

Agent	Emerging treatments for acute and chronic pain				Development Status, Route, Contact information				Update Status
	Function / Target	Description / Mechanism of Action	Indication / Other Comments	Sponsor / Originator	Status	Opioid (Y/No)	Route	URL	

2019 UPDATES / CONTINUING PRODUCTS FROM 2018

1	1% diacerein (AC-203 / CCP-020)	caspase-1 inhibitor	Small molecule, inhibition of caspase-1, block activation of NLRP3 inflammasomes; reduced IL-1beta and IL-18	Inherited Epidermolysis Bullosa	TWi Biotechnology / Castle Creek Pharmaceuticals	Phase 2	No	Topical	www.twibiotech.com	
2	AB001	NSAID	Small molecule; topical NSAID formulation (nondisclosed active ingredient)	Chronic low back pain	Frontier Biotechnologies	Phase 2	No	Topical	www.frontierbiotech.com/en/products/1.html	
3	AC-201 CR	Uricosuric + xanthine oxidase	Small molecule; oral uricosuric / anti-inflammatory agent + febuxostat (xanthine oxidase inhibitor); inhibition of NLRP3 inflammasome assembly, reduced production of caspase-1 and cytokine IL-1Beta	Gout in patients taking urate-lowering therapy; Gout; Epidermolysis Bullosa Simplex (EBS)	TWi Biotechnology	Phase 2	No	Oral	www.twibiotech.com/rAndD_11	
4	AK-1830 (ARRY-954)	TrkA	Small molecule; tropomyosin receptor kinase A (TrkA) inhibitor	Pain, inflammation	Array BioPharma / Asahi Kasei Pharma	Phase 1	No	Oral	www.arraybiopharma.com/our-science/our-pipeline www.asahi-kasei.co.jp/asahi/en/news/2016/e160401_2.html	A
5	Altius System	Neurostimulator	Medical device; neurostimulator	Post-amputation pain	Neuros Medical	Phase 2	No	Implanted device	www.neurosmedical.com/clinical-research www.clinicaltrials.gov/ct2/show/NCT02221934?term=%22Neuro+Medical%22&rank=1	
6	AMG0101 AMG0103	NF-kB	Biologic; NF-kappaB decoy oligo DNA decoy	Discogenic low back pain	AnGes MG	Phase 1b	No	Intra-discal	www.anges.co.jp/en/project/proj_pipeline.html	S
7	AmiKet	Amitriptyline + ketamine	Small molecule; combination of amitriptyline + ketamine	Topical analgesic cream; peripheral neuropathies including diabetes (DPN), chemotherapy (CPN), and shingles (PHN)	EpiCept / Immune Pharmaceuticals / Maxim Pharmaceuticals	Phase 2	No	Topical	www.immunepharma.com/products/amiket-2	
8	AmnioFix	dHACM	Biologic; micronized dehydrated human amnion/chorion membrane (dHACM) injection	Knee osteoarthritis, plantar fasciitis. FDA RMAT (Regenerative Medicine Advanced Therapy) designation.	MiMedx	Phase 2b	No	Intra-articular	https://mimedx.qcs-web.com/news-releases/news-release-details/amniifix-injectable-granted-regenerative-medicine-advanced	S
9	Ampion	DA-DKP	Biologic; low molecular weight fraction of human serum albumin (HSA); active moiety is dipeptide aspartyl-alanyl diketopiperazine (DA-DKP)	Knee osteoarthritis (intra-articular injection), Phase 3; hand osteoarthritis (Phase 1)	Ampion	BLA Not Approved; Phase 3 ongoing	No	IA	http://ampiopharma.com/pipeline/ampion	S
10	AOB202	Nitric oxide	Biologic; Ammonia Oxidizing Bacteria (AOB); microbiome origin; Nitrosomonas euro convert ammonia to nitric oxide	Prevention of episodic migraine	AOBiome Therapeutics	Phase 2	No	IN	www.aobiome.com/aobiome-therapeutic-pipeline www.aobiome.com/aob-inflammatory-conditions-and-systemic-effects	
11	APD37	CB2	Small molecule; CB2 agonist	Pain	Arena Pharmaceuticals	Phase 2	No	Oral	www.arenapharm.com/pipeline/apd371	
12	AQU-005	MMP2 + MMP9	Small molecule; dual inhibitor of matrix metalloprotease (MMP) type 2 and 9	Neuropathic pain; diabetic polyneuropathy, postherpetic neuralgia, HIV-induced neuralgia, sensory neuropathy, and other kinds of neuropathy	NeuroMax / Aquilus Pharmaceuticals	Phase 1	No	UNK	http://neuromax.ru/en/products/aqu-005	S
13	Arhalofenate	URAT1	Small molecule; antagonist to renal uric acid transporter URAT1 + blockade of urate crystal-induced production of IL-1β	Reduction of gout flares	CymaBay Therapeutics / Kowa Pharmaceuticals America	Phase 2b	No	Oral	www.cymbabay.com/pipeline_arhalofenate.html	
14	ASP0819	K ⁺ Channel	Small molecule; Calcium2+-activated K ⁺ channel opener	Fibromyalgia	Astellas	Phase 2	No	Oral	https://sw4503.swcms.net/en/library/pipeline/inframe/main/01/teaserItems/1/0/linkList/0/link/3q2019_pipeline_en.pdf	

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15	ATB-346	H ₂ S-NSAID	Small molecule; hydrogen sulfide (H ₂ S)-releasing derivative of naproxen (COX inhibitor)	Osteoarthritis; NSAID with improved safety	Antibe	Phase 2 (Canada)	No	Oral	https://antibethera.com/pipeline/overview	S
16	Atogepant (AGN-241689, MK-8031)	CGRP	Small molecule CGRP receptor antagonist	Chronic migraine prevention, episodic migraine	Allergan	Phase 3	No	Oral	www.allergan.com/research-and-development/pipeline	S
17	Aximris XR (Rexista, oxycodone ER)	Mu opioid	Small molecule; oxycodone extended-release formulation	Chronic pain, abuse-deterrent formulation	Intellipharma	NDA Submitted	Y	Oral	www.intellipharma.com/product-pipeline/oxycodone-hydrochloride-er	S
18	AXS-02	Bisphosphonate	Small molecule; disodium zoledronate tetrahydrate	Knee osteoarthritis (OA) associated with bone marrow lesions (BMLs) and chronic low back pain (CLBP) associated with Modic changes (MCs). FDA Fast Track.	Axsome Therapeutics	Phase 3	No	Oral	https://axsome.com/axs-pipeline/axsome-pain-and-primary-care	S
19	BCG vaccine	BCG vaccine	Biologic; Bacillus Calmette–Guérin (BCG) vaccine, stimulation of peripheral blood mononuclear (PBM) cells	Fibromyalgia; companion diagnostic (FM/a test)	EpicGenetics	Phase 2	No	Intra-dermal	www.biospace.com/article/-cp8r-epicgenetics-and-massachusetts-general-hospital-to-launch-fibromyalgia-clinical-trial ; https://fmtest.com	
20	Bedrocan	Cannabis with high THC content; CB1 receptor	Small molecule; natural product	Fibromyalgia	Bedrocan International	Phase 2	No	Vaporizer (inhalation)	https://bedrocan.com/fibromyalgia-study-proves-effectiveness-of-bedrocans-products	
21	BMP-7	BMP-7	Biologic; autologous bone morphogenetic protein (BMP-7)	Knee osteoarthritis; prevention of cartilage loss, potential anabolic effects	Ember Therapeutics	Phase 2	No	IA	www.embertx.com/pipeline.html	
22	Brivolidge (AYX1)	EGR1	Biologic; inhibition of transcription factor EGR1	Acute postoperative pain; single intrathecal injection prior to surgery; reduction of acute pain and the prevention of chronic pain following surgery	Adynxx	Phase 2b	No	IT	www.adynxx.com/avx1	
23	Buprenorphine sublingual spray	Mu opioid	Small molecule; buprenorphine formulation	Acute pain (sublingual)	Insys Therapeutics	Phase 3	Y	SL	www.insysrx.com/products/in-development	S
24	CA-008	TRPV1	Small molecule; capsaicin prodrug.	Acute post-surgical pain. FDA Breakthrough Therapy, Fast Track.	Concentric	Phase 2	No	Local Injection	www.concentricanalgesics.com/pipeline	
25	Cebranopadol	Mu opioid + NOP opioid	Small molecule: dual-acting agonist at nociceptin (NOP) and mu-opioid (MOR) receptors	Chronic pain [painful diabetic peripheral neuropathy (PDPN), osteoarthritis (OA) and chronic lower back pain]	Grünenthal / Depomed	Phase 2	Y	Oral	www.grunenthal.com/en/r-d-vision-mission/pipeline	S
26	CGS-200-1 CGS-200-5	TRPV1	Small molecule; 1% / 5% trans - capsaicin formulations	Knee osteoarthritis; musculoskeletal pain	Vizuri Health Sciences	Phase 2	No	Topical	http://vizuriusa.com/products/prescription-products www.clinicaltrials.gov/ct2/show/NCT03528369?term=vizuri&rank=1	
27	Cibinetide (ARA 290)	IRR	Biologic; Innate Repair Receptor peptide, IRR); synthetic 11-amino-acid peptide	Peripheral neuropathy, EPO analog, inflammation and sarcoidosis pain (rare disease)	Araim Pharmaceuticals	Phase 2	No	SC	http://araimpharma.com/our-clinical-focus	
28	Cingal	Sodium hyaluronate + steroid	Biologic + small molecule; combination of sodium hyaluronate + triamcinolone hexacetonide	Knee osteoarthritis; viscosupplement + steroid (intra-articular injection)	Anika Therapeutics	Phase 3 (Approved in Canada)	No	IA	www.anikatherapeutics.com/technology/pipeline	
29	CL-HIT	Sumatriptan + promethazine	Small molecule; combination of sumatriptan, promethazine	Migraine	Charleston Laboratories	Phase 2	No	Oral	https://charlestonlabs.com/pipeline	
30	CLOX-315	Mu opioid combination	Small molecule; combination of oxycodone, promethazine	Acute pain	Charleston Laboratories	Phase 2	Y	Oral	https://charlestonlabs.com/pipeline	S
31	CLP-417	Mu opioid combination	Small molecule; combination of tramadol, promethazine	Acute pain	Charleston Laboratories	Phase 1	Y	Oral	https://charlestonlabs.com/pipeline	S
32	CLP-517	Mu opioid combination	Small molecule; combination of hydromorphone, promethazine	Acute pain	Charleston Laboratories	Phase 1	Y	Oral	https://charlestonlabs.com/pipeline	S

