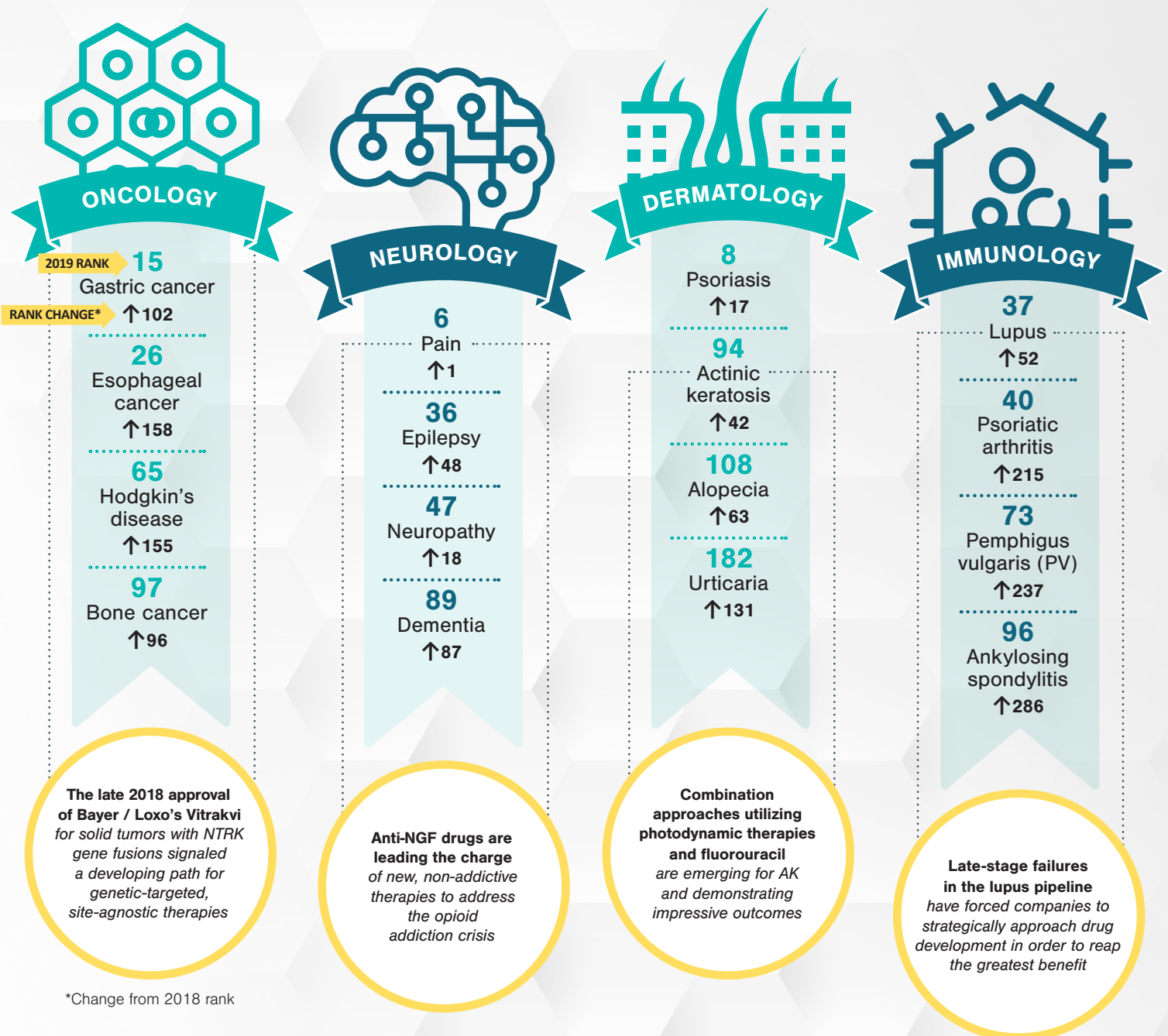


HOT INDICATIONS LIST 2019

Kx Advisors' 5th annual analysis of global R&D investment has identified the top indications for industry focus in 2019 across 21 therapeutic areas (TAs). There were impressive changes in market focus and investment over the past year. Novel approaches to established treatment pathways drove top movers on the 2019 list, including **Pancreatic Cancer (#15)** and **Ulcerative Colitis (#25)**. In Immunology, excitement surrounds the recent clinical successes of JAK inhibitors in indications such as **rheumatoid arthritis (#17)**, fueling increased hope that they could also be used in other autoimmune diseases such as **lupus (#37)**, **psoriatic arthritis (#40)** and **ankylosing spondylitis (#96)**. The late 2018 approval of Vitrakvi catalyzed the ever-growing Oncology space, opening the door to innovation in site-agnostic tumor therapies and immunotherapies across indications, especially in rare cancers. Developments in gene therapy also exploded, with R&D funding exceeding \$4B, and prices skyrocketing: Novartis' recent approval of Zolgensma for **SMA (#151)** shattered the record as the most expensive drug in the world, at \$2.1M per treatment. With the market rapidly evolving in response to growing needs, companies are being challenged to capitalize on strategic R&D opportunities through clinical innovation at an accelerated pace. To learn more about the Kx Advisors Hot Indications methodology, see page 4.



POCKETS OF OPPORTUNITY

Outside of the top-moving indications, Kx Advisors performed an analysis of the most crowded TAs to identify indications with relatively high unmet need and relatively low clinical trial failure rates and numbers of programs in development. These pockets of opportunity are the most attractive, least competitive indications within the hottest TAs, where companies can get ahead of the curve to establish a unique position in competitive markets. These pockets of opportunity include high unmet need Oncology markets, such as Bladder Cancer (#16), where competition is less intense than in banner indications such as Breast Cancer (#1). Advancements in gene

therapy and increased funding for rare disease research have made ALS (#147) one of the most interesting indications in the rapidly growing Neurology space. Fringe autoimmune diseases such as Myasthenia Gravis (#129) present a light pipeline as an opportunity for companies to innovate beyond JAK inhibitors. Finally, companies should consider indications such as Alopecia (#108) due to their favorable funding and potential orphan drug designation to drive growth in a crowded Dermatology market. To learn more about potential opportunities for investment, check out Kx Advisors' upcoming deep dives.

