In just a few years, rare diseases have moved from neglected "orphan" status into the mainstream of drug development, with a growing number of pharmaceutical companies acquiring and investing in life-saving treatments that benefit targeted groups of patients.

Now they are converging with the broader trend of "personalised medicine" that is transforming research, outcomes and the economics of the industry more widely: "We're moving from blockbusters to niche-busters," says Hilary Thomas, chief medical adviser at KPMG.

Many thousands of orphan conditions affecting small numbers of patients with unusual conditions remain poorly researched with few medical options for treatment and poor prognoses.

However, a growing number — from Gaucher’s disease, which can cause an enlarged spleen and liver as well as skeletal disorders, to cystic fibrosis, which affects mainly the lungs — have potent treatments that were inconceivable until recently.

That is reflected in growing corporate investment. In January, Sanofi paid nearly $12bn for Bioverativ, a US company focused on haemophilia and other rare blood conditions. Shire, which acquired Baxalta for $32bn in 2016 to strengthen its rare disease portfolio, has been subject to fresh speculation that it will itself be bought after a previous thwarted takeover bid by AbbVie.

EvaluatePharma, a research group, estimates total orphan drug sales will rise from $127bn for 2017 to $217bn in 2022, while their share of the revenue from all prescription medicines will increase from 16 per cent to 21 per cent.

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Value of niche drugs market is expected to balloon

Continued from page 1

Targeted response such as enzyme replacement. "You often have a monogenic [controlled by one gene] disease with one cause, compared with other medical conditions such as hypertension which are multi-causal," says Andreas Busch, chief scientific officer at Shire.

One of the most striking evolutions in the field has been in oncology, the study and treatment of cancer and tumours, where previously broad-brush treatments are being replaced with therapies for smaller patient populations. For these patients, the therapy is targeted and suitable for so few that the treatments are also classified as orphans.

EvaluatePharma’s largest sales forecasts are for cancer treatments: it estimates that in 2017 orphan drugs will have generated $12.4bn in annual sales for Novartis, the Swiss pharmaceutical group, and $10.7bn for Celsgene in the US. Its Revlimid (the top-selling rare disease drug) for multiple myeloma, a cancer of the blood, alone accounted for $8bn.

"In breast and lung cancer, there is a lot of work to identify the specificities of populations where certain drugs may work in the best possible way," says Samit Hirawat, head of oncology global development at Novartis. "Large diseases are converting to smaller, rare diseases" that are being replaced with therapies for smaller populations of patients. "How can you maintain the impetus towards innovation if diseases are too small for industry to see a return on investment or only at a price healthcare systems cannot afford to pay?" he asks.

Last year, GSK’s Strimvelis gene therapy for adenosine deaminase deficiency or "bubble baby" syndrome, won draft approval by the UK’s National Institute for Health and Care Excellence (Nice), the NHS’ drugs advisory body — at £700,000 per treatment. Yet in February, Nice decided not to recommend BioMarin’s Brineura for Batten disease, another very rare genetic disease that affects the nervous system. It concluded that at £500,000 per treatment, the drug did not offer sufficient proven value.

"Quick and dirty development is not possible any more," says Jan-Anders Karlsson, chief executive of Verona Pharma, which works on respiratory diseases including cystic fibrosis. "It’s going to be less and less attractive unless you truly have a cure or a very targeted molecular mechanism."

Mr Kent cautions: "We have to find a way of creating an environment that is sustainable, with a reasonable prospect of patients getting treated, the industry rewarded and with treatments that are affordable in the long term for the health system, or it will crash and burn."

"It was really a cottage industry, but now it’s an absolute boom area. It’s a remarkable time for medicine," he likens gene therapy to receiving a transplant rather than conventional drug treatments, which typically “don’t cure you but just keep disease at bay.”

These advances are challenging some longer-established rare disease treatments. In cystic fibrosis, for instance, Vertex’s ivacaftor works on an estimated 8 per cent of patients with specific gene mutations.

Yet this trend of personalisation creates multiple difficulties. The first is the risk of undermining some of the exceptional power of small but united patient groups for rare diseases, which have been a force for lobbying and recruitment for clinical trials to ease new drug development.

“We are seeing that the fragmentation of common diseases is replicated for rare diseases,” says Alastair Kent, ambassador for Genetic Alliance UK, the patient advocacy group. “That risks putting patients into different camps and fragmenting the solidarity that has been a characteristic of patient support organisations.”

There is a trade-off to make between creating economic incentives to tackle rare diseases and the spiralling cost of treating growing numbers of ever-smaller populations of patients. “How can you maintain the impetus towards innovation if diseases are too small for industry to see a return on investment or only at a price healthcare systems cannot afford to pay?” he asks.

In more personalised cancer treatment, there are challenges of toxicity, complexity and the need for precise diagnostics. That has sparked a shift towards immunotherapy, such as around individualised CAR T-cell therapy which collects and uses patients’ own immune cells to treat their cancer.

There is a broader interest in individualised gene therapies that extract, modify and return genes to the body of each patient.

“This is a completely new arm of medicine and we believe it’s going to be the next big thing,” says Keith Thompson, chief executive of the UK’s Cell and Gene Therapy Catapult, which supports research and manufacture in the field. “It was really a cottage industry, but now it’s an absolute boom area. It’s a remarkable time for medicine.”

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Discovery will aid fight against the horrifying birth defect caused by Zika

Breakthrough: a team led by Brazilian scientist Mayana Zatz has found that only babies with a genetic predisposition are born with microcephaly after infection with the Zika virus. Page 3 — Hseae Media/Dado Galdieri for Financial Times

Drugs: the industry has changed

Targeted: smaller can be better