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33	CNTX-0290	SSTR4	Small molecule; somatostatin SSTR4 agonist	Neuropathic, inflammatory, and mixed pain; chronic low back pain	Lilly / Centrexion	Phase 1	No	Oral	www.lilly.com/discovery/pipeline; https://centrexion.com/science/pipeline	S
34	CNTX-2022	Local anesthetic	Small molecule; topical 40% lidocaine gel	Superficial musculoskeletal pain, neuropathic pain, dermatologic pain	Centrexion	Phase 1	No	Topical	https://centrexion.com/science/pipeline	S
35	CNTX-4975	TRPV1	Small molecule; trans-capsaicin injection	Morton's Neuroma (rare disease); osteoarthritis pain. FDA Fast Track.	Centrexion	Phase 3	No	Local Injection / IA	https://centrexion.com/science/pipeline	S
36	CNTX-6016	CB2	Small molecule; CB2 agonist	Diabetic and autoimmune neuropathic pain and chemotherapy-induced neuropathy	Lilly / Centrexion	Phase 1	No	Oral	www.lilly.com/discovery/pipeline; https://centrexion.com/science/pipeline	A
37	CNTX-6970	CCR2	Small molecule; cytokine CCR2 antagonist	Inflammatory pain	Centrexion	Phase 1	No	Oral	https://centrexion.com/science/pipeline	S
38	Condoliase (SI-6603)	Chondroitin sulfate	Biologic; chondroitin-sulfate-ABC endolyase	Radicular leg pain (e.g. sciatica) due to lumbar disc herniation	Seikagaku / Ferring	Phase 3	No	Intervertebral disc injection	https://www.seikagaku.co.jp/en/development/status.html	S
39	CTX001	Hemoglobin gene replacement	Biologic; CRISPR-edited hemoglobin gene	Sickle cell disease, β-thalassemia; FDA Fast Track designation	CRISPR Therapeutics / Vertex	Phase 1/2	No	Trans-plant	www.crisprtx.com/programs/pipeline; www.crisprtx.com/programs/hemoglobinopathies	S
40	CX1739	AMPA	Small molecule; ampakine to enhance glutamate at AMPA glutamate receptors	Treatment of opioid respiratory depression	RespireRx Pharmaceuticals	Phase 2a (on hold)	No	Oral	www.respirex.com/development/cx1739.html	A
41	CYT-1010	Endomorphin opioid	Small molecule; stable synthetic analog of Endomorphin-1	Acute postoperative pain	Cytogel	Phase 1	Y	IV	www.cytogelpharma.com/analgesics.html	S
42	DEN-181 (Rheumavax)	CCP	Biologic; anti-CCP vaccine (citrullinated peptide dendritic cell immunotherapy)	Rheumatoid arthritis; disease-modifying therapy (intradermal injection 2x)	Dendright / Janssen / Univ. Queensland	Phase 1b	No	SC	www.dendright.com.au/news/dendright-announces-first-human-dose-den-181-phase-1b-clinical-trial	S
43	Dex-IN (dexmedetomidine)	Alpha ₂	Small molecule; dexmedetomidine intranasal formulation	Acute peri-procedural pain (Phase 2); breakthrough cancer pain (Phase 1)	Recro Pharma	Phase 2 Phase 1	No	IN	www.recropharma.com/product-pipeline/overview	
44	Dusquetide (SGX942)	IDR	Biologic; innate defense regulator (IDR); short, synthetic peptide	Oral mucositis (OM) in head and neck cancer patients undergoing chemoradiation therapy (CRT); FDA Fast Track	Soligenics	Phase 3	No	IV	www.soligenix.com/pipeline/biotherapeutics/sqx942-oral-mucositis	
45	EB-101	Stem cells	Biologic; genetically-engineered allogenic adipose-derived mesenchymal stem cells	Recessive Dystrophic Epidermolysis Bullosa (RDEB); rare disease; painful blisters. FDA Breakthrough Therapy designation	Abeona / Anterogen	Phase 3	No	Topical	www.abeonatherapeutics.com/clinical-trials/rdeb	A
46	EC5026	Soluble epoxide hydrolase (sEH)	Small molecule; inhibitor of soluble epoxide hydrolase (sEH)	Chronic pain; painful diabetic neuropathy. NIH Blueprint Neurotherapeutics program.	EicOsis	Phase 1	No	Oral	www.eicosis.com/pr20160108.html	A
47	ECCO-50	Stem cells	Biologic; autologous adipose-derived regenerative cells; isolation device + therapeutic	Knee osteoarthritis	Cytori	Phase 2	No	IA	www.cytori.com/pipeline	
48	Egalet-002	Mu opioid	Small molecule; oxycodone extended-release formulation	Chronic pain, abuse-deterrent formulation	Egalet	Phase 3	Y	Oral	http://egalet.com/rd/pipeline	
49	EGP-437	Steroid	Small molecule; dexamethasone iontophoretic formulation + EyeGate II delivery system	Post-cataract surgery pain and inflammation	EyeGate / Valeant	Phase 3	No	Ocular	www.evegatepharma.com/pipeline/egp-437	
50	ELI-200	Opioid (undisclosed)	Small molecule; unspecified opioid, extended-release	Chronic pain, abuse-deterrent formulation	Elite Pharmaceuticals / Epic Pharma	Phase 3	Y	Oral	www.elitepharma.com/pipeline-branded	

