Pharma compounds at the crossroads

By Michael J. Haas, Senior Writer

The NIH's National Center for Advancing Translational Sciences (NCATS) has disclosed details about the first library of therapeutics in its Discovering New Therapeutic Uses for Existing Molecules program (see Table 1, "Repurposing pharma compounds"). The compounds

provided by the program's eight pharma participants have completed at least Phase I testing but did not reach registration for that indication and are available to researchers for experimentation. Although it is not yet clear how researchers will use the library, hints about potential therapeutic avenues can be gleaned from similar compounds in development and from highlights of translational research in the literature. A complete list of library compounds, compound data provided by the participating companies and details about the NIH/NCATS program are available on the agency's [website](#).

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COMPANIES AND INSTITUTIONS MENTIONED

National Center for Advancing Translational Sciences,
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National Institutes of Health, Bethesda, Md.

Table 1. Repurposing pharma compounds.

Source: BCIQ: BioCentury Online Intelligence; National Center for Advancing Translational Sciences [website](#)

Company	Compound	Mechanism	Original indication(s) ^A	In commercial development ^B	Literature-based indication(s) ^C
Sanofi (Euronext:SAN; NYSE:SNY)	Canosimibe (AVE5530)	Sterol O-acyltransferase (SOAT; ACAT) inhibitor	Phase III to treat hypercholesterolemia	1 to treat atherosclerosis	Alzheimer's disease (AD)
Pfizer Inc. (NYSE:PFE)	Senicapoc (PF-05416266; ICA-17043)	Potassium channel KCa3.1 (KCNN4) inhibitor	Phase IIa to treat asthma, sickle cell disease (SCD)	Not available	Inflammatory bowel disease (IBD), renal fibrosis
Abbott Laboratories (NYSE:ABT)	ABT-639	Calcium channel voltage- dependent T type- α 1H subunit (CACNA1H; Cav3.2) inhibitor	Phase II to treat diabetic neuropathic pain (DNP)	1 to treat neuropathic pain	Hypertension, obesity
Pfizer	Otenabant (CP- 945598)	Cannabinoid CB ₁ receptor (CNR1) antagonist	Phase III to treat obesity in type 2 diabetes	4 to treat diabetes, obesity, dyslipidemia, liver disease	Pain
Eli Lilly and Co. (NYSE:LLY)	LY2828630	Cannabinoid CB ₂ receptor (CNR2) agonist	Phase II to treat pain in osteoarthritis (OA)	6 to treat pain, IBD, autoimmune disease, inflammatory disease	Brain inflammation, cocaine addiction, bone marrow transplant (BMT)
AstraZeneca plc (LSE:AZN; NYSE:AZN)	AZD1981	Prostaglandin D ₂ receptor subtype DP2 antagonist	Phase II to treat asthma, chronic obstructive pulmonary disease (COPD)	8 to treat asthma, COPD, allergy, inflammation	Alopecia (prostaglandin D ₂ receptor (CRTH2; GPR44; CD294) subtype unspecified)
AstraZeneca	AZD2423	CC chemokine receptor 2 (CCR2; CD192) antagonist	Phase IIa to treat pain and COPD	4 to treat diabetes, diabetic neuropathy, HIV/AIDS, inflammatory disease	Metastatic breast cancer, AD
Pfizer	PF-04136309		Phase II to treat HCV infection, pain in OA		
Pfizer	CE-326597	Cholecystokinin A receptor (CCKAR; CCK1R) agonist	Phase II to treat obesity in type 2 diabetes	1 to treat IBD	Hyperglycemia

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Table 1. Repurposing pharma compounds (continued)

