

# **A new generation** of allergy treatments

**Annual report and accounts 2014**

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## **Circassia in brief**

Circassia is a specialty biopharmaceutical company focused on the development and commercialisation of a range of allergy immunotherapy product candidates. Established in 2006, the Company has used its proprietary ToleroMune® technology to develop a new class of therapies, Synthetic Peptide Immuno-Regulatory Epitopes (SPIREs), which have the potential to revolutionise allergy treatment.

The Company's portfolio of SPIREs is designed to treat a broad range of seasonal and perennial allergies. The most advanced, Cat-SPIRE, targets cat allergy and is currently in phase III development. Three other product candidates, targeting house dust mite, ragweed and grass allergies, have completed clinical proof-of-concept phase IIb studies.

## Allergies are a serious global health issue...

Allergic rhinitis is the world's most prevalent chronic non-communicable disease.

Allergic diseases affect around 1 billion people and can devastate sleep, work and social life. Today, allergy is greatly underserved by the pharmaceutical industry.

**1bn**

People are affected by allergic diseases around the world

See page 04

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## ...current treatments are significantly inadequate...

Our SPIRE treatments target the cause of the underlying disease, not just the symptoms.

SPIREs show long-lasting efficacy after a simple short course, have their strongest effect in those who suffer the worst symptoms, and have a superior overall safety and tolerability profile.

**Our SPIREs have a favourable safety profile and long-lasting efficacy**

See page 06

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## ...our therapies could transform the market.

Current immunotherapy treatments can take several years. Our SPIREs offer the potential of a short course of treatment, patient-friendly administration and long-lasting efficacy. As a result, market research shows our SPIREs have a major commercial opportunity.

**\$2.6bn**

**Our four lead SPIREs have a \$2.6 billion peak sales opportunity in the US alone**

See page 08

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# Chairman's statement

**The last year has been a period of great transformation for Circassia. We successfully listed on the London Stock Exchange, raising over £200 million and completing the UK's largest ever biotech Initial Public Offering (IPO) fundraising. During 2014, we have been putting this investment to work, undertaking studies in all our late-stage clinical programmes and building the team to support our anticipated first product launch. As a result, we are increasingly well positioned to capitalise on the significant potential value offered by our innovative allergy treatments.**

## **IPO strategy**

Our IPO in early 2014 represents a step-change in our ambitions to bring our products to market, and follows several years of strong progress as a private company. Since Circassia was established in 2006, we successfully completed a number of clinical studies and advanced our lead allergy treatment into phase III development, supported by £105 million of pre-IPO investment from highly supportive technology commercialisation and institutional investors.

In late 2013, with our phase III programme ongoing, we received encouraging clinical results that presented the opportunity to accelerate our strategy and seek the significant funding needed to develop our late-stage clinical products in parallel, and also make the preparations to independently commercialise our first product in the US and key EU markets. This strategy was strongly supported by investors, and Circassia came to the public market in March 2014.

## **2014: a year of progress**

During the last year, we have continued to build the foundations required to bring our novel allergy treatments to the marketplace, and have made good progress towards our objective of creating a successful, self-sustaining specialty biopharmaceutical company. We completed a number of encouraging long-term follow-up studies, maintained the progress of our phase III study and gained important insights from our ragweed allergy programme that are informing our next steps. In addition, we have begun the commercial infrastructure build to support a successful product launch.

## **Maintaining momentum**

In the coming year, we plan to maintain the momentum established in 2014, both clinically and commercially. We anticipate advancing our grass allergy treatment towards phase III development and completing recruitment into our phase IIb field study in house dust mite allergy. We also plan to advance our commercial strategy, building our capabilities in key markets and exploring potential acquisitions that could accelerate our commercial ambitions. Overall, we are ensuring preparations are in place for 2016, when we anticipate results from the pivotal phase III study of our cat allergy treatment.

## **Encouraging outlook**

Looking to the longer term, the outlook is highly encouraging, with the marketplace undergoing positive developments after a long period of inactivity. Indeed, for much of the pharmaceutical industry, the allergy field had been of little strategic interest for many years. Whole allergen immunotherapy, which remains the mainstay of disease-modifying treatment, was first used over 100 years ago, and with no major breakthroughs in the intervening decades, the allergy field was poorly served.

However, this situation is changing rapidly. During 2014, the Food and Drug Administration (FDA) approved three new sublingual whole allergen immunotherapies for grass and ragweed allergies, opening the market to new treatment approaches. With these products now promoted by significant industry players, the allergy market appears set to gather significant momentum. We believe this creates a major opportunity for Circassia, as our treatments have a number of significant potential benefits over existing products, including those launched recently. In the coming years, we intend to capitalise on these positive developments by bringing our own treatments to market and transforming Circassia into a successful specialty biopharmaceutical commercial business.

**Dr Francesco Granata**  
Chairman

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# 5 x phase II

Studies completed across our development programmes in 2014

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# US operations

US subsidiary established and commercial team recruitment underway

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# £202m

Successful flotation on the London Stock Exchange raised £202.0 million (£192.4 million net): fully funded to bring lead product to market

### Cat-SPIRE

- Completed recruitment for phase III registration study (CATALYST); on track to report results in H1 2016
- Initiated two-to-five year follow-on study (CP007A); 138 subjects from CATALYST enrolled to date
- On track to complete paediatric safety study (CP009) in H2 2015
- Paediatric study plan agreed with FDA

### HDM-SPIRE (House Dust Mite)

- Positive results from two-year follow-up phase IIb study (TH002A)
- Excellent safety profile demonstrated in controlled asthmatic study (TH004)
- Completed observational study (TH003) to inform field study design
- Initiated large phase IIb field study (TH005)

### Grass-SPIRE

- Highly encouraging results from third season follow-up phase IIb study (TG002B)
- Initiated phase II safety study in controlled asthmatics (TG004)
- Initiated observational study (TG003) to inform phase III design

### Ragweed-SPIRE

- Symptoms reduced in phase IIb chamber study (TR006); results suggest optimal dose not tested
- Supportive subsequent field data from TR006; reduction in symptoms and rescue medication use
- Follow-up study (TR006A) planned to assess effect of allergen exposure during further ragweed season
- Positive results from safety study (TR007) support inclusion of controlled asthmatics in future studies
- Additional phase IIb dose ranging study planned

### Commercialisation progress

- Appointed Chief Commercial Officer; US subsidiary established
- Building US and EU market access and medical affairs team to expand relationships with allergists
- Positive research with specialists, patients and payers in US and key EU markets
- US patent term extended for Cat-SPIRE, HDM-SPIRE and Grass-SPIRE; protection to at least 2030

### Financial highlights

- Successful flotation on the London Stock Exchange raised £202.0 million (£192.4 million net)
- Increased investment in research and development to £38.6 million (2013: £21.1 million)
- Loss for the year £35.1 million (2013: £20.0 million)
- Strong balance sheet with £186.6 million cash and deposits at 31 December 2014 (31 December 2013: £30.6 million)

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# Allergies are a serious global health issue...

In Europe, allergy is considered a public health pandemic. It affects over 150 million people, making it the continent's most prevalent chronic disease. In the US, allergic disease including asthma is the fifth most prevalent chronic disease, and the third most common in children. Nasal allergies alone affect approximately 50 million Americans.

“ ...the general public confronts huge direct and indirect costs with major effects on macroeconomics due to healthcare, loss of productivity and absenteeism...”

EAACI Global Atlas of Allergy 2014

”

“ ...I'm physically exhausted and I feel like I have a constant cold!

Cat allergy patient: GfK research 2014

”

## 10-20%

Allergic rhinitis affects 10 – 20% of the world's population, making it the most prevalent chronic non-communicable disease

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## Allergies cause chronic misery

### Can't work, can't sleep, can't function

Allergic diseases can cause long-term misery, affecting sleep, work and lifestyle. With 150 million Europeans 'trapped' by allergy, and even more affected in the US and elsewhere, the economic and social impacts are significant, and often overlooked.

- In the US allergy has the greatest impact on work productivity of all medical conditions
- Approximately 10,000 children a day miss school in the US due to allergic rhinitis
- In Europe up to 20% of those with allergy have debilitating disease
- Those with the most severe allergy are at risk of a potentially life-threatening asthma attack or anaphylaxis

### Common symptoms of allergic conditions

- Blocked, itching, running nose
- Coughing
- Sneezing
- Itching, red, streaming eyes
- Swollen eyelids
- Itching mouth and throat
- Urticaria (itching, red skin)

“...I feel sad and lonely  
and especially isolated...”

Cat allergy patient: GfK research 2014

”

### Common allergies

Allergy is a hypersensitivity of the immune system leading to disease. Allergy can occur in almost every organ, but is most common in the skin and mucous membranes that form the boundary with the outside environment. Of the wide range of allergy-related conditions, allergic rhinitis and conjunctivitis are the most common, and often occur together.

#### Cat allergy

Cats are responsible for the sensitisation of over 50 million Americans and 30-37 million Europeans, making cat allergens the sixth and third most common cause of allergic sensitisation respectively.

#### House dust mite allergy

Skin pricking tests show more people are sensitised to house dust mites in Europe and the US than any other allergen. In each region this equates to over 80 million people.

#### Grass allergy

Grass pollens are a common cause of hay fever. In Europe and the US, grasses cause the greatest sensitisation of all seasonal allergens, affecting over 60 million and 80 million people respectively.

#### Ragweed allergy

Ragweed allergy is a major problem in the US, where over 80 million people are sensitised to its pollen. In Europe, ragweed is spreading and in heavily infested areas of France and Italy up to 12% of the population are allergic to its pollen.

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# ...current treatments are significantly inadequate...

Current treatments for patients with moderate or severe allergy are inadequate. Avoidance is difficult or impossible. Pharmacological treatments (antihistamines and corticosteroids) provide short-term symptom relief only, and are only partially effective. Whole allergen immunotherapy is the only treatment to address the underlying disease, but is lengthy and can have unpleasant side effects with the potential for anaphylaxis.

## Current immunotherapies have inherent problems

### Subcutaneous immunotherapy

- Allergen injected into skin
- Requires complicated dose escalation
- Treatment is lengthy
- Potential for anaphylaxis
- Patient compliance is poor

# 3-5yrs

Subcutaneous immunotherapy requires multi-year treatment

“Pollens... may be ubiquitous... so avoidance measures are impossible”

EAACI Global Atlas of Allergy 2014

### Sublingual immunotherapy

- Allergen administered under the tongue
- Lengthy treatment
- Poor patient compliance
- Side effects are extremely common
- Long-term treatment is costly

# \$9,000

Three years of daily sublingual immunotherapy is expensive

# 65-85%

Adverse reactions to sublingual immunotherapy are extremely common

# 7%

Only 7% of patients complete three years of sublingual immunotherapy



# Our SPIREs are designed to revolutionise treatment

## MicronJet™ administration

Our SPIRE allergy therapies can be delivered with the patient-friendly MicronJet™ system. This novel device is mounted on a standard syringe and allows simple intradermal administration via microscopic hollow crystals of pure silicon. MicronJet™ is approved for use in Europe and the US, providing consistent, patient-friendly, intradermal administration.

## Modern production

Our treatments are manufactured using modern synthetic pharmaceutical processes, unlike existing immunotherapies that rely on complex techniques to produce and process whole allergens. This gives us a number of benefits:

- Totally synthetic products
- Highly controllable processes
- Well characterised products
- Consistent quality
- Standardised doses

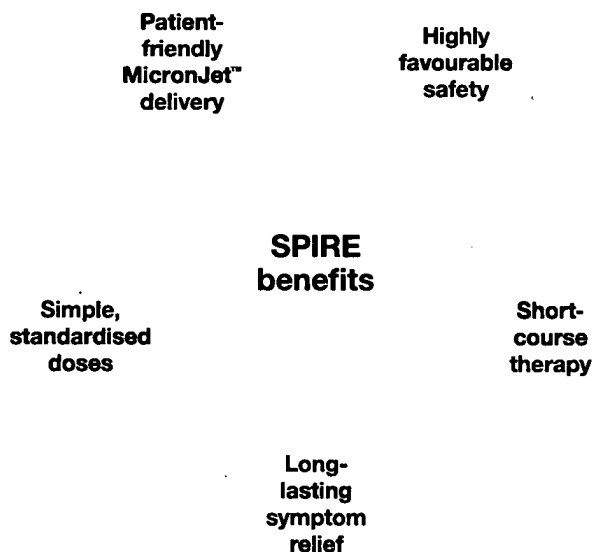
## Targeting key allergies

Our SPIRE therapies are designed to treat some of the most common allergies:

- Cat-SPIRE targets cat allergy
- HDM-SPIRE is targeting house dust mite allergy
- Grass-SPIRE targets allergy to grass pollen
- Ragweed-SPIRE is targeting ragweed pollen allergy
- Birch-SPIRE targets allergy to birch pollen
- Japanese cedar-SPIRE is targeting allergy to Japanese cedar pollen
- Alternaria-SPIRE targets allergy to Alternaria mould

## Making strong clinical progress

- Four programmes in phase II/III
- 22 studies complete
- Six studies ongoing
- 3,500 subjects in clinical studies



## Our therapies: designed to transform therapy

We are developing a totally new class of therapies, the Synthetic Peptide Immuno-Regulatory Epitopes (SPIREs). This new type of treatment is designed to build on the efficacy of whole allergen therapy while overcoming its drawbacks. SPIREs use a novel mix of small peptides to restore immunological balance and induce tolerance to naturally occurring allergens. Our research shows this approach offers major potential benefits compared with existing immunotherapies:

- Short, simple treatment
- Long-lasting efficacy
- Strongest against worst symptoms
- Safety profile similar to placebo
- Patient-friendly MicronJet™ delivery

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# **...our therapies could transform the market.**

We've undertaken extensive research showing our new generation treatments have the potential to transform the marketplace and give us a major commercial opportunity.

- >\$500m US peak sales potential for Cat-SPIRE
- \$2.6bn US opportunity for our four lead products
- \$2,600 pricing potential per Cat-SPIRE short course

**Our territories:  
North America**

## **100 → 3,500**

**100-strong sales force  
to initially target 3,500  
allergists in North America**

**Our target**  
We are targeting allergists and specialists who treat patients with moderate and severe allergies

**Circassia's target population in the USA for Cat-SPIRE**

**24m people**

Cat-allergic individuals in the United States

**1.3m**

Of the 24 million cat-allergic individuals, 1.3 million new patients consult an allergist every year about symptoms

**Secondary Circassia focus**  
Patients not offered IT

**1m**

Of the 1.3 million seeking help, 1 million are suitable for immunotherapy and are offered the existing treatment options

**Primary Circassia focus**  
Patients declining IT

**378,000**

Of the 1 million who are offered whole allergen immunotherapy, less than half actually accept it

**Secondary Circassia focus**  
Patients failing to complete IT

**60,000**

Only 60,000 people of the 378,000 who accept treatment actually complete the course

#### **Serving the underserved**

Current treatments underserve many allergy patients. Of those offered immunotherapy by their specialist, the vast majority either decline or fail to complete treatment. Targeting this population would give us a major market opportunity, and allow allergists to maintain their patient relationships. Also targeting patients not currently offered immunotherapy would boost the opportunity further.

In the US, treating just 200,000 patients with Cat-SPIRE out of the more than 1 million who are currently not offered, decline or do not complete immunotherapy, could result in peak sales of over \$500 million.

#### **Commercialisation strategy**

Our strategy is to target the concentrated group of specialists who treat patients with moderate and severe allergies, giving us the opportunity to commercialise our products independently in key markets while licensing or forming partnerships elsewhere.

