Addiction treatment specialist **Indivior's (INDV)** shares marched almost 20% higher to 359.6p on 17 August 2016 thanks to news about a phase III clinical trial.

The late stage tests appear to prove the £2.3 billion cap's opioid addiction treatment works, moving it closer to market approval and $500 million of potential sales by 2020, according to stockbroker Numis.

The market's very positive reaction to the news highlights how clinical trial results can impact sentiment for a pharmaceutical or biotech's investment case.

Assessing the probability of a clinical-phase drug company getting a treatment to market is crucial to backing the next healthcare hero. Getting it wrong could mean waving goodbye to your cash.

Circassia (CIR) is an example of what can happen when management tells investors their money has been wasted. In June, phase III clinical trials proved that its severe cat allergy candidate did not work. Investors raced to dump the stock, wiping 62% off the biotech's market value.

SUCCESS RATE

Picking a winner among clinical-phase drugmakers is not easy. Less than one in 10 treatments entering the three-stage clinical trial process secures sales approval in the lucrative US market, according to trade body the Biotechnology Innovation Organisation (BIO).

Circassia's situation highlights how companies must clear all three clinical trial hurdles in order to achieve success. The cat allergy candidate had passed two earlier clinical trials before falling in the third round.

Clinical trials are designed to show how a new drug performs versus an existing similar treatment. They also seek to prove that a drug is safe, identify any side effects and establish the correct dosage.

The process can take years and millions of pounds of investors' cash before a dossier is handed to a regulator. It can then take up to two years for a decision to be made on whether or not the medicine can be prescribed by a doctor. As such, investors in biotech and pharmaceutical stocks need to be very patient.

EQUITY SELECTIONS

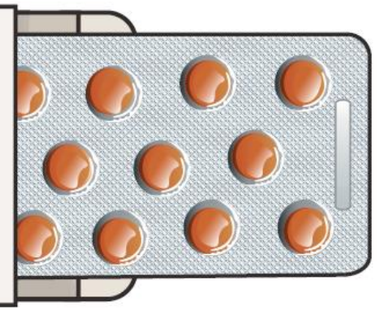
The healthcare market has a lot of smaller players, many of which trade on AIM and are yet to generate their first £1 of revenue.

A company the size of FTSE 100 member **AstraZeneca (AZN)** may only experience a mere ripple in its share price if one of its drug candidates is spat out by the clinical trials process. Such a result, however, would be a nightmare for a smaller company reliant on a single product, potentially putting it out of business.

Phytopharm will be forever associated with such a scenario. The failure of a Parkinson's treatment in 2013 saw management use its remaining £5 million cash to reinvent the business. The company took a 45% stake in brain health specialist **IXICO (IXI:AIM)** and adopted the investee company's name.

Factoring in the probability of a certain treatment reaching the market into your investment research may not guarantee success. But it could help you avoid taking unnecessary risks.

CLINICAL TRIALS:
An overview*



GETTING A DRUG TO MARKET – STEP BY STEP

- Pre-clinical (animal) testing
- Submit an Investigational New Drug (IND) application to FDA
- Clinical trial phase I
- Clinical trial phase II
- Clinical trial phase III
- A new drug application (NDA) is submitted to the FDA
- If the NDA is accepted, the drug candidate is evaluated for safety and efficacy
- A decision is made on whether the drug can be sold to the general public or not

Source: FDA

PHASE I

AIM: Test for safety and assess dosage

SAMPLE: Between 20 to 100 healthy volunteers or people suffering from the disease/ condition

LENGTH OF STUDY: Several months

Percentage of drugs that move to the next phase:

70%

Source: FDA

PHASE II

AIM: Test for efficacy and to assess any side effects

SAMPLE: Several hundred sufferers of the condition/ disease

LENGTH OF STUDY: Several months to two years

Percentage of drugs that move to the next phase:

