



2020 Global Drug Delivery & Formulation

R E P O R T

Part Four of a Four-Part Series

Part 1: A Review of 2020 Product Approvals

Part 2: Notable Drug Delivery and Formulation
Product Approvals of 2020

Part 3: Notable Drug Delivery & Formulation
Transactions and Technologies of 2020

Part 4: The Drug Delivery and Formulation Pipeline

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Introduction

The pharmaceutical pipeline in 2020 developed in two ways that would have been surprising the year before. The first of these was the introduction of thousands of products into development for the treatment of Infectious Disease to treat COVID-19. There are currently more than 2,500 identified products in development for COVID-19. This includes products newly designed and developed for either prevention or treatment, products found in the pipeline cupboard and dusted off in hopes of success, and products approved for a variety of non-COVID-19 indications that offer important adjunctive benefits. One of the most critical adjunctive products, one that surprisingly requires FDA approval, is Oxygen. Its shortage in many parts of the world is leading to many avoidable deaths. A summary of the current COVID-19 pipeline is presented later in this report.

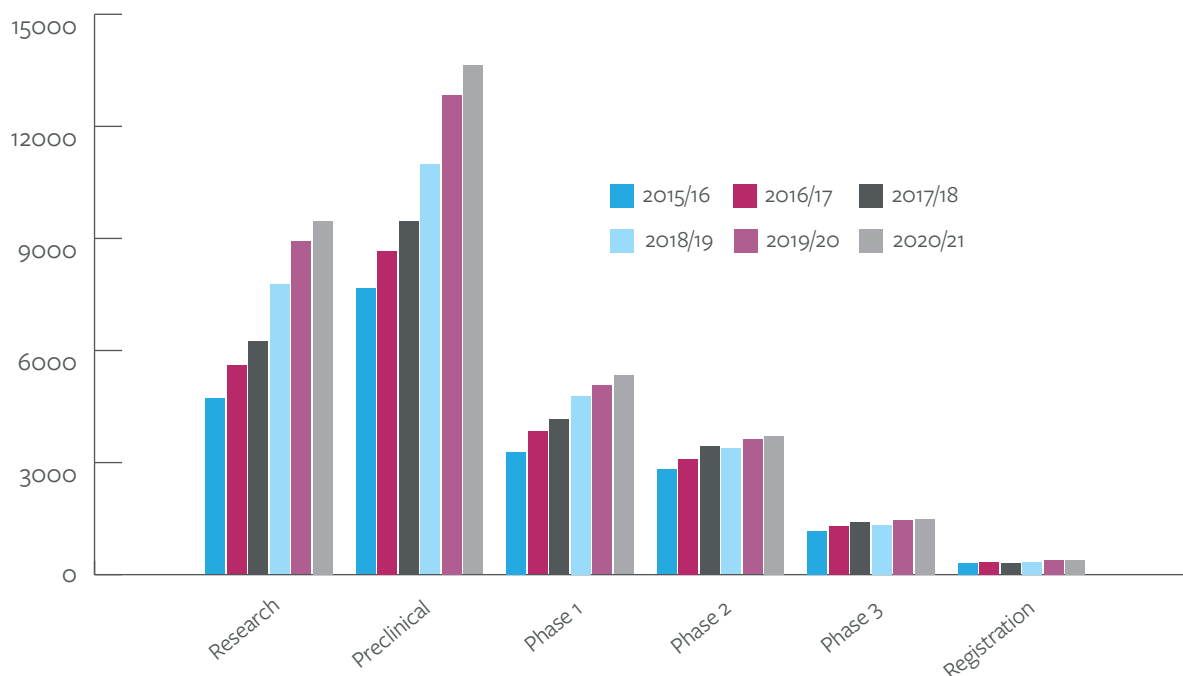
A second surprise is the large number of Cell Therapy products that have entered Phase 1 development. There are more than 2,000 cell therapies approved or at some stage of development, including more than 550 in Phase 1 development and some 1,275 products at a Research or Preclinical stage of development. A significant number of the Phase 1 products are being developed by companies based in China.

Beyond these two outliers, the development pipeline continued to show strong growth as more and more investment money rushes in to capture the financial potential of the new ideas bubbling up from emerging companies hoping to treat disease with new molecular and therapeutic strategies.

Once again, this year's Drug Delivery and Formulation Pipeline analysis leans on PharmaCircle's Pipeline Dynamics companion module to the Pipeline & Products Intelligence module and covers 6 years of the pharmaceutical pipeline history. By capturing detailed records annually of what products were at what stage of development from 2014/15 through to 2020/21, it is now possible to visualize the dynamic history of pharmaceutical product development. The following pages include pipeline snapshots and comparisons for a number of parameters that are of most interest to drug delivery and formulation professionals – Disease Area, Molecule Type, and Delivery Route.