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51	Engensis (donaperminogen e seltoplasmid; VM202)	HGF	Biologic; plasmid gene therapy encoding hepatocyte growth factor (HGF)	Neuropathic pain; painful diabetic neuropathy; i.m. administration (4x in calf muscle); angiogenic + neurotrophic effects to form new microvasculature and regenerate nerve cells. FDA RMAT (Regenerative Medicine Advanced Therapy) designation	Helixmith (formerly ViroMed / VM BioPharma)	Phase 3	No	IM	www.helixmith.com/engensis_dpn#first	S
52	Eptinezumab (ALD403)	CGRP	Biologic; humanized monoclonal antibody, calcitonin gene-related peptide (CGRP) receptor antagonist	Episodic and chronic migraine prevention (i.v. dosing q. 12 weeks)	Lundbeck (Alder BioPharmaceuticals)	BLA Submitted	No	IV SC IM	www.alderbio.com/pipeline/eptinezumab www.lundbeck.com/global/brain-disorders/pipeline	A
53	Etoricoxib (TRM-359)	NSAID	Small molecule; COX-2 inhibitor	"Serious pediatric orphan disease for which high-potency opioid therapies are the only available therapies"	Tremeau Pharmaceuticals	Phase 2	No	Oral	www.tremeaux.com/pipeline-1	
54	Fado (fadolmidine)	Alpha ₂	Small molecule; peripheral alpha-2 agonist	Pain or anesthesia (IT dosing): potential topical use to treat neuropathic pain	Recro Pharma	Phase 2	No	IT	www.recropharma.com/product-pipeline/fadolmidine	
55	Fasinumab (REGN475)	NGF	Biologic; fully human NGF monoclonal antibody	Osteoarthritis of the hip or knee; chronic low back pain	Regeneron / Teva	Phase 3	No	SC	www.regeneron.com/pipeline	
56	FCX-007	Type VII gene replacement	Biologic; lentiviral vector gene therapy, autologous fibroblast transduced with COL7 producing gene (COL7A1)	Pediatric recessive dystrophic epidermolysis bullosa (RDEB); FDA Rare Pediatric Disease, Orphan Drug, Regenerative Medicine Advanced Therapy (RMAT), and Fast Track Designation	Fibrocell Science / Intrexon Corporation	Phase 3	No	Intra-dermal	http://fibrocell.com/pipeline-clinical-trials https://clinicaltrials.gov/ct2/show/NCT04213261?term=fibrocell&draw=2&rank=2	A
57	Filgotinib (GLPG0634)	JAK1	Small molecule; highly selective JAK1 inhibitor	Rheumatoid arthritis, Crohn's disease, ulcerative colitis, psoriatic arthritis, ankylosing spondylitis; FDA priority review	Gilead / Galapagos NV	NDA Submitted	No	Oral	www.gilead.com/science-and-medicine/pipeline www.gilq.com/clinical-pipelines	A
58	Funapide (TV-45070, XEN402)	Nav 1.7	Small molecule / modulates voltage-gated Nav 1.7 sodium channels	Neuropathic pain (topical) (failed OA clinical trial)	Teva / Xenon	Phase 2b	No	Topical	www.xenon-pharma.com/product-candidates/pain/pain-teva	
59	GC4419	Superoxide dismutase mimetic	Small molecule; synthetic enzyme to convert superoxide free radicals to molecular oxygen and hydrogen peroxide	Severe oral mucositis (SOM); FDA Breakthrough Therapy and Fast Track designations	Galera Therapeutics	Phase 2	No	IV infusion	www.galeratx.com/our-pipeline/gc4419	
60	GLPG1972 / S201086	ADAMTS-5 (cartilage degrading enzyme)	Small molecule; inhibitor of ADAMTS-5 (A Disintegrin and Metalloproteinase with Thrombospondin Motif)	Knee osteoarthritis [disease-modifying osteoarthritis drug (DMOAD) candidate]; goal to reduce cartilage loss after 52 weeks of treatment; FDA Fast Track designation	Galapagos-Sevier	Phase 2	No	Oral	www.gilq.com/gilq-1972 http://hugin.info/133350/R/2201467/853828.pdf	S
61	Halneuron (Tetradotoxin, TTX)	Sodium channel blocker	Biologic; peptide inhibitor of voltage-gated sodium channels (VGSCs) in peripheral sensory neurons	Chemotherapy induced neuropathy (CINP); cancer pain	Wex Pharmaceuticals	Phase 3	No	SC	www.wextech.ca	
62	HPI201	HPI201	Small peptide; tetrapeptide, selective κ-opioid agonist, peripherally-acting	Acute, chronic, and neuropathic pain	JP Pharmaceuticals	pre-IND	Y	Oral	www.jp-pharmaceuticals.com/main/pain-pipeline	S
63	HTX-011	Local anesthetic + NSAID	Small molecule; combination of bupivacaine (targets sodium channels) and meloxicam (targets nociceptors)	Postoperative pain	Heron Therapeutics	NDA Submitted	No	Local injection	www.heronrx.com/HTX-011	S

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64	Hydorex (CL-108)	Mu opioid combination	Small molecule; combination of hydrocodone, acetaminophen, promethazine	Osteoarthritis; moderate to severe pain, reduced Opioid-Induced Nausea and Vomiting (QINV)	Charleston Laboratories	NDA Submitted	Y	Oral	https://charlestonlabs.com/pipeline	S
65	IMC-1	NSAID + antiviral	Small molecule; combination of famciclovir + celecoxib	Fibromyalgia; antiviral + COX-2 inhibitor; infectious disease theory of fibromyalgia. FDA Fast Track.	Innovative Med Concepts	Phase 2	No	Oral	http://innovativemedconcepts.com/pipeline.html	
66	Inclacumab	P-selectin	Biologic; P-selectin monoclonal antibody	Vaso-occlusive crises (VOC) in patients with sickle cell disease (SCD)	Global Blood Therapeutics / Roche	Phase 1	No	IV	www.gbt.com/programs/scd/inclacumab ; www.gbt.com/programs/overview	S
67	Inotersen (IONIS-TTR)	Transthyretin (TTR) protein	Biologic; antisense drug designed to decrease the amount of mutant and normal TTR	Transthyretin (TTR) familial amyloid polyneuropathy (FAP)	Ionis Pharmaceuticals	Phase 3	No	SC	http://ir.ionispharma.com/news-releases/news-release-details/ionis-pharmaceuticals-provides-update-ionis-ttr-rx-program	
68	INP104 (dihydro-ergotamine nasal)	Ergot alkaloid	Small molecule; nasal formulation of dihydroergotamine mesylate (DHE)	Acute migraine	Impel NeuroPharma	Phase 3	No	IN	https://impelnp.com/treatments	S
69	Invossa (TissueGene-C; TG-C)	Stem cells	Biologic; allogeneic cell therapy (cartilage cells + cells with a growth factor promoting cell differentiation)	Knee osteoarthritis (intra-articular injection)	Kolon TissueGene	Phase 3	No	Intra-articular	https://www.tissuegene.com/en_US/product-pipeline	S
70	IV meloxicam (N1539)	NSAID	Small molecule; meloxicam i.v. formulation	Acute postoperative pain (NDA submitted, i.v.); Acute pain (Phase 2, i.m.)	Baudax Bio (formerly Recro Pharma)	NDA Resubmitted	No	IV IM	https://www.baudaxbio.com/product-pipeline/meloxicam	S
71	JointStem	Stem cells	Biologic; autologous mesenchymal stem cell therapy	Osteoarthritis	Nature Cell Co.	Phase 2	No	Intra-articular	www.naturecell.co.kr/en ; www.clinicaltrials.gov/ct2/show/NCT02674399?term=%22Nature+Cell%22&rank=2	
72	Kevzara (sarilumab)	IL-6	Biologic targets IL-6, fully human monoclonal antibody	Polyarticular-course juvenile idiopathic arthritis (BLA approval for adult rheumatoid arthritis)	Sanofi, Regeneron	Phase 2 (BLA Approval)	No	SC	www.regeneron.com/pipeline ; www.regeneron.com/kevzara-injection	
73	Korsuva (difelikefalin, CR845)	Kappa opioid	Small peptide; tetrapeptide, selective κ-opioid agonist, peripherally-acting	Uremic pruritus (parenteral); chronic kidney disease-associated pruritus (CKD-aP), chronic liver disease-associated pruritus (CLD-aP), acute and chronic pain, postop nausea & vomiting (PONV); FDA Breakthrough Therapy designation for uremic pruritus	Cara Therapeutics, Enteris BioPharma	Phase 3 Phase 2	Y	IV Oral	www.caratherapeutics.com/pipeline-technology/our-pipeline	S
74	KPI-121	Corticosteroid	Small molecule; nanoparticle loteprednol etabonate MPP (mucus-penetrating particle) formulation (0.25%)	Postoperative cataract surgery; treatment of ocular inflammation and pain; topical application 2x or 4x daily	Kala Pharmaceuticals	Phase 3	No	Topical	http://kalarx.com/pipeline	S
75	Krystexxa (pegloticase)	Uric acid reduction	Biologic; PEGylated uric acid specific enzyme	Uncontrolled gout; goal is persistently lowering of serum uric acid; combination with methotrexate to reduce immune response to Krystexxa	Horizon Pharma	Phase 3b/4	No	IV	http://ir.horizon-pharma.com/news-releases/news-release-details/horizon-pharma-plc-initiates-clinical-trial-evaluate-krystexxa ; www.horizonpharma.com/our-pipeline	
76	L-4 chloro-kynurenine (AV-101)	NMDA / GlyB	Small molecule, NMDA (N-methyl-D-aspartate) receptor glycine B antagonist	Major depressive disorder, neuropathic pain. FDA Fast Track	VistaGen Therapeutics	Phase 2	No	Oral	www.vistagen.com/pipeline/av-101/neuropathic-pain	
77	Linzagolix (OBE2109)	GnRH	Small molecule; gonadotropin-releasing hormone (GnRH) receptor antagonist	Endometriosis-associated pain	ObsEva Therapeutic	Phase 3	No	Oral	www.obseva.com/pipeline	
78	LIQ865	Local anesthetic	Small molecule; bupivacaine extended-release formulation	Postoperative pain	Liquidia	Phase 1	No	SC	http://liquidia.com/pipeline	S