2019 Ranking	Indication	Therapeutic Area	2018 Ranking	Change
1	Breast cancer	Oncology	3	↑ 2
2	Non-small cell lung cancer (NSCLC)	Oncology	4	↑ 2
3	Diabetes	Endocrinology	1	↓-2
4	Non-Hodgkin's lymphoma (NHL)	Oncology	6	↑ 2
5	Colorectal cancer	Oncology	16	↑ 11
6	Pain	Neurology	7	↑ 1
7	Ovarian cancer	Oncology	23	↑ 16
8	Psoriasis	Dermatology	25	↑ 17
9	Acute myelogenous leukemia (AML)	Oncology	8	↓-1
10	Melanoma	Oncology	13	↑ 3
11	Head & neck cancers	Oncology	19	↑ 8
12	Liver cancer	Oncology	9	↓-3
13	Multiple myeloma (MM)	Oncology	27	↑ 14
14	Glioblastoma multiforme (GBM)	Oncology	34	↑ 20
15	Gastric cancer	Oncology	117	↑ 102
16	Bladder cancer	Oncology	46	↑ 30
17	Rheumatoid arthritis (RA)	Immunology	20	↑ 3
18	Pancreatic cancer	Oncology	26	↑ 8
19	Parkinson's disease (PD)	Neurology	17	↓-2
20	Renal cancer	Oncology	103	↑ 83
21	Prostate cancer	Oncology	5	↓-16
22	Dermatitis	Dermatology	11	↓-11
23	HIV / AIDS	Infectious Disease	10	↓-13
24	Crohn's disease	Gastroenterology	69	↑ 45
25	Ulcerative colitis	Gastroenterology	81	↑ 56
26	Esophageal cancer	Oncology	184	↑ 158
27	Hyperlipidemia	Endocrinology	53	↑ 26
28	Acute lymphoblastic leukemia (ALL)	Oncology	104	↑ 76
29	Myelodysplastic syndrome (MDS)	Oncology	111	↑ 82
30	Cystic fibrosis (CF)	Pulmonology	42	↑ 12
31	Neuroendocrine tumors	Oncology	175	↑ 144
32	Bone repair	Musculoskeletal	61	↑ 29
33	Dermal ulcers	Dermatology	122	↑ 89
34	Osteoarthritis	Immunology	24	↓-10
35	Respiratory syncytial virus (RSV)	Infectious Disease	37	↑ 2
36	Epilepsy	Neurology	84	↑ 48
37	Lupus	Immunology	89	↑ 52
38	Uveitis	Ophthalmology	167	↑ 129
39	Respiratory infection	Pulmonology	48	↑ 9
40	Psoriatic arthritis	Immunology	255	↑ 215
41	Congestive heart failure (CHF)	Cardiovascular	80	↑ 39
42	Asthma	Inflammatory	14	↓-28
43	Alzheimer's disease (AD)	Neurology	2	↓-41
44	Glioma	Oncology	75	↑ 31
45	Cytomegalovirus (CMV)	Infectious Disease	126	↑ 81
46	Chronic kidney disease (CKD)	Nephrology	158	↑ 112
47	Neuropathy	Neurology	65	↑ 18
48	Thalassemia	Hematology	252	↑ 204
49	Age-related macular degeneration (AMD)	Ophthalmology	18	↓-31
50	Uterine cancer	Oncology	129	↑ 79

2019 Ranking	Indication	Therapeutic Area	2018 Ranking	Change
51	Graft-versus-host disease (GvHD)	Transplant	70	↑ 19