**Our territories:**  
**Europe**

**Our territories:**  
**rest of world**

**90 → 6,600**

**90-strong sales force to target high prescribers among 6,600 allergists in Europe**

**License or partner in Japan and other key markets**

## Chief Executive's review

**2014 has been transformational for Circassia. In March, we raised over £200 million through a successful IPO, and now have the funds to accelerate our late-stage clinical portfolio and establish the infrastructure to independently commercialise our first next generation allergy treatment. During the year, we made good progress towards meeting these goals. We completed recruitment for our phase III Cat-SPIRE registration study, which remains on track to report in H1 2016, and completed five further clinical trials across our portfolio. We are committed to bringing our innovative allergy products to market, and during the year we began to build our commercial organisation. With the US allergy immunotherapy marketplace opening up to new treatment approaches, we are well positioned to exploit the growing interest in this poorly served field.**

### **Advancing our portfolio**

Our novel SPIRE treatments offer significant potential benefits compared with existing immunotherapies, in both seasonal and perennial allergies. During 2014, we made good clinical progress with our portfolio, completing studies across our development programmes. We also completed recruitment into our pivotal phase III CATALYST study, recruiting 19% more subjects than our initial minimum target, and extending the trial to Russia to support a potential future filing in this significant market. We have a further six clinical trials ongoing, and anticipate completing three of these by the end of this year, and our CATALYST study in the first half of 2016.

### **Encouraging results**

The results from the studies we completed in 2014 continued to confirm the potential of our short-course treatments to improve patients' allergy symptoms. During the year, we received positive long-term data from two of our programmes. These showed ongoing efficacy in two-year and three-season follow-ups with our HDM-SPIRE and Grass-SPIRE treatments respectively, despite subjects not receiving any further doses.

In December, we announced top-line chamber results from a Ragweed-SPIRE phase IIb study. The results suggested we may not yet have tested the optimal dose for this treatment, and a higher dose may be necessary to achieve greater symptom improvements. This conclusion was supported by encouraging field results from the same study. We intend to capitalise on these learnings by conducting a longer-term follow-up of these subjects in the field, and to use the insights we gain in the design of a dose ranging study, before moving Ragweed-SPIRE into phase III.

### **Establishing our infrastructure**

With our lead product on track to complete its registration study next year, we plan to file for marketing approval, dependent on the results, in the second half of 2016. Consequently, we have completed the manufacturing scale-up for commercial supply and begun marketing preparations to ensure a successful launch. We intend to commercialise our products independently in key markets, and to partner elsewhere, and during 2014 we made good progress in implementing this approach. We are recruiting medical science liaisons in the US and the five largest EU markets to establish links with allergists, opinion leaders and payers, and intend to complement this team with market access and marketing specialists, as we begin major global research to inform our core marketing plans.

### **Robust financial position**

Following our successful flotation in 2014, we have maintained a strong balance sheet and remain fully funded to complete our phase III study and bring our first innovative new allergy treatment to market. During the year, we accelerated the clinical development of our pipeline, and substantially expanded our R&D team to support this activity. As a result, our R&D investment increased significantly, reaching £38.6 million, up from £21.1 million the year before. With £186.6 million of cash and deposits at the end of the year, we are well positioned to continue investing in our development programmes to deliver on the promise of our unique product candidates.

### **Positive outlook**

During 2014, the allergy market continued to develop. In the US, the FDA approved a number of sublingual immunotherapies, which will be promoted by significant players Merck and Greer. This is an important opportunity to open the market to new treatment approaches, and provide renewed vigour to a field that has been largely ignored for many years. Both of these companies have announced robust pricing for their new products, which supports our research suggesting Circassia's novel therapies have a major commercial opportunity. This positive outlook is further supported by a payer study we undertook during 2014. The results show pricing for Cat-SPIRE may be greater than the \$2,600 per course indicated in our previous research, which suggested a peak sales opportunity of over \$500 million for the product in the US alone.

Following a year of strong progress in 2014, we look forward to continuing our positive momentum in the year ahead. We plan to complete three clinical studies to support phase III programmes for Cat-SPIRE and Grass-SPIRE, to fully recruit subjects for our HDM-SPIRE field study and to advance Ragweed-SPIRE towards phase III. At the same time, we intend to establish the foundations of a strong commercial team to prepare for our first product launch. With the allergy market entering an exciting period, the outlook is extremely encouraging.

**Steve Harris**  
Chief Executive

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## Business model

Our management team has a proven track record of developing successful biopharmaceutical businesses. We leverage the team's experience to manage an efficient outsourced business model. This allows us to retain key functions in-house, such as strategy, intellectual property, clinical study design, regulatory affairs and commercialisation, while also drawing on third-party expertise by outsourcing non-core activities to well-established contract research organisations and pharmaceutical manufacturers. We are currently establishing our commercial organisation to sell our products directly in key markets, while partnering elsewhere, and as part of this process may acquire appropriate infrastructure and complementary products.

### Our global partnership network

- InVentiv Health, Quintiles and Pharm-Olam International for clinical studies;
- Bachem for pharmaceutical ingredient production, Patheon for lyophilisation fill-finish and Nova Laboratories for formulation services for clinical studies;
- Adiga Life Sciences (our 50/50 joint venture with McMaster University) for epitope discovery and mechanistic clinical studies;
- Aptuit and Sequani for toxicology services;
- NanoPass for production and licensing to us the MicronJet™ delivery device.

#### Circassia development

#### Circassia

#### Circassia commercialisation

#### Development partners

#### Manufacturing partners

#### Commercial collaborations

#### Circassia development

- Management
- Study design
- Regulatory
- CMC

#### Development partners

- CROs
- Pre-clinical testing

#### Circassia

- Strategy
- Technology
- IP

#### Manufacturing partners

- Clinical supplies
- Commercial production

#### Circassia commercialisation

- USA
- Key EU markets

#### Commercial collaborations

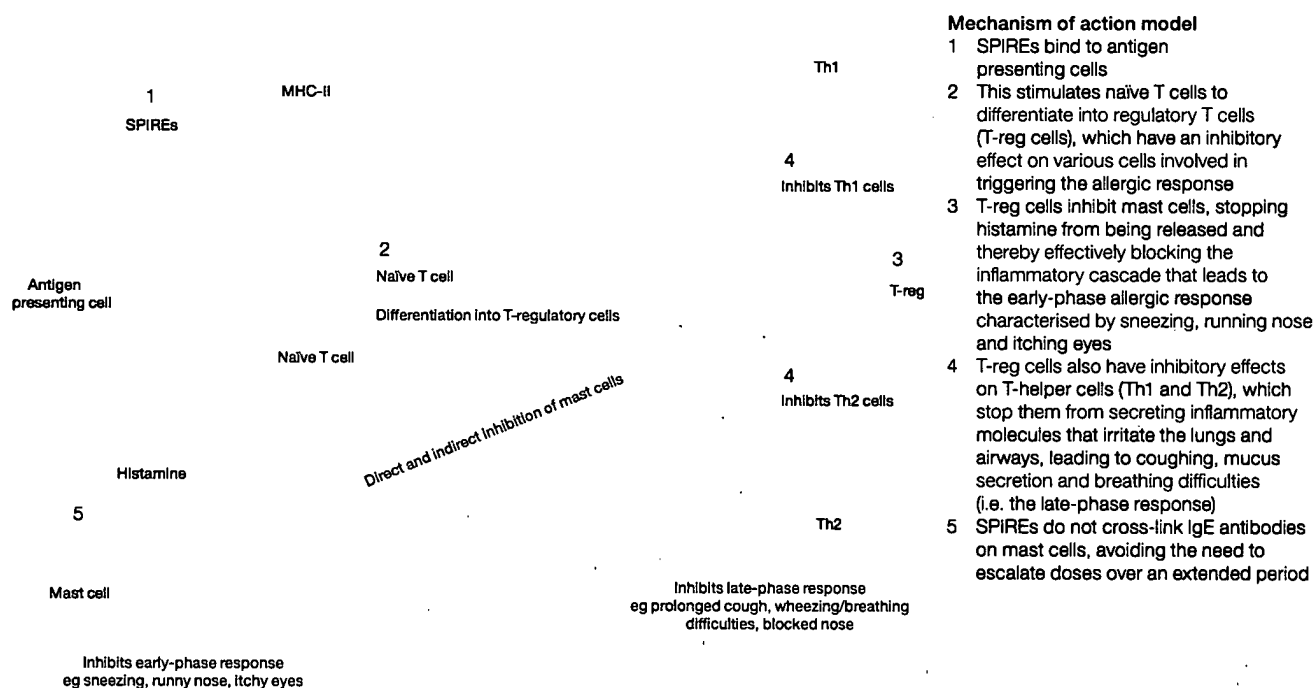
- License/partner in rest of world

## Our technology

Our Toleromune® technology is a unique platform designed to discover the next generation of allergy treatments.

Rather than using whole allergens as treatments, Toleromune® technology identifies short peptide epitopes from sequenced allergens that can stimulate a T-cell response. Toleromune® specifically selects novel mixtures of these peptides to induce rapid immune tolerance, with a short course of treatment of four or eight injections over 12-14 weeks. The peptides are manufactured synthetically rather than extracted from whole allergens, and as a result this new class of treatment is called Synthetic Peptide Immuno-Regulatory Epitopes, or SPIREs.

T-cell epitopes are selected from sequenced whole allergens. Final products are vials of room-temperature stable, lyophilised mix of peptides for intradermal administration



## Our pipeline

We are developing a range of innovative SPIRE treatments, targeting some of the most common allergies. We currently have four late-stage clinical development programmes, with three further products progressing towards the clinic.

Product	Research	Pre-clinical	Phase 1	Phase 2	Phase 3
<b>Cat-SPIRE</b>					
<b>Grass-SPIRE</b>					
<b>House Dust Mite-SPIRE</b>					
<b>Ragweed-SPIRE</b>					
<b>Birch-SPIRE</b>					
<b>Japanese cedar-SPIRE</b>					
<b>Alternaria-SPIRE</b>					

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## Our portfolio

Our seven innovative treatments currently in development have the potential to revolutionise allergy therapy, and transform the lives of millions of sufferers.

### **Cat-SPIRE** for cat allergy

# 83-90m

**Population sensitised to cat allergens  
in the US and Europe**

#### **Cat allergy**

Cat allergy, one of the most common allergies, is triggered by allergens found in cat saliva, notably the protein Fel d 1, which cats spread over their bodies when they groom themselves. In Europe and the US, between 8% and 17% of the population are sensitised to the proteins in cat saliva, urine and skin flakes (dander) that are responsible for allergic reactions. These allergens are widespread in the environment and therefore difficult to avoid. Cat allergy is a perennial condition that reduces sufferers' quality of life and impacts social lives, preventing visits to friends and relatives with cats. As cat allergen is present in many public places it causes problems in schools and in the workplace.

#### **Cat-SPIRE**

Circassia's novel product candidate Cat-SPIRE contains seven synthetically produced peptides identified from Fel d 1, which is the main allergen responsible for allergy to cats. Cat-SPIRE has successfully completed a number of phase II studies, and achieved impressive results. The studies showed that a short course of treatment with Cat-SPIRE substantially reduced patients' symptoms. In a long-term follow-up study, patients' symptoms remained greatly improved two years after the start of the study, despite no further treatment after the initial four-dose, 12-week course of Cat-SPIRE. Cat-SPIRE has demonstrated a favourable safety profile and is currently in a pivotal phase III trial, which is fully recruited and due to report in H1 2016.



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**HDM-SPIRE**  
for house dust mite allergy

**168m**

Population sensitised to house dust mite allergens  
in the US and Europe

**Grass-SPIRE**  
for grass allergy

**147m**

Population sensitised to grass pollen  
in the US and Europe

**House Dust Mite (HDM)  
allergy**

In Europe and the United States, more people are sensitised to house dust mites than any other common allergen. House dust mites are small translucent organisms belonging to the arachnid class. They are found globally in mattresses, pillows, sofas and carpets where they can reach a constant source of food (human skin scales) and humidity is high enough to permit their survival. Throughout their lifetime of approximately three months, house dust mites produce around 2,000 faecal pellets, each containing digestive enzymes and other proteins. The allergens found in the faecal pellets play a major part in the development of allergic asthma, rhinoconjunctivitis and eczema. In Europe and the US, between 22% and 28% of the population are sensitised to the allergens found in house dust mite faeces. House dust mite allergy is a perennial condition and can have a significant impact on sufferers' quality of life.

**HDM-SPIRE**

Circassia's novel product candidate HDM-SPIRE contains seven synthetically produced peptides identified from the key allergens found in house dust mite faecal pellets. It is designed to generate a similar frequency of T-cell response to that generated by whole house dust mite allergen. HDM-SPIRE has achieved positive results in a phase IIb clinical study, significantly reducing patients' allergic reactions while demonstrating a favourable safety profile. A two-year follow-up study also demonstrated encouraging trends that suggest HDM-SPIRE has a long-lasting effect with no further injections. Building on the encouraging data generated from the HDM-SPIRE clinical programme to date, Circassia has initiated a phase IIb field study in 660 subjects.

**Grass allergy**

Grass allergy, a common cause of hay fever, is extremely prevalent. In Europe and the US, 17% – 27% of the population are sensitised to grass pollen allergens. Grass pollen allergens are universally recognised as a major cause of allergic diseases in humans, including asthma, allergic rhinoconjunctivitis and dermatitis. Grass allergy is a seasonal condition and can debilitate sufferers during the months when pollen is released, resulting in significant healthcare costs, workplace/school absences and the inability to spend time outdoors.

**Grass-SPIRE**

Circassia's novel product candidate Grass-SPIRE contains a mixture of seven peptides designed to generate a similar frequency of T-cell response to that generated by whole grass allergen. The product candidate contains epitopes derived from Rye, Timothy and Bermuda grass, and these epitopes are conserved in other grasses, including Velvet, Orchard, Kentucky blue and Canary grass. In a phase IIb clinical study, a short course of Grass-SPIRE therapy demonstrated a significant improvement in symptoms at the end of the season compared with placebo. Efficacy was also demonstrated after a second grass season, and in patients who were followed over three consecutive pollen seasons the initial treatment effect was maintained despite no further doses.

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## Our portfolio continued

### **Ragweed-SPIRE** for ragweed allergy

# 82m

Population sensitised to ragweed pollen in the US

### **Birch-SPIRE** for birch allergy

# 22m

Population sensitised to birch pollen in Europe

#### **Ragweed allergy**

"Ragweed" refers to a group of approximately 40 species of annual weed plants most of which are native to North America. The two species most closely associated with allergy and asthmatic symptoms are short ragweed (*Ambrosia artemisiifolia*) and giant ragweed (*Ambrosia trifida*), although the latter is much less abundant. Allergy to ragweed pollen is widespread in the United States, where approximately 26% of the population are sensitised to the allergen, and is commonly considered a form of hay fever. Although the prevalence is lower in Europe, ragweed allergy is affecting a growing proportion of the population. The ragweed season begins in mid-August and is a significant problem for people allergic to its pollen.

#### **Ragweed-SPIRE**

Circassia's novel product candidate Ragweed-SPIRE contains seven synthetically produced peptides identified from the key allergen found in short ragweed pollen. It is designed to generate a similar frequency of T-cell response to that generated by whole ragweed allergen. In a large phase IIb study, patients with more severe symptoms who received higher-dose treatment had improved symptoms following just eight doses of Ragweed-SPIRE. In a second phase IIb chamber study, Ragweed-SPIRE demonstrated a clear dose response, with the higher dose improving subjects' symptoms, although the outcome appeared significantly influenced by a marked placebo effect that was greater than in similar subjects in the earlier study.

