class	Y
1993	Kytril	Granisetron Hydrochloride	serotonin-3 (5-HT3) receptor antagonist	Addition to Class	Y
1993	Betaseron	Interferon beta-1b	recombinant human interferon beta	First in Class	
1993	Livostin	Levocabastine Hydrochloride	histamine-1 (H1) receptor antagonist	Advance in Class	Y

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1993	Orlaam	Levomethadyl Acetate Hydrochloride	opioid antagonist	Advance in Class	
1993	Alomide	Lodoxamide Tromethamine	mast cell stabilizer	Addition to Class	
1993	Claritin	Loratadine	histamine-1 (H1) receptor antagonist	Addition to Class	Y
1993	Aceon	Perindopril Erbumine	angiotensin converting enzyme inhibitor	Addition to Class	Y
1993	Flumadine	Rimantadine Hydrochloride	influenza A M2 protein inhibitor	Advance in Class	
1993	Risperdal	Risperidone	atypical antipsychotic	Advance in Class	Y
1993	Metastron	Strontium Chloride, SR-89	radioactive therapeutic agent	Advance in Class	
1993	Cognex	Tacrine Hydrochloride	cholinesterase inhibitor	First in Class	Y
1993	Zosyn	Tazobactam Sodium/Piperacillin Sodium	Penicillin class antibacterial and beta-lactamase inhibitor	Addition to Class	Y
1993	Demadex	Torsemide	loop diuretic	Addition to Class	
1993	Neutrexin	Trimetrexate Glucuronate	folate analog metabolic inhibitor	Advance in Class	
1993	Effexor	Venlafaxine Hydrochloride	serotonin and norepinephrine reuptake inhibitor (SNRI)	First in Class	Y
1994	ReoPro	Abciximab	Glycoprotein IIb/IIIa inhibitor	First in Class	
1994	Semprex-D	Acrivastine, Pseudoephedrine Hydrochloride	histamine-1 (H1) receptor antagonist; alpha adrenergic agonist	Addition to Class	Y
1994	Rhinocort	Budesonide	corticosteroid	Addition to Class	
1994	Cystagon	Cysteamine Bitartrate	cysteine depleting agent	First in Class	
1994	Fragmin	Dalteparin Sodium	low molecular weight heparin (LMWH)	Addition to Class	Y
1994	Trusopt	Dorzolamide Hydrochloride	carbonic anhydrase inhibitor	First in Class	Y
1994	Famvir	Famciclovir	nucleoside Analog Herpes virus DNA Polymerase Inhibitor	Addition to Class	Y
1994	Luvox	Fluvoxamine Maleate	selective serotonin reuptake inhibitor (SSRI)	Addition to Class	
1994	Cerezyme	Imiglucerase	hydrolytic lysosomal glucocerebrosidase-specific enzyme	Advance in Class	
1994	Lamictal	Lamotrigine	antiepileptic	Advance in Class	Y
1994	Serzone	Nefazodone Hydrochloride	serotonin reuptake inhibitor	Addition to Class	Y
1994	Oncaspar	Pegaspargase	asparagine-specific enzyme	Addition to Class	
1994	Vexol	Rimexalone	corticosteroid	Advance in Class	
1994	Zemuron	Rocuronium Bromide	nondepolarizing neuromuscular blocker	Addition to Class	
1994	Serevent	Salmeterol Xinafoate	beta-2 adrenergic agonist	Advance in Class	Y
1994	Renormax	Spirapril Hydrochloride	angiotensin converting enzyme inhibitor	Addition to Class	
1994	Zerit	Stavudine	HIV nucleoside analog reverse transcriptase inhibitor (HIV-1 NRTI)	Advance in Class	Y

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1994	Prograf	Tacrolimus	calcineurin inhibitor immunosuppressant	Advance in Class	
1994	Navelbine	Vinorelbine Tartrate	vinca alkaloid	Advance in Class	Y
1995	Precose	Acarbose	alpha glucosidase inhibitor	First in Class	Y
1995	Fosamax	Alendronate Sodium	bisphosphonate	Advance in Class	Y
1995	Ethyol	Amifostine	cytoprotective agent - renal toxicity associated with repeated administration of cisplatin	First in Class	
1995	Arimidex	Anastrozole	aromatase inhibitor	First in Class	Y
1995	Azelex	Azelaic Acid	dicarboxylic acid	First in Class	
1995	Casodex	Bicalutamide	androgen receptor inhibitor	Addition to Class	Y
1995	Coreg	Carvedilol	alpha/beta-adrenergic blocker	Addition to Class	Y
1995	Cedax	Ceftibuten	cephalosporin antibacterial	Addition to Class	Y
1995	Zyrtec	Cetirizine	histamine-1 (H1) receptor antagonist	Addition to Class	Y
1995	Zinecard	Dexrazoxane	cytoprotective agent - anthracycline extravasation	First in Class	
1995	Dynabac	Dirithromycin	macrolide antimicrobial	Addition to Class	Y
1995	Eprex/Procrit	Epoetin alfa	erythropoiesis-stimulating agent (ESA)	Advance in Class	Y
1995	Flolan	Epoprostenol Sodium	prostacycline vasodilator	First in Class	Y
1995	Amaryl	Glimepiride	sulfonylurea	Addition to Class	
1995	Corvert	Ibutilide Fumurate	antiarrhythmic - Class III	Addition to Class	Y
1995	Epivir	Lamivudine	HIV nucleoside analog reverse transcriptase inhibitor (HIV-1 NRTI)	Advance in Class	Y
1995	Prevacid	Lansoprazole	proton pump inhibitor	Addition to Class	Y
1995	Cozaar	Losartan Potassium	angiotensin 2 receptor blocker	First in Class	Y
1995	Glucophage	Metformin Hydrochloride	biguanide	Advance in Class	
1995	Univasc	Moexipril Hydrochloride	angiotensin converting enzyme inhibitor	Addition to Class	
1995	Cellcept	Mycophenolate Mofetil	antimetabolite immunosuppressant	Advance in Class	Y
1995	Revex	Nalmefene Hydrochloride	opioid antagonist	Addition to Class	
1995	Sular	Nisoldipine	dihydropyridine calcium channel blocker	Addition to Class	Y
1995	Photofrin	Porfimer Sodium	photoactivated radical generator	First in Class	
1995	Rilutek	Riluzole	benzothiazole	First in Class	Y
1995	Invirase	Saquinavir	HIV protease inhibitor	First in Class	Y
1995	Ultane	Sevoflurane	general anesthetic	Addition to Class	Y
1995	Ultram	Tramadol Hydrochloride	opioid agonist	Addition to Class	Y
1996	Differin	Adapalene	retinoid	Addition to Class	
1996	Albenza	Albendazole	anthelmintic - benzimidazole	Advance in Class	Y
1996	Aphthasol	Amlexanox	anti-inflammatory oral paste	Advance in Class	
1996	Lipitor	Atorvastatin Calcium	HMG CoA-reductase inhibitor	Advance in Class	Y