The Research and Preclinical Pipeline Continues to Outpace Clinical Stage Products in Terms of Growth

Pharma Pipeline Product Development, 2015/16 to 2020/21 (Most Advanced Phase)



Source: PharmaCircle Pipeline & Products Intelligence Module (Pipeline Dynamics). The 2020/21 pipeline data covers the 12 months ending March 2021.

The constant influx of funding for new companies has fueled a boom in new product development from Research and Preclinical through to all stages of Clinical development. The impact of early stage investments over the past few years is seen in the number of early stage clinical products. This has not yet led to a significant increase in later-stage clinical products. This may be a result of less selective criteria for products to enter early stage clinical development or possibly the simple economics of late-stage development that limit development to only the very best candidates. The relative ratio of Research and Preclinical products to Clinical Stage products in 2020/21 is 2 to 1, compared with a 1.6 to 1 ratio in 2015/16.

A Surprise in 2020/21 was the Sharp Increase in Clinical Stage Cell Therapy Products

Molecule Type as a Share of All Clinical Stage Products, 2020/21

	Phase 1	Phase 2	Phase 3	Registration	Share of All Clinical Products (2020/21)	Share of All Clinical Products (2015/16)
Small Molecule	51%	61%	66%	73%	57%	62%
Antibody	12%	10%	11%	10%	11%	9%
Protein	6%	8%	7%	7%	7%	10%
Peptide	5%	6%	5%	4%	5%	7%
Cell & Gene Therapy	17%	7%	4%	2%	11%	8%
Oligonucleotide & RNA	2%	1%	1%	0%	2%	2%
Stem Cell	4%	2%	2%	1%	3%	0%
Carbohydrate	1%	1%	2%	1%	1%	1%
All Other	1%	2%	3%	3%	3%	0%

Source: PharmaCircle Pipeline & Products Intelligence Module (Pipeline Dynamics). The 2020/21 pipeline data covers the 12 months ending March 2021.

The increasing lean toward Biologics seen over the past few years continued in 2020/21. For the 12 months ending April 2021, the share of clinical-stage products accounted for by Small Molecules dropped to 57% as compared with 62% in 2014/15. This represented a relatively large drop when compared with the year earlier when Small Molecule products held a 60% share.

A very notable shift was seen in the number of Cell Therapy products identified as in Phase 1, a total of 543 products. Combined with Gene Therapy products, the two accounted for 17% of the Phase 1 product pipeline, significantly exceeding the Antibody product share of 12%. The Gene and Cell Therapy share drops in Phases 2 and 3. It remains to be seen if this large Phase 1 cohort will translate into more later-stage products in the years to come.

Stem Cell products also seem to be in favor as evidenced by a reasonably large bump in Phase 1 products in development. This contrasts with no negligible share for Stem Cell products in 2015/16.

The share of Antibody products in clinical development are up by a third over 2015/16. Clinical-stage Peptide and Protein products are down sharply in terms of share.

RNA and Oligonucleotide products still represent a very small share of the clinical development pipeline, with perhaps some evidence of future increases based on the growth of the Phase 1 product pipeline.

Infectious Disease Products, Unexpectedly Showed the Greatest Increase in Clinical Stage Products

Active Clinical Stage Programs by Disease Area, 2014/15 to 2020/21

	2014/15	2020/21	Change
Cancer	1,642	3,140	91%
Infectious Disease	886	2,073	134%
CNS	686	1,024	49%
Endocrine/Metabolism	519	629	21%
Inflammation/Immune	461	611	33%
Skin Disorders	295	437	48%
Cardiovascular Diseases	306	375	23%
Pain Management	263	317	21%
Respiratory	257	280	9%
Eye Diseases	164	332	102%
All Other	1,103	1,027	-7%
Total	6,582	10,915	66%

Source: PharmaCircle Pipeline & Products Intelligence Module (Pipeline Dynamics). The 2020/21 pipeline data covers the 12 months ending March 2021. (The figures here represent programs rather than products.)

The sharp rise in the Infectious Disease pipeline was unexpected but is not surprising given the attention paid to therapeutics and vaccines for the treatment of COVID-19. Every company it seems dug into their product cupboard to see what might be useful for the treatment of COVID-19. The urgency to develop life-saving therapeutics allowed many companies to enter the clinic with more hope than supporting data. Both prophylactic and therapeutic approaches received considerable attention and investment.

Cancer and Eye Disease programs continued to be a major area of clinical trial activity and investment. The Cancer pipeline increase was largely a result of new molecular strategies being identified and the development of novel molecular motifs to take advantage of these insights.