#### **Birch allergy**

Birch trees (*Betula verrucosa*) are widespread across the northern hemisphere, particularly in Northern Europe, and approximately 6% of the European population are sensitised to birch pollen. Bet v 1 is the major birch allergen, and is highly cross-reactive with many plant foods. Birch allergy sufferers also suffer from Oral Allergy Syndrome (OAS) or Pollen Food Syndrome (PFS), and the allergen can trigger oral symptoms such as swelling or itching of the lips, mouth and throat when people eat certain fresh fruits or raw vegetables.

#### **Birch-SPIRE**

Circassia is evaluating a novel product candidate for the treatment of birch allergy, which is currently in pre-clinical development. The first clinical study is planned to begin in H2 2015.

**Japanese cedar-SPIRE  
for Japanese cedar allergy**

**71m**

**Population sensitised to Japanese cedar pollen in Japan**

**Alternaria-SPIRE  
for Alternaria allergy**

**52m**

**Population sensitised to Alternaria mould  
in the US and Europe**

**Japanese cedar allergy**

Pollen from the Japanese cedar tree (*Cryptomeria japonica*) is the cause of one of the most common allergic diseases in Japan. From 1949 to 1970, large numbers of fast growing Japanese cedar trees were planted for use in the construction industry, and planted Japanese cedar forests account for approximately 12% of the country's total area (45,000km<sup>2</sup>). It is estimated that 56% of the Japanese population is sensitised to Japanese cedar, and during the pollen season weather forecasts typically provide information on the pollen count and sufferers wear masks and eyewear to reduce exposure to the allergen.

**Japanese cedar-SPIRE**

Cry j 1 and Cry j 2 are the main allergens responsible for allergy to Japanese cedar. Circassia is currently evaluating a novel product candidate for the treatment of Japanese cedar allergy, which is currently in pre-clinical studies.

**Alternaria allergy**

*Alternaria alternata* (Ascomycete fungi) is one of the most common fungi associated with allergy in humans. It is ubiquitous in the environment and a natural part of fungal flora almost everywhere. *Alternaria* can be found in soils, corn silage, rotten wood, compost, bird nests and various forest plants and it is frequently found on water condensed on window frames. In Europe and the US, between 3% and 13% of the population are sensitised to the allergen.

**Alternaria-SPIRE**

Alt a 1 is the major allergen responsible for allergy to *Alternaria*. Circassia is evaluating a novel product candidate for the treatment of *Alternaria* allergy, which is currently in pre-clinical studies.

## Strategy and progress against objectives

Circassia's strategy is to build a successful biopharmaceutical company with a strong pipeline of product candidates, and a broad and balanced portfolio of innovative products independently commercialised in the US and key European markets and partnered in other regions.

By establishing or acquiring the relatively modest infrastructure required to target specialists in the US and main European markets, we will also have the opportunity to license or acquire complementary products that we can commercialise by leveraging the same infrastructure, completing our transformation into a successful specialty biopharmaceutical business.

### Strategic objectives

#### **Complete the clinical development of our innovative product candidates**

We are focused on completing the clinical development of our new generation of allergy treatments. Cat-SPIRE is in an ongoing, fully recruited phase III registration study, and we expect to have the results available in H1 2016. Subject to the results of this study, we intend to submit applications for marketing approval for Cat-SPIRE to the FDA, Health Canada and the EMA later the same year.

In parallel, we intend to complete the development of our other late-stage product candidates, HDM-SPIRE, Ragweed-SPIRE and Grass-SPIRE, which have each demonstrated clinical proof-of-concept in phase IIb studies. We expect that phase III data for Grass-SPIRE will be available in 2017, and for HDM-SPIRE in 2019. For Ragweed-SPIRE, we are planning to complete a confirmatory dose ranging study, before moving to phase III.

#### **Independently commercialise our products in North America and major EU markets**

We have retained full global commercialisation rights for all of our product candidates and intend to establish our own sales and marketing capabilities in North America and major EU markets, initially focusing on allergists. We believe the allergist population is sufficiently concentrated to enable us to commercialise products effectively with a specialist sales and marketing group. We are also exploring additional options for commercialisation, including acquiring companies that have appropriate infrastructure.

#### **Establish commercial partnerships in other regions of the world**

In other markets, such as Japan, we intend to commercialise our products through partnerships rather than establishing our own dedicated infrastructure. We have a number of options to achieve this, including out-licensing commercialisation rights or collaborating with regional or global pharmaceutical companies.

#### **Leverage our ToleroMune® technology to expand our portfolio of development programmes**

We believe that we can leverage our ToleroMune® technology to expand our portfolio of product candidates, both in the field of allergy as well as immune disorders more generally. We also have the opportunity to leverage our broader expertise in allergy and immunology to enhance our pipeline, such as through in-licensing or the acquisition of complementary product candidates or technologies.

#### **Maintain and strengthen our intellectual property portfolio**

Our patent portfolio provides broad effective protection for our technology and pipeline to at least 2030 in the US and 2028 in Europe, with potential significant further patent extensions available post-approval. We intend to continue to leverage this protection to develop and commercialise our novel product candidates. We will also continue to file new patent applications and expand and strengthen our wider intellectual property portfolio, including through potential in-licensing and acquisition.

*Achieving our strategic objectives involves risks and uncertainties, which are detailed in the section entitled 'Risks and risk management'.*

## **Build broad and balanced portfolio**

Unique ToleroMune® technology with four late-stage clinical products and three pre-clinical programmes

## **Deliver the pipeline**

Clinical trials in over 3,500 subjects with 22 studies complete and six ongoing

## **Market novel products**

Independently commercialise products in North America and major EU markets; commercial partnerships in other regions

# Progress in 2014

**During 2014, we made significant progress in advancing our strategy, with a clear focus on accelerating the clinical development of our portfolio of innovative SPIRE allergy treatments. In parallel, we successfully completed our IPO on the London Stock Exchange to raise the significant funds required to support the development of our pipeline and establish the infrastructure to commercialise our specialist therapies.**

### **Cat-SPIRE progress**

By the end of 2014 we had successfully completed recruitment for our pivotal phase III study, extended the trial to support a potential filing in Russia and initiated a two-to-five year follow-up study of the phase III subjects.

### **HDM-SPIRE progress**

We reported positive results from both a phase IIb two-year follow-up study and a safety study in controlled asthmatics. We also successfully completed an observational field study and started a large multi-centre field trial in North America, South Africa and Europe.

### **Grass-SPIRE progress**

We announced highly encouraging results from a three-season follow-up phase IIb study. We also initiated a safety study in controlled asthmatics and an observational study to monitor subjects' allergy symptoms and rescue medication use during the pollen season.

### **Ragweed-SPIRE progress**

We reported top-line results from a phase IIb study, and based on the full dataset plan to undertake a further dose ranging study to identify the optimal regimen for phase III. We also completed a successful safety study in controlled asthmatics.

### **Commercialisation progress**

We appointed a Chief Commercial Officer and established our US subsidiary. We are recruiting medical science liaisons in the US and Europe, and plan to strengthen the marketing and market access team in the coming months. We also completed successful market research with allergists, payers and patients in the US and EU.

### **Commercial partnership progress**

We plan to enter discussions with potential partners after reporting our Cat-SPIRE phase III results, to maximise value. These will cover the commercialisation of our product candidates in a wide range of territories around the world.

### **ToleroMune® progress**

We continued to advance the three earlier-stage pre-clinical products we have developed with our unique technology. We also progressed a number of studies to help further leverage the platform, exploring novel biomarkers and immunological mechanisms.

### **Intellectual property progress**

We extended protection in the US to 2030 for Cat-SPIRE, HDM-SPIRE and Grass-SPIRE through patent term adjustments. During 2014, we also had 13 new patents granted and completed an additional six filings in key territories.

# Strategic review

Circassia's overarching objective is to build a successful biopharmaceutical company with a strong pipeline of treatments in development and a broad, balanced portfolio of innovative marketed products that are commercialised independently in the US and key European markets and partnered in other regions.

During 2014, we made good progress towards this objective. We advanced our clinical programmes, progressed our earlier-stage pre-clinical candidates and continued to lay the foundations for the successful commercialisation of our next generation allergy treatments. Over the next three years, we intend to deliver against each element of our strategy to transform Circassia into a financially self-sustaining specialty biopharmaceutical business.

# 1,409 subjects

Cat-SPIRE phase III recruitment completed with 19% more subjects than minimum target

## Clinical progress

### **Cat-SPIRE: phase III fully recruited; two-to-five year follow-up initiated; paediatric safety study progressing**

Cat-SPIRE is Circassia's lead product candidate. This innovative cat allergy treatment has achieved impressive clinical results to date, with a short course of four doses given over 12 weeks reducing allergy symptoms over a two-year period without further dosing. Cat-SPIRE is currently undergoing phase III testing in a single pivotal field trial, conducted under the name CATALYST, in subjects aged 12–65 years with moderate to severe allergy symptoms. By the end of 2014, we had completed recruitment into this double-blind, randomised, placebo-controlled, multi-centre study, enrolling 1,409 subjects, 19% above the minimum target. During the year, we extended CATALYST to include Russia, where we recruited 91 subjects to support a potential regulatory filing in this significant market. The phase III study is currently ongoing in centres across North America, Europe and Russia, where it is evaluating a single and two sequential short courses of Cat-SPIRE, each of four doses administered over 12 weeks. With the primary endpoint assessing the effect on symptom scores and rescue medication use one year after the start of treatment, CATALYST remains on track to report in H1 2016, and subject to the results, we plan to file for marketing approval in key markets later the same year.

In the first half of 2014, we initiated a long-term study (CP007A) to follow-up subjects from the CATALYST trial. This follow-on is designed to assess the ongoing efficacy of Cat-SPIRE without subjects receiving any further doses, and will record symptom scores and use of rescue medication annually for up to five years after the start of treatment in the initial phase III study. To date we have enrolled 138 subjects who have completed the CATALYST final one-year assessment.

We have also made progress with our Cat-SPIRE paediatric development plan. In Europe, our paediatric safety study (CP009) will enrol at least 12 subjects in two groups, and the first, aged 9–12 years old (n=8), is now recruited, and we anticipate completing the study in H2 2015. In the US, the FDA has approved our initial paediatric study plan, which, in line with the usual regulatory process, will await product approval for finalisation.

### **HDM-SPIRE: positive two-year follow-up and asthmatic safety results; large phase IIb study initiated**

HDM-SPIRE is Circassia's innovative treatment for house dust mite allergy. In an earlier proof-of-concept phase IIb trial (TH002), subjects who received a short course of four doses of HDM-SPIRE over 12 weeks had a significant improvement in their allergy symptoms compared with placebo a year after the start of treatment (p=0.02). In June 2014, we announced the completion of a two-year follow-up (TH002A) in 72 of these subjects, which assessed the ongoing effect of treatment without further doses of HDM-SPIRE. The results demonstrated persistent symptom reduction compared with placebo two years after the start of treatment, which was equivalent to that achieved after one year in the same subjects. The results also showed a greater effect in those with more severe symptoms, as has been seen in other SPIRE studies. This finding is important because research shows this group is more likely to seek treatment due to the impact of their allergy.

**Highly encouraging three-season follow-up**

In the phase IIb follow-up, subjects who received two different Grass-SPIRE regimens had a continued reduction in allergy symptoms when assessed in an environmental chamber three pollen seasons after receiving treatment

“ In 2014 we started a large HDM-SPIRE field study in North America, Europe and South Africa ”

During 2014, we also successfully completed two studies to inform the design of a large HDM-SPIRE phase IIb field trial. The first, an observational field study (TH003), enrolled 109 subjects with house dust mite allergy and monitored them over six weeks to determine the most relevant symptoms for assessment, the optimal duration for recording symptoms and screening measures to identify appropriate subjects. The second study (TH004) was a phase II double-blind, placebo-controlled safety trial in 30 controlled asthmatics, which demonstrated an excellent safety profile for HDM-SPIRE.

These studies enabled the initiation of a large phase IIb field study (TH005) in Q3 2014, which includes enrolment of controlled asthmatic subjects. This randomised, double-blind, placebo-controlled study will enrol 660 subjects aged 18–65 years old in North America, Europe and South Africa, and will compare the optimal short course of treatment from the previous phase IIb trial, a double course and a short course of higher dose HDM-SPIRE. Currently, the study has enrolled 103 subjects.

**Grass-SPIRE: highly encouraging results from three-season follow-up; two support studies initiated**

Grass-SPIRE is Circassia's novel product candidate for the treatment of grass pollen allergy, which is a common cause of hay fever. Previously, in a phase IIb clinical proof-of-concept study (TG002) in 282 subjects, the optimal short course of Grass-SPIRE administered before the grass pollen season significantly reduced subjects' symptoms compared with placebo at the end of the season ( $p=0.035$ ).

In November 2014, we announced positive results from a follow-up study (TG002B) that enrolled 85 subjects from the original proof-of-concept trial. In the phase IIb follow-up, subjects who received two different Grass-SPIRE regimens had a continued reduction in allergy symptoms three pollen seasons after receiving treatment. In those who returned for assessment after both the second and third seasons, their symptom improvement was statistically significant compared with placebo, despite the small sample size and no further dosing over the 30 month period.

During 2014, we initiated two clinical studies to support the design of our Grass-SPIRE phase III trial, which remains on track to begin in H1 2016. The first of these studies (TG004) is in controlled asthmatics, and will evaluate the safety and tolerability of two Grass-SPIRE regimens. The study is now fully recruited with 54 subjects enrolled. The results are anticipated in H1 2015, which if positive will allow the inclusion of subjects with controlled asthma into the phase III trial. The second study is also fully recruited, with 108 subjects enrolled, and we expect to receive the results in the first half of 2015. This observational study will inform the design of the phase III trial, and is monitoring the symptoms and rescue medication use of grass allergy sufferers during the pollen season.

### Supportive field results

Higher-dose Ragweed-SPIRE regimen improved combined scores of symptoms and rescue medication use by 33% compared with placebo

‘ We have three further SPIRE programmes advancing towards the clinic ’

### Ragweed-SPIRE: phase IIb study completed; successful controlled asthmatic safety study

Circassia's novel product candidate Ragweed-SPIRE is designed to treat ragweed pollen allergy. In an earlier proof-of-concept phase IIb trial (TR002) conducted in 2011, subjects with more severe symptoms who received eight higher doses of Ragweed-SPIRE over 14 weeks had a significant improvement in their allergy symptoms compared with placebo ( $p=0.04$ ).

In December 2014, we announced top-line results from a further phase IIb chamber study (TR006) that compared this higher-dose regimen with two lower-dose courses of Ragweed-SPIRE. In this study, a marked placebo effect, which was greater than that seen in the earlier trial, appeared to influence the outcome, and although the higher-dose regimen achieved a robust reduction in subjects' allergy symptoms this did not reach significance compared with placebo ( $p=0.149$ ). The top-line results also indicated a dose response effect consistent with the treatment having a positive effect on symptoms, and suggesting that a higher dose than those tested to date may have greater efficacy.

Subsequently, we have received full results from the study, including data on symptom improvement and rescue medication use measured in the field during the ragweed pollen season. These field results show a treatment effect consistent with that observed in the chamber setting. Similarly, the higher-dose regimen performed better than the lower doses, and improved combined scores of symptoms and rescue medication use by 33% compared with placebo, which approached statistical significance ( $p=0.09$ ). We have used these data and the results from the earlier phase IIb study to inform the next steps for Ragweed-SPIRE (see below).