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1996	Astelin	Azelastine Hydrochloride	histamine-1 (H1) receptor antagonist	Addition to Class	
1996	IVY Block	Bentoquatam	poison ivy protectant	First in Class	
1996	Cystadane	Betaine Anhydrous	methylating agent	First in Class	
1996	Alphagan	Brimonidine Tartrate	ophthalmic alpha adrenergic agonist	Addition to Class	
1996	Mentax	Butenafine Hydrochloride	benzylamine antifungal	Addition to Class	
1996	Dostinex	Cabergoline	ergot-derived dopamine receptor agonist	Addition to Class	Y
1996	Maxipime	Cefepime Hydrochloride	cephalosporin antibacterial	Addition to Class	Y
1996	Vistide	Cidofovir	nucleotide analog CMV DNA polymerase inhibitor	Addition to Class	
1996	Orgaran	Danaparoid Sodium	heparin derivative	Addition to Class	
1996	Taxotere	Docetaxel	Microtubule Inhibitor - taxane	Advance in Class	Y
1996	Aricept	Donepezil Hydrochloride	cholinesterase inhibitor	Advance in Class	
1996	Allegra	Fexofenadine Hydrochloride	histamine-1 (H1) receptor antagonist	Addition to Class	Y
1996	Monurol	Fosfomycin Tromethamine	phosphonic acid antibacterial	First in Class	
1996	Cerebyx	Fosphenytoin Sodium	antiepileptic	Addition to Class	Y
1996	Gemzar	Gemcitabine Hydrochloride	nucleoside Metabolic Inhibitor - Pyrimidine analog	Advance in Class	Y
1996	Copaxone	Glatiramer Acetate	Immunomodulator - MS specific	First in Class	
1996	Crixivan	Indinavir Sulfate	HIV protease inhibitor	Advance in Class	Y
1996	Avonex	Interferon beta-1a	recombinant human interferon beta	Advance in Class	
1996	Camptosar	Irinotecan Hydrochloride	topoisomerase I inhibitor	Advance in Class	Y
1996	Stromectol	Ivermectin	antiparasitic - macrocyclic lactone	First in Class	Y
1996	Xalatan	Latanoprost	prostaglandin analog	First in Class	Y
1996	Humalog	Lispro Insulin	insulin analog	Addition to Class	Y
1996	Merrem	Meropenem	penem antibacterial	Addition to Class	Y
1996	ProAmatine	Midodrine Hydrochloride	alpha adrenergic agonist	First in Class	
1996	Glyset	Miglitol	alpha glucosidase inhibitor	Addition to Class	Y
1996	Remeron	Mirtazapine	antidepressant - atypical	Addition to Class	
1996	Viramune	Nevirapine	HIV nonnucleoside analog reverse transcriptase inhibitor (HIV-1 NNRTI)	First in Class	Y
1996	Nilandron	Nilutamide	androgen receptor inhibitor	Addition to Class	
1996	Zyprexa	Olanzapine	atypical antipsychotic	Addition to Class	Y
1996	Patanol	Olopatadine Hydrochloride	histamine-1 (H1) inhibitor; mast cell stabilizer	Addition to Class	
1996	Denavir	Penciclovir	nucleoside Analog Herpes virus DNA Polymerase Inhibitor	Addition to Class	Y
1996	Elmiron	Pentosan Polysulfate Sodium	glycosaminoglycan	First in Class	
1996	Ultiva	Remifentanyl Hydrochloride	opioid agonist	Addition to Class	Y

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1996	Retavase	Reteplase	tissue plasminogen activator (TPA)	Addition to Class	
1996	Norvir	Ritonavir	HIV protease inhibitor	Advance in Class	Y
1996	Naropin	Ropivacaine Hydrochloride Monohydrate	amide local anesthetic	Addition to Class	
1996	Buphenyl	Sodium Phenylbutyrate	nitrogen binding agent	Advance in Class	
1996	Zagam	Sparfloxacin	fluoroquinolone antimicrobial	Addition to Class	Y
1996	Zanaflex	Tizanidine Hydrochloride	alpha-2 adrenergic agonist	First in Class	
1996	Topamax	Topiramate	antiepileptic	Addition to Class	Y
1996	Hycamtin	Topotecan Hydrochloride	topoisomerase I inhibitor	First in Class	Y
1996	Mavik	Trandolapril	angiotensin converting enzyme inhibitor	Addition to Class	
1996	Diovan	Valsartan	angiotensin 2 receptor blocker	Addition to Class	Y
1996	Accolate	Zafirlukast	leukotriene modifiers	First in Class	Y
1996	Zyflo	Zileuton	leukotriene modifiers	Addition to Class	Y
1997	Trovan	Alatrofloxacin Mesylate	fluoroquinolone antimicrobial	Addition to Class	Y
1997	Agrylin	Anagrelide Hydrochloride	platelet-reducing agent	Advance in Class	
1997	Normiflo	Ardeparin Sodium	low molecular weight heparin (LMWH)	Addition to Class	Y
1997	Regranex	Becaplermin	human platelet-derived growth factor	First in Class	Y
1997	Duract	Bromfenac Sodium	Nonsteroidal anti-inflammatory drug - acetic acid derivative	Addition to Class	Y
1997	Infasurf	Calfactant	surfactant	Addition to Class	
1997	Omnicef	Cefdinir	cephalosporin antibacterial	Addition to Class	Y
1997	Baycol	Cerivastatin Sodium	HMG CoA-reductase inhibitor	Addition to Class	Y
1997	Plavix	Clopidogrel Bisulfate	P2Y12 platelet inhibitor	Advance in Class	
1997	Zenapax	Daclizumab	interleukin-2 receptor blocking antibody	First in Class	Y
1997	Rescriptor	Delavirdine Mesylate	HIV nonnucleoside analog reverse transcriptase inhibitor (HIV-1 NNRTI)	Advance in Class	Y
1997	Anzemet	Dolasetron Mesylate	serotonin-3 (5-HT3) receptor antagonist	Addition to Class	Y
1997	Emadine	Emedastine Difumarate	histamine-1 (H1) receptor antagonist	Addition to Class	Y
1997	Teveten	Eprosartan Mesylate	angiotensin 2 receptor blocker	Addition to Class	Y
1997	Corlopan	Fenoldopam Mesylate	Dopaminergic Agonist - D1-like receptor agonist	First in Class	
1997	Antizol	Fomepizole	antidote - ethylene glycol poisoning	Addition to Class	
1997	Raxar	Grepafloxacin Hydrochloride	fluoroquinolone antimicrobial	Addition to Class	Y
1997	Aldara	Imiquimod	Immunomodulator - cutaneous immune response modifier	First in Class	
1997	Infergen	Interferon alfacon-1	interferon alpha	Addition to Class	Y
1997	Avapro	Irbesartan	angiotensin 2 receptor blocker	Addition to Class	

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Approval Year	Trade Name	Active Ingredient(s)	Drug Class	Innovation Category	Top 25 Company
1997	Femara	Letrozole	aromatase inhibitor	Addition to Class	Y
1997	Posicor	Mibefradil Dihydrochloride	dihydropyridine calcium channel blocker	Addition to Class	Y
1997	Viracept	Nelfinavir Mesylate	HIV protease inhibitor	Advance in Class	
1997	Neumega	Oprelvekin	megakaryocyte growth factor	First in Class	
1997	Mirapex	Pramipexole Dihydrochloride	nonergot dopamine agonist	First in Class	Y
1997	Seroquel	Quetiapine Fumarate	atypical antipsychotic	Addition to Class	Y
1997	Evista	Raloxifene Hydrochloride	estrogen agonist/antagonist - osteoporosis	First in Class	Y
1997	Prandin	Repaglinide	glinide	First in Class	
1997	Rituxan	Rituximab	CD20-directed cytolytic antibody	First in Class	
1997	Requip	Ropinirole Hydrochloride	nonergot dopamine agonist	Addition to Class	Y
1997	Quadramet	Samarium SM 153 Lexidronam	radioactive therapeutic agent	Addition to Class	
1997	Meridia	Sibutramine Hydrochloride	norepinephrine, serotonin, and dopamine reuptake inhibitor anorectic	First in Class	
1997	Flomax	Tamsulosin Hydrochloride	alpha adrenergic blocker	Addition to Class	Y
1997	Tazorac	Tazarotene	retinoid	Addition to Class	
1997	Gabitril	Tiagabine Hydrochloride	antiepileptic	Addition to Class	Y
1997	Skelid	Tiludronate Disodium	bisphosphonate	Addition to Class	
1997	Fareston	Toremifene Citrate	estrogen agonist/antagonist	Addition to Class	
1997	Rezulin	Troglitazone	thiazolidinedione	First in Class	Y
1997	Trovan	Trovafoxacin Mesylate	fluoroquinolone antimicrobial	Addition to Class	Y
1997	Zomig	Zolmitriptan	serotonin (5-HT) 1b/1d receptor agonist	Addition to Class	Y
1998	Ziagen	Abacavir Sulfate	HIV nucleoside analog reverse transcriptase inhibitor (HIV-1 NRTI)	Advance in Class	Y
1998	Simulect	Basiliximab	interleukin-2 receptor blocking antibody	Advance in Class	Y
1998	Azopt	Brinzolamide	carbonic anhydrase inhibitor	Addition to Class	
1998	Atacand	Candesartan Cilexetil	angiotensin 2 receptor blocker	Addition to Class	Y
1998	Xeloda	Capecitabine	nucleoside Metabolic Inhibitor - Pyrimidine analog	Advance in Class	Y
1998	Celebrex	Celecoxib	Nonsteroidal anti-inflammatory drug - Cox-2 Inhibitor	First in Class	Y
1998	Celexa	Citalopram Hydrobromide	selective serotonin reuptake inhibitor (SSRI)	Addition to Class	
1998	Sustiva	Efavirenz	HIV nonnucleoside analog reverse transcriptase inhibitor (HIV-1 NNRTI)	Advance in Class	
1998	Integrilin	Eptifibatide	Glycoprotein IIb/IIIa inhibitor	Advance in Class	
1998	Enbrel	Etanercept	tumor necrosis factor (TNF) blocker	Advance in Class	
1998	Vitravene	Fomivirsen Sodium	human cytomegalovirus (CMV) antisense inhibitor	First in Class	