33%

Source: FDA

PHASE III

AIM: Testing for efficacy and monitoring of adverse reactions

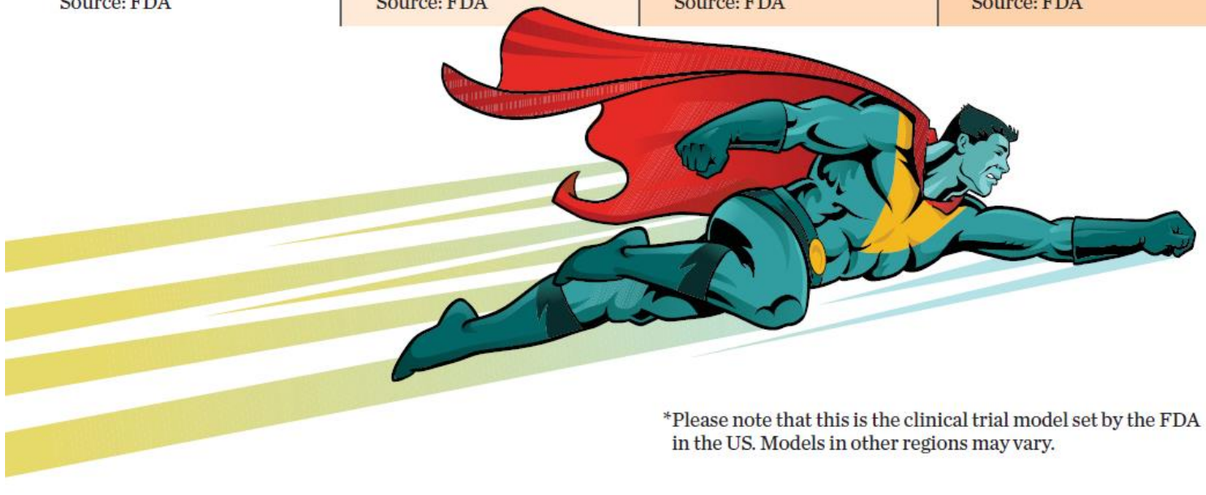
SAMPLE: 300 to 3,000 sufferers of the condition/ disease

LENGTH OF STUDY: One to four years

Percentage of drugs that move to the next phase:

25% TO 30%

Source: FDA



*Please note that this is the clinical trial model set by the FDA in the US. Models in other regions may vary.

THE ODDS OF a new drug being administered in hospitals are heavily stacked against investors. Nine out of every 10 drug candidates given to volunteers on the first day of phase I clinical trials do not reach the point where a regulator says 'you can sell it'.

One tactic that investors employ could be to back companies with drugs in later stage trials. The logic could be that if a drug has progressed through one or two phases then the chances of success have increased. Research says otherwise.

A report compiled by a trio of organisations, including trade body BIO, shows that the first phase has a higher success rate than the two stages that follow.

The likelihood of a treatment moving to phase II trials from phase I is 63.2%, according to *Clinical Development Success Rates 2006-2015*. Of those making it through, only 30.7% will probably move onto the third and final phase, based on a sample of 7,455 treatments that entered US trials over a 10-year period.

The chances of a treatment in phase III being handed to the regulator so that the final decision can be made improves to 58.1%.

Do not fall into the trap of believing that a drug has an increased chance of success because it has shown signs of efficacy and safety. Those doubting the research should remember Circassia's sorrows which we discussed earlier in this article. The phase III failure made the headlines of newspapers across the country; such was the scale of investor disappointment.

The stage where there is the highest probability of success is when a dossier of the trial's results has been handed to the regulator for assessment. Only 15% of candidates reaching this stage fail.

BIO's figures are different from those on US regulator the Food & Drug Administration's (FDA) website.

The first two phases are similar at 70% and 33% compared to 63.2% and 30.7%, respectively. But the FDA believes there is only a 25% to 30% chance of a candidate progressing beyond phase III, compared to 58.1% in BIO's research.

THREE TESTS

The varying probabilities of success for each stage of the process are down to each phase having a different goal. The number of people taking part is also a factor, so too is safety.

One reason why share prices are sensitive to phase I clinical trial data is that this is the first time a drug candidate would have been tested on people.

In the lab the drugs will be tested on animals to assess toxicity. This is not adequate to prove the treatment is safe for people.

The first task when entering clinical trials is to test that it is safe, not that it works. This involves anything up to 100 people who do not suffer from the ailment that the drug has been designed to treat. This stage is designed to ensure the drug is safe, identify any side effects and to set the dosage.