At the end of 2014, we also completed a phase II safety study (TR007) of Ragweed-SPIRE in controlled asthmatics. The results demonstrated a positive safety and tolerability profile, and will support the inclusion of subjects with controlled asthma in future studies.

### Ragweed-SPIRE: next steps underway

Our first phase IIb chamber study undertaken in 2011 indicated that higher doses of Ragweed-SPIRE produced a greater response. The data from our most recent phase IIb study continue to support this observation, and also suggest that the doses tested to date may not have achieved the peak response. As a result, we intend to conduct an additional phase II dose ranging trial designed to identify the optimal regimen of Ragweed-SPIRE to advance into phase III testing. In addition, we plan to conduct a follow-on field study in TR006 subjects to determine the effect of exposure to naturally occurring ragweed pollen during a further season without additional treatment. We aim to incorporate the learnings from this follow-up into the design of the dose ranging study, and to discuss the details of our development plan with regulators. We anticipate the study may enrol approximately 500 subjects and could include the best performing dose of Ragweed-SPIRE tested to date and at least one regimen of higher-dose Ragweed-SPIRE. We plan to initiate the study and complete recruitment and dosing prior to the 2017 pollen season, with results anticipated in H1 2018.



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# ~500 subjects

Ragweed-SPIRE dose ranging study may enrol approximately 500 subjects

“ Our Adiga joint venture completed two successful clinical immunology studies in 2014 ”

#### **Pipeline progress**

##### **Birch-SPIRE: toxicology studies initiated; chemistry progressing**

Birch-SPIRE is Circassia's novel product candidate for the treatment of birch pollen allergy, and is currently in pre-clinical development. During 2014, we initiated Birch-SPIRE toxicology studies and progressed manufacturing chemistry of the product peptides in preparation for advancing into the clinic in H2 2015.

##### **Japanese cedar-SPIRE: pre-clinical studies initiated; regulatory discussions advancing**

Our novel product candidate designed for the treatment of Japanese cedar allergy is also in pre-clinical development. We have identified candidate epitopes for the product, and during 2014 initiated studies to confirm they do not cause histamine release in blood samples from allergy sufferers. We expect to select the lead candidate in H1 2015, and are currently discussing toxicology study requirements with the Japanese regulators.

##### **Alternaria-SPIRE: histamine release studies initiated**

Alternaria-SPIRE is Circassia's product candidate targeting allergy to the common mould Alternaria. Development is at a similar stage to Japanese cedar-SPIRE, with histamine release studies ongoing in blood from allergic subjects. We anticipate selecting a lead candidate in H2 2015, which we plan to progress into toxicology testing in 2016.

##### **ToleroMune® development: immunology studies complete**

During 2014, we undertook a number of studies to support the efficient leveraging of our ToleroMune® technology. We completed two successful clinical trials as part of our Adiga joint venture with McMaster University. These were designed to assist in the development of future products, and are evaluating a number of mechanistic aspects of SPIRE treatment, such as the identification of novel biomarkers. In addition, our collaboration with Professor Mark Larché at McMaster, which is funded by the NIH, continued to make good progress and provided important immunology data associated with SPIRE treatment. During the year, we also progressed additional work evaluating immunological mechanisms, such as the detection of treatment-related changes in gene expression in allergen-specific T cells.

### **Manufacturing progress**

#### **Production milestones achieved for clinical programmes and to support commercial launch**

As part of our outsourcing strategy we work with established manufacturers for the production of our products. During 2014, we continued our work with Bachem and Patheon to produce study supplies and prepare for commercial production. As a result, Active Pharmaceutical Ingredient (API) manufacturing is now at commercial scale for all four of our late-stage products and the commercial fill-finish process is in place for three of the treatments, and work on the fourth is underway.

During the year, Bachem completed the production of the Cat-SPIRE API validation batches required for regulatory approval, and Patheon completed validation batches of drug product. Bachem also produced initial API validation batches for HDM-SPIRE, and Patheon established the product's lyophilisation process at commercial scale. For Ragweed-SPIRE, the API commercial scale manufacture has been established in the US, and the fill-finish process has completed scale-up. For Grass-SPIRE, the initial API pre-validation batches are being produced, and transfer of the lyophilisation process to the commercial manufacturing site is progressing well.

### **Commercialisation progress**

#### **Chief Commercial Officer appointed; team recruitment underway; positive market research results**

In November 2014, we announced the appointment of our Chief Commercial Officer, who will establish and lead our global commercial operations in preparation for the launch of our first next generation allergy treatment. Linda Szyper, who brings over 20 years' experience of product commercialisation, will also head our newly established US subsidiary. Following Linda's appointment, we have begun to expand our commercialisation infrastructure, starting with the recruitment of US medical science liaisons who will focus on working with key opinion leaders and allergists, as well as supporting our clinical programmes. We plan to mirror this approach in the five key European markets, and are currently recruiting in each of these countries. At the same time, we plan to build our internal market access capabilities, and intend to recruit experts in both the US and Europe in the coming months.

During 2014, we also progressed our pre-launch activities for Cat-SPIRE, including the development of the product's brand name. Following successful initial research with healthcare professionals and patients we are currently testing a panel of four potential names. In the coming months, we intend to select the final name and file trade mark applications. During 2014, we also commissioned a range of market research with allergists, payers and patients in the US and key European markets. Positive results show that all groups welcomed the product profile presented for Cat-SPIRE, and the outcomes will be used to inform our message development, product positioning and value proposition for launch. Importantly, the recent results from US payers suggest Cat-SPIRE has a pricing opportunity that is potentially greater than that identified in research we conducted before the 2014 US approvals of sublingual whole allergen therapies for grass and ragweed allergies.

### **Manufacturing progress**

Our active pharmaceutical ingredient manufacturing is at commercial scale for all four lead programmes

**Commercial fill-finish**  
The commercial fill-finish process is in place for three of our four lead programmes and work on the fourth is underway

### **Building our team**

#### **Teams strengthened to support phase III programmes and commercialisation**

During the year we accelerated our clinical portfolio, initiating a large number of studies and preparing to begin others, including a pivotal phase III trial for Grass-SPIRE. We also progressed our launch preparations for our lead product. To support this rapid advance, we have recruited experts to join our medical, clinical, regulatory, quality and Chemistry, Manufacturing and Control (CMC) teams, and are currently building our commercial organisation. As a result, Circassia's team more than doubled during 2014, growing from 25 employees at the start of the period to 56 at the end of the year.

### **Intellectual property progress**

#### **US protection extended to 2030; 13 patents granted; opposition successfully defended**

During 2014, we continued to invest in our intellectual property to protect our ToleroMune® technology and product portfolio. In the US, we succeeded in obtaining patent term adjustments for Cat-SPIRE, HDM-SPIRE and Grass-SPIRE, and protection will run to 2030 for each of these treatments, with the potential for further significant patent extensions available post-approval. During the year, we also created additional layers of protection, with 13 new patents granted, of which six relate to Cat-SPIRE, HDM-SPIRE and Grass-SPIRE in the US, Japan, and China. In addition, we completed six new filings in key markets to provide additional protection for these products. We also made progress defending our intellectual property position. In November 2014, we were successful at a European Patent Office opposition hearing, at which the Opposition Division upheld the validity of our patent covering Ragweed-SPIRE.

### **Outlook**

#### **Clinical progress continuing; commercial plans accelerating; US immunotherapy market advancing**

During 2015, we plan to continue advancing our clinical portfolio, with six studies ongoing of which three are scheduled for completion in support of our phase III programmes. The first two, an observational study and a controlled asthmatic safety trial, will support the design of our Grass-SPIRE phase III pivotal study, which remains on track to begin in H1 2016. The third, a paediatric safety study, will support our ongoing Cat-SPIRE phase III study as part of our European regulatory filing strategy. We continue on track to complete our phase III study in H1 2016, and, subject to the results, plan to file for marketing approval in North America and Europe later that year.

Alongside our clinical plans, we intend to further develop our commercial organisation in preparation for the launch of our first product, and are currently building the foundations while continuing to review opportunities to accelerate our commercialisation strategy, including through acquisition. As part of this process, we are recruiting medical science liaisons in the US and Europe, and we intend to augment our commercial team with market access and marketing specialists during 2015. In addition, we plan to finalise the brand name for Cat-SPIRE, and to initiate large-scale global research that will provide the foundations for our future marketing programmes.

Over the longer term, we believe Circassia is well placed to capitalise on a renewed focus on the allergy field. With the recent approval of sublingual immunotherapies in the US, 2015 is likely to see the opening up of the market to new treatments. We welcome these positive developments, and believe the allergy field, which has long been poorly served by the pharmaceutical industry, is poised to undergo a resurgence that Circassia is well positioned to exploit.

During the year, the Company transformed its financial position through a successful flotation on the London Stock Exchange. The proceeds have supported greater investment in R&D, with a number of new clinical studies initiated, and an expansion of the Company's R&D team to manage the increased activity. At the end of the year, the Group's balance sheet remains strong, with cash, cash equivalents and short-term deposits of £186.6 million.

## Admission to London Stock Exchange

On 18 March 2014, the Company completed a landmark Initial Public Offering and was admitted to the London Stock Exchange. The Company offered approximately 64.5 million Ordinary shares at 310p each, raising gross proceeds of £200.0 million. It also offered 0.6 million shares from the over-allotment option at the same price, raising additional gross proceeds of £2.0 million.

## Research and development activities

During the period, the Group increased its investment in research and development to £38.6 million (2013: £21.1 million). This covered a number of activities:

- Initiation of new clinical trials, including a phase III follow-on study for Cat-SPIRE (CP007A), a phase II controlled asthmatic study for Ragweed-SPIRE (TR007) and a phase IIb field study of HDM-SPIRE (TH005)
- Completion of recruitment into the Cat-SPIRE phase III registration study (CP007)
- Completion of a phase IIb chamber study of Ragweed-SPIRE (TR006)
- Manufacture of clinical trial supplies for Cat-SPIRE, HDM-SPIRE and Ragweed-SPIRE, and production of validation batches for Cat-SPIRE
- Increase in R&D headcount to 44 at the end of the year (2013: 16)
- Award of new share options with a charge to the income statement of £0.7 million (2013: £nil)

## Administrative expenditure

Commercial infrastructure and administrative expenses, including corporate overheads, centrally-managed support functions and corporate costs, increased to £7.2 million (2013: £3.8 million). This expenditure covered a number of costs:

- Increase in headcount to 12 at the end of the year (2013: 9)
- Award of new share options with a charge to the income statement of £0.5 million (2013: £nil)
- Professional fees including public company costs and patent costs of £3.5 million (2013: £1.3 million)
- IPO-related costs not available for offset against the share premium account of £0.2 million (2013: £nil)
- Commercial infrastructure build costs of £0.8 million (2013: £0.3 million)

## Financial income

Net finance income increased by £1.3 million to £1.9 million, due to higher average cash balances following admission.

## Operating loss

Operating loss for the year ended 31 December 2014 was £45.8 million (2013: £24.5 million). This increase reflects the greater number of clinical trials undertaken and more advanced stage of product development across the Group's portfolio. Average headcount also increased from 20 during 2013 to 49 during 2014 to manage this increase in activity.

## R&D tax credits

The Group recorded a tax credit for the year of £8.9 million (2013: £3.9 million) in the income statement, relating to qualifying research and development expenditure. The increase reflects the higher R&D investment during the year, and an increase in the R&D tax credit rate from 11% to 14.5% from 1 April 2014.

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# £38.6m

Increased investment in research and development to £38.6 million (2013: £21.1 million)

# £7.2m

Administration expenditure increased to £7.2 million (2013: £3.8 million) reflecting larger company cost base

# £8.9m

The Group recorded a tax credit for the year of £8.9 million (2013: £3.9 million) in the income statement, relating to qualifying research and development expenditure

# £186.6m

The Group's balance sheet remains strong with cash, cash equivalents and short-term deposits of £186.6 million at 31 December 2014 (31 December 2013: £30.6 million)

## Loss per share

Basic loss per share decreased to 21p (2013: 126p after adjustment for the re-capitalisation). This reflects an increased loss after tax of £35.1 million (2013: £20.0 million), which was significantly more than offset by the increase in Ordinary share capital of the Company following admission. Note 21 to the financial statements provides a full explanation of the change in share capital.

## Financial position

The Group's net assets of £190.8 million were significantly higher at the end of the year compared to the previous year (2013: £30.0 million), largely due to the increase in cash following admission. Costs relating to admission amounted to £9.6 million, of which, £9.4 million was offset against the share premium account and £0.2 million of indirect admission costs were included in the income statement. Current tax assets stood at £8.8 million at the end of the year (2013: £4.0 million), representing the R&D tax credit for the year. Trade and other payables increased by £3.8 million to £9.8 million, mainly due to year-end accruals of supplier invoices and annual year-end bonuses.

## Cash flow and position

The Group's cash position (including short-term deposits) increased significantly from £30.6 million at the end of 2013 to £186.6 million at 31 December 2014. This reflects a number of changes:

- Net proceeds of £192.4 million from shares issued on admission (2013: £1,928 for issued shares)
- Net cash used in operating activities increased to £36.7 million (2013: £17.9 million) due to higher investment in research and development and an increase in administrative expenditure
- Receipt of £4.1 million R&D tax credit from HMRC (2013: £3.0 million)
- Interest from bank deposits decreased to £0.2 million (2013: £1.3 million) due to the timing of the maturity of fixed-term deposits
- Capital expenditure of £0.3 million (2013: £nil) for fit out of additional R&D office space

## Summary and outlook

During 2014, Circassia's admission to the London Stock Exchange transformed the Company's financial position. The funds raised at the flotation supported increased R&D investment during the year as the Company conducted a greater number of clinical studies across its portfolio. The balance sheet remains robust, and the Company anticipates maintaining momentum in its clinical development programmes during 2015. With the phase III registration study of the Company's lead product on track to complete in H1 2016, Circassia remains funded to bring its first allergy treatment to market.

## Julien Cotta

Chief Financial Officer

# Corporate social responsibility

**The Directors recognise the importance of corporate social responsibility, and seek to take account of the interests of all the Group's stakeholders, including its investors, customers, suppliers, partners, and employees when operating the business. The Board believes that fostering an environment in which employees act in an ethical and socially responsible fashion is critical to its long-term success. The Group strives to be a good corporate citizen and respects the laws of the countries in which it operates.**

## People

Attracting, motivating and retaining a highly skilled workforce is key to the Group's long-term success. The policies put in place by the Group accord with best practice, and stipulate that there should be equal opportunities and an absence of discrimination for all employees.

## Diversity

The importance of diversity within the Group is also reflected in its policies and procedures. The Group does not have formal diversity quotas but recognises that a diverse employee profile is of significant benefit. The table below shows the gender profile at different levels of the Group as at 31 December 2014.

Member	Male	Female	Total	%Male	%Female
Plc Board including Non-Executive Directors	9	1	10	90	10
Senior Managers excluding Directors	4	2	6	67	33
All other employees	24	23	47	51	49
<b>Total</b>	<b>37</b>	<b>26</b>	<b>63</b>	<b>59</b>	<b>41</b>

## Employee welfare and involvement

The maternity and paternity leave and pay policies of the Group meet all statutory requirements. In addition, the Group has implemented a flexible working policy which, with suitable authorisation and where responsibilities allow, permits employees to work from home at certain times.

The Employees are regularly provided with information about the Group, for example through regular 'open house' sessions at which the CEO and other members of the management team present on various topics such as strategic and operational progress, and employee-related policies. Feedback is frequently sought by line managers and the senior management team through team meetings, and in 2014 a formal Employee Survey took place which led to the implementation of several proposals from employees.