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1998	Remicade	Infliximab	tumor necrosis factor (TNF) blocker	First in Class	
1998	Arava	Leflunomide	antirheumatic - Pyrimidine synthesis inhibitor	First in Class	
1998	Refludan	Lepirudin	direct thrombin inhibitor	First in Class	Y
1998	Lotemax	Loteprednol Etabonate	corticosteroid	Addition to Class	
1998	Provigil	Modafinil	sympathomimetic-like agent	First in Class	
1998	Singulair	Montelukast Sodium	leukotriene modifiers	Addition to Class	Y
1998	Amerge	Naratriptan	serotonin (5-HT) 1b/1d receptor agonist	Addition to Class	Y
1998	Synagis	Palivizumab	RSV anti-F protein monoclonal (mAb)	First in Class	
1998	Zemplar	Paricalcitol	vitamin D3 analog	Addition to Class	Y
1998	Priftin	Rifapentine	rifamycin antimycobacterial	Advance in Class	Y
1998	Actonel	Risedronate Sodium	bisphosphonate	Addition to Class	
1998	Maxalt	Rizatriptan Benzoate	serotonin (5-HT) 1b/1d receptor agonist	Addition to Class	Y
1998	Sucraid	Sacrosidase	sucrose specific enzyme	First in Class	
1998	Renagel	Sevelamer Hydrochloride	phosphate binder	Addition to Class	
1998	Viagra	Sildenafil Citrate	phosphodiesterase-5 (PDE-5) inhibitor	First in Class	Y
1998	Micardis	Telmisartan	angiotensin 2 receptor blocker	Addition to Class	Y
1998	Thalomid	Thalidomide	Immunomodulator - Thalidomide and IMiD derivatives	First in Class	
1998	Aggrastat	Tirofiban Hydrochloride	Glycoprotein IIb/IIIa inhibitor	Advance in Class	Y
1998	Tasmar	Tolcapone	catechol o-methyl transferase (COMT) inhibitor	First in Class	Y
1998	Detrol	Tolterodine Tartrate	muscarinic antagonist	Addition to Class	Y
1998	Herceptin	Trastuzumab	HER2 receptor antagonist	First in Class	
1998	Valstar	Valrubicin	anthracycline topoisomerase inhibitor	Advance in Class	
1999	Panretin	Alitretinoin	retinoid	Advance in Class	
1999	Levulan Kerastick	Aminolevulinic Acid Hydrochloride	porphyrin precursor	First in Class	
1999	Agenerase	Amprenavir	HIV protease inhibitor	Advance in Class	Y
1999	Targretin	Bexarotene	retinoid	Advance in Class	
1999	Pletal	Cilostazol	phosphodiesterase-3 inhibitor - antiplatelet	First in Class	
1999	Synercid	Dalfopristin, Quinupristin	streptogramin antibacterial	First in Class	Y
1999	Ontak	Denileukin diftitox	CD25-directed cytotoxin	First in Class	
1999	Precedex	Dexmedetomidine Hydrochloride	selective alpha2-agonist	Addition to Class	Y
1999	Tikosyn	Dofetilide	antiarrhythmic - Class III	Addition to Class	Y
1999	Hectorol	Doxercalciferol	vitamin D2 analog	Addition to Class	
1999	Comtan	Entacapone	catechol o-methyl transferase (COMT) inhibitor	Addition to Class	

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1999	Ellence	Epirubicin Hydrochloride	anthracycline topoisomerase inhibitor	Advance in Class	Y
1999	Aromasin	Exemestane	aromatase inhibitor	Addition to Class	Y
1999	Antagon	Ganirelix Acetate	gonadotropin releasing hormone (GnRH) antagonist	First in Class	
1999	Tequin	Gatifloxacin	fluoroquinolone antimicrobial	Addition to Class	Y
1999	Wellferon	Interferon alfa-n1 (Lymphoblastoid)	interferon alpha	Addition to Class	Y
1999	Zaditor	Ketotifen Fumarate	histamine-1 (H1) receptor antagonist	Advance in Class	Y
1999	Keppra	Levetiracetam	antiepileptic	Addition to Class	
1999	Solage	Mequinol, Tretinoin	skin lightening agent; retinoid	Addition to Class	Y
1999	Avelox	Moxifloxacin Hydrochloride	fluoroquinolone antimicrobial	Addition to Class	Y
1999	INOmax	Nitric Oxide	pulmonary vasodilator	First in Class	
1999	Xenical	Orlistat	intestinal lipase inhibitor	First in Class	Y
1999	Tamiflu	Oseltamivir Phosphate	influenza neuraminidase inhibitor	Advance in Class	Y
1999	Alamast	Pemirolast Potassium	mast cell stabilizer	Advance in Class	
1999	Actos	Pioglitazone Hydrochloride	thiazolidinedione; peroxisome proliferator-activated receptor (PPAR) gamma agonist	Advance in Class	
1999	Curosurf	Poractant	surfactant	Addition to Class	
1999	Aciphex	Rabeprazole Sodium	proton pump inhibitor	Addition to Class	
1999	Raplon	Rapacuronium Bromide	nondepolarizing neuromuscular blocker	Addition to Class	
1999	Vioxx	Rofecoxib	Nonsteroidal anti-inflammatory drug - Cox-2 Inhibitor	Advance in Class	Y
1999	Avandia	Rosiglitazone Maleate	thiazolidinedione; peroxisome proliferator-activated receptor (PPAR) gamma agonist	Advance in Class	Y
1999	Rapamune	Sirolimus	mTor inhibitor immunosuppressant	First in Class	Y
1999	Ferrlecit	Sodium Ferric Gluconate Complex	parenteral iron replacement	Advance in Class	
1999	Temodar	Temozolomide	alkylating drug	Advance in Class	Y
1999	Sonata	Zaleplon	non-benzodiazepine hypnotic	Addition to Class	Y
1999	Relenza	Zanamivir	influenza neuraminidase inhibitor	First in Class	Y
2000	Lotronex	Alosetron Hydrochloride	serotonin-3 (5-HT3) receptor antagonist - IBS	First in Class	Y
2000	Acova	Argatroban	direct thrombin inhibitor	Addition to Class	
2000	Trisenox	Arsenic Trioxide	differentiating agent	Advance in Class	
2000	Septocaine	Articaine Hydrochloride 4%;Ephinephrine	amide local anesthetic	Addition to Class	
2000	Colazal	Balsalazide Disodium	aminosalicylate	Addition to Class	
2000	Angiomax	Bivalirudin	direct thrombin inhibitor	Addition to Class	
2000	Myobloc	Botulinum Toxin Type B	acetylcholine release inhibitor	Addition to Class	