One reason why the progression rate is so high is that BIO's study points to some larger companies not reporting failed Phase I trials to the public as they do not consider them 'material'.

Phase II is where, for the first time, the company looks for signs that the treatment works. Hundreds of people suffering from the condition/ disease are tested over months or even several years.

NEW REVOLUTION

Drugs affect people in different ways – which has given birth to the personalised medicines revolution. With this in mind, the drug company continues to monitor any side effects that the volunteers might suffer during phase II.

This is also the stage where the company funding the drug candidate has to decide if it is worth spending years and millions of dollars of shareholders' cash to move the treatment into phase III trials.

Any concerns that a drug candidate might not produce good enough results to win sales approval could prompt management to cut their losses or take it back to the lab in an attempt to improve the formula.

The third and final stage is where the treatment is tested on thousands of sufferers to ensure the drug has a positive effect on a large number of people.

The treatment is tested against the market leader or a placebo and has to show a clear improvement over either one. This is where Circassia failed. The placebo effect was measured at 60%.

A decision on whether a treatment is approved for sale can take between 1.1 years from filing for oncology to two years for neurology. The average time for the regulator to make a decision is 1.6 years, according to BIO.

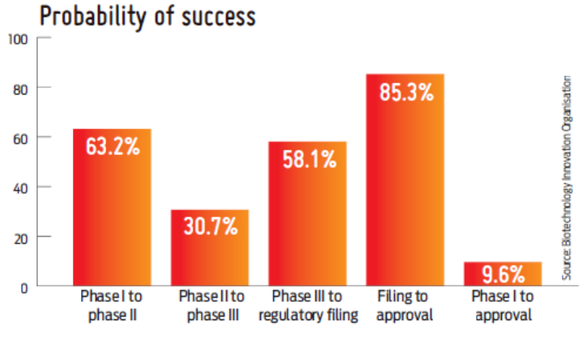
There is a phase IV, where regulators continue to monitor the treatment once it is being used in hospitals or sold in chemists. They want to make sure there have been no mistakes.

THE TREND IS YOUR FRIEND

Drugs seeking to treat certain ailments will have varying chances of successfully passing trials and reaching the market.

Candidates focused on hematology, conditions and diseases of the blood, were the most likely to achieve sales clearance after entering clinical trials with a 26.1% success rate, according to BIO data. Infectious diseases are close behind on 19.1%.

Oncology is at the foot of the table with only 5.1% of candidates entering clinical



trials gaining marketing approval, according to the study by BIO.

Oncology is the term often used to describe cancer treatments. It is one of the largest markets in healthcare and led the way in terms of volume with 1,222 candidates examined as part of BIO's study. This compares to the 462 candidates in neurology, the second largest group.

The failure rate among cancer drugs brings down the overall clinical trial success rate. Cancer is the market with potentially the biggest rewards, but also carries the highest risk.

Any drug reaching phase III has more than a 50% chance of being filed with the regulator, according to BIO. The only exception is oncology, which only has a 40% probability of being put in the decision-maker's hands.

RARE DISEASES

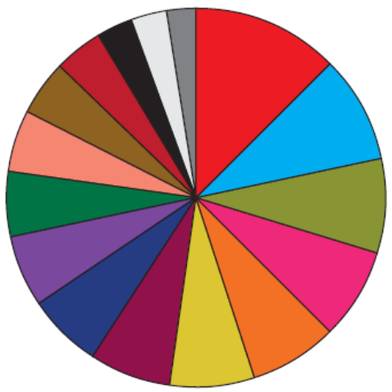
There is one area of the healthcare market where the success rate is almost three times higher than the 9.6% for the whole market. Rare diseases, which have only a few hundred thousand sufferers, have a 25.3% chance of gaining sales approval, claims BIO. Chronic conditions trail behind with an 8.7% probability of success.

Rare disease treatments lead the way in all stages of the clinical testing programme, including a 50% success rate in phase II compared to 30% for all diseases.

The research puts this down to more money backing niche treatments in recent years, tempted by lower development costs, higher prices and longer exclusivity periods. It points to around 7,000 rare diseases, many of which have no cure or treatment.