Company	Compound	Mechanism	Original indication(s) ^A	In commercial development ^B	Literature-based indication(s) ^C
Bristol-Myers Squibb Co. (NYSE:BMJ)	Pexacerfont (BMS-562086)	Corticotropin-releasing factor 1 (CRF1) antagonist	Phase II to treat major depressive disorder (MDD), generalized anxiety disorder (GAD), irritable bowel syndrome (IBS)	2 to treat depression, post-traumatic stress disorder (PTSD), glioblastoma multiforme (GBM), breast cancer, colon cancer	AD
AstraZeneca	Zibotentan (ZD4054)	Endothelin A receptor antagonist	Phase III to treat castration-resistant prostate cancer (CRPC); Phase II to treat non-small cell lung cancer (NSCLC), ovarian cancer; Phase I to treat solid tumors	5 to treat prostate cancer, pulmonary arterial hypertension (PAH), renal disease, shock/trauma	SCD, tumor imaging
Pfizer	Prinaberele (PF-00913086; ERB-041)	Estrogen receptor- β agonist	Phase II to treat endometriosis, rheumatoid arthritis (RA); Phase I to treat Crohn's disease	9 to treat menopause, pain, Parkinson's disease (PD), multiple sclerosis (MS), cancer, endocrine disease	Not available
Eli Lilly	LY500307		Phase II to treat lower urinary tract symptoms (LUTS) in benign prostatic hyperplasia (BPH)		
Sanofi	Riferminogene pectaplasamid (temusi; NV1FGF; XRP0038)	Nonviral DNA plasmid encoding fibroblast growth factor 1 (FGF1)	Phase III to treat critical limb ischemia	6 to treat spinal cord injury (SCI), coronary artery disease (CAD), peripheral vascular disease (PVD), dermal ulcers, wounds, Huntington's disease (HD)	Diabetes, peripheral neuropathy
AstraZeneca	AZD7325	GABA _A receptor agonist	Phase IIa to treat GAD	16 to treat insomnia, seizures, epilepsy, cognitive impairment in both schizophrenia and AD	Not available
AstraZeneca	Lesogaberan (AZD3355)	GABA _B receptor agonist	Phase IIb to treat gastroesophageal reflux disease (GERD)	5 to treat incontinence, spasticity, autism, fragile X syndrome	Not available
Pfizer	PF-05190457	Ghrelin receptor (GHSR) antagonist	Phase I to treat type 2 diabetes	2 to treat obesity, diabetes	Alcohol dependence
AstraZeneca	AZD1656	Glucokinase (GCK; GK) activator	Phase IIb to treat type 2 diabetes	8 to treat diabetes	Not available
Bristol-Myers Squibb	BMS-820132		Phase I to treat type 2 diabetes		
Pfizer	PF-03463275	Glycine transporter type 1 (GlyT1; SLC6A9) inhibitor	Phase II to treat schizophrenia	4 to treat schizophrenia, cognitive dysfunction	Not available
Sanofi	Ataciguat (HMR1766)	Soluble guanylyl cyclase (sGC) activator	Phase II to treat peripheral artery disease (PAD), neuropathic pain, angina pectoris	2 to treat heart failure, hypertension	Attention deficit hyperactivity disorder (ADHD)
Abbott	ABT-288	Histamine H3 receptor (HRH3) antagonist	Phase II to treat cognitive impairment in both schizophrenia and AD	8 to treat cognitive dysfunction, AD, schizophrenia, narcolepsy, cataplexy, rhinitis, obesity	Not available
Pfizer	PF-03654746		Phase II to treat ADHD, narcolepsy, rhinitis; Phase I to treat cognitive impairment in both schizophrenia and AD		
GlaxoSmithKline plc (LSE:GSK; NYSE:GSK)	GSK1004723	Dual HRH1 and HRH3 antagonist	Phase II to treat allergic rhinitis	19 to treat allergy, rhinitis, conjunctivitis, urticaria, insomnia, emesis	Malaria
GSK	GSK835726				
Pfizer	CE-210666	Serotonin (5-HT _{1B}) receptor antagonist	Phase III to treat MDD	7 to treat migraine, ADHD	Not available
Pfizer	Elzasonan (CP-448187)		Phase II to treat MDD		
Pfizer	Deramciclane (EGIS-3886; PH-670187)	Dual serotonin (5-HT _{2A}) receptor and serotonin (5-HT _{2C}) receptor antagonist	Phase III to treat GAD	6 to treat schizophrenia, psychosis, bipolar disorder, mania, depression, arterial thrombosis	Not available
				1 to treat OA	Post-SCI muscle spasticity

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Table 1. Repurposing pharma compounds (continued)