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2000	Cetrotide	Cetrorelix Acetate	gonadotropin releasing hormone (GnRH) antagonist	Addition to Class	
2000	Evoxac	Cevimeline Hydrochloride	cholinergic agonist	Addition to Class	
2000	Welchol	Colesevelam Hydrochloride	bile acid sequestrant	Addition to Class	
2000	Abreva	Docosanol	topical antiviral - herpes labialis	First in Class	
2000	Mylotarg	Gemtuzumab Ozogamicin	CD33-directed cytotoxin	First in Class	Y
2000	NovoLog	Insulin Aspart Recombinant	insulin analog	Addition to Class	
2000	Lantus	Insulin Glargine	insulin analog	Addition to Class	Y
2000	Zyvox	Linezolid	oxazolidinone antibacterial	First in Class	Y
2000	Kaletra	Lopinavir, Ritonavir	HIV protease inhibitor	Advance in Class	Y
2000	Mobic	Meloxicam	Nonsteroidal anti-inflammatory drug - enolic acid derivative	Addition to Class	Y
2000	Mifeprex	Mifepristone	progestin antagonist	First in Class	
2000	Starlix	Nateglinide	glinide	Addition to Class	Y
2000	Trileptal	Oxcarbazepine	antiepileptic	Addition to Class	Y
2000	Protonix	Pantoprazole Sodium	proton pump inhibitor	Addition to Class	Y
2000	Exelon	Rivastigmine Tartrate	cholinesterase inhibitor	Addition to Class	Y
2000	TNKase	Tenecteplase	tissue plasminogen activator (TPA)	Addition to Class	
2000	Innohep	Tinzaparin Sodium	low molecular weight heparin (LMWH)	Addition to Class	
2000	Trelstar Depot	Triptorelin Pamoate	gonadotropin releasing hormone (GnRH) agonist	Addition to Class	
2000	Rescula	Unoprostone Isopropyl	prostaglandin analog	Advance in Class	Y
2000	Visudyne	Verteporfin	photoenhancer	First in Class	
2000	Zonegran	Zonisamide	antiepileptic	Addition to Class	
2001	Campath	Alemtuzumab	CD52-directed cytolytic antibody	First in Class	
2001	Axert	Almotriptan Malate	serotonin (5-HT) 1b/1d receptor agonist	Addition to Class	Y
2001	Kineret	Anakinra	interleukin-1 (IL-1) receptor antagonist	First in Class	Y
2001	Lumigan	Bimatoprost	prostaglandin analog	Advance in Class	
2001	Tracleer	Bosentan	endothelin receptor antagonist	First in Class	
2001	Cancidas	Caspofungin Acetate	echinocandin antifungal	First in Class	Y
2001	Spectracef	Cefditoren Pivoxil	cephalosporin antibacterial	Addition to Class	Y
2001	Aranesp	Darbepoetin alfa	erythropoiesis-stimulating agent (ESA)	Addition to Class	Y
2001	Clarinx	Desloratadine	histamine-1 (H1) receptor antagonist	Addition to Class	Y
2001	Yasmin	Drospirenone/Ethinyl Estradiol	estrogen/progestin COC	Addition to Class	
2001	Xigris	Drotrecogin alfa (Activated)	recombinant activated protein C	First in Class	Y
2001	Avodart	Dutasteride	5-alpha reductase inhibitor	Addition to Class	Y
2001	Invanz	Ertapenem Sodium	penem antibacterial	Addition to Class	Y

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2001	NuvaRing	Ethinyl Estradiol, Etonogestrel	estrogen/progestin COC	Addition to Class	
2001	Ortho Erva	Ethinyl Estradiol/Norelgestromin	estrogen/progestin COC	Addition to Class	Y
2001	Arixtra	Fondaparinux Sodium	factor Xa inhibitor	First in Class	
2001	Foradil	Formoterol Fumarate	beta-2 adrenergic agonist	Addition to Class	Y
2001	Frova	Frovatriptan	serotonin (5-HT) 1b/1d receptor agonist	Addition to Class	
2001	Reminyl	Galantamine Hydrobromide	cholinesterase inhibitor	Addition to Class	Y
2001	Gleevec	Imatinib Mesylate	kinase Inhibitor - Bcr-Abl tyrosine kinase inhibitor	First in Class	Y
2001	Natrecor	Nesiritide	natriuretic peptide	First in Class	
2001	Peg-Intron	Peginterferon alfa-2b	interferon alpha	Addition to Class	Y
2001	Elidel	Pimecrolimus	calcineurin inhibitor immunosuppressant	Addition to Class	Y
2001	Viread	Tenofovir Disoproxil Fumarate	HIV nucleotide analog reverse transcriptase inhibitor (HIV-1 NtRTI)	Advance in class	
2001	Travatan	Travoprost	prostaglandin analog	Advance in Class	
2001	Bextra	Valdecoxib	Nonsteroidal anti-inflammatory drug - Cox-2 Inhibitor	Addition to Class	Y
2001	Geodon	Ziprasidone Hydrochloride	atypical antipsychotic	Addition to Class	Y
2001	Zometa	Zoledronic Acid	bisphosphonate	Advance in Class	Y
2002	Humira	Adalimumab	tumor necrosis factor (TNF) blocker	Addition to Class	Y
2002	Hepsera	Adefovir Dipivoxil	HBV nucleotide analog reverse transcriptase inhibitor (HBV-NtRTI)	Advance in class	
2002	Abilify	Aripiprazole	atypical antipsychotic - dopamine system stabilizers	First in Class	
2002	Strattera	Atomoxetine Hydrochloride	selective norepinephrine reuptake inhibitor	First in Class	Y
2002	Relpax	Eletriptan Hydrobromide	serotonin (5-HT) 1b/1d receptor agonist	Addition to Class	Y
2002	Inspra	Eplerenone	aldosterone antagonist	Addition to Class	Y
2002	Zetia	Ezetimibe	dietary cholesterol absorption inhibitor	First in Class	
2002	Faslodex	Fulvestrant	estrogen agonist/antagonist - oestrogen receptor (ER) down-regulators	First in Class	Y
2002	Zevalin	Ibritumomab tiuxetan	CD20-directed radiotherapeutic antibody	First in Class	
2002	Extraneal	Icodextrin	peritoneal dialysis solution	Addition to Class	
2002	Rebif	Interferon beta-1a	recombinant human interferon beta	Addition to Class	
2002	Alinia	Nitazoxanide	antiprotozoal - Thiazolide	First in Class	
2002	Orfadin	Nitisinone	hydroxyphenyl-pyruvate dioxygenase inhibitor	First in Class	
2002	Benicar	Olmesartan Medoxomil	angiotensin 2 receptor blocker	Addition to Class	