### Health and safety

The Group is committed to protecting the health and safety of its employees and endeavours to maintain an effective health and safety culture.

The Group provides ongoing training to individuals who are responsible for health and safety and all staff are notified of health and safety practices. The Group continuously monitors its health and safety policy and practices to ensure they are robust, appropriate, and reflect changes in best practice.

### Ethical and social policies

The Group is a pharmaceutical group and accordingly operates in a highly regulated ethical framework. It complies fully with these laws and regulations. The Company has a clear anti-bribery policy and political donations by the Group are not permitted.

### Product development

The Company's ToleroMune® technology undertakes early development efficacy testing in blood samples taken from human volunteers with allergies. The Group commissions third-party laboratories to conduct the minimum necessary pre-clinical product safety testing in animal models as required by regulatory authorities before commencing clinical studies. Regulators have required the Group to commission this safety testing.

### Environment

The Group is committed to minimising the impact of its activities on the environment. As its employees operate out of two modern office suites, and the Group has no production facilities, it believes that efficient use of energy and materials in those offices is the most important means of climate protection currently available to it. Initiatives to reduce waste have been adopted, which include recycling of paper waste, cans, plastics and printer toners/cartridges.

### Greenhouse gas emission

This section of the Annual report constitutes the Group's disclosure of its greenhouse gas (GHG) emissions in accordance with the Companies Act 2006 (Strategic Report and Directors' Report Regulations 2013).

The Group considers that its current activities have a low environmental impact. Nonetheless, it still actively seeks to make energy savings in a fashion which is environmentally responsible and cost effective.

This is the first year in which the Group has reported on GHG emissions and so no comparative data is available for the year ended 31 December 2013. The baseline year for this report is the year ended 31 December 2014.

Greenhouse gas emissions by source 2014	Tonnes of carbon dioxide
Scope 1	–
Scope 2	17
<b>Total emissions</b>	<b>17</b>

GHG emissions are reported in metric tonnes of carbon dioxide equivalents and calculated using the energy calculator provided by the National Energy Foundation (which uses the Defra conversion factors).

Gas and electricity usage information has been obtained from purchase invoices and verified by reference to meter readings.

In order to express annual emissions in relation to a quantifiable factor associated with the Group's business, an intensity ratio has been calculated which shows emissions reported per square metre of the office space occupied by the Group. This shows that the Group uses approximately 47 kilogrammes of carbon dioxide per m<sup>2</sup>.

# Risks and risk management

**The management of risks is a key responsibility of the Board of Directors of the Company. The Board ensures that the risks taken by the Group are understood, and are appropriate in the light of the Company's strategy and objectives, and that internal controls are in place to effectively identify, assess, and manage important risks.**

The risk management strategy adopted by the Company has a number of facets. A risk register has been created and is updated on an annual basis by those individuals in the business who manage risks on a day to day basis. This process is coordinated by the Chief Financial Officer. The register is reviewed by the Board of Directors and the Senior Management Team, with a particular emphasis on ensuring that the risk appetite of the Board is fully understood by the relevant employees. The register also sets out activities which are designed to mitigate the identified risks, and again the Board and the Senior Management Team analyse these mitigation strategies and ensure that the approach taken is consistent with the nature and degree of risks which are considered acceptable by the Board. Aside from the review, risk owners across the business are responsible for reporting any significant issues on an ongoing basis up to the Senior Management Team and for ensuring that other members of their teams are aware of the risk management process. The Senior Management Team will, in turn, update the Board on a timely basis where important developments occur. Within the R&D function, project team meetings take place once a month at which progress and risks of each individual project is discussed. These discussions are then documented in detailed reports which are circulated to the Senior Management Team. The risk management system is designed to manage risks, rather than eliminate them at the expense of achieving corporate objectives. Accordingly, it can only provide a reasonable and not an absolute assurance against material misstatement or loss.

## Principal risks

The main risks relevant to the Group have been identified below, together with an explanation of how they are managed and controlled. Some risks are common across the pharmaceutical industry, while others reflect the Group's specific strategy. The Company considers all of these risks relevant to any decision to invest in the Company.

## Regulatory approvals

The Company may not obtain regulatory approval for its products. Even if products are approved, subsequent regulatory difficulties may arise, or the conditions relating to the approval may be more onerous or restrictive than the Company expects.

The pharmaceutical industry is highly regulated. Regulatory authorities across the world enforce a range of laws and regulations which govern the testing, approval, manufacturing, labelling and marketing of pharmaceutical products. Stringent standards are imposed which relate to the quality, safety and efficacy of these products. These requirements are a major determinant of whether it is commercially feasible to develop a drug substance given the time, expertise, and expense which must be invested. Moreover, approval in one territory offers no guarantee that regulatory approval will be obtained in any other territory.

The Company's lead product candidate is Cat-SPIRE, which it is developing for the treatment of cat allergy. Failure to obtain regulatory approval for this lead product, or significant delays in obtaining approval, would have a material adverse effect on the Company's business. This risk can be further divided into a number of component risks, each of which require distinct mitigation strategies. These include a failure to complete the phase III registration study and supporting studies; inability to demonstrate efficacy of the product after moving to field studies from chamber studies; and any problems which might arise in validating the manufacturing process for the active pharmaceutical ingredient in the product.

In order to obtain regulatory approval for the Company's products, it will be necessary to successfully complete the supporting clinical studies. Clinical studies are typically expensive, complex and time-consuming, and have uncertain outcomes. Conditions in which clinical studies are conducted differ, and results achieved in one set of conditions could be different from the results achieved in different conditions or with different subject populations. Regulatory authorities or institutional review boards may suspend or terminate clinical studies at any time if the subjects participating in such studies are being exposed to unacceptable health risks or may require additional studies to be performed. Difficulties or delays in the enrolment of subjects could result in significant delays in the completion of those studies and even in their abandonment.

The Company relies on third-party sub-contractors and service providers for the execution of most aspects of its development programs. Failure of these third parties to provide services of a suitable quality within acceptable timeframes – for example due to technical reasons or bankruptcy of the provider – may cause the failure or delay of these development programs.

Even where approval is obtained, regulatory authorities may still impose significant restrictions on the indicated uses or marketing of the product or impose costly, ongoing requirements for post-marketing surveillance or post-approval studies.



### **Mitigating activities**

The Group manages its regulatory risk by employing highly experienced clinical managers and regulatory affairs professionals who, where appropriate, will commission advice from external advisers and consult with the regulatory authorities on the design of the Group's pre-clinical and clinical programs. These in-house experts ensure that high quality protocols and other documentation are submitted during the regulatory process, and that well-reputed contract research organisations with global capabilities are retained to manage the trials.

With regard to the risks specifically identified in relation to Cat-SPIRE, it is of note that recruitment for the phase III study has now been successfully completed; allergen levels used in the exposure chamber have been shown to be comparable to those experienced with an indoor cat which reduces the risk that it will not be possible to show efficacy moving from chamber studies to field studies; and three validation batches of Cat-SPIRE have now been manufactured, giving comfort that the manufacturing process is robust.

### **Unforeseen side effects**

Unforeseen side effects may result from the use of the Company's products or product candidates.

There is a risk of adverse reactions with all drugs. If any of the Company's products are found to cause adverse reactions or unacceptable side effects, then product development may be delayed, additional expenses may be incurred if further studies are required, and, in extreme circumstances, it may prove necessary to suspend or terminate development. This may occur even after regulatory approval has been obtained, in which case additional trials may be required or the approval may be suspended or withdrawn or additional safety warnings may have to be included on the label.

Adverse events or unforeseen side effects may also potentially lead to product liability claims being raised against the Company as the developer of the products and sponsor of the relevant clinical trials.

### **Mitigating activities**

The Company conducts extensive pre-clinical and clinical trials which test for and identify any adverse side effects. A robust pharmacovigilance plan is in place to ensure any safety issues are identified and reported. A Risk Evaluation and Mitigation Strategy (REMS) has also been developed to ensure that the benefits of Cat-SPIRE are balanced against any risks. Insurance is in place to cover product liability claims which may arise during the conduct of clinical trials.

### **Commercial success**

The Company's products may not be commercially successful.

The Company may not be able to sell its products profitably if reimbursement from third-party payers such as private health insurers and government health authorities is restricted or not available because for example it proves difficult to build a strong enough economic case based on the burden of illness and population impact. Third-party payers are increasingly attempting to curtail healthcare costs by challenging the prices that are charged for pharmaceutical products and denying or limiting coverage and the level of reimbursement. Moreover, even if the products can be sold profitably, they may not be accepted by patients and the medical community.

Alternatively, the Company's competitors – many of whom have considerably greater financial and human resources – may develop safer or more effective products or be able to compete more effectively in the markets targeted by the Company. New companies may enter these markets and novel products and technologies may become available which are more commercially successful than those being developed by the Company.

Factors that may undermine the Company's efforts to commercialise its products include: the inability to train and retain effective sales and marketing personnel; a failure to persuade prescribers to prescribe products; and higher costs of marketing and promotion than are anticipated by the Company.

### **Mitigating activities**

In the context of Cat-SPIRE, thorough market research will be carried out prior to product launch and the findings will be used to generate effective and appropriately resourced marketing campaigns. These will emphasise the attributes which differentiate the product from its competitors, for example its short dosing regimen and lack of side effects. A disease awareness campaign will be developed and implemented. Pricing and reimbursement studies and health economic data will be used to support the value proposition which will be presented to payers.

### **Supply chain**

The Group relies on third-party contractors for the supply of key materials and services. Problems with contractors, such as technical issues, contamination, and regulatory actions may lead to delays or even loss of supply or inadequate supply of these materials and services either prior to launch or thereafter. Some materials may only be available from one source, as is currently the case for the peptides contained in the Cat-SPIRE product, and regulatory requirements may make substitution costly and time-consuming, particularly where the product is regulated as a biologic.

### **Mitigating activities**

Audits of sub-contractors are routinely conducted according to procedures set out in the Company's quality system. Dual sourcing is being investigated where this is practicable. Manufacturing sites are well established regulator approved facilities.

# Risks and risk management continued

## Research and development risks

The Company may not be successful in its efforts to use and expand its technology platform, ToleroMune®, to build a pipeline of products and develop marketable products. This would have a material impact on the long-term success of the business. Failure of programs could result from lack of internal resources or capabilities, or from not obtaining the desired pre-clinical and clinical results.

## Mitigating activities

The Company has recruited highly experienced R&D executives. Projects are closely monitored against goals and regularly reported to the Senior Management Team and the Board, and external resources are retained where this is deemed appropriate. In addition, the Company will seek, through business development activity, to identify opportunities which would expand and diversify its portfolio.

## Intellectual property, know how, and trade secrets

The Company may be subject to challenges relating to the validity of its patents. If these challenges are successful then the Company may be exposed to generic competition. Four of the Company's granted European patents (three patents relevant to Cat-SPIRE and a fourth relevant to Ragweed-SPIRE) are currently the subject of opposition proceedings at the European Patent Office by anonymous opponents. If the opponents are successful then the patent protection for these products in Europe will be reduced or even eliminated.

Alternatively, the Company may be sued for infringement of third-party patent rights. If these actions are successful then it may have to pay substantial damages and potentially remove its products from the market.

Such litigation, particularly in the US, involves significant costs and uncertainties.

It is possible that the Company will not be able to secure intellectual property protection, or sufficient protection, in relation to products which are acquired or in development. Similarly, a failure by the Company to maintain or renew key patents would lead to the loss of such protection. In both cases the potential of the Company to earn revenue from its products could be compromised as it would be less difficult for third parties to copy the products.

The Company may rely upon know how and trade secrets to protect its products and maintain a competitive advantage. This may be especially important where patent protection is limited or lacking. Conversely, the Company may be subject to claims that its employees or agents have wrongfully used or disclosed the confidential information of third parties which could lead to damages or injunctions which affect particular products.

The Company licenses certain intellectual property rights from third parties. If the Company fails to comply with its obligations under these agreements it may enable the other party to terminate the agreement. This could impair the Company's freedom to operate and potentially lead to third parties preventing it from selling certain of its products.

## Mitigating activities

Detailed responses have been filed to the four oppositions commenced against the Company. The oral hearing relating to the European Ragweed-SPIRE patent took place in November 2014 and the Opposition Division of the European Patent Office upheld the validity of the patent and rejected all grounds of opposition. Important products are covered by more than one patent family and oppositions to patents are defended using carefully selected external patent attorneys and lawyers. A robust system is in place which ensures patents are renewed on time. Third-party patent filings are monitored to ensure the Company continues to have freedom to operate and oppositions against third-party patents are filed where this is considered expedient. Confidential information (both of the Company and belonging to third parties) is protected through use of confidential disclosure agreements with third parties, and suitable provisions relating to confidentiality and intellectual property exist in the Company's employment contracts. Licences are monitored for compliance with their terms.

## Organisational capabilities and capacity

The Company may be unable to successfully implement its plans for growth if it does not attract and retain employees with the requisite capabilities and experience, in appropriate numbers. More particularly, the rapid development which is envisaged may place unsupportable demands on the Company's current managers and employees, particularly if it cannot attract sufficient new employees. The Company depends on the skills and experience of its current management team and employees, and is generally subject to competition for, and may fail to retain, skilled personnel.

Existing employees, investigators, consultants and commercial partners may engage in misconduct or improper activities, including non-compliance with regulatory standards and laws.

Where the Company acquires complementary technologies, products, or businesses it may not be able to integrate those acquisitions effectively or realise their expected benefits.

The Company may be vulnerable to disruption and damage as a result of failures of its computer systems.

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**Mitigating activities**

The Company has budgeted for substantial growth in headcount over the next three years. The management team has already been strengthened in the course of 2014 by the recruitment of a General Counsel, Chief Medical Officer, Chief Commercial Officer, and Vice President of Human Resources. Remuneration packages are competitive, and incentive plans based on the contingent award of shares, are in place to attract, motivate and retain staff.

Disciplinary and whistleblowing policies exist to address misconduct by employees and officers, and committee structures have been established with the Contract Research Organisations instructed by the Company, to monitor and manage the conduct of the Company's clinical trials.

The Senior Management Team has considerable experience of integrating acquired businesses and assets, and will assess opportunities using conservative assumptions.

To address IT risks, a disaster recovery plan has been developed. Data is backed up daily on off-site servers and the Company operates from two physically separate sites.

**Financial operations**

The Group has incurred significant losses since its inception and anticipates that it will continue to do so, at least until it is able to launch products.

Foreign exchange fluctuations may adversely affect the Group's results and financial condition. The Group records its transactions and prepares its Financial Statements in pounds sterling, but a significant proportion of its expenditure is in US dollars, Canadian dollars, Swiss Francs, or Euros.

Adverse decisions of regulators, including tax authorities, or changes in tax treaties, laws, or the interpretation of those laws, could reduce or eliminate research and development tax credits which the Group, and its joint venture Adiga Life Sciences Inc. currently receive in the United Kingdom and Canada respectively.

**Mitigating activities**

The Group has prepared a detailed budget for the next three years and, if it achieves its objectives, this shows that the current business plan is sufficient to support the business through to commercialisation of Cat-SPIRE.

Forward purchases of foreign currencies are made when exchange rates are favourable to provide for expenditure in those currencies. Markets are monitored on a daily basis.

If tax credits are lost in the future then action would be taken to reduce discretionary expenditure in order to help ensure there remained sufficient cash to support the business through to commercialisation of Cat-SPIRE.