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79	Lu AG09222 (ALD1910)	PACAP-38	Biologic; monoclonal antibody (mAb) designed to inhibit pituitary adenylate cyclase-activating polypeptide (PACAP) for migraine prevention	Migraine prevention	Lundbeck (Alder BioPharmaceuticals)	Phase 1	No	SC	www.lundbeck.com/global/brain-disorders/pipeline	A
80	LX9211 (BMS-986176)	AAK1	Small molecule; selective inhibitor of AAK1 (adapter-associated kinase)	Neuropathic pain	Lexicon Pharma	Phase 1	No	Oral	www.lexpharma.com/pipeline	S
81	M6495 (ALX-1141)	ADAMTS-5 protein inhibitor	Biologic; nanobody / single-domain antibody fragment, undisclosed target	Osteoarthritis; disease-modifying therapy	Merck KGaA (formerly Ablynx)	Phase 1	No	SC	www.emdgroup.com/en/research/biopharma-pipeline.html	S
82	Maxigesic IV (APAP + ibuprofen)	APAP + NSAID	Small molecule; combination product of acetaminophen + ibuprofen	Treatment of postoperative pain	AFT Pharmaceuticals	Phase 3	No	IV	www.aftpharm.com/news/positive-result-from-large-us-clinical-trial-for-maxigesic-iv-intravenous	
83	MEB-1166, MEB-1170	Mu opioid	Small molecule; G protein-biased agonist to mu opioid receptor	Acute postoperative pain; anticipated reduced adverse effect profile, low abuse liability	Mebias Discovery	Pre-IND	Y	UNK	http://mebiasdiscovery.com/pipeline ; https://mebiasdiscovery.com/wp-content/uploads/2019/07/Mu-Opioid-Receptor.pdf	S
84	MepiGel	Local anesthetic	Small molecule; mepivacaine formulation	Neuropathic pain (postherpetic neuralgia (PHN), and HIV-associated neuropathy); topical application to feet	Relmada Therapeutics	pre-IND	No	Topical	www.relmada.com/product-candidates/rel-1021-mepigel	S
85	Mirogabalin	α2δ-1	Small molecule; α2δ-1 inhibitor, long duration of action	Diabetic peripheral neuropathic pain (DPND), postherpetic neuralgia (PHN), fibromyalgia (FMS)	Daiichi-Sankyo	Phase 3	No	Oral	www.daiichisankyo.com/rd/pipeline/products/index.html	
86	MPC-06-ID	Stem cells	Biologic; allogeneic mesenchymal precursor cell (MPC) product	Chronic discogenic low back pain; single injection alone or combined with hyaluronic acid into the painful intervertebral disc	Grünenthal / Mesoblast Limited	Phase 3	No	Intra-articular	www.mesoblast.com/product-candidates/lead-product-candidates ; http://investorsmedia.mesoblast.com/static-files/d03b7388-da1a-4172-b614-9a5f66523f43	S
87	Nalbuphine ER	Mu opioid	Small molecule; extended-release formulation	Prurigo Nodularis (PN); uremic pruritus	Trevi Therapeutics	Phase 3 Phase 2	Y	Oral	www.trevitherapeutics.com/pipeline	A
88	namilumab (IZN-101) (AMG203)	GM-CSF	Biologic; anti GM-CSF monoclonal antibody	Ankylosing spondylitis	Izana Bioscience / Takeda	Phase 2	No	SC	https://izanabio.com	
89	Neosaxitoxin (NeoSTX)	Sodium channel blocker	Biologic; site-1 specific sodium channel blocker	Long-acting local anesthetic; postoperative analgesia; acute pain, chronic pain; acts synergistically with local anesthetics (local infiltration)	Grünenthal / Proteus	Phase 2	No	Local injection	www.grunenthal.com/en/r-d-vision-mission/pipeline	S
90	Neridronic acid	Bisphosphanate	Small molecule; oral and i.v. formulations	Complex regional pain syndrome (CRPS). FDA Orphan Drug, Fast Track, Breakthrough Therapy designations	Grünenthal / Abiogen Pharma	Phase 3	No	IV	www.grunenthal.com/en/r-d-vision-mission/pipeline	S
91	NKTR-181	Mu opioid	Small molecule polymer conjugate; μ opioid receptor agonist	Chronic pain, slower brain uptake and anticipated lower abuse liability than reference oxycodone	Nektar Therapeutics	NDA Submitted	Y	Oral	www.nektar.com/pipeline/rd-pipeline/nktr-181	S
92	NOP	NOP opioid	Small molecule; nociceptin (NOP) receptor agonist	Unknown	Grünenthal	Phase 2	Y	Topical	www.grunenthal.com/en/r-d-vision-mission/pipeline	S
93	NTM-001	NSAID	Small molecule; ketorolac infusion formulation	Acute postoperative pain	Neumentum	Phase 1	No	IV	http://neumentum.com/pipeline	A
94	NYX-2925	NMDA	Small molecule; NMDA antagonist	Painful diabetic peripheral neuropathy; fibromyalgia	Aptinyx	Phase 2	No	Oral	www.aptinyx.com/pipeline	S

Agent	Emerging treatments for acute and chronic pain				Development Status, Route, Contact information				Update Status	
	Function / Target	Description / Mechanism of Action	Indication / Other Comments	Sponsor / Originator	Status	Opioid (Y/No)	Route	URL		
95	Olinciguat (IW-1701)	Soluble guanylate cyclase (sGC)	Small molecule; soluble guanylate cyclase (sGC) stimulator; modulation of nitric oxide/soluble guanylate cyclase/cyclic guanosine monophosphate (NO/sGC/cGMP) signaling pathway	Sickle cell disease; FDA orphan drug designation	Cyclerion Therapeutics / Ironwood Pharmaceuticals	Phase 2	No	Oral	www.cyclerion.com/pipeline	S
96	Olinvo (oliceridine, TRV130)	Mu opioid	Small molecule; G protein-biased agonist to mu opioid receptor	Acute postoperative pain (parenteral); faster onset and stronger analgesia than morphine with lower AE profile, anticipated low abuse liability; FDA Breakthrough Therapy designation	Trevena	Phase 3	Y	IV	https://www.trevena.com/pipeline/iv-oliceridine	S
97	ONO-5704 / SI-613 (diclofenac etalhyaluronate sodium)	Hyaluronic acid-NSAID	Small molecule; diclofenac salt	Knee osteoarthritis (NDA filed in Japan; Phase 2, USA)	ONO Pharmaceutical / Seikagaku	Phase 2	No	IA	https://www.ono.co.jp/eng/investor/dp.html	S
98	Opiranserin (VVZ-149)	GlyT2, 5HT2A	Small molecule, inhibitor of GlyT2 and 5HT2A receptors	Postoperative pain; lumbar radiculopathy. FDA Fast Track.	Vivozon	Phase 3	No	IV	www.vivozon.com	A
99	Otilimab (GSK3196165 / MOR103)	GM-CSF inhibitor	Biologic; fully human HuCal antibody versus granulocyte-macrophage colony-stimulating factor (GM-CSF)	Rheumatoid arthritis, combination with methotrexate	GSK / MorphoSys	Phase 3	No	SC	www.gsk.com/en-gb/research-and-development/our-pipeline www.morphosys.com/pipeline/proprietary-product-portfolio/mor103	A
100	PACAP38 Antibody	PACAP38	Biologic; neutralizing monoclonal antibody with reactivity to PACAP38	Treatment of pain (unspecified)	Lilly	Phase 1	No	UNK	www.lilly.com/discovery/pipeline	S
101	PF329	Mu opioid	Small molecule; hydromorphone prodrug	Chronic pain (opioid prodrug); TAAP technology prevents non-oral abuse	Ensysce Biosciences	Phase 1	Y	Oral	https://ensysce.com/our-pipeline	S
102	PF614	Mu opioid	Small molecule; oxycodone prodrug	Chronic pain (opioid prodrug); TAAP technology prevents non-oral abuse	Ensysce Biosciences	Phase 1	Y	Oral	https://ensysce.com/our-pipeline	S
103	PL265	Enkephalinase inhibitor	Small molecule; dual enkephalinase inhibitor (DENKI); target enzymes aminopeptidase N (NEP) and neprilysin (APN)	Neuropathic pain (Phase 1); ocular pain/dry eye syndrome (preclinical)	PharmaLeads	Phase 1	Y	Oral	www.pharmaleads.com/pharmaleads-pipeline/pl265 ; www.pharmaleads.com/pharmaleads-pipeline/pipeline-chart	S
104	PL37	Enkephalinase inhibitor	Small molecule; dual enkephalinase inhibitor (DENKI); target enzymes aminopeptidase N (NEP) and neprilysin (APN)	Acute post-surgical, traumatic, and breakthrough cancer pain; acute migraine pain	PharmaLeads	pre-IND	Y	IV (formerly oral)	Switch from oral to IV development: www.pharmaleads.com/pharmaleads-pipeline/pipeline-chart	N
105	Posimir (Posidur; SABER-bupivacaine)	Local anesthetic	Small molecule; bupivacaine extended-release formulation	Acute postoperative pain (local injection depot)	Durect / Sandoz	NDA Submitted	No	Local Injection	www.durect.com/pipeline/development/posimir	A
106	PPS	PPS	Small molecule; pentosan polysulfate sodium (PPS)	Knee osteoarthritis with concurrent bone marrow lesions (intra-articular injection)	Paradigm Biopharmaceuticals	Phase 2b	No	Intra-articular	www.paradigmbiopharma.com/clinical/clinical-trials	
107	Progenza	Stem cells	Biologic; allogenic adipose mesenchymal stem cells & secretions	Osteoarthritis; intra-articular injection	Regeneus Ltd	Phase 1	No	Intra-articular	http://regeneus.com.au/product-pipeline/progenza	S
108	Provant Therapy System	Neurostimulator	Medical device; topical stimulator	Painful Diabetic Distal Symmetric Peripheral Neuropathy (DSPN)	Regenesis	Phase 2	No	Topical	https://chqcp.net/clinical-trials-registry/NCT03455543	
109	Qtrypta (M207)	Triptan	Small molecule; zolmitriptan in adhesive dermally applied microarray (ADAM) microneedle formulation	Acute migraine	Zosano Pharma	NDA Submitted	No	Topical Patch	www.zosanopharma.com/pipeline	A