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2002	Eloxatin	Oxaliplatin	platinum-based drug	Advance in Class	
2002	Neulasta	Pegfilgrastim	leukocyte growth factor - Granulocyte colony-stimulating factor (G-CSF)	Addition to Class	Y
2002	Pegasys	Peginterferon alfa-2a	interferon alpha	Addition to Class	Y
2002	Elitek	Rasburicase	uric acid specific enzyme	First in Class	
2002	Xyrem	Sodium Oxybate	central nervous system depressant	Advance in Class	
2002	Zelnorm	Tegaserod Maleate	serotonin-4 (5-HT ₄) receptor antagonist	First in Class	Y
2002	Remodulin	Treprostinil Sodium	prostacycline vasodilator	Advance in Class	
2002	VFEND	Voriconazole	Azole antifungal - Triazole	Addition to Class	Y
2003	Plenaxis	Abarelix	gonadotropin releasing hormone (GnRH) antagonist - Prostate Cancer	First in Class	
2003	Fabrazyme	agalsidase beta	hydrolytic lysosomal neutral glycosphingolipid-specific enzyme	First in Class	
2003	Amevive	Alefacept	CD2-directed LFA-3/Fc fusion protein	First in Class	
2003	Uroxatral	Alfuzosin Hydrochloride	alpha adrenergic blocker	Addition to Class	Y
2003	Emend	Aprepitant	substance P/neurokinin-1 (NK-1) receptor antagonist	First in Class	Y
2003	Reyataz	Atazanavir Sulfate	HIV protease inhibitor	Advance in Class	Y
2003	Velcade	Bortezomib	proteasome inhibitor	First in Class	
2003	Cubicin	Daptomycin	lipopeptide antibacterial	First in Class	
2003	Raptiva	Efalizumab	CD11a-directed humanized IgG1 antibody	First in Class	Y
2003	Emtriva	Emtricitabine	HIV nucleoside analog reverse transcriptase inhibitor (HIV-1 NRTI)	Addition to Class	
2003	Fuzeon	Enfuvirtide	HIV fusion inhibitor (HIV-1 FI)	First in Class	Y
2003	Elestat	Epinastine Hydrochloride	histamine-1 (H ₁) inhibitor; mast cell stabilizer	Addition to Class	
2003	Iressa	Gefitinib	kinase Inhibitor - EGFR tyrosine kinase inhibitor	First in Class	Y
2003	Factive	Gemifloxacin Mesylate	fluoroquinolone antimicrobial	Addition to Class	
2003	Boniva	Ibandronate Sodium	bisphosphonate	Addition to Class	Y
2003	Aldurazyme	Laronidase	hydrolytic lysosomal glycosaminoglycan (GAG)-specific enzyme - MPS I	First in Class	
2003	Namenda	Memantine Hydrochloride	N-methyl-D-aspartate (NMDA) receptor antagonist	First in Class	Y
2003	Zavesca	Miglustat	glucosylceramide synthase inhibitor	First in Class	
2003	Xolair	Omalizumab	anti-IgE	First in Class	Y
2003	Aloxi	Palonosetron Hydrochloride	serotonin-3 (5-HT ₃) receptor antagonist	Addition to Class	

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2003	Somavert	Pegvisomant	growth hormone receptor antagonist	First in Class	Y
2003	Crestor	Rosuvastatin Calcium	HMG CoA-reductase inhibitor	Addition to Class	
2003	Ertsczo	Sertaconazole Nitrate	Azole Antifungal - topical	Addition to Class	
2003	Cialis	Tadalafil	phosphodiesterase-5 (PDE-5) inhibitor	Addition to Class	Y
2003	Bexxar	Tositumomab and Iodine 131 Tositumomab	CD20-directed radiotherapeutic antibody	Advance in Class	
2003	Levitra	Vardenafil Hydrochloride	phosphodiesterase-5 (PDE-5) inhibitor	Addition to Class	Y
2004	Campral	Acamprosate Calcium	NMDA partial agonist	First in Class	
2004	Apokyn	Apomorphine Hydrochloride	nonergot dopamine agonist	Advance in Class	
2004	Vidaza	Azacitidine	nucleoside Metabolic Inhibitor - DNA Demethylation agent	First in Class	
2004	Avastin	Bevacizumab	Vascular Endothelial Growth Factor (VEGF) directed antibody	First in Class	Y
2004	Erbitux	Cetuximab	epidermal growth factor receptor (EGFR) antagonist	First in Class	
2004	Sensipar	Cinacalcet Hydrochloride	calcium-sensing receptor agonist	First in Class	Y
2004	Clolar	Clofarbine	nucleoside Metabolic Inhibitor - purine analog	Advance in Class	
2004	Enablex	Darifenacin Hydrobromide	muscarinic antagonist	Addition to Class	Y
2004	Cymbalta	Duloxetine Hydrochloride	serotonin and norepinephrine reuptake inhibitor (SNRI)	Addition to Class	Y
2004	Tarceva	Erlotinib Hydrochloride	kinase Inhibitor - EGFR tyrosine kinase inhibitor	Advance in Class	
2004	Lunesta	Eszopiclone	non-benzodiazepine hypnotic	Addition to Class	
2004	Ventavis	Iloprost	prostacycline vasodilator	Advance in Class	
2004	Apidra	Insulin Glulisine	insulin analog	Addition to Class	Y
2004	Fosrenol	Lanthanum Carbonate Hydrate	phosphate binder	Addition to Class	
2004	Tysabri	Natalizumab	integrin receptor antagonist	First in Class	
2004	Omacor	Omega-3-Acid Ethyl Esters	omega-3 fatty acid	First in Class	Y
2004	Kepivance	Palifermin	mucocutaneous epithelial cell growth factor	First in Class	Y
2004	Macugen	Pegaptanib Sodium	ophthalmic VEGF-directed antibody	First in Class	
2004	Alimta	Pemetrexed Disodium	folate analog metabolic inhibitor	Advance in Class	Y
2004	Lyrica	Pregabalin	calcium channel alpha2delta protein ligand	Advance in Class	Y
2004	Xifaxan	Rifaximin	rifamycin antibacterial	Addition to Class	
2004	VESIcare	Solifenacin Succinate	muscarinic antagonist	Addition to Class	
2004	Ketek	Telithromycin	ketolide antibacterial	First in Class	Y
2004	Spiriva Handihaler	Tiotropium Bromide	anticholinergic	Addition to Class	Y
2004	Sanctura	Trospium Chloride	muscarinic antagonist	Addition to Class	

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2004	Prialt	Ziconotide	N-type calcium channel antagonist	First in Class	
2005	Orencia	Abatacept	human CTLA-4 and Fc-IgG1 recombinant fusion protein	First in Class	Y
2005	Vaprisol	Conivaptan Hydrochloride	vasopressin antagonist	First in Class	
2005	Exjade	Deferasirox	iron chelator	Advance in Class	Y
2005	Baraclude	Entecavir	HBV nucleoside analog reverse transcriptase inhibitor (HBV-NRTI)	Advance in Class	Y
2005	Byetta	Exenatide	GLP-1 receptor agonist	First in Class	
2005	Naglazyme	Galsulfase	hydrolytic lysosomal glycosaminoglycan (GAG)-specific enzyme - MPS VI	First in Class	
2005	Levemir	Insulin Detemir	insulin analog	Addition to Class	
2005	Revlimid	Lenalidomide	Immunomodulator - Thalidomide and IMiD derivatives	Advance in Class	
2005	Increlex	Mecasermin [rDNA Origin]	insulin-like growth factor-1 (IGF-1)	First in Class	
2005	Iplex	Mecasermin Rinfabate [rDNA Origin]	insulin-like growth factor-1 (IGF-1)	Advance in Class	
2005	Mycamine	Micafungin Sodium	echinocandin antifungal	Advance in Class	
2005	Arranon	Nelarabine	nucleoside Metabolic Inhibitor - DNA Demethylation agent	Advance in Class	Y
2005	Nevanac	Nepafenac	Nonsteroidal anti-inflammatory drug - acetic acid derivative	Advance in Class	
2005	Symlin	Pramlintide Acetate	amylin analog	First in Class	
2005	Rozerem	Ramelteon	melatonin receptor agonist	First in Class	Y
2005	Nexavar	Sorafenib Tosylate	kinase Inhibitor - multi-kinase inhibitor (VEGFR and PDGFR)	First in Class	
2005	Tygacil	Tigecycline	Tetracycline class antibacterial - glycylcycline	First in class	Y
2005	Aptivus	Tipranavir	HIV protease inhibitor	Advance in Class	Y
2006	Myozyme	Alglucosidase alfa	hydrolytic lysosomal glycogen-specific enzyme	First in Class	
2006	Eraxis	Anidulafungin	echinocandin antifungal	Addition to Class	
2006	Pylera	Biskalcitrate; Metronidazole; Tetracycline Hydrochloride	Bismuth and Nitroimidazole Antimicrobial and Tetracycline-class Antibacterial	Addition to Class	
2006	Omnamis	Ciclesonide	corticosteroid	Addition to Class	
2006	Prezista	Darunavir	HIV protease inhibitor	Advance in Class	
2006	Sprycel	Dasatinib	kinase Inhibitor - Bcr-Abl tyrosine kinase inhibitor	Advance in Class	Y
2006	Dacogen	Decitabine	nucleoside Metabolic Inhibitor - DNA Demethylation agent	Addition to Class	
2006	Elaprase	Idursulfase	hydrolytic lysosomal glycosaminoglycan (GAG)-specific enzyme - Hunter syndrome	First in Class	