The increase in the Eye Disease pipeline is a result of increasing needs with an aging population and a relatively attractive reimbursement environment. This is a market that has largely focused on small molecule therapeutics but has now come to embrace the potential of biologics. Non-small products now constitute almost 50% of the Eye Disease clinical pipeline.

Injectables Continue to Take Share from All Other Delivery Routes

Delivery Route Products as a Share of All Clinical Stage Products, 2020/21

	2014/15	2020/21
Injection	46%	51%
Oral	40%	38%
Topical	5%	4%
Ophthalmic	2%	2%
Inhalation	3%	2%
Nasal	2%	2%
Transdermal	2%	1%

Source: PharmaCircle Pipeline & Products Intelligence Module (Pipeline Dynamics). The 2020/21 pipeline data covers the 12 months ending April 2021. (Early-stage clinical programs, notably Phase 1, products often do not provide information regarding Delivery Route. These products are not included in the analysis.)

The continuing adoption of Injection-based products reflects the previously noted shift of the pharmaceutical product development pipeline to Cancer and Infectious Disease products that require more precise dosing and are generally administered in the in-patient setting. The development of patient-friendly injection devices has further extended the use of injectables to more chronic out-patient indications, such as rheumatoid arthritis and multiple sclerosis.

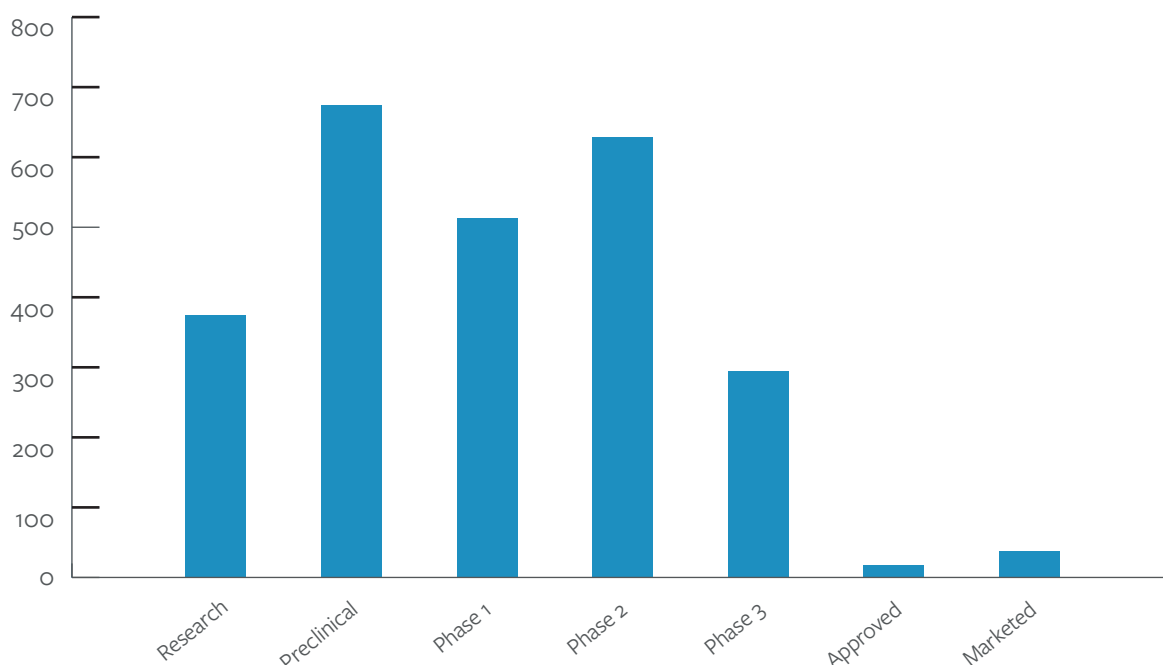
Inhalation has become a less popular route for new product delivery as the number of respiratory product opportunities has decreased. This is partly a result of newer products targeting more severe respiratory conditions with Biologics. The historically important Respiratory indications of Asthma and Chronic Obstructive Pulmonary Disease are now largely managed with inhaled generic products, creating a huge challenge in terms of cost effectiveness for any new inhaled products hoping to address these conditions.

Nasal and Transdermal delivered products face a similar challenge. Generics have captured the previously important therapeutic opportunities suitable for Nasal and Transdermal delivery, and the newer Biologics are not suited for delivery by either route. Historically, these routes have been an important option for the more convenient dosing of small molecules not suitable for Oral dosing.