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The Strategic report on pages 01 to 33 has been approved by the Board.

**Steven Harris**  
Chief Executive Officer

# Board of Directors

## **1 Dr Francesco Granata Chairman, 64**

Dr Francesco Granata, joined Circassia as Chairman on 1 September 2013. He is also Chairman of the Nomination Committee.

Francesco is senior advisor at Warburg Pincus International LLC. Prior to this he was Executive Vice President at Biogen Idec Inc., and before that he was Group Vice President and President responsible for Canada and major European markets at Schering-Plough Corporation. Previously, he served as Regional President for Northern Europe and also Middle East and Africa at Pfizer Inc., and as Managing Director of Pharmacia & Upjohn Inc. in Italy. He is currently a Board member of Italfarmaco SpA, a leading Italian pharmaceutical group that operates in both the pharma and chemical sectors; BSP Pharmaceuticals srl, an Italian CMO; Prismic Pharmaceuticals Inc., a US based medical food company; and a member of the strategic advisory committee at Lupin, a leading Indian global pharmaceutical company. Prior to his career in industry, Francesco practised as a medical doctor specialising in cardiology. He holds a degree in medicine and surgery from the University of Pavia, Italy, and was formerly a member of the Board of the European Federation of Pharmaceutical Industry Associations.

## **2 Steven Harris Chief Executive Officer, 48**

Steven Harris co-founded Circassia on 19 May 2006 and has led the Company as Chief Executive Officer since then.

Steven has extensive experience of leading specialty pharmaceutical companies. Prior to co-founding Circassia, he was a founding member of the management team that grew Zeneus Pharma Limited into a successful specialty pharmaceutical company and managed its acquisition by Cephalon Inc. (now part of Teva Pharmaceutical Industries Limited). Prior to this he served for seven years as Chief Financial Officer of PowderJect Pharmaceuticals plc and was a key member of the management team which grew the organisation from a private biotechnology company to the world's fifth largest vaccines business, before it was acquired by Chiron Corporation in 2003. He holds a BSc from Southampton University and is a Chartered Accountant and a member of the Institute of Chartered Accountants of England and Wales (ICAEW).

## **3 Julien Cotta Chief Financial Officer, 51**

Julien Cotta joined Circassia as Chief Financial Officer on 5 January 2012 and was appointed a Director on 26 November 2013.

Julien has significant financial management experience in the healthcare industry. Prior to joining Circassia, he was Chief Financial Officer of the Finnish medical technology company, Inion Oy, and before this Group Financial Controller at Whatman plc (now part of GE Healthcare). Previously, he served as Vice President of Financial Accounting at Chiron Corporation and Group Financial Controller at PowderJect Pharmaceuticals plc (prior to its acquisition by Chiron in 2003). Before this he held senior financial management roles at Scotia Pharmaceuticals Limited, and Sanofi S.A., having begun his pharmaceutical career as a sales representative at Merck Sharpe & Dohme Corporation. He completed his accountancy training at Coopers & Lybrand (now PricewaterhouseCoopers LLP). Julien holds a BSc (Hons) in Pharmacology from University College London and is a Chartered Accountant and a member of the ICAEW.

## **4 Dr Rod Hafner Director and Senior Vice President Research & Development, 49**

Dr Rod Hafner joined Circassia on 1 March 2007 and became Senior Vice President of Research & Development and a Director on 10 March 2008.

Rod has many years of experience at a senior level in the life sciences industry and is a named inventor on numerous granted patents and patent applications. Before joining Circassia, he led the UK operating company of the Scandinavian drug delivery business, OptiNose AS (now OptiNose US Inc.) and prior to that was Director of Programme Management and Vice President of Research & Development Portfolio Management at PowderJect. Other roles have included Head of Project Management at Cortecs International Limited and positions at Wyeth Pharmaceuticals, Inc. (now Pfizer) and The Procter & Gamble Company. Rod has led Circassia's research and development function since joining in 2007. He has a BSc (Hons) in Biochemistry from Edinburgh University and a PhD in Biochemistry from the University of Cambridge.

## **5 Dr Jean-Jacques Garaud Senior Independent Non- Executive Director, 59**

Dr Jean-Jacques Garaud, the Senior Independent Non-Executive Director joined Circassia as a Non-Executive Director on 1 November 2012. He is Chairman of the Remuneration Committee and a Member of the Audit Committee and the Nomination Committee.

Jean-Jacques has extensive pharmaceutical research and development experience having held senior roles at companies in the United States and Europe. Until recently he was Global Head of Pharma Research and Early Development and a member of the extended corporate executive committee at F Hoffmann-La Roche Inc. having joined the company in 2007 as Global Head of Pharmaceutical Development and Chief Medical Officer. Prior to this he was Global Head of Clinical Research and Development and Global Head of Exploratory Development at Novartis and held roles at Schering-Plough Corporation, Rhone-Poulenc Rorer Limited and Merrell Dow Pharmaceuticals Inc. Before working in industry, Jean-Jacques practised medicine at the Claude Bernard Hospital in Paris, France after gaining his medical degree at the University of Paris. He is a Non-Executive Director at MedDay SAS, Inaterys SAS and Polyphor Limited and Chairman of the Inserm Transfert Initiatives Investment Committee.

## **6 Dr Tim Corn Independent Non-Executive Director, 63**

Dr Tim Corn joined Circassia as an Independent Non-Executive Director on 1 August 2006. He is a Member of the Audit Committee, the Remuneration Committee, and the Nomination Committee.

Tim was previously Chief Medical Officer at EUSA Pharma (Europe Limited), an international division of Jazz Pharmaceuticals plc. In the course of his career, he has played a key role in the regulatory approval of numerous products in the fields of neurology and oncology. Tim qualified in medicine at King's College Hospital, London, after gaining an MSc in Biochemistry from Imperial College, London. He has been a Fellow of the Faculty of Pharmaceutical Medicine since 1996 and a Fellow of the Royal College of Psychiatrists since 1998. He is Chairman of the Board of Trustees of the Neuro Foundation and a Non-Executive Director of Remeuron plc.

## **7 Russell Cummings Non-Executive Director, 50**

Russell Cummings joined Circassia as a Non-Executive Director on 25 January 2007. He is Chief Executive Officer of Imperial Innovations Group plc, having joined as Chief Investment Officer in 2006. From 2003 to 2006, he held roles at the growth equity and venture capital firm Scottish Equity Partners LLP, and prior to this spent 16 years at the international venture capital company 3i Group plc, latterly as a Director in its UK Technology Group. He holds a BSc (Eng) in Mechanical Engineering from Imperial College, London. Russell is also a Non-Executive Director of Nexxon Limited.

## **8 Paul R Edick Non-Executive Director, 59**

Paul Edick joined Circassia as an Independent Non-Executive Director on 3 April 2013.

Until 18 November 2014 Paul was Chief Executive Officer of Durata Therapeutics Inc. which was acquired by Actavis plc. Prior to this he was Chief Executive Officer of Ganix Pharmaceuticals Inc., a Warburg Pincus investment vehicle disbanded in June 2010. From 2006 to 2008 he served as Chief Executive Officer of MedPointe Healthcare Inc., following a period as President. After MedPointe was acquired by Meda in late 2007, he continued in office until mid-2008 and then acted as a consultant for the rest of the year. Earlier roles included a number of senior positions at GD Searle & Company, and Pharmacia Corporation (now Pfizer Inc.), following the acquisition of Searle by Pharmacia, culminating in his appointment as Pharmacia's Group Vice President and President, Asia Pacific/Latin America Operations. Paul holds a BA in Psychology from Hamilton College. He currently sits on the board of NewLink Genetics Corporation and was previously chairman of the Danish biotechnology company, Life Cycle Pharma A/S.

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**9 Cathrin Petty**

**Non-Executive Director, 41**

Cathrin Petty joined Circassia as a Non-Executive Director on 8 March 2010. She was Chair of the Audit Committee throughout 2014.

Cathrin is Co-Head of EMEA Healthcare at J.P. Morgan, and has extensive senior level experience of the life sciences industry. She has held a number of non-executive roles, most recently at ICON plc and at the NHS Strategic Health Authority for Greater London. She has previously worked as Special Partner at Vitruvian Partners LLP, Partner at Apax Partners LLP, and at Schroders and Schroder Ventures Life Sciences. She holds an MA in Natural Sciences from the University of Cambridge and a post-graduate Diploma in Management Studies from the Judge Institute, Cambridge.

**10 Charles Swingland**

**Non-Executive Director, 62**

Charles Swingland is a Non-Executive Director and co-founder of Circassia.

Charles was General Counsel, Company Secretary and Deputy Chairman of Circassia from May 2006 until March 2014. Prior to founding Circassia with Steven Harris, he was a Director and General Counsel at Zeneus Pharma Limited from 2004 to 2006 and before this was Executive Director, General Counsel and Company Secretary at PowderJect, until it was sold to Chiron in 2003. Before working in industry, Charles practised as a lawyer in the City of London for over 15 years.

**11 Lota S Zoth**

**Independent Non-Executive Director, 55**

Lota Zoth was appointed to the Board as an Independent Non-Executive Director and a member of the Remuneration Committee on 9 February 2015.

She will become Chair of the Audit Committee on 27 February 2015. She is an experienced Board member, and has significant financial experience gained in a number of global public companies. Most recently she was CFO at MedImmune, and previously held senior positions at PSINet, Sodexo Marriott, PepsiCo and Ernst & Young. She is currently a Non-Executive Director at Hyperion Therapeutics Inc, NewLink Genetics Corporation and Orexigen Therapeutics Inc. She is also Chair of Aeras, a non-profit product development organisation focused on tuberculosis and funded by The Bill and Melinda Gates Foundation, and until 2014 was a Non-Executive Director at privately-held biopharmaceutical company Ikaria Inc. She has over 30 years' experience as a Certified Public Accountant, and holds a Bachelor of Business Administration from Texas Tech University.

# Corporate governance

## Dear Shareholders

On behalf of the Board, I am pleased to present Circassia's Corporate governance report for the year ended 31 December 2014. It describes how the Board and its Committees apply the principles of good corporate governance set out in the UK Corporate Governance Code issued by the Financial Reporting Council on 28 September 2012 (the "Code"). The Code became effective for the Group as a result of its listing on the London Stock Exchange on 18 March 2014.

High standards of corporate governance are fundamental to our business and are implemented and supported through appropriate internal policies and procedures. The responsibility for ensuring this framework is effective lies with the Board, and we are constantly striving to improve standards while building a successful company.

One area on which the Board has focused in particular since Listing relates to its composition. As we explained at the time of Listing, the Board believes that at this critical point in its development the Group benefits from the knowledge and experience of the full range of its Non-Executive Directors but had been looking to appoint a further independent Non-Executive Director with recent and relevant financial experience, to Chair the Audit Committee. I am therefore pleased to report that on 9 February 2015, Ms Lota Zoth joined the Board as an Independent Non-Executive Director, and will be appointed Chair of the Audit Committee on 27 February 2015.

Maintaining good communication with our Shareholders is extremely important to us. During the year, Steve Harris, our CEO has held a number of meetings with investors and presented at several conferences which were attended by existing and potential Shareholders.

I, together with other members of the Board, will be present at our Annual General Meeting on 20 May 2015 and I would encourage all Shareholders to participate.

**Dr Francesco Granata**  
Chairman

## Corporate governance report

### Compliance with the UK Corporate Governance Code

The UK Corporate Governance Code (the "Code") sets out the principles of good practice in relation to corporate governance which should be followed by companies with a listing on the London Stock Exchange. The Code is published by the Financial Reporting Council ("FRC") and can be found on their website ([www.frc.org.uk](http://www.frc.org.uk)).

The principles of the Code are divided into five sections. Each section sets out the main principles relating to Leadership; Effectiveness; Accountability; Remuneration; and Relations with Shareholders. This report explains how Circassia has applied these principles.

The Directors support high standards of corporate governance. However, the Company has not complied with the recommendations of the Code that at least half the Board should comprise independent Non-Executive Directors and that the Audit Committee should comprise only independent Non-Executive Directors. In addition, for a short part of the year the Remuneration and Nomination Committees did not comply with the membership requirements for independence. However, following the membership changes on the Remuneration and Nomination Committees, they complied with the membership requirements of the Code for independence. Following the membership change on the Audit Committee on 27 February 2015, the Audit Committee will comply with the membership requirements of the Code for independence.

Following Admission the Board consisted of ten members. Of these, three were independent Non-Executive Directors for the period 1 January 2014 to 14 September 2014 and from 15 September 2014 to 31 December 2014, two of these three were considered by the Board to be independent. Of the other seven Directors, for the period from 1 January to 18 March 2014 there were two Non-Executive Directors not considered independent, four Executive Directors, and the Chairman (who was independent on appointment). From 18 March 2014 to 31 December 2014 there were three Non-Executive Directors not considered independent, three Executive Directors, and the Chairman. Charles Swingland was an Executive Director for the period 1 January 2014 to 18 March 2014. On 18 March, he became a Non-Executive Director. The Audit Committee has consisted of two independent Non-Executive Directors and one Non-Executive Director.

The Board believes that at this point in the Group's development it is important that it has access to the expertise and knowledge of all current Non-Executive Directors. Moreover, as was its stated intention in the Prospectus, the Company has been successful in recruiting an additional independent Non-Executive Director with recent and relevant financial experience who will join the Audit Committee and replace Cathrin Petty as Committee Chair. From 9 February 2015 the Board consisted of three independent Non-Executive Directors (as well as the Chairman) and from 27 February 2015 will comply with the recommendation that the Audit Committee should comprise only independent Non-Executive Directors.

The composition of the three Board Committees throughout the year and the extent to which their composition complied with the provisions of the Code, was as follows:

— **Nomination Committee**

The Code requires that a majority of the members of the Committee should be independent Non-Executive Directors and the Committee should be chaired by the Chairman or an independent Non-Executive Director. The Committee was constituted on 21 February 2014 with three members: Dr Francesco Granata (Chairman and Chair of the Committee); Dr Tim Corn and Mr Paul Edick. For the period from 21 February to 14 September all three members of the Committee were considered to be independent. Mr Edick ceased to be independent from 15 September, but remained on the Committee. He resigned from the Committee on 25 November and Dr Jean-Jacques Garaud, who is independent, was appointed to the Committee on the same date. Therefore, for the period from 15 September 2014 to 25 November 2014 a majority of the members of the Committee, excluding the Chairman, were not independent and from the appointment of Dr Jean-Jacques Garaud on 25 November 2014 all members of the Committee (excluding the Chairman) were independent.

— **Remuneration Committee**

The Code requires that the Committee should comprise a minimum of three Directors, all of whom should be independent. The Committee was re-constituted on 21 February 2014 with three members: Dr Jean-Jacques Garaud (Chair of the Committee); Dr Tim Corn and Mr Paul Edick. For the period from 21 February to 14 September all three members of the Committee were considered to be independent. However, Mr Edick ceased to be independent from 15 September, but remained on the Committee until 9 February 2015 when he was replaced by Ms Lota Zoth, who is independent. Therefore, for the period from 15 September 2014 to 9 February 2015 the composition of the Committee did not comply with the requirements of the Code insofar as they relate to the number of independent Directors. On 9 February, following the appointment of Ms Lota Zoth, the Committee complied with the membership requirements of the Code for independence.