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2006	Veregen	Kunecatechins	Botanical Antiviral - catechins	First in Class	
2006	Amitiza	Lubiprostone	chloride channel activator	First in Class	
2006	Invega	Paliperidone	atypical antipsychotic	Addition to Class	Y
2006	Vectibix	Panitumumab	epidermal growth factor receptor (EGFR) antagonist	Advance in Class	Y
2006	Noxafil	Posaconazole	Azole antifungal - Triazole	Advance in Class	Y
2006	Lucentis	Ranibizumab	ophthalmic VEGF-directed antibody	Advance in Class	Y
2006	Ranexa	Ranolazine	antianginal - Partial fatty acid oxidation (pFOX) inhibitor	First in Class	
2006	Azilect	Rasagiline Mesylate	monoamine oxidase inhibitor (MAOI)	Addition to Class	Y
2006	Januvia	Sitagliptin Phosphate	dipeptidyl peptidase 4 (DPP-4) inhibitor	First in Class	Y
2006	Sutent	Sunitinib Malate	kinase Inhibitor - multi-kinase inhibitor (VEGFR and PDGFR)	Advance in Class	Y
2006	Tyzeka	Telbivudine	HBV nucleoside analog reverse transcriptase inhibitor (HBV-NRTI)	Addition to Class	
2006	Chantix	Varenicline	partial nicotine agonist	First in Class	Y
2006	Zolinza	Vorinostat	histone deacetylase (HDAC) inhibitor	First in Class	Y
2007	Tekturna	Aliskiren	renin inhibitor	First in Class	Y
2007	Letairis	Ambrisentan	endothelin receptor antagonist	Advance in Class	
2007	Doribax	Doripenem	penem antibacterial	Addition to Class	Y
2007	Soliris	Eculizumab	complement inhibitor	First in Class	
2007	Ixempra	Ixabepilone	Microtubule inhibitor - epothilone	First in Class	Y
2007	Somatuline	Lanreotide	somatostatin analog	Addition to Class	
2007	Tykerb	Lapatinib	kinase Inhibitor - dual kinase inhibitor (HER2 and EGFR)	Advance in Class	Y
2007	Vyvanse	Lisdexamfetamine dimesylate	central nervous system stimulant	Addition to Class	
2007	Selezentry	Maraviroc	CCR5 co-receptor antagonist	First in Class	Y
2007	Bystolic	Nebivolol	beta adrenergic blocker	Addition to Class	Y
2007	Tasigna	Nilotinib	kinase Inhibitor - Bcr-Abl tyrosine kinase inhibitor	Addition to Class	Y
2007	Mircera	Pegzerepoetin alfa	erythropoiesis-stimulating agent (ESA)	Addition to Class	Y
2007	Isentress	Raltegravir Potassium	human immunodeficiency virus integrase strand transfer inhibitor (HIV-1 INSTI)	First in Class	Y
2007	Altabax	Retapamulin	pleuromutilin antibacterial	First in Class	Y
2007	Neupro	Rotigotine	nonergot dopamine agonist	Addition to Class	
2007	Kuvan	Sapropterin Dihydrochloride	phenylalanine hydroxylase-stimulating protein	First in Class	
2007	Torisel	Temsirolimus	kinase Inhibitor - mTOR kinase inhibitor	First in Class	Y

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Approval Year	Trade Name	Active Ingredient(s)	Drug Class	Innovation Category	Top 25 Company
2008	Entereg	Alvimopan	peripherally acting μ -opioid receptor antagonist	Addition to Class	
2008	Cimzia	Certolizumab pegol	tumor necrosis factor (TNF) blocker	Addition to Class	
2008	Cleviprex	Clevidipine	dihydropyridine calcium channel blocker	Addition to Class	
2008		Degarelix	gonadotropin releasing hormone (GnRH) antagonist - Prostate Cancer	Addition to Class	
2008	Pristiq	Desvenlafaxine	serotonin and norepinephrine reuptake inhibitor (SNRI)	Addition to Class	Y
2008	Durezol	Difluprednate	corticosteroid	Advance in Class	
2008	Promacta	Eltrombopag	thrombopoiesis stimulating agent	Advance in Class	Y
2008	Intelence	Etravirine	HIV nonnucleoside analog reverse transcriptase inhibitor (HIV-1 NNRTI)	Advance in Class	Y
2008	Toviaz	Fesoterodine fumarate	muscarinic antagonist	Addition to Class	Y
2008	Lusedra	Fospropofol disodium	sedative-hypnotic agent	Addition to Class	Y
2008	Vimpat	Lacosamide	antiepileptic	Addition to Class	
2008	Relistor	Methylnaltrexone	peripherally acting μ -opioid receptor antagonist	First in Class	
2008	Mozobil	Plerixafor	hematopoietic stem cell mobilizer	First in Class	
2008	Arcalyst	Rilonacept	interleukin-1 (IL-1) receptor antagonist	Advance in Class	
2008	Nplate	Romiplostim	thrombopoiesis stimulating agent	First in Class	Y
2008	Banzel	Rufinamide	antiepileptic	Addition to Class	Y
2008	Rapaflo	Silodosin	alpha adrenergic blocker	Addition to Class	Y
2008		Tapentadol	opioid agonist	Addition to Class	Y
2008	Xenazine	Tetrabenazine	vesicular monoamine transporter 2 (VMAT) inhibitor	First in Class	
2009	Dysport	Abobotulinumtoxin A	acetylcholine release inhibitor	Addition to Class	
2009	Coartem	Artemether; Lumefantrine	antimalarial - artemisininins	First in Class	Y
2009	Saphris	Asenapine	atypical Antipsychotic	Addition to Class	
2009	Bepreve	Bepotastine besilate	histamine-1 (H1) receptor antagonist	Addition to Class	
2009	Besivance	Besifloxacin	fluoroquinolone antimicrobial	Addition to Class	
2009	Ilaris	Canakinumab	interleukin-1 (IL-1) receptor antagonist	Advance in Class	Y
2009	Multaq	Dronedarone	antiarrhythmic - Class III	Advance in Class	Y
2009	Kalbitor	Ecallantide	plasma kallikrein inhibitor	First in Class	
2009	Afinitor	Everolimus	kinase Inhibitor - mTOR kinase inhibitor	Advance in Class	Y
2009	xanthine oxidase inhibitor	Febuxostat	xanthine oxidase inhibitor	Addition to Class	Y