52	Skin cancer	Oncology	59	↑ 7
53	Sarcoma	Oncology	146	↑ 93
54	Urea cycle disorders (UCD)	Endocrinology	114	↑ 60
55	Small cell lung cancer	Oncology	41	↓-14
56	Severe combined immunodeficiency (SCID)	Endocrinology	334	↑ 278
57	Cervical cancer	Oncology	132	↑ 75
58	Biliary cancer	Oncology	123	↑ 65
59	Chronic lymphocytic leukemia (CLL)	Oncology	88	↑ 29
60	Pulmonary fibrosis	Pulmonology	99	↑ 39
61	Influenza virus	Infectious Disease	12	↓-49
62	Non-alcoholic steatohepatitis (NASH)	Hepatology	95	↑ 33
63	Dry eye	Ophthalmology	77	↑ 14
64	Coronary artery bypass graft (CABG) surgery	Cardiovascular	424	↑ 360
65	Hodgkin's disease	Oncology	220	↑ 155
66	Cough	Pulmonology	102	↑ 36
67	Staphylococcus	Infectious Disease	31	↓-36
68	Lung cancer, general	Oncology	71	↑ 3
69	Multiple sclerosis (MS)	Immunology	36	↓-33
70	Hepatitis B virus (HBV)	Hepatology	21	↓-49
71	Schizophrenia	Psychiatry	58	↓-13
72	Depression	Psychiatry	54	↓-18
73	Pemphigus vulgaris (PV)	Immunology	310	↑ 237
74	Vasculitis	Inflammatory	371	↑ 297
75	Duchenne muscular dystrophy	Musculoskeletal	94	↑ 19
76	Pulmonary hypertension	Pulmonology	57	↓-19
77	Bone marrow transplant (BMT)	Transplant	195	↑ 118
78	Hemophilia	Hematology	91	↑ 13
79	Incontinence	Urology and Women's Health	32	↓-47
80	Anemia	Hematology	28	↓-52
81	Overactive bladder	Urology and Women's Health	190	↑ 109
82	Inflammatory bowel disease (IBD)	Gastroenterology	139	↑ 57
83	Metachromatic leukodystrophy	Endocrinology	355	↑ 272
84	Wiskott-Aldrich syndrome	Hematology	431	↑ 347
85	Idiopathic thrombocytopenic purpura (ITP)	Immunology	417	↑ 332
86	Epidermolysis bullosa	Dermatology	43	↓-43
87	Migraine	Neurology	30	↓-57
88	Chronic granulomatous disease (CGD)	Inflammatory	416	↑ 328
89	Dementia	Neurology	176	↑ 87
90	Myelofibrosis	Hematology	207	↑ 117
91	Obesity	Endocrinology	15	↓-76
92	Glaucoma	Ophthalmology	56	↓-36
93	Chronic obstructive pulmonary disease (COPD)	Pulmonology	29	↓-64
94	Actinic keratosis	Dermatology	136	↑ 42
95	Anaphylaxis	Inflammatory	219	↑ 124
96	Ankylosing spondylitis	Immunology	382	↑ 286
97	Bone cancer	Oncology	193	↑ 96
98	Acromegaly	Endocrinology	199	↑ 101
99	Hidradenitis suppurativa	Dermatology	311	↑ 212
100	Emesis	Gastroenterology	83	↓-17