Company	Compound	Mechanism	Original indication(s) ^A	In commercial development ^B	Literature-based indication(s) ^C
Pfizer	PF-04995274	Serotonin (5-HT ₄) receptor agonist	Phase I to treat cognitive impairment in AD	12 to treat GERD, constipation, gastroparesis, IBS, gastrointestinal dysfunction, gastrointestinal motility disorder, cognitive dysfunction, AD	Not available
AstraZeneca	MEDI2338	IL-18 inhibitor	Phase I to treat COPD	1 to treat metabolic syndrome	MS, neuropathic pain
Pfizer	PF-04191834	5-Lipoxygenase (ALOX5; 5-LO) inhibitor	Phase II to treat asthma, pain in OA	1 to treat asthma	Inflammation, chronic myelogenous leukemia (CML)
Pfizer	SD-7300 (SC-81490)	Inhibitor of matrix metalloproteinase 2 (MMP2), MMP9 and MMP13	Phase I to treat myocardial infarction (MI), OA	Not available	Cancer, congestive heart failure (CHF), thrombosis, OA, neuropathic pain, acute myelogenous leukemia (AML), tuberculosis (TB), vaginal prolapse
AstraZeneca	AZD1236	Dual MMP9 and MMP12 inhibitor	Phase IIa to treat COPD	1 to treat COPD, MS, liver fibrosis	Asthma, emphysema, bacterial infection
Bristol-Myers Squibb	BMS-830216	Melanin-concentrating hormone receptor 1 (MCHR1; GPR24) antagonist	Phase I/II to treat obesity	Not available	IBD
AstraZeneca	AZD5904	Myeloperoxidase (MPO) inhibitor	Phase I to treat COPD and MS	1 to treat PD	Atrial fibrillation (AF)
Abbott	ABT-089	Nicotinic acetylcholine receptor $\alpha_4\beta_2$ agonist	Phase II to treat ADHD, AD	2 to treat AD, ADHD	Not available
AstraZeneca	AZD0328	Nicotinic acetylcholine receptor α_7 (CHRNA7) agonist	Phase IIa to treat cognitive impairment in schizophrenia	3 to treat ADHD, AD, schizophrenia, cognitive dysfunction	Epilepsy, brain damage associated with cardiac arrest/stroke
Johnson & Johnson (NYSE:JNJ)	JNJ-39393406		Phase I to treat AD, cognitive impairment in schizophrenia		
GSK	GW274150	Inducible nitric oxide synthase 2 (NOS2; iNOS) inhibitor	Phase II to treat RA, migraine; Phase I to treat asthma	3 to treat neuropathic pain, postherpetic neuralgia (PHN), mucositis	Brain cancer, arthritis, inflammation, genetic association with psoriasis
Pfizer	SD-6010 (SC-84250)		Phase III to treat pain in OA, asthma		
AstraZeneca	AZD7268	Opioid receptor $\delta 1$ (OPRD1; DOR) agonist	Phase II to treat MDD	1 to treat pain in OA	Not available
Sanofi	AVE8134	Peroxisome proliferation-activated receptor- α (PPARA; PPAR α) agonist	Phase II to treat type 2 diabetes	13 to treat diabetes, dyslipidemia, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, metabolic syndrome, cardiovascular disease	Not available
Sanofi	AVE0847	Dual PPAR α and PPAR γ (PPARG) agonist	Phase I to treat type 2 diabetes	6 to treat diabetes, dyslipidemia, AD, cardiovascular disease	Not available
Pfizer	PF-05019702 (PRA-27)	Progesterone receptor antagonist	Phase I to treat endometriosis	1 to treat depression, Cushing's disease	Not available

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Table 1. Repurposing pharma compounds (continued)

Company	Compound	Mechanism	Original indication(s) ^A	In commercial development ^B	Literature-based indication(s) ^C
AstraZeneca	AZD9056	Purinergic receptor P2X ligand-gated ion channel 7 (P2RX7; P2X7) antagonist	Phase II to treat COPD, RA, Crohn's disease	5 to treat pain, RA, OA, MS	Cancer, MI, heart failure, arterial thrombosis, graft-versus-host disease (GvHD), SCL, PD, neuroinflammatory diseases
Eli Lilly	LY2245461	Selective estrogen receptor modulator (SERM)	Phase unknown, to treat hot flashes in postmenopausal women	10 to treat osteoporosis, menopause, androgen deficiency, hypogonadism, breast cancer, pain	Cervical cancer
Sanofi	SAR115740	Transient receptor potential vanilloid 1 (TRPV1; VR1) antagonist	Phase I to treat acute and chronic pain	7 to treat pain, itch, rhinitis, incontinence	Not available
AstraZeneca	Recentin cediranib (AZD2171)	Inhibitor of VEGF receptor 1 (FLT1; VEGFR-1), VEGFR-2 (KDR/Flk-1) and VEGFR-3 (FLT4)	Phase II or III to treat multiple solid tumor types	4 to treat multiple solid tumors, lymphoma, sarcoma, age-related macular degeneration (AMD)	Not available

^ADenotes the disease indication(s) in which the company has already tested the compound in the clinic; in most cases, the company discontinued development of the compound because of lack of efficacy, failure to meet trial endpoint(s) or for undisclosed reasons. ^BDenotes the number of compounds with the same mechanism of action that at least one company has or had in preclinical and/or clinical development to treat the listed indication(s). ^CDenotes additional disease indications in which a compound with the same mechanism of action could have efficacy, based on preclinical results reported in selected scientific literature.