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Approval Year	Trade Name	Active Ingredient(s)	Drug Class	Innovation Category	Top 25 Company
2009	Simponi	Golimumab	tumor necrosis factor (TNF) blocker	Addition to Class	Y
2009	Fanapt	Iloperidone	atypical antipsychotic	Addition to Class	
2009	Savella	Milnacipran hydrochloride	serotonin and norepinephrine reuptake inhibitor (SNRI)	Addition to Class	
2009	Arzerra	Ofatumumab	CD20-directed cytolytic antibody	Advance in Class	Y
2009	Votrient	Pazopanib	kinase Inhibitor - multi-kinase inhibitor (VEGFR, PDGFR, c-kit)	Addition to Class	Y
2009	Livalo	Pitavastatin	HMG CoA-reductase inhibitor	Addition to Class	
2009	Folotyn	Pralatrexate	folate analog metabolic inhibitor	Advance in Class	
2009	Effient	Prasugrel	P2Y12 platelet inhibitor	Advance in Class	Y
2009	Istodax	Romidepsin	histone deacetylase (HDAC) inhibitor	Addition to Class	
2009	Onglyza	Saxagliptin	dipeptidyl peptidase 4 (DPP-4) inhibitor	Addition to Class	Y
2009	Vibativ	Telavancin	lipoglycopeptide antibacterial	Addition to Class	
2009	Samsca	Tolvaptan	vasopressin antagonist	Addition to Class	Y
2009	Stelara	Ustekinumab	interleukin-12 and -23 antagonist	First in Class	Y
2009	Sabril	Vigabatrin	antiepileptic	Addition to Class	
2010	Lastacraft	Alcaftadine	histamine-1 (H1) receptor antagonist	Addition to Class	
2010	Lumizyme	Alglucosidase alfa (2000L)	hydrolytic lysosomal glycogen-specific enzyme	Advance in Class	
2010	Jevtana	Cabazitaxel	Microtubule Inhibitor - taxane	Advance in Class	Y
2010	Carbaglu	Carglumic acid	Carbamoyl Phosphate Synthetase 1 (CPS 1) activator	First in Class	
2010	Teflaro	Ceftaroline fosamil	cephalosporin antibacterial	Addition to Class	
2010	Xiaflex	Clostridial collagenase	collagenase	First in Class	
2010	Pradaxa	Dabigatran etexilate mesylate	direct thrombin inhibitor	Advance in Class	Y
2010	Ampyra	Dalfampridine	potassium channel blocker	First in Class	
2010	Prolia	Denosumab	RANK ligand (RANKL) inhibitor	First in Class	Y
2010	Natazia	Dienogest; Estradiol Valerate	estrogen/progestin COC	Addition to Class	
2010	Halaven	Eribulin mesylate	microtubule inhibitor - halichondrin	First in Class	Y
2010	Gilenya	Fingolimod	sphingosine 1-phosphate receptor modulator	First in Class	Y
2010	Xeomin	Incobotulinumtoxin A	acetylcholine release inhibitor	Addition to Class	
2010	Victoza	Liraglutide	GLP-1 receptor agonist	Addition to Class	Y
2010	Latuda	Lurasidone hydrochloride	atypical antipsychotic	Addition to Class	
2010	Krystexxa	Pegloticase	PEGylated uric acid specific enzyme	First in Class	
2010	Asclera	Polidocanol	sclerosing agent	Addition to Class	
2010	Egrifta	Tesamorelin	growth hormone releasing factor (GRF)	First in Class	

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Approval Year	Trade Name	Active Ingredient(s)	Drug Class	Innovation Category	Top 25 Company
2010	Actemra	Tocilizumab	interleukin-6 (IL-6) receptor inhibitor	First in Class	Y
2010	Ella	Ulipristal acetate	progesterone agonist/antagonist	Addition to Class	
2010	Vpriv	Velaglucerase Alfa	hydrolytic lysosomal glucocerebroside-specific enzyme	Advance in Class	
2011	Zytiga	Abiraterone Acetate	CYP17 inhibitor	First in Class	Y
2011	Eylea	Aflibercept	ophthalmic VEGF-directed antibody	Advance in Class	
2011	Edarbi	Azilsartan medoxomil	angiotensin 2 receptor blocker	Addition to Class	Y
2011	Nulojix	Belatacept	selective T-cell costimulation blocker	First in Class	Y
2011	Benlysta	Belimumab	B-lymphocyte stimulator (BLyS)-specific inhibitor	First in Class	
2011	Victrelis	Boceprevir	hepatitis C virus (HCV) NS3/4A protease inhibitor	First in Class	Y
2011	Adcetris	Brentuximab vedotin	CD30-directed antibody-drug conjugate	First in Class	
2011	Onfi	Clobazam	benzodiazepine	Addition to Class	
2011	Xalkori	Crizotinib	kinase inhibitor - ALK inhibitor	First in Class	Y
2011	Ferriprox	Deferiprone	iron chelator	Addition to Class	
2011	Erwinaze	Erwinia L-asparaginase	asparagine-specific enzyme	Advance in Class	
2011	Potiga	Ezogabine	potassium channel opener antiepileptic drug	First in Class	
2011	Dificid	Fidaxomicin	macrolide antibacterial	Advance in Class	
2011	Firazyr	Icatibant	bradykinin B2 receptor antagonist	First in Class	
2011	Arcapta	Indacaterol	beta-2 adrenergic agonist	Addition to Class	Y
2011	Yervoy	Ipilimumab	cytotoxic T-lymphocyte antigen 4 (CTLA-4)-blocking antibody	First in Class	Y
2011	Tradjenta	Linagliptin	dipeptidyl peptidase 4 (DPP-4) inhibitor	Addition to Class	Y
2011	Edurant	Rilpivirine	HIV nonnucleoside analog reverse transcriptase inhibitor (HIV-1 NNRTI)	Addition to Class	Y
2011	Xarelto	Rivaroxaban	factor Xa inhibitor	Addition to Class	Y
2011	Dailresp	Roflumilast	selective phosphodiesterase 4 (PDE4) inhibitor	First in Class	Y
2011	Jakafi	Ruxolitinib	kinase inhibitor - JAK inhibitor	First in Class	
2011	Natroba	Spinosad	pediculicide	Addition to class	
2011	Incivek	Telaprevir	hepatitis C virus (HCV) NS3/4A protease inhibitor	Advance in Class	
2011	Brilinta	Ticagrelor	P2Y12 platelet inhibitor	Addition to Class	Y
2011	Caprelsa	Vandetanib	kinase Inhibitor - multi-kinase inhibitor (EGFR, VEGFR, RET, BRK, TIE2)	Advance in Class	Y
2011	Zelboraf	Vemurafenib	kinase inhibitor - BRAF Inhibitor	First in Class	Y

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Approval Year	Trade Name	Active Ingredient(s)	Drug Class	Innovation Category	Top 25 Company
2011	Viibryd	Vilazodone	selective serotonin reuptake inhibitor (SSRI)	Addition to Class	

Appendix Exhibit B

Additional Methodology for Defining Drug Classes

Because we lack a formal definition of what constitutes a new drug class, or a “first-in-class” drug, the primary challenge we faced upon embarking on this study was to develop a list of distinct drug classes that would serve as the basis of our analysis. Our objective in identifying drug classes was to group together drugs in a logical and consistent way that took into account the mechanism through which a drug produces an effect as well as the disease or condition which the drug is intended to treat. Although we considered using existing drug classification systems such as the World Health Organization (WHO) Anatomical Therapeutic Classification (ATC) classification systems and IMS Health Uniform System of Classification (USC) codes^{1,2}, the hierarchical structures used in these classification systems, based primarily on drug markets and primary indicated use of the drug, presented a number of challenging situations where class terms alone failed to categorize drugs at the level of detail needed to identify a drug’s mechanism of action or indicated use.