Oral delivery remains the patient preferred route of delivery. The increasing number of biologics, generally not suitable for oral delivery, is contributing to the decreasing share of oral products in the development pipeline. This trend is likely to continue until some sort of oral enabling or enhancing technology making some of the smaller Biologics reasonable candidates for oral delivery.

COVID-19 Vaccines and Therapeutics - A Robust Clinical Pipeline

COVID-19 Products in Development by Most Advanced Phase



Source: PharmaCircle Pipeline & Products Intelligence Module as of mid-April 2021.

COVID-19 Products in Development by Delivery Route

	Research	Preclinical	Phase 1	Phase 2	Phase 3	Approved	Marketed
Oral	30	83	132	275	153	1	18
Nasal	10	53	26	17	4	1	1
Injection	177	346	277	271	112	16	17
Inhalation	12	40	34	40	13	0	0
Buccal or	0	9	5	4	1	0	1
All Other	5	10	6	1	0	0	1

Source: PharmaCircle Pipeline & Products Intelligence Module as of mid-April 2021. Note: Research and Preclinical stage products may not have disclosed delivery routes.

The COVID-19 development pipeline includes a variety of novel vaccines and therapeutics as well as a number of previously approved products that are being applied to provide supportive treatment. A good example are steroids like dexamethasone that are used with seriously ill COVID-19 patients to manage overactive immune responses.

Unsurprisingly, Injection medications are the most common given that treatment is usually administered in a critical care setting. Both Nasal and Inhalation delivery are being explored as more convenient and efficacious routes to address COVID-19 symptoms at earlier prehospitalization stages of infection.

An overview of the COVID-19 pipeline is available at www.PharmaCircle.com. This includes a detailed summary of therapeutics and vaccines in development as well as ongoing clinical trials along with the latest epidemiology statistics.

Final Thoughts

Beyond the surprises noted earlier with respect to COVID-19 and Cell Therapy products, the pipeline in 2020 developed much as it had for the past decade. Increased investments in emerging companies and novel therapeutic concepts have created a larger research and preclinical pipeline with some spillover seen in the larger Phase 1 product cohort. These investments have not yet impacted the Phase 3 pipeline. All of this is reasonable as approvals and pipelines reflect events and efforts of the past. In this sense, the 2020 pipeline is the result of work and investments in 2019 and before. With the restrictions and refocusing demanded by COVID-19, it is not clear what the future pipeline will look like. Will 2020 be a “dip” a “recession” or a “depression” to use economic terms? Did 2020 provide companies the opportunity to rethink their strategies going forward and reconfigure operations to also meet non-pandemic challenges? Next year’s pipeline analysis will provide a sense of how COVID-19 has impacted drug development, but it will still take 3 years or more to properly understand the full impact.

Some additional trends not properly captured in the charts and tables presented in these four articles include:

1. A continued shift to Injectables as a consequence of the focus on Biologics.
2. An expansion of the investment in next-generation Biologics, particularly variations on nucleic acid chemistry and function.
3. CDMO/CMO/CRO further validated their importance to the development of innovator products. Companies small and large are not just contracting out work, they are contracting out responsibility and decision-making to these expert suppliers.
4. Diagnostics are less and less an afterthought or nice to have. Diagnostics are critical to identifying responding patient subpopulations during clinical trials and supporting the mega dollar prices for orphan drug products. As we saw in 2020, the rapid development and deployment of COVID-19 diagnostics was a critical part of the strategy for fighting the pandemic.
5. There is considerable interest and investment in Artificial Intelligence and Machine Learning. The fruits of this investment are yet to be realized. As with many technologies, it can take a decade or more for the benefits of technology to be seen.

An early indicator of the impact of COVID-19 on the pharmaceutical product pipeline will be FDA approvals for 2021. A quick look at FDA approval numbers for “innovative” products (Type1, Type 1,4 and Type 4) at the FDA through mid-May 2021 finds 19 approvals. This compares with 22 approvals the year earlier. These numbers are the tip of the iceberg and too close to draw any conclusions in terms of where the pharmaceutical pipeline might be headed as a result of COVID-19.

We will be back next year with 2021 approval and pipeline information that may help us understand if we experienced a COVID-19 dip, recession, depression, or just business as usual.

About the Authors

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Kurt Sedo earned his BS in Chemistry and Mathematics from the University of Wisconsin Stevens Point. Prior to joining PharmaCircle in 2003, he held various R&D Scientist positions within Searle/Pharmacia’s Pharmaceutical Sciences Department in Analytical Development and Drug Delivery. Mr. Sedo’s responsibilities with PharmaCircle include oversight of data integrity, product development, project management and customer service. In addition to authoring articles, Mr. Sedo regularly presents overviews of the state of drug delivery and formulation at industry conferences.

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