Agent	Emerging treatments for acute and chronic pain				Development Status, Route, Contact information				Update Status	
	Function / Target	Description / Mechanism of Action	Indication / Other Comments	Sponsor / Originator	Status	Opioid (Y/No)	Route	URL		
110	RDD-1219	Calcium channel blocker	Small molecule; coated nifedipine suppository	Chronic Anal Fissure	RDD Pharma	Phase 3 (Europe)	No	Topical	www.rddpharma.com	
111	ReActiv8	Neurostimulator	Medical device; neurostimulator	Chronic low back pain; implanted neuromuscular stimulator	Mainstay Medical	Phase 3	No	Implant	www.mainstay-medical.com/us/about	
112	ReJoin	Stem cells	Biologic; mesenchymal progenitor cells (haMPC), human adipose-derived	Osteoarthritis; intra-articular injection of haMPC	Cellular Biomedicine Group	Phase 2b	No	IA	www.cellbiomedgroup.com/stem-cells/rejoiako	
113	Resiniferatoxin	TRPV1	Small molecule; TRPV1 agonist	Intractable terminal cancer pain (intrathecal); pre-IND cancer pain (epidural); osteoarthritis pain (intra-articular)	Sorrento	Phase 1	No	IT, Epidural, Intra-articular	https://sorrentotherapeutics.com/pipeline	S
114	Rituxan (rituximab)	CD20	Biologic; CD20 chimeric monoclonal antibody	Pemphigus Vulgaris (PV); rare disease; Orphan Drug Designation; FDA Breakthrough Therapy designation	Genentech	Phase 3	No	IV	www.gene.com/stories/understanding-pemphigus-vulgaris	
115	Rivipansel (GMI-1070)	Pan-selectin	Small molecule (carbohydrate mimetic); pan-selectin inhibitor	Sickle cell disease; treatment of vaso-occlusive crisis (infused i.v. q. 12 hr; not a primary analgesic; used in combination with i.v. morphine); FDA Orphan Drug and Fast Track designations	Pfizer / GlycoMetics	Phase 3	No	IV	www.pfizer.com/science/drug-product-pipeline ; www.pfizer.com/news/press-release/press-release-detail/pfizer-announces-phase-3-top-line-results-for-rivipansel-in-patients-with-sickle-cell-disease-experiencing-a-vaso-occlusive-crisis	S
116	Rofecoxib (TRM-201)	NSAID	Small molecule; COX-2 inhibitor	Hemophilic arthropathy (joint pain). FDA Fast Track and Orphan Drug designation.	Tremeau Pharmaceuticals	Phase 3	No	Oral	www.tremeaux.com/pipeline-1	
117	Ropivacaine (PRF-110)	Local anesthetic	Small molecule; liposomal product formulation	Postoperative pain; soft and hard tissue	PainReform	Phase 3	No	IM	www.painreform.com/product.php?ID=1	
118	RVT-1801	Hemoglobin gene replacement	Biologic; lentiviral-modified fetal hemoglobin gene	Sickle cell disease, beta-thalassemia	Aruvant Sciences	Phase 2	No	Transplant	http://aruvant.com	
119	S1A (MR309, E-52862)	Sigma ₁	Small molecule; sigma-1 antagonist	Neuropathic pain (diabetic neuropathy; post-surgical; nerve injury); acute post-operative pain	Mundipharma / Purdue Pharma / Esteve	Phase 2	No	Oral	www.purduepharma.com/news-media/2016/05/mundipharma-and-purdue-pharma-expand-pain-pipeline-with-new-deal-for-first-in-class-sigma-1-antagonist-s1a-or-mr309e-52862-from-estevae/	S
120	SB-061	Aggrecan	Biologic; prevention of cartilage degradation by mimicking the protective effect of the proteoglycan aggrecan	Osteoarthritis	Symic Biomedical	Phase 1 / 2	No	Intra-articular	www.symic.bio/pipeline/osteoarthritis	S
121	SD-101 (formerly Zorblisa)	Allantoin	Small molecule; 6% allantoin cream	Epidermolysis bullosa (rare disease)	Amicus	Phase 3	No	Topical	www.amicusrx.com/clinical_studies_eb	
122	SEL-212	Uricase + immunosuppressant	Biologic; non-immunogenic encapsulated rapamycin + pegsitticase (pegylated uricase) Biologic; chemical	Treatment of refractory and tophaceous gout	Selecta Biosciences	Phase 2	No	IV	https://selectabio.com/pipeline/chronic-severe-gout	
123	Sevuparin	Heparin analog	Biologic; chemical depolymerization of heparin to optimize its anti-adhesive and anti-inflammatory effects and remove anti-thrombin binding sites	Acute vaso-occlusive crisis in subjects with sickle cell disease	Modus / Karolinska Institutet and Uppsala University	Phase 2 (EU) Phase 1 (US)	No	IV SC	www.modustx.com/modus-therapeutics-announces-fda-acceptance-sevuparin-ind-treatment-sickle-cell-disease	
124	SM04690	Wnt	Small molecule; inhibitor of Wnt pathway	Knee osteoarthritis; potential disease modifying osteoarthritis drug (DMOAD)	Samumed	Phase 3	No	Intra-articular	www.samumed.com/pipeline/default.aspx	A
125	Tanezumab	NGF	Biologic; humanized NGF monoclonal antibody	Osteoarthritis, chronic low back pain, cancer pain. FDA Fast-Track.	Pfizer / Lilly	Phase 3	No	SC	www.lilly.com/discovery/pipeline	S
126	TLC599	Corticosteroid	Small molecule; extended-release dexamethasone	Knee osteoarthritis	TLC Biopharmaceuticals	Phase 3	No	Intra-articular	www.tlcbio.com/en-global/pipeline/index/pain-management/TLC599#product_info	A

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		Function / Target	Description / Mechanism of Action	Indication / Other Comments	Sponsor / Originator	Status	Opioid (Y/No)	Route	URL	
127	Topofen (ELS-M11)	NSAID	Small molecule; 5% ketoprofen gel (migraine); 2% ketoprofen gel (OA)	Acute and chronic migraine; topical administration to skin in facial trigeminal nerve branches; osteoarthritis	Achelios	Phase 1b / 2a	No	Topical	http://achelios.com/programs-pipeline	S
128	TPM / Oxycodone Transdermal Matrix Patch	Mu opioid	Small molecule; oxycodone transdermal patch formulation	Chronic pain	Phosphagenics	Phase 1 / 2	Y	TD	www.phosphagenics.com/research/pipeline	S
129	TPM / Oxycodone Transdermal Matrix Patch	Mu opioid	Small molecule; oxycodone transdermal patch formulation	Chronic pain	Phosphagenics	Phase 1 / 2	Y	TD	www.phosphagenics.com/research/pipeline	S
130	TPX-100	Cartilage repair	Small peptide; 23-amino acid chondrogenic peptide	Knee osteoarthritis; patello-femoral osteoarthritis; intra-articular injection; tissue-specific hard tissue repair and regeneration molecule (cartilage, bone, and dentin defects)	OrthoTropix	Phase 2	No	Intra-articular	www.orthotropix.com/products-tpx-100.html	S
131	Tramadol IV	Mu opioid / NE-5HT uptake	Small molecule; tramadol in i.v. formulation	Moderate to moderately severe post-operative pain	Avenue Therapeutics	NDA Submitted	Y	IV	www.avenuetx.com/pipeline	A
132	TRV250	Delta opioid	Small molecule; delta opioid receptor agonist	Acute migraine	Trevena	Phase 1	Y	Oral, SC	https://www.trevena.com/pipeline/trv250	S
133	TRV734	Mu opioid	Small molecule; G protein-biased agonist to mu opioid receptor	Opioid use disorder (formerly acute postoperative pain); anticipated reduced adverse effect profile, low abuse liability	Trevena	Phase 1	Y	Oral	www.trevena.com/pipeline/trv734	S
134	Turmeric	Turmeric	Small molecule; natural product	Basal joint arthritis	Massachusetts General Hospital	Phase 1	No	Oral	www.clinicaltrials.gov/ct2/show/NCT03017118?term=Turmeric+arthritis&rank=2	S
135	UBX0101	MDM2/p53 inhibitor	Small molecule; senolytic inhibitor of the MDM2/p53 protein interaction.	Knee osteoarthritis; triggers elimination of senescent cells, reduces pain, prompts cartilage regrowth.	Unity Biotech	Phase 2	No	IA	https://unitybiotechnology.com/pipeline	A
136	Unnamed	Topical analgesic	Small molecule; rapidly acting topical analgesic made of volatile anesthetics (unnamed)	Topical analgesic; rapid onset	Vapogenix	Phase 2	No	Topical	www.vapogenix.com/pipeline.html	
137	URG101	Local anesthetic + heparin	Small molecule; combination of heparin sodium + lidocaine HCl	Bladder pain syndrome/interstitial cystitis (BPS/IC); intravesical administration	Urigen	Phase 2	No	IVS	www.urigen.com/urg101.htm	
138	VM-902A	TrkA	Small molecule; allosteric selective inhibitor of tropomyosin kinase A (TrkA) receptor [inhibitor of nerve growth factor (NGF) receptor]	Chronic pain	Purdue Pharma / VM Pharma	Phase 2	No	Oral	www.purduepharma.com/news-media/2015/09/purdue-pharma-l-p-announces-acquisition-of-trka-program-from-vm-pharma-lc	
139	VX-150	Nav 1.8	Small molecule; Nav1.8 inhibitor	Acute postoperative pain; knee osteoarthritis; small fiber neuropathic pain	Vertex Pharmaceuticals	Phase 2	No	Oral	www.vrtx.com/pipeline-medicines/investigational-medicines-pipeline	
140	Xaracoll	Local anesthetic + collagen	Biologic + small molecule; collagen + bupivacaine bioresorbable implant	Acute postoperative pain; implant delivers high dose local anesthetic to the surgical site, low systemic bioavailability	Innocoll	Phase 3	No	Local implant	www.innocoll.com/products.aspx	S
141	XT-150	IL-10	Biologic; IL-10 gene therapy, suppression of activated glial activity in the spinal cord	Osteoarthritis	Xalud Therapeutics	Phase 2a	No	IA	www.xaludthera.com/pipeline/	
142	Zalviso	Mu opioid	Small molecule; sufentanil formulation	Acute postoperative pain (sublingual), pre-programmed, patient-controlled analgesia device; alternative to i.v. PCA opioids	AcelRx	Phase 3	Y	SL	www.acerlx.com/pipeline/zalviso-us.php	S