In our search for a classification standard to apply to this project, we also identified FDA’s the Established Pharmacologic Class as a potential means for establishing a set of meaningful

¹ The World Health Organization ATC codes are a drug classification system developed and maintained by the World Health Organization. ATC classification groups related drugs at five different levels based on the organ or system on which they act and their therapeutic, pharmacologic, and chemical attributes. Additional details on ATC classes can be found at <http://www.who.int/classifications/atcddd/en/>

² The USC classification system is a drug classification system developed by IMS Health primarily geared toward grouping pharmaceutical products that compete within the same market. Similar to ATC codes the USC system classified drugs based on a hierarchical structure based on numerous attributes including general therapeutic category, pharmacology, chemical structure, and indicated use. Additional detail on USC classes can be found at http://www.imshealth.com/deployedfiles/ims/Global/Content/Insights/Health%20Services%20Research%20Network/USC_Classification_Process_2011.pdf

distinct drug classes. The established pharmacologic class is a term found in the Highlights of the Prescribing Information in an approved drug label. According to FDA guidance³, an Established Pharmacologic Class is a group of drugs that share scientifically documented properties on the basis of mechanism of action, physiologic effect, or chemical structure. The established pharmacologic class of a drug or biological product is a clinically meaningful term or phrase, such as calcium channel blocker, HIV Protease Inhibitor, or macrolide antibacterial, that helps medical professionals understand the physiological effects or anticipate possible undesirable side effects known to be associated with a drug or other members in its class. An FDA established pharmacologic class of a drug is one that is supported by documented empirical evidence showing that the drug's pharmacologic class is not theoretical and is relevant to the uses indicated in the product labeling. Because the established pharmacologic class determinations emphasize the use of terms that are clinically meaningful, we found this approach to be a desirable basis for our drug classification strategy. Additional detailed information on how FDA determines the FDA established pharmacological class, including specific examples of how a pharmacologic class term is identified, is described in more detail the aforementioned FDA guidance (3).

We derived the established pharmacological class terms based on the approved FDA Labeling⁴ and through listings of pharmacological class codes available on FDA's website.⁵ Using these two sources we identified a documented FDA-established pharmacologic class for 86% of the

³ See "Guidance for Industry and Review Staff: Labeling for Human Prescription Drug and Biological Products – Determining Established Pharmacologic Class for Use in the Highlights of Prescribing Information", October, 2009 <http://www.fda.gov/downloads/Drugs/Guidances/ucm186607.pdf>

⁴ A searchable database of FDA approved products, including approved labeling is available at the Drugs@FDA website, <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/>

⁵ A downloadable listing of FDA Established Pharmacologic Class is available on FDA's website. <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/ucm162549.htm>

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NMEs included in our study. We note that for some drugs, there is not a documented established pharmacologic class term. Examples of drugs without an FDA pharmacologic classification fall generally fall into one of two categories: 1) Drugs whose mechanism of action is not known or is unclear (and also do not have a clinically meaningful term attributed to its physiological effect or chemical structure), or 2) older products which are no longer marketed, and thus do not have a recently revised labeling that would reflect the pharmacologic class term. For these remaining 14% in our dataset, we referenced commercial databases, such as Drug Facts and Comparisons and PharmaProjects which track numerous characteristics of prescription drug products, including pharmacology and therapeutic class.

Once an appropriate drug class term was identified for all 645 drugs in our study, we reviewed the list to make sure that these drug classes provide for appropriate differentiations based on our objective to group drugs that were similar pharmacologically and clinically. In conducting this review we referenced the *description* and *clinical pharmacology* sections of approved labeling, Center for Drug Evaluation and Research (CDER) review documents, formularies, and literature sources, to determine if additional stratification of certain drugs classes would be appropriate. Through this process, we identified examples of broad established pharmacologic classes that appeared to encompass meaningful subclasses; for example, drugs that had similar mechanisms of action, but substantively different clinical uses.

In certain instances, a novel application of an existing class of drugs was considered first in class for the purposes of our study. For example, Nimotop (nimodipine) is a calcium channel blocker which, unlike others primarily used to treat hypertension, has a unique use in patients who suffer a type of stroke known as subarachnoid hemorrhage. Additionally, Lotronex (alosetron) is a 5-

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HT3 receptor antagonist used to treat irritable bowel syndrome whereas other 5-HT3 receptor antagonists are indicated for use as treatment of nausea resulting from chemotherapy. In both instances we determined that the unique clinical application of each of these drugs merited placement of the drug in a separate and distinct class.

A small number of established pharmacologic classes were determined to be overly broad, and appeared to have clinical or pharmacologically meaningful sub categories. In such instances we identified these subcategories, and identified these as separate classes of drugs. Examples of additional sub categorization include kinase inhibitors used to treat various forms of cancer, which we delineated by molecular target (e.x. Bcr-Abl, BRAF, JAK, mTOR, ALK). Similarly, nonsteroidal antiinflammatory drugs (NSAIDs) were also placed in to sub classes. For example NSAIDS identified as selective Cox-2 inhibitors, which were considered a separate class of NSAID from older existing NSAID products. In yet another instance, Platelet aggregation inhibitors, used to prevent blood clot formation and life-threatening thrombotic events, work through different mechanisms (P2Y12, Glycoprotein IIb/IIIa, and PDE-3 inhibitors) and thus were identified as separate classes based on these more granular mechanisms.

To further ensure that drug classifications and class distinctions were appropriate, the list of the proposed classes for this study was reviewed by specialists and scientific staff in FDA's Office of New Drugs and other Center for Drug Evaluation and Research offices to ensure such distinctions were appropriate. We incorporated feedback received from our subject matter experts in the final determination of the drug classes that we used.

At the conclusion of this exercise, 80% of the drugs in our study in a drug class that was either the same as the established pharmacologic class or, for drugs lacking an established

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pharmacologic class term, were closely related to other drugs that did have a pharmaceutical class term. Only 20% of products in our dataset were placed in a drug class based on additional refinements based on supplementary sources of information.

We acknowledge that the determination of what constitutes a separate drug class is always going to involve a degree of subjectivity. However, based on our use of FDA's established pharmacologic class, FDA approved labeling, supplementary sources, and input from FDA scientific staff, we believe the process used to determine the drug classes used in this study was robust and produced valid and consistent results.

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Appendix Exhibit C

Selected Examples of Drug Classes and Innovation Categories

Drug Class	Therapeutic Use	First-in-Class Drug	Advance-in-Class Drugs	Addition-to-Class Drugs
Cholinesterase inhibitor	Alzheimer's	Cognex (1993)	Aricept (1996)	Exelon (2000), Reminyl(2001)
HMG CoA reductase inhibitor (statins)	Cholesterol lowering	Mevacor (1987)	Lipitor (1996)	Pravachol (1991), Zocor (1991), Lescol (1993), Baycol (1997), Crestor (2003), Livalo (2009)
Selective serotonin reuptake inhibitors (SSRI)	Depression / OCD	Prozac (1987)		Zoloft (1991), Paxil (1992), Luvox (1994), Celexa (1998), Viibryd (2011)
Proton pump inhibitors	GERD / erosive esophagitis	Prilosec (1989)		Prevacid (1995), Aciphex (1999), Protonix(2000)
HIV nucleoside analog reverse transcriptase inhibitors (HIV NRTI)	HIV	Retrovir (1987)	Videx (1991), Hivid (1992), Zerit (1994), Epivir(1995), Ziagen(1998)	Emtriva(2003)
Angiotensin 2 receptor blocker(ARB)	Hypertension	Cozaar (1995)		Diovan (1996), Teveten (1997), Avapro (1997), Atacand (1998), Micardis (1998), Benicar (2002), Edarbi (2011)
Tumor necrosis factor (TNF) blocker	Inflammatory diseases	Remicade (1998)	Enbrel (1998)	Humira (2002), Cimzia (2008), Simponi(2009)
Serotonin (5 HT) 1b/1d receptor agonist	Migraine	Imitrex (1992)		Zomig (1997), Maxalt (1998), Amerge (1998), Axert (2001), Frova (2001), Relpax (2002)
Recombinant human interferon beta	Multiple sclerosis	Betaseron (1993)	Avonex (1996)	Rebif (2002)