METHODOLOGY

The Kx Advisors methodology is designed to assess investment intensity of drug development for each indication through a comprehensive and balanced analysis of the key drivers and metrics.

Our Hot Indications analysis framework considers the volume of ongoing scientific investigation, as well as the types of companies and level of funding supporting these trials. Our analysis evaluated 36,785 drug programs ongoing in 2018, categorized them into 612 unique indications, and compared available data for these indications across three main criteria:

1. PIPELINE SCORE

The Pipeline Score measures the overall level of drug development activity for an indication. The score gives greater value to later-stage programs, higher volumes of programs overall, and indications with greater numbers of companies with programs.

2. R&D FUNDING

R&D Funding estimates the availability of financing to support the development of each drug program to its reasonable endpoint. For some programs, this endpoint will be FDA approval, while for others it will be discontinuation in preclinical or Phase I.

The score measures availability of funds and willingness to invest based on two main inputs for each indication. First, the R&D FundingScore quantifies the historical track record of sponsor companies, based on the number of drugs each company has successfully developed. Second, the score measures initial public offering and venture capital investment fundraising activity in

2018 for each indication, with the expectation that the financing from such events will be major contributors in supporting ongoing R&D programs.

3. ACADEMIC FOCUS

Academic Focus measures the overall publication activity for each indication, based on the absolute number and the one-year change in publications citing the indication for the evaluation period.

Hot Indications Ranking

For each of the 612 indications, the overall ranking score is calculated by a weighted average of Pipeline Score (50%), R&D Funding (40%) and Academic Focus (10%).

Therapeutic Areas

Each indication is categorized into one of 21 TAs, which include 20 major fields of medicine and an “Other” group. In general, indications are categorized based on the medical specialty most likely to treat patients with a disease or disorder.

Systemic diseases, such as autoimmune disorders, or TAs representing a variety of medical specialties, such as Musculoskeletal, are grouped on a case-by-case basis. For example, Crohn’s disease and ulcerative colitis are included in Gastroenterology rather than Immunology, whereas Multiple Sclerosis is included in Immunology due to the variety of symptoms it presents.

ABOUT KX ADVISORS

For more than 30 years, Kx Advisors (operating as Kaiser Associates' healthcare practice) has provided strategy consulting services to help healthcare executives achieve critical business growth goals. With a highly collaborative approach they have developed pragmatic solutions for leading pharmaceutical, biotechnology, medical device, health IT, and digital health clients, with data-driven insights to give those clients the tools to compete and win across the healthcare industry.

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