Chronic illnesses, which include lifestyle conditions such as diabetes, have seen lower funding and the researchers question if this is because there are 'higher hurdles' to gaining approval for preventable conditions.

Likelihood of approval from Phase I



Hematology	26.1%	Respiratory	12.8%
Infectious disease	19.1%	Urology	11.4%
Ophthalmology	17.1%	Autoimmune	11.1%
Other	16.3%	All indications	9.6%
Metabolic	15.3%	Neurology	8.4%
Gastroenterology	15.1%	Cardiovascular	6.6%
Allergy	14.7%	Psychiatry	6.2%
Endocrine	13.2%	Oncology	5.1%

Source: Biotechnology Innovation Organisation

IMMUPHARMA (IMM:AIM) 39P

DRUG DEVELOPER **ImmuPharma (IMM:AIM)** is likely to feature in investors' research into a type of treatment with a higher probability of passing successfully through the clinical trial process.

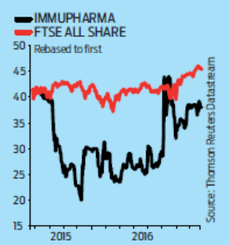
Its lead drug is a treatment for Lupus, an auto-immune disease, and is currently in phase III clinical trials. Results are expected at the end of 2017.

Lupuzor intends to relieve sufferers of Lupus' symptoms, which include fatigue and rashes. It could be launched in 2019 if trials go to plan. Analysts believe it has the potential to generate multi-billion dollar sales every year.

Lupus is a rare condition, and treatments have a 25.3% probability of reaching the market and a 73% chance of being filed with the regulator, based on BIO's study data.

ImmuPharma's drug candidate has been awarded fast-track status from the FDA. A decision to clear the treatment for sale could take around six months.

The only relevant product on the market is **GlaxoSmithKline's (GSK)** Benlysta. There are question marks over the level of efficacy and its side effects.



MEREO BIOPHARMA (MPH:AIM) 312.5P

CLINICAL-PHASE BIOTECH **Mereo BioPharma (MPH:AIM)** has three treatments in clinical trials, all of which were invented by Swiss drug giant **Novartis (NOVN:VTX)**.

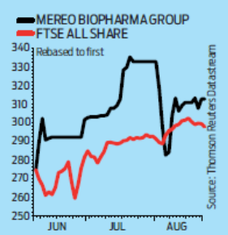
Mereo, backed by high profile fund manager Neil Woodford, has a smokers' cough treatment undergoing phase II tests. Results are expected towards the end of 2017.

Such types of treatment have a 12.8% chance of reaching the market, according to BIO, falling into the respiratory category. They have a 29% chance of progressing to phase III.

Having a higher chance of success is the brittle bone disease treatment, which is scheduled to start the third stage of tests in the second half of 2016, if it hasn't already. The drug candidate has fast-track status with brittle bone disease classed as a rare condition. Expect the first results in 2018.

This type of treatment, according to BIO's research, has a 25.3% probability of reaching the market, while there is a 13% probability it will not reach the regulator.

Mereo also has a drug that restores normal testosterone levels in overweight men, which is in phase II trials.



DIURNAL (DNL:AIM) 143.5P

HORMONE DISEASE-FOCUSED drug developer **Diurnal (DNL:AIM)** recently posted positive results from phase III tests on its Infacort candidate. The treatment proved successful in increasing cortisol levels in those suffering from a deficiency.

If this leads to a market launch within the next two years it would be the first adrenal insufficiency treatment for children under six years old in Europe. The condition causes weight loss, muscle weakness, fatigue and low blood pressure due to the adrenal glands not producing enough of the hormone cortisol.

Diurnal's second treatment is Chronocort, which targets congenital adrenal hyperplasia (CAT). The condition affects one in every 15,000 adults causing infertility and development defects such as stunted height and genital deformities. Its treatment is also in phase III trials in Europe and phase II in the US. If approved, it would be the first such treatment for adults in Europe.

Subject to approval, these treatments – which have orphan drug status from the FDA – will be launched into markets worth more than $11 billion a year, believes Diurnal.

Infacort could potentially be on the market by 2018 with Chronocort following in 2019.