Agent	Emerging treatments for acute and chronic pain				Development Status, Route, Contact information				Update Status
	Function / Target	Description / Mechanism of Action	Indication / Other Comments	Sponsor / Originator	Status	Opioid (Y/No)	Route	URL	
143 Zydis (rimegepant, (BHV-3000)	CGRP	Small molecule; CGRP antagonist	Acute migraine, FDA priority review	Biohaven Pharmaceuticals	NDA Submitted	No	Oral	www.biohavenpharma.com/science-pipeline/our-pipeline	A

NDA / BLA APPROVED PRODUCTS FOR 2019

1	Adakveo (crizanlizumab, SEG101, SelG1)	P-selectin	Biologic; humanized anti-P-selectin monoclonal antibody	Acute vaso-occlusive crisis in subjects with sickle cell disease; sickle cell crisis	Novartis / Selexys Pharmaceuticals	BLA Approval	No	IV	www.novartis.com/news/media-releases/new-novartis-medicine-adakveo-crizanlizumab-approved-fda-reduce-frequency-pain-crisis-individuals-living-sickle-cell-disease	A
2	Aimovig (erenumab; AMG 334)	CGRP	Biologic; fully human monoclonal antibody, calcitonin gene-related peptide (CGRP) receptor antagonist	Chronic migraine prevention (s.c. monthly dosing)	Amgen / Novartis	BLA Approval	No	SC	www.aimoviq.com	A
3	Emgality (galcanezumab-gnlm; (LY2951742)	CGRP	Biologic; humanized monoclonal antibody, calcitonin gene-related peptide (CGRP) receptor antagonist	Cluster headache prevention (s.c. monthly dosing) (New Indication)	Lilly	BLA Approval (cluster headache)	No	SC	https://investor.lilly.com/news-releases/news-release-details/fda-approves-emgalityr-galcanezumab-qnm-first-and-only	A
4	Oxbryta (voxelotor, GBT440)	HbS	Small molecule; hemoglobin S allosteric modulator; increases hemoglobin affinity for oxygen	May be disease-modifying for sickle cell disease (SCD). FDA Breakthrough, Fast Track and Orphan Drug designation; Rare Pediatric Disease status	Global Blood Therapeutics	NDA Approval	No	Oral	www.gbt.com/our-medicine	A
5	Reyvow (lasmiditan, (LY573144, COL-144)	5-HT _{1f}	Small molecule; 5-HT _{1f} antagonist	Acute migraine	Lilly / Colucid	NDA Approval	No	IV	https://investor.lilly.com/news-releases/news-release-details/lillys-reyvowtm-lasmiditan-first-and-only-medicine-new-class	A
6	Rinvoq (upadacitinib, ABT-494)	JAK1	Small molecule; selective JAK1 inhibitor	Rheumatoid arthritis, atopic dermatitis, axial SpA, Crohn's disease, psoriatic arthritis, ulcerative colitis, giant cell arteritis	AbbVie	NDA Approval	No	Oral	www.abbvie.com/our-science/pipeline/upadacitinib.html	A
7	Taltz (ixekizumab, LY2439821)	IL-17	Biologic; humanized IgG4-type monoclonal antibody to IL-17	Axial spondyloarthritis, psoriatic arthritis, plaque psoriasis, rheumatoid arthritis	Lilly	BLA Approval	No	SC	https://investor.lilly.com/news-releases/news-release-details/lilly-receives-us-fda-approval-taltzr-ixekizumab-treatment	A
8	Ubrovelvy (ubrogepant, (MK-1602)	CGRP	Small molecule CGRP receptor antagonist	Acute treatment of migraine	Allergan	NDA Approval	No	Oral	www.allergan.com/research-and-development/pipeline	A

NEW PRODUCTS FOR 2019

1	Atexakin alfa (SON-080)	r-IL-6	Biologic; low-dosage recombinant IL-6 formulation	Chemotherapy-induced peripheral neuropathy (CIPN)	Sonnet BioTherapeutics / Relief Therapeutics (Merck Serono)	Phase 1	No	SC	www.sonnetbio.com/pipeline ; https://relieftherapeutics.com/compounds-2	N
2	AXS-06	Meloxicam + esomeprazole	Small molecule; combination of meloxicam (COX-2 anti-inflammatory) + esomeprazole (PPI, prevention of GI ulceration)	Chronic pain; osteoarthritis, rheumatoid arthritis	Axsome Therapeutics	Phase 3 (planned)	No	Oral	https://axsome.com/axs-pipeline/axsome-pain-and-primary-care	N
3	AXS-07	Meloxicam + rizatriptan	Small molecule; combination of meloxicam (COX-2 anti-inflammatory) + rizatriptan (5-HT _{1B/D} agonist)	Acute migraine	Axsome Therapeutics	Phase 3	No	Oral	https://axsome.com/axs-pipeline/about-axs-07	N