— **Audit Committee**

The Code requires that the Committee should comprise a minimum of three Directors, all of whom should be independent. The Committee was constituted on 21 February 2014 with three members: Ms Cathrin Petty (Chair of the Committee); Dr Tim Corn; and Dr Jean-Jacques Garaud. Ms Petty has recent and relevant financial experience but is not considered to be independent. She will remain on the Committee until 27 February 2015 when she will be replaced by Ms Lota Zoth, who is independent. Therefore, for the period from 21 February 2014 to 27 February 2015 the composition of the Committee does not comply with the requirements of the Code insofar as they relate to the number of independent Directors. Following the appointment of Ms Lota Zoth on 27 February 2015, the Audit Committee will comply with the membership requirements of the Code for independence.

The Board confirms that in all other respects, the Group has fully complied with the principles of the Code throughout the year to 31 December 2014 and up to the date of this report. Details of Directors' remuneration, as required by the Code and Part 4 to Schedule 8 of the Large and Medium-sized Companies and Groups (Accounts and Reports) (Amendment) Regulations 2013, are set out in the Remuneration Committee report.

The Group's Auditor, PricewaterhouseCoopers LLP, is required to review whether this Corporate governance statement properly reflects the Group's compliance with certain provisions of the Code and to report any non-compliance. The Group confirms that no report of non-compliance has been made other than in respect of the matters identified above in relation to Board composition.

**Leadership**

**The role of the Board**

The Board is responsible for the leadership and long-term success of the business. It has a schedule of matters which are reserved for its review. These include the review and approval of strategic plans, financial statements and budgets, financing, acquisitions and disposals, major capital expenditure, dividend policy, and Executive remuneration and appointments.

At each meeting, the Board will assess the progress of the Group when measured against its objectives, particularly those which relate to its clinical trials programme, and will review financial performance against the budget.

**Roles and responsibilities**

The Board is currently composed of the Chairman, three Executive Directors, and seven Non-Executive Directors. The biographies of the members of the Board who served during the year to 31 December 2014 are set out in the Corporate governance report.

The Executive Directors have direct responsibility for the business operations of the Company. The Non-Executive Directors, by virtue of their wide range of industry experience and skills, bring an informed view to the decision making process.

The roles of the Chairman and Chief Executive Officer are clearly delineated. This division of responsibilities has been set out in writing and approved by the Board.

**Chairman**

Dr Francesco Granata, Chairman, is responsible for the leadership of the Board and its effectiveness by ensuring that:

- the agenda for meetings is appropriate, and the Board is provided with the information it needs for high quality decision making in a timely fashion;
- the Board plays a full and constructive role in shaping the strategy of the Group;
- the Board environment is productive and utilises the skills and experience of all members;
- the Board complies with the appropriate standards of corporate governance;
- the Committees are properly structured and resourced;
- the performance of the Board, its committees, and individual Directors are evaluated each year; and
- there is effective communication with Shareholders.

The Chairman and the Non-Executive Directors meet in the absence of the Executive Directors as appropriate.

**Chief Executive Officer**

Steven Harris, Chief Executive Officer, is responsible for the day to day management of the Company and for formulating and implementing the strategy which has been reviewed and approved by the Board. He is also responsible for ensuring effective communication with Shareholders, brokers, and analysts.

# Corporate governance continued

## Senior Independent Non-Executive Director

Dr Jean-Jacques Garaud has been Senior Independent Non-Executive Director since 21 February 2014. He works closely with the Chairman to resolve any significant issues which may arise and is responsible for the annual evaluation of the Chairman's performance, for leading the other Non-Executive Directors in their oversight of the Chairman, and for ensuring there is a clear division of responsibilities between the Chairman and the Chief Executive Officer. He is available to communicate directly with Shareholders if they have concerns which cannot be resolved through the normal channels of the Chairman, Chief Executive Officer, or Chief Financial Officer.

## Non-Executive Directors

The role of the Non-Executive Directors, and of the Committees of which they are members, is to scrutinise the performance of management, satisfy themselves that the financial and risk control mechanisms are robust, and determine appropriate levels of Executive pay. They have wide ranging experience of industry and bring their judgement to bear in the decision making process of the Board. Their seniority and range of skills ensure that no one individual can dominate this process.

## Board Committees

The Board has three Committees: the Audit Committee; the Nomination Committee; and the Remuneration Committee, to which it delegates specific responsibilities. The reports of these Committees and details of their composition form part of the Corporate governance report.

Each Committee has full terms of reference which have been approved by the Board and also appear on the website at [www.circassia.co.uk](http://www.circassia.co.uk). These terms of reference are reviewed annually. The Board provides the Committees with sufficient resources, including access to external advisers, as may be required in order to fulfil their roles.

## Board meetings

The Board aims to meet at least five times during the year. Additional meetings may be arranged where urgent matters arise. These additional meetings may be held by telephone.

The table below sets out the attendance of the Directors, while they were Board members, at scheduled meetings which occurred during the year to 31 December 2014.

	Committee Memberships <sup>6</sup>	Independent status	Board	Nomination Committee	Audit Committee	Remuneration Committee
<b>Executive Directors</b>						
Steven Harris	n/a	n/a	7 (7)	3 (3) <sup>1</sup>	3 (3) <sup>1</sup>	4 (4) <sup>1</sup>
Julien Cotta	n/a	n/a	7 (7)	3 (3) <sup>2</sup>	3 (3) <sup>2</sup>	4 (4) <sup>2</sup>
Rod Hafner	n/a	n/a	7 (7)	–	–	–
Charles Swingland <sup>3</sup>	n/a	n/a	3 (3)	–	–	–
<b>Non-Executive Directors</b>						
Francesco Granata	N (Chair)	Yes	7 (7)	3 (3)	–	–
Jean-Jacques Garaud	A, R (Chair), N <sup>4</sup>	Yes	7 (7)	–	3 (3)	4 (4)
Tim Corn	N, A, R	Yes	7 (7)	3 (3)	3 (3)	4 (4)
Russell Cummings	–	No	7 (7)	–	–	1 <sup>1</sup>
Paul R Edick	N <sup>5</sup> , R	Yes <sup>7</sup> No <sup>8</sup>	7 (7)	3 (3)	–	4 (4)
Cathrin Petty	A (Chair)	No	7 (7)	–	3 (3)	1 <sup>1</sup>
Charles Swingland	–	No	4 (4)	–	–	–

<sup>1</sup> By invitation

<sup>2</sup> In the capacity of Secretary to the Committee

<sup>3</sup> Charles Swingland was an Executive Director from 1 January 2014 to 18 March 2014 and was appointed a Non-Executive Director on 18 March 2014

<sup>4</sup> Jean-Jacques Garaud was appointed to the Nomination Committee on 25 November 2014

<sup>5</sup> Paul Edick resigned from the Nomination Committee on 25 November 2014

<sup>6</sup> N = Nomination Committee, R = Remuneration Committee, A = Audit Committee

<sup>7</sup> Independent for the period 1 January 2014 to 14 September 2014

<sup>8</sup> Not independent for the period 15 September 2014 onwards



### Board activity

The Board's main activities during the course of the year included:

- Preparation for and oversight of the Company's successful Initial Public Offering of its shares on the Main Market of the London Stock Exchange;
- Reviews of the progress of the Group's clinical trials;
- Reviews of the progress of business and corporate development activity and opportunities;
- Assessment of the financial performance against the budget for FY 2014;
- Approval of the budget for FY 2015 – 2017;
- Completion of a Board evaluation exercise;
- Approval of terms of reference for the committees.

### Effectiveness

#### Independence

The Board reviews the independence of its Non-Executive Directors each year. For the period 1 January to 20 February 2014, excluding the Chairman, four of the nine Board members were Non-Executive Directors who were considered by the Board to be independent. For the period 21 February to 14 September, three out of nine were considered to be independent and from 15 September to 31 December two out of nine were considered to be independent.

Dr Tim Corn, Paul R Edick, and Dr Jean-Jacques Garaud have all participated in the Company's unapproved share option scheme in the past. However, this scheme is unrelated to performance, such participation was historic, and no further share options will be granted to any of these Directors. The Board has therefore determined that it regards Dr Tim Corn, Paul R Edick and Dr Jean-Jacques Garaud as independent Non-Executive Directors within the meaning of "independent" as defined in the Code for the period 1 January 2014 to 14 September 2014. From 15 September 2014, Mr Paul Edick was determined by the Board to no longer be independent as Mr Edick's wife began employment with the Group as Chief Commercial Officer.

The Board also carefully reviews any actual or potential conflicts of interest that may arise due to the commercial interests of Non-Executive Directors and they are required to make a declaration in respect of any such situations. The Board can confirm that no such conflicts of interest arose in the year. As is noted in their respective biographies, Cathrin Petty is an employee of JP Morgan and Russ Cummings is an employee of Imperial Innovations. For these reasons, Russ Cummings and Cathrin Petty are considered by the Board not to be independent.

The Code indicates that a tenure of more than nine years as a Non-Executive Director could be relevant to a determination of independence. It is confirmed that none of the Independent Non-Executive Directors have served for more than nine years.

The Board further confirms that Dr Francesco Granata was independent upon his appointment.

#### Appointments to the Board

The procedure for appointment of new Directors to the Board is formal, rigorous and transparent. The process is led by the Nomination Committee which comprises the Chairman and independent Non-Executive Directors. Shortlisted candidates are interviewed by members of the Committee before a recommendation is made to the Board.

### Diversity

The Board recognises the value of diversity at all levels of the Group. The Group has an Equal Treatment, Equal Opportunities and Diversity policy which extends to the Board. This provides that the Group will take all reasonable steps to employ and promote employees on the basis of their abilities and qualifications without regard to age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race (including colour, nationality and ethnic or national origins), religion or belief, sex and/or sexual orientation. The Group appoints, trains, develops and promotes on the basis of merit and ability alone.

### Induction and training

Upon appointment, each Director receives a comprehensive induction package which includes written materials relevant to their responsibilities. In addition, meetings are organised with other Board members and with members of the Company's management team.

All Directors have direct access to the advice of the Company Secretary. Whenever it is considered necessary, the Company Secretary can arrange the appointment of professional advisers at the Group's expense to assist Board members in their roles.

Directors receive frequent updates on commercial developments affecting the business as well as regulatory and legislative changes. Directors are invited, during the annual evaluation procedure, to identify any training which they feel might benefit them.

### Information

In advance of each Board Meeting, Directors receive a full agenda and a comprehensive set of papers which include commercial and functional reports. A procedure is in place to ensure that these materials are delivered to the Board in a timely fashion. Senior employees of the business regularly attend meetings in order to enhance the Non-Executive Directors' understanding of current issues and give them the opportunity to ask detailed questions.

### Commitment

The Board is satisfied that the other commitments of the Chairman and Non-Executive Directors – which are set out in their biographies – leave them with sufficient time to diligently perform their role for the Group.

### Performance evaluation

Formal Board evaluations are carried out once a year, and informal evaluations are carried out on a continuing basis throughout the year. The formal evaluation commences with the circulation of a written questionnaire which has been prepared by the Company Secretary with the assistance of the Auditors. This invites Directors to rate and comment on the performance of the Board in a number of areas, including the conduct of Board meetings; the standard and timeliness of information; the balance of skills of the members of the Board; the roles and responsibilities of individual Directors; and compliance with good corporate governance practices. A detailed, anonymised analysis of these responses is then prepared by the Company Secretary and reviewed and discussed by the Board.

The Board intends to subject itself to an external review every third year.

### Re-election

All Directors have service contracts which are capable of termination on giving a fixed period of notice. In the case of the Executive Directors this notice period is six months and in the case of the Non-Executive Directors and Chairman it is three months.

All Directors are subject to re-election by Shareholders on an annual basis.

# Corporate governance continued

## Accountability

The Board acknowledges its duty to present a fair, balanced and understandable view of the Group's position and prospects. A description of the Group's business model is contained in the Strategic report. The Statement of Directors' responsibilities sets out information regarding the Directors' responsibility to prepare financial statements. The Independent Auditors' report includes a statement by the Auditor on its reporting responsibilities.

The role of the Audit Committee is set out in detail in the Audit Committee report.

The Board is responsible for determining the significant risks which the Group is prepared to take in order to attain its strategic objectives, and keeps the risk management procedures and internal controls of the business under regular review. The Board confirms that it is satisfied that the current procedures and controls are sufficient to ensure compliance with the Code.

After taking advice from the Audit Committee, the Board is able to confirm that the Annual report and accounts, taken as a whole is fair, balanced, and understandable and provides the information necessary for Shareholders to judge the Group's strategy, business model and performance.

## Risk management system

The risk management system is set out in the Corporate governance report. The system is designed to manage risks, not to eliminate them completely, and can only provide a reasonable degree of assurance against material misstatement or loss. Inherent in the concept of reasonable assurance is the recognition that the cost of a control procedure should not exceed its anticipated benefits. The significant risks facing the Group are set out in the Strategic review.

The Board confirms that it has conducted a review of the Group's risk management and internal controls systems, including financial, operational and compliance controls and has found them to be effective.

## Internal controls

The Audit Committee reviews the Group's financial controls on an annual basis and makes recommendations to the Board where improvements are required. The efficacy of non-financial control systems are reviewed by the full Board as required by the Turnbull guidance.

Circassia's primary risk control systems are as follows:

## Management structure

- There is a management structure with clear lines of responsibility and accountability. Employees are recruited when they have the appropriate skills and experience to perform their intended roles.
- The Board sets the overall strategy and reviews the performance of the Group.
- The Group's Senior Management Team, chaired by the Chief Executive Officer, is responsible for day to day operations. Other team members include the Chief Financial Officer and senior staff members from the business. This team meets weekly.

## Written policies and procedures

- There are documented quality procedures which ensure regulatory compliance. Regular reviews take place to ensure standards are maintained and the Company is fully prepared for a regulatory inspection. The Head of Quality and her team monitor internal and external (Contract Research Organisation) compliance with Good Manufacturing Practice, Good Clinical Practice, and Good Laboratory Practice and organise training for employees.
- There are controls in place which determine how financial information is validated, consolidated and reviewed.
- There are specific controls on expenditure. Material investments or capital expenditure must be approved by the Board. Normal expenditure is controlled by setting limits which are determined by the CEO and CFO within a general framework approved by the Board.
- Detailed management accounts are prepared on a monthly basis and provided to the Board. Accompanying reports will explain any variances between these results and the budget.
- R&D Committee meets on a weekly basis to review performance of the various clinical trials and implement action plans to prevent delays.
- The Patents Committee meets regularly to assess the scope of protection provided by pending and granted patents, organise the defence of granted patents, and plan new filings where appropriate. This group also manages registered trade marks.
- There are physical and electronic procedures in place to ensure the security and integrity of data and confidential information. A Data Protection Policy is in place.
- An established policy exists for share dealing by employees or connected persons.
- There is a Health and Safety Officer and a documented Health and Safety Policy.
- There is a Whistleblowing Policy which enables employees to communicate concerns regarding improper activity to a trusted individual who is not their line manager or a member of the operational management team.
- There is a documented anti-bribery and corruption policy.
- There is a Disclosure Committee, as required by the Market Abuse Directive, comprising the Chief Executive Officer, Chief Financial Officer, and the Head of Corporate Communications. This group maintains an Insider List recording employees and external parties who may have access to inside information. Individuals are notified of their addition to and removal from the list and are appraised of their responsibilities.

No failure of controls or breach of internal policies was recorded during the year to 31 December 2014 and up to the date of this report.

## Remuneration

The Board has adopted a remuneration policy which it believes is sufficient to attract, retain, and motivate Directors of the quality required to run the Group successfully, but which does not result in payment of more than is necessary for this purpose. A significant proportion of Executive Directors' pay is linked to corporate and individual performance. Full details of the policy are set out in the Remuneration Committee report.