Agent	Emerging treatments for acute and chronic pain				Development Status, Route, Contact information				Update Status	
	Function / Target	Description / Mechanism of Action	Indication / Other Comments	Sponsor / Originator	Status	Opioid (Y/No)	Route	URL		
4	Bercolagene telsepavec (KB103)	Mutations in the COL7A1 gene encoding type VII collagen (COL7)	Biologic; gene therapy to restore functional collagen VII	Dystrophic epidermolysis bullosa (DEB); FDA Orphan Drug Designation; FDA Rare Pediatric Disease Designation; FDA Fast-track Designation; FDA RMAT designation	Krystal Biotech	Phase 2	No	Topical	www.krystalbio.com/focus/pipeline ; www.krystalbio.com/focus/about-dystrophic-eb	N
5	Bermekimab	IL-1	Biologic; mAb, IgG1k isotype targeting IL-1 alpha	Hidradenitis suppurativa (painful skin lesions, inflammation and infection of sweat glands)	Janssen / Xbiotech	Phase 2	N	SC	www.xbiotech.com/about/janssen.php www.jni.com/janssen-to-acquire-investigational-bermekimab-from-xbiotech	N
6	Brazikumab (MEDI2070)	IL-23 antibody	Biologic; human monoclonal antibody to IL-23	Ulcerative colitis, Crohn's disease	Allergan / AstraZeneca (MedImmune)	Phase 2 / 3	No	IV / SC	www.allergan.com/research-and-development/pipeline	N
7	C213	Triptan	Small molecule; zolmitriptan in adhesive dermally applied microarray (ADAM) microneedle formulation	Cluster Headache	Zosano Pharma	Phase 2/3	N	Patch	www.zosanopharma.com/pipeline	N
8	Cannabis extract	Cannabis; CB1 receptor	Small molecule; tetrahydrocannabinol (THC) extract	Chronic pain; pain in chronic kidney disease	Panaxia Pharmaceutical	Clinical	No	SL	https://panaxia.co.il/research-tech	N
9	CR4056	Imidazoline-2 (I2) agonist	Small molecule; facilitate descending noradrenergic inhibitory pathways	Knee osteoarthritis; neuropathic pain	Rottapharm Biotech S.r.l.	Phase 2	No	Oral	www.rottapharmbiotech.com/pipeline ; www.rottapharmbiotech.com/cr4056	N
10	CT-044	Peroxynitrite catalytic inactivation	Small molecule; Radical Species Decomposition Accelerant (RSDAx) of peroxyxynitrite and hydrogen peroxide	Acute and chronic pain including acute post-surgical pain and painful diabetic neuropathy	CerSci Therapeutics	Phase 1	No	Oral	https://cersci.com/development-pipeline	N
11	CTL-X	Cannabis with high THC content; CB1 receptor	Small molecule; natural product	Acute postoperative pain; vaporized administration	Veritas	Phase 1	N	Inhalation	http://veritaspharmainc.com/product-pipeline	N
12	Diepalestat (BNV-222)	Aldos reductase inhibitor (ARI)	Small molecule; co-crystal of epalrestat, an aldose reductase inhibitor	Diabetic peripheral neuropathy (DPN); potential indication: diabetic retinopathy, diabetic neuropathy, diabetic cardiomyopathy	Neuromax / Bionevia Pharmaceuticals	Phase 2	No	Oral	http://neuromax.ru/en/products/bnv-222 ; www.new-bionevia.com/services.html	N
13	FX201 (human-takinogene hadenovec)	IL-1 antagonist	Biologic; human IL-1 receptor antagonist (IL-1Ra) gene therapy; adenovirus vector	Knee osteoarthritis; expect one dose administration to produce analgesia for one year	Flexion Therapeutics	Phase 1	No	IA	https://flexiontherapeutics.com/our-pipeline/#FX201	N
14	IMR-687	PDE9 Inhibitor	Small molecule; phosphodiesterase 9 inhibition designed to increase fetal globin, decrease RBC and WBC adherence to blood vessel endothelium	Sickle cell disease (SCD); FDA Fast Track designation	Imara	Phase 2	No	Oral	https://imaratx.com/our-programs/#imr	N
15	ISC 17536 (GRC-17536)	TRPA1 antagonist	Small molecule; transient receptor potential ankyrin-1 (TRPA 1) antagonist	Neuropathic pain; painful diabetic peripheral neuropathy	Ichnos Sciences (formerly Glenmark)	Phase 2	No	Oral	www.ichnoscience.com/approach	N
16	ISC 27864 (GRC-27864)	Prostaglandin-E synthase inhibitor	Small molecule; microsomal prostaglandin E synthase-1 (mPGES-1) inhibitor	Osteoarthritis of the hip or knee	Ichnos Sciences (formerly Glenmark)	Phase 2	No	Oral	www.ichnoscience.com/approach	N
17	Lanraplenib (GS-9876)	Syk inhibitor	Small molecule; spleen tyrosine kinase inhibitor ...	Sjogren's syndrome, lupus, ulcerative colitis	Gilead	Phase 2	No	Oral	www.gilead.com/science-and-medicine/pipeline	N
18	LentiGlobin (HGB-206)	Hemoglobin gene	Biologic; lentiviral vector hemoglobin gene therapy	Sickle cell disease (SCD)	Bluebird Bio	Phase 1/2	No	IV	www.bluebirdbio.com/our-science/pipeline	N
19	Lu AG06466 (ABX-1431)	MGLL	Small molecule; inhibitor of the serine hydrolase monoacylglycerol lipase (MGLL); potentiation of endocannabinoid signalling	Neuropathic pain, chronic central pain (Phase 2 in Tourette's syndrome)	Lundbeck (Abide Therapeutics)	Phase 1	No	Oral	www.lundbeck.com/global/brain-disorders/pipeline	N

Agent	Emerging treatments for acute and chronic pain				Development Status, Route, Contact information				Update Status	
	Function / Target	Description / Mechanism of Action	Indication / Other Comments	Sponsor / Originator	Status	Opioid (Y/No)	Route	URL		
20	MD-7246	Guanylate cyclase-C agonists	Small molecule; release of linaclotide (Linzess) in the distal ileum near the ileocecal junction	Abdominal pain associated with IBS with diarrhea (IBS-D)	Allergan / Ironwood Pharmaceuticals	Phase 2	No	Oral	www.ironwoodpharma.com/pipeline/md-7246	N
21	MEDI7352	NGF/TNF inhibitor	Biologic; NGF/TNF bispecific monoclonal antibody	Osteoarthritis, painful diabetic neuropathy	AstraZeneca / MedImmune	Phase 2	No	IV	https://www.astrazeneca.com/our-science/pipeline.html	N
22	Oxycodone IR	Mu agonist	Small molecule; oxycodone formulation (contains dye)	Acute pain	Pharmaceutical Manufacturing Research Services (PMRS)	NDA Not Approved	Y	Oral	www.prnewswire.com/news-releases/pharmaceutical-maker-sues-fda-for-rejecting-new-approach-to-detering-opioid-abuse-300920993.html	N
23	Oxytocin	CGRP; physiological antagonism	Small peptide; unique formulation + delivery system	Acute migraine	Trigemina	Phase 2	N	IN	http://trigemina.com	N
24	PVA Hydrogel	Visco-supplementation	Small molecule; synthetic polymer of vinyl alcohol (polyvinyl alcohol; PVA)	Osteoarthritis; intra-articular viscosupplementation with long half life	Rottapharm Biotech S.r.l.	Phase 1	No	IA	www.rottopharmbiotech.com/pipeline ; www.rottopharmbiotech.com/pva-hydrogel	N
25	shRNA (mir)	BCL11A (fetal to adult globin switch)	Biologic; lentiviral vector, autologous gene therapy targeting BCL11A protein	Sickle cell disease (SCD)	Bluebird Bio	Phase 1	No	IV	www.bluebirdbio.com/our-science/pipeline	N
26	SI-722	Chondroitin sulfate + steroid conjugate	Biologic; conjugated to unnamed steroid	Interstitial Cystitis, Bladder Pain Syndrome; extended release steroid	Seikagaku	Phase 1/2	No	IVS	www.seikagaku.co.jp/en/development/status.html ; www.seikagaku.co.jp/en/news/news-5685669025233081251/main/0/link/20191108_e.pdf	N
27	Sprifermin	Fibroblast growth factor-18	Biologic; recombinant human fibroblast growth factor-18	Osteoarthritis; possible disease-modifying	Merck KGaA	Phase 2	No	IA	www.emdgroup.com/en/research/biopharma-pipeline.html	N
28	STS101	Ergot alkaloid	Small molecule; powdered nasal formulation of dihydroergotamine mesylate (DHE)	Acute migraine	Satsuma Pharmaceuticals	Phase 3	No	IN	www.satsumarx.com/lead-candidate	N
29	TD-1473	pan-JAK inhibitor	Small molecule; gut-selective JAK inhibitor	Ulcerative colitis, Crohn's disease	Janssen / Theravance	Phase 2 / 3	No	Oral	www.theravance.com/our-pipeline	N
30	TLC590	Local anesthetic	Small molecule; ropivacaine extended-release formulation (96 hours)	Acute postoperative pain; single intrathecal injection prior to surgery	The Liposome Company	Phase 2	N	Local injection	www.tlcbio.com/en-global/pipeline/index/pain-management/TLC590	N
31	TLC590	Local anesthetic	Small molecule; extended-release liposomal ropivacaine formulation	Acute postoperative pain	TLC Biopharmaceuticals	Phase 2	No	Local infiltration	www.tlcbio.com/en-global/pipeline/index/pain-management/TLC590#product_info	N
32	TLC599	Corticosteroid	Small molecule; dexamethasone sodium phosphate (DSP) extended-release (24 month) formulation	Osteoarthritis	The Liposome Company	Phase 3	N	IA	www.tlcbio.com/en-global/pipeline/index/pain-management/TLC599	N
33	Tonmya (TNX-102 SL)	5-HT2 antagonist	Small molecule; cyclobenzaprine formulation; centrally acting muscle relaxant	Fibromyalgia	Tonix	Phase 2	No	SL	www.tonixpharma.com/news-events/press-releases/detail/1011/tonix-pharmaceuticals-completes-enrollment-in-phase-3	N
34	Tramadol + celecoxib (E-58425)	Mu opioid + COX-2 combination	Small molecule; co-crystal formulation of tramadol + celecoxib	Acute pain	Esteve	NDA Submitted	Y	Oral	https://www.esteve.com/global/research-development/pipeline	N
35	Vasegepant (BHV-3500)	CGRP	Small molecule; CGRP antagonist	Acute migraine	Biohaven Pharmaceuticals	Phase 2/3	No	IN	www.biohavenpharma.com/science-pipeline/our-pipeline	N
36	VIB4920	CD40L-Tn3 blocker	Biologic; anti-CD40L-Tn3 fusion protein that blocks human CD40L and inhibits activation of B cells	Rheumatoid arthritis; Sjögren's syndrome	Viela Bio	Phase 1	No	IV	https://vielabio.com/product-candidates/pipeline	N

DISCONTINUED / UNCERTAIN PRODUCTS IN 2019

1	Asalhydro-morphine (Asal-HM) (KP511/FR)	Mu opioid	Small molecule; hydromorphone prodrug	Chronic pain (opioid prodrug)	KemPharm	Phase 1	Y	Oral	https://kempharm.com/pipeline-products	D
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Agent	Emerging treatments for acute and chronic pain				Development Status, Route, Contact information				Update Status	
	Function / Target	Description / Mechanism of Action	Indication / Other Comments	Sponsor / Originator	Status	Opioid (Y/No)	Route	URL		
2	Asahydro-morphone (Asal-HM) (KP511/IR)	Mu opioid	Small molecule; hydromorphone prodrug	Acute pain (opioid prodrug)	KemPharm	Phase 1	Y	Oral	https://kempharm.com/pipeline-products	D
3	ASP1807 (CC8464)	Nav 1.7	Small molecule sodium channel blockade (Nav 1.7 selective)	Neuropathic and inflammatory pain. FDA Fast Track.	Astellas / Chromocell	Phase 1	No	Oral	No longer in Astellas development pipeline: https://sw4503.swcms.net/en/ir-library/pipeline/inframe/main/01/teaserItems/1/0/linkList/0/link/2q2019_rd_en.pdf	D
4	ASP6294	Biologic; NGF neutralizing antibody	Biologic; nerve growth factor antibody	Bladder pain syndrome / interstitial cystitis	Astellas	Phase 2	No	SC	https://sw4503.swcms.net/en/ir-library/pipeline/inframe/main/01/teaserItems/1/0/linkList/0/link/2q2019_rd_en.pdf	D
5	ASP7962	TrkA	Small molecule; TrkA inhibitor	Osteoarthritis	Astellas	Phase 2 (EU)	No	Oral	No longer on Astellas development pipeline: https://sw4503.swcms.net/en/ir-library/pipeline/inframe/main/01/teaserItems/1/0/linkList/0/link/3q2019_pipeline_en.pdf	D
6	Axelopran / oxycodone FDC	Mu opioid + peripheral antagonist	Small molecule; combination of axelopran (TD-1211) and oxycodone	Chronic pain, abuse-deterrent formulation; opioid pain relief without opioid-induced constipation (OIC)	Theravance	Phase 1	Y	Oral	No longer in Theravance development pipeline: www.theravance.com/our-pipeline	D
7	BuTab (REL-1028)	Mu opioid	Small molecule; buprenorphine formulation	Chronic pain	Relmada Therapeutics	Phase 1	Y	Oral	No current studies planned: www.relmada.com/product-candidates/rel-1028-butab	??
8	Clazakizumab (ALD518)	IL-6	Biologic; humanized IL-6 monoclonal antibody	Rheumatoid arthritis; patients who have experienced an inadequate response to TNF inhibitors	Vitaeris / Alder BioPharmaceuticals	Phase 2b	No	SC	No longer in RA; Phase 3 shift to renal allograft loss from antibody mediated rejection: https://vitaerisbio.com/clazakizumab	??
9	Dextromethadone (d-Methadone, REL-1017)	NMDA	Small molecule; single enantiomer of d,l-methadone	Neuropathic pain; NMDA receptor antagonist, expected to have no opioid activity at expected therapeutic doses	Relmada Therapeutics	Phase 2	Y	Oral	Current studies shifted to Major Depressive Disorder: www.relmada.com/product-candidates/rel-1017-dextromethadone-in-depression	D
10	Egalet-004	Mu opioid	Small molecule; hydrocodone extended-release formulation	Chronic pain, abuse-deterrent formulation	Zyla Life Sciences (formerly Egalet)	Phase 1	Y	Oral	Company bankruptcy; changed focus: www.egalet.com/?s=egalet	D
11	KP201/IR	Mu opioid	Small molecule; benzhydrocodone	Acute pain (opioid prodrug)	KemPharm	Phase 1	Y	Oral	https://kempharm.com/pipeline-products	D
12	LEVI-04	p75NTR-Fc	Biologic; p75 neurotrophin receptor fusion protein (p75NTR-Fc); modulation of NGF activity	Neuropathic pain, knee osteoarthritis	Levicept	Phase 1	No	IV	(website suspended; update not confirmed): www.levicept.com/science	??
13	LevoCap ER (REL-1015)	Mu opioid	Small molecule; levorphanol extended-release formulation	Chronic pain, abuse-deterrent formulation; expected dual action (opioid + noradrenaline reuptake inhibition)	Relmada Therapeutics	Phase 1	Y	Oral	No current studies planned: www.relmada.com/product-candidates/rel-1015-levocap-er	??
14	Lpathomab (LT3015, LT3000)	LPA	Biologic; antibody targeting lysophosphatidic acid (LPA)	Chronic pain; reduction in bioactive lipids involved in chronic pain and neuropathic pain	Apollo Endoscopy / Lpath	Phase 1	No	IV	No longer in Apollo Endoscopy development pipeline: https://apolloendo.com	D
15	LTX-03	Mu opioid combination	Small molecule; combination of hydrocodone + acetaminophen	Acute pain, abuse-deterrent formulation	Acura Pharmaceuticals	Phase 1	Y	Oral	No active development: http://acurapharm.com/productpipeline	??
16	LTX-04	Mu opioid	Small molecule; hydromorphone immediate release	Acute pain, abuse-deterrent formulation	Acura Pharmaceuticals	Phase 1	Y	Oral	No active development: http://acurapharm.com/productpipeline	??
17	Mesenchymal trophic factors (MTF)	Stem cells	Biologic; mesenchymal stem cell trophic factors, umbilical cord tissue derived	Osteoarthritis; intra-articular injection of MSC (single injection) or weekly s.c. injection x 12 weeks	Translational Biosciences	Phase 1 / 2	No	Intra-articular; SC	No active development: www.translationalbiosciences.com/human-umbilical-cord-mesenchymal-stem-cell-therapy-for-osteoarthritis	??
18	MM-II	Phospholipids	Small molecule; liposomal product with 2 known phospholipids (undisclosed)	Knee osteoarthritis	Moebius Medical / Sun Pharma	Phase 1 / 2	No	Intra-articular	No active development: http://moebiusmedical.com/mm-ii	??
19	MNK-812 (oxycodone)	Mu agonist	Small molecule; abuse deterrent immediate release formulation	Acute pain	Mallinckrodt-SpecGx	NDA Not Approved	Y	Oral	No longer in Mallinckrodt development pipeline: www.mallinckrodt.com/research/science-technology/pipeline	D

Agent	Emerging treatments for acute and chronic pain				Development Status, Route, Contact information				Update Status	
	Function / Target	Description / Mechanism of Action	Indication / Other Comments	Sponsor / Originator	Status	Opioid (Y/No)	Route	URL		
20	NKT120	NK T cells	Biologic; humanized monoclonal antibody that selectively depletes invariant natural killer T cells	Sickle cell disease; reduce organ damage, inflammation, and pain; FDA Fast Track.	NKT Therapeutics	Phase 1	No	IV	Development uncertain: www.nktr.com/company.html	??
21	Olodanrigan (EMA401)	AT2	Small molecule; angiotensin II type 2 (AT2) receptor antagonist	Neuropathic pain; post-herpetic neuralgia	Novartis / Spinifex	Phase 2 (Discontinued?)	No	Oral	www.novartis.com/sites/www.novartis.com/files/novartis-pipeline-2018-annual-report.pdf	D
22	Remoxy ER	Mu opioid	Small molecule; oxycodone extended-release formulation	Chronic pain, abuse-deterrent formulation	Cassava Sciences (Pain Therapeutics)	Discontinued (NDA Not Approved)	Y	Oral	https://www.cassavasciences.com/news-releases/news-release-details/pain-therapeutics-announces-name-change-cassava-sciences-inc	D
23	TRK-750	Undisclosed	Undefined mechanism	Peripheral Neuropathic Pain	Toray	Phase 1	No	Oral	No longer in Toray development pipeline: www.toray.com/technology/organization/laboratories/lab007.html	D
24	UC-MSC (OA)	Stem cells	Biologic; Mesenchymal Stem Cells (MSC), umbilical cord tissue derived	Osteoarthritis; intra-articular injection of MSC (single injection)	Translational Biosciences	Phase 1 / 2	No	Intra-articular; IV	No active development: www.translationalbiosciences.com/human-umbilical-cord-mesenchymal-stem-cell-therapy-for-osteoarthritis	??
25	UC-MSC (RA)	Stem cells	Biologic; Mesenchymal Stem Cells (MSC), umbilical cord tissue derived	Rheumatoid arthritis; patients resistant to DMARD therapy; MSC injected i.v. daily x 5 days	Translational Biosciences	Phase 1 / 2	No	IV	No active development: www.translationalbiosciences.com/human-umbilical-cord-mesenchymal-stem-cell-therapy-for-osteoarthritis	??
26	VBY-036	Cathepsin S	Small molecule; cathepsin S inhibitor	Neuropathic pain; Chemotherapy-Induced Peripheral Neuropathy Disease (CINP)	Virobay	Phase 1	No	Oral	(website inactive; company dissolved): www.virobayinc.com/	D
27	Zoledronic acid (T121)	Bisphosphanate	Small molecule; oral and i.v. formulations of zoledronic acid	Complex regional pain syndrome (CRPS).	Grünenthal / Thar Pharmaceuticals	Phase 3	No	Oral IV	No longer in Grunenthal development pipeline: www.grunenthal.com/r-d-vision-mission/pipeline	D