## Relations with Shareholders Dialogue with Shareholders

The Board maintains regular communication with Shareholders. Meetings between material Shareholders and the Executive Directors take place throughout the year. The Chairman and Senior independent Non-Executive Director and other Directors are available to meet with major Shareholders on request.

All meetings with Shareholders are held in a manner which ensures price sensitive information which has not been made available to Shareholders generally is protected from disclosure.

The Chief Executive Officer and the Chief Financial Officer give annual and six-monthly presentations to institutional investors, analysts, and the media. These presentations are available on the website. Annual and Interim reports and all press releases are also published on the website as are the terms of reference of the three Board committees. Paper copies of the report and accounts are mailed to those Shareholders who have elected to receive them.

The Directors receive a report from the Corporate Communications department at each Board Meeting giving information on material changes in shareholdings and collating feedback from the Company's brokers and investors.

## Annual General Meeting

The AGM provides an opportunity for all Shareholders to meet Board members and have the opportunity to ask about the proposed resolutions and the business in general.

In addition, the Chairs of the Audit, Nomination, and Remuneration Committees will be present at the AGM to answer Shareholders' questions.

Notice of the AGM is posted to Shareholders not less than 20 working days prior to the date of the AGM and is also available to Shareholders on the website at [www.circassia.co.uk](http://www.circassia.co.uk). The letter accompanying the Notice will include details of the proposed resolutions and an explanation of their content.

At the AGM the number of proxy votes cast for, against, or abstaining from each resolution will be disclosed. Results of voting are posted on the website and announced to the market as soon as possible after the AGM.

The Group does not currently consider it appropriate to introduce mandatory poll voting on all resolutions put to the Shareholders but will keep this position under review.

## Audit Committee report

### Dear Shareholder

On behalf of the Board I am pleased to present Circassia's Audit Committee report for the year ended 31 December 2014.

The Audit Committee is the key independent oversight Committee at Circassia. It monitors and reviews the effectiveness of the Group's risk management framework and internal controls.

This report sets out how the Committee has discharged its responsibilities under the UK Corporate Governance Code (the "Code"). It also contains a summary of the activities of the Committee throughout the year.

### Cathrin Petty

Chair of the Audit Committee

26 February 2015

## Responsibilities

The Committee has responsibility for monitoring the integrity of the financial statements of the Group, and for reviewing the effectiveness of the Group's internal control systems and risk management systems, including reviewing its risk profile.

Accordingly, the Committee performs a detailed review of the interim and annual financial statements, considering whether the accounting policies have been applied properly and consistently and whether the disclosures made in the Annual report and accounts are compliant with financial reporting standards, and with corporate governance and regulatory requirements.

The Committee also manages the relationship with the external Auditors on behalf of the Board. It monitors the independence of the Auditor and reviews the effectiveness of the audit procedure. The Committee makes recommendations to the Board regarding the appointment of the external Auditors and reviews their terms of engagement. The Committee has access to the services of the external Auditors and, if necessary, may appoint external accounting and legal advisers to assist it with its work.

The Committee's terms of reference are available on the website. They cover issues such as membership, the frequency of meetings, together with requirements for a quorum and the right to attend meetings. The duties of the Committee as set out in the terms of reference include financial and regulatory reporting; internal controls; internal audit; external audit; risk management; and reporting responsibilities.

## Membership

The names of the members of the Audit Committee, their dates of appointment, and the number of meetings attended during the year are set out in the table below:

Member	Date of appointment	Meetings attended (held)
C Petty	21 February 2014	3 (3)
T Corn	21 February 2014	3 (3)
J-J Garaud	21 February 2014	3 (3)

The Committee was chaired throughout the year by Cathrin Petty, who has recent and relevant financial experience.

## Corporate governance continued

The Code provides that all members of the Audit Committee should be independent Non-Executive Directors. Cathrin Petty is not considered by the Board to be independent and so the Company has not complied with the provisions of the Code in this respect throughout the year. However Lota Zoth has been appointed as an additional independent Non-Executive Director. Ms Zoth was appointed to the Board on 9 February 2015 and will be appointed as the new Chair of the Audit Committee on 27 February 2015. Ms Zoth has significant recent and relevant financial experience. She is currently a Non-Executive Director, Compensation Committee Member and the Audit Committee Chair at Hyperion Therapeutics Inc and NewLink Genetics Corporation. She is also a Non-Executive Director and the Audit Committee Chair at Orexigen Therapeutics Inc., She was also Chief Financial Officer and Senior Vice President at MedImmune, LLC from 2004 to 2007. The Audit Committee will therefore be in compliance with the Code's requirement for membership of independent Non-Executive Directors from 27 February 2015 following the appointment of Lota Zoth.

The Company Secretary acts as the Secretary to the Committee. The CEO attends Committee meetings at the invitation of the Chair. The Chairman meets with the external Auditors at least once a year in the absence of management.

A summary of the matters considered by the Committee since the last financial statements is shown in the table below and explained in further detail in the subsequent text:

### Financial reporting

During the year to 31 December 2014 and up to the date of this report, the Committee reviewed the interim management statements, the Interim report and accounts for the period ended 30 June 2014, and the preliminary announcement and Annual report and accounts for the year ended 31 December 2014.

### Significant accounting matters

The Committee considered the following key accounting issues, judgements and disclosures during the course of the year:

- Completeness of accruals;
- Measuring the fair value of awards under new share option schemes and the related accounting treatment;
- Accounting for IPO costs;
- Accounting for the changes in the capital structure as a result of the IPO; and
- Going concern and liquidity.

Area of review	Activities undertaken
Financial reporting	Review of the interim and full year results. Consideration of whether the Annual report is fair, balanced, and understandable. Review of the external Auditors' reports on the interim and full year results. Review of trading updates. Review of significant accounting issues (see below). Review of anticipated changes in accounting standards and their impact. Review of the going concern basis of preparation of the financial statements.
External Auditor	Review of external Auditors' independence. Review of Auditors compliance with ethical and professional guidance on audit partner rotation. Assess effectiveness of audit process. Recommend re-appointment of Auditors.
Risk management and internal control	Review of risk management systems, internal controls, and anti-corruption and anti-bribery procedures. Review of internal compliance monitoring. Review of the Whistleblowing policy.
Governance	Review of the Committee's terms of reference.

### **Completeness of accruals**

The Group is a clinical-stage specialty biopharmaceutical group focused on the development and commercialisation of a range of immunotherapy products for the treatment of allergies.

The research operations of the Group are outsourced to Clinical Research Organisations (CROs) who submit applications for payment at regular intervals throughout the clinical trials.

During the year research and development costs for the Group totalled £38.8 million of which £4.5 million was accrued at year end in relation to invoices not yet received.

The appropriate timing and accuracy of these costs between financial periods requires close monitoring. Submissions for payment by suppliers do not always correspond to the periods in which the underlying activities occurred, making the underlying calculations for the accruals more complex.

### **Measuring the fair value of awards under new share option schemes and the related accounting treatment**

The accounting treatment for share options can be complex and involve judgement regarding the appropriate treatment and calculation of fair values. Prior to the IPO, Circassia had a small number of share options under EMI approved schemes which gave rise to a charge of £98,000 in the year ended 31 December 2013. Following the IPO process a further 2,206,611 share options were issued under a new performance share scheme.

The newly granted share options were valued under the Black Scholes model or Monte Carlo model dependent on the performance vesting conditions.

The fair value determined drives the charge recognised by the Company.

The IPO has increased the value of the shares in the Group used in the share options calculation and therefore has increased the share options charge. As a result the risk of a material error or misstatement is significantly increased. In addition the new scheme includes market vesting performance conditions for some of the options granted which makes the fair value calculation more complex.

As a result there is a risk that the fair value of options could be measured incorrectly.

### **Accounting for IPO costs**

The Group incurred £9.6 million of costs in completing the IPO in March 2014. Incremental costs that are directly attributable to the equity transaction are accounted for through equity, with the remaining costs through the income statement. There is an element of judgement and allocation in this treatment.

Management performed an allocation of IPO related transaction costs by considering the type of expenditure incurred and whether it meets the criteria to be considered directly attributable to the issue of shares. From this determination, £9.4 million was attributed to equity. There is a risk that these costs do not qualify as directly attributable to the equity transaction and, as such, should have been recorded in the income statement.

### **Accounting for the changes in the capital structure as a result of the IPO**

Immediately prior to the admission of shares onto the main market for listed securities of the London Stock Exchange, the Company converted Preference shares into Ordinary shares and issued liquidation shares to the Preference Shareholders. Loan notes were also converted into Ordinary shares.

On 18 March 2014 each 10p Ordinary share was subdivided into 125 x 0.08p Ordinary shares. In addition, new Ordinary shares were issued as part of the admission onto the London Stock Exchange on 18 March.

Share options have also been exercised by employees during the year under the EMI option scheme.

As a result of these transactions, the capital structure of the Company has been significantly altered. There is a risk that the accounting and disclosure implications of these agreements have not been correctly reflected in the financial statements.

### **Risk management and internal control**

The Board has overall responsibility for the review of the Group's risk management framework and the level of risk which is acceptable in order to achieve its strategic objectives. The Committee, on behalf of the Board, undertakes the detailed monitoring of the risk management framework and system of internal controls and reports to the Board on their suitability and efficacy annually.

In order to discharge its duties in this respect, the Committee receives and reviews reports from the Group's management team. The Committee continues to assess what is an acceptable level of risk in key areas, and the best strategy for mitigating those risks given the cost and time constraints which exist.

### **Whistleblowing**

A confidential whistleblowing procedure has been put in place to enable employees to raise concerns regarding possible improprieties in relation to financial or other matters. This procedure has been communicated to all staff. The Committee has reviewed these arrangements and is satisfied that the current procedure allows for proportionate and independent investigation of such disclosures, and for appropriate follow up actions to be taken. In accordance with the current policy, concerned employees may raise matters directly with the Chair of the Committee.

### **UK Bribery Act**

The Group has an anti-corruption and anti-bribery policy which has been communicated to all staff. This policy ensures full compliance with the UK Bribery Act 2010. The policy extends to carrying out due diligence on new key business partners who are judged to be acting on behalf of the Group in high risk areas.

### **Internal audit**

This year the Committee considered whether there is a need for an internal audit function and concluded that, given the scale of operations at this time, it is not currently necessary. The Board accepted this recommendation. This decision will be kept under review.

### **External audit**

The Group's external Auditor, PricewaterhouseCoopers LLP (PwC), is engaged to express its opinion on the Group's financial statements.

# Corporate governance continued

## Effectiveness

The effectiveness of the external audit process is reviewed annually by the Committee. This review encompasses an examination of the independence, qualifications, capabilities, and remuneration of the Auditor. If issues are identified which may affect the effectiveness of the process then actions will be agreed. No such issues were identified in the year to 31 December 2014 or up to the date of this report.

At the end of the audit for the year ended 31 December 2014 the Committee formally evaluated the performance of PwC. To conduct this evaluation the Committee completed a questionnaire to assess robustness of the audit process, quality of its delivery, quality of reporting, and quality of the individuals and service. Moreover, the Committee takes into account the quality of its interactions with the Auditor in forming a view on their effectiveness.

## Independence

The Committee is responsible for reviewing the independence and objectivity of the external Auditor. Each year the external Auditor confirms its policies for ensuring its independence and provides the Committee with written confirmation that they continue to be independent.

The Committee pays careful regard to whether non-audit work is carried out by the Auditor so as to ensure that the provision of such additional services does not impair its independence or objectivity. A formal process exists for approving the use of the Auditor for non-audit work. There is no automatic restriction on the Auditor providing such services, but the Auditor should not be appointed to provide non-audit services which might put the Auditor in the position of auditing its own work or create a mutual interest between the Group and the Auditor or result in the Auditor acting as an advocate, manager, or employee of the Group.

PwC undertook non-audit services for the Group in the course of the year to 31 December 2014 which are summarised in the table below. These services were provided in compliance with the policy outlined above and no conflicts of interest were considered to have arisen.

Committee approval required?	Nature of work	Fees £'000
	Other assurance services	223
No	Taxation	5
No	Treasury services	10

The total fees paid to the Auditor are shown in note 7 of the financial statements. The other assurance services during the year related to procedures performed as reporting accountant on historical financial information. The Committee believes that the use of PwC was appropriate in the circumstances and that independence was preserved as the nature of the non-audit services was such that the external Auditor was best placed to perform this work due to their skills and experience and the fees paid were insignificant in the context of the overall revenues earned by PwC.

In summary, the Committee confirms that the Group has received an independent audit service in the year to 31 December 2014 and up to 26 February 2015.

## Audit partner rotation

PwC adheres to a rotation policy which complies with the ethical standards of the Audit Practices Board (the "APB") and the audit partner is rotated every five years. Simon Ormiston, the current audit partner was appointed for the year ended 31 December 2014 and is not due for rotation until completion of the year ended 31 December 2018.

## Tendering

PwC has been the Company's Auditor since the year ended 31 December 2007. The Committee is actively monitoring the EU audit directive and ongoing discussions in this area at the Financial Reporting Council, the EU and the Competition Commission. In view of the changes to the regulatory requirements relating to mandatory audit tendering, the Committee expects to conduct an audit tender at the latest prior to contracting the 2017 year-end audit.

## Reappointment

Each year the Committee considers the reappointment of the external Auditor and makes a recommendation to the Board. In doing so the Committee considers the effectiveness and independence of the external Auditor. The judgement of the Committee is that PwC continues to deliver an effective and independent service.

Accordingly, the Committee has recommended to the Board that PricewaterhouseCoopers LLP be reappointed as the Company's Auditor for a further year. This recommendation has been accepted by the Board.

The Committee will continue to monitor the changes proposed by the UK Competition Commission and European Commission in respect of Auditor services and re-tendering.

## Committee evaluation

A review of the effectiveness of the Committee was carried out in November 2014 as part of the process of evaluating Board effectiveness.

## Cathrin Petty

Chair of the Audit Committee

26 February 2015

## Nomination Committee report

### Dear Shareholder

On behalf of the Board, I am pleased to present Circassia's Nomination Committee report for the year ended 31 December 2014. The key objective of the Committee is to ensure the Board is made up of a range of individuals who together have the appropriate mixture of skills and experience to lead the Group.

During the year the Committee considered and made recommendations to the Board regarding the appointment of Charles Swingland as a Non-Executive Director. Shortly after the year end, the Committee considered and recommended the appointment of Lota Zoth as an independent Non-Executive Director, and recommended that she be appointed as Chair of the Audit Committee in the place of Cathrin Petty and be appointed to the Remuneration Committee.

There follows a summary of the activities of the Committee.

### Dr Francesco Granata

Chair of the Nomination Committee

26 February 2015

### Responsibilities

The Committee must review the size, structure, and composition of the Board and the Committees evaluating the balance of skills, experience, independence, and diversity of the Board as a whole. On the basis of this evaluation it will then make recommendations to the Board on any appointments. As part of this process, the Committee will prepare a description of the skills, experience and other characteristics required, and identify through a transparent procedure, individuals who are capable of filling those roles.

The Committee also plans for the orderly succession of Directors to the Board and recommends to the Board the membership and chairmanship of the Audit and Remuneration Committees.

The full terms of reference of the Committee can be found on the website.

### Membership and meetings

The Committee was constituted on 21 February 2014 and comprised Dr Tim Corn, Paul Edick and Dr Francesco Granata, the Chairman. All members of the Nomination Committee (excluding the Chairman) were considered by the Board to be independent from the period 21 February 2014 to 14 September 2014. On 15 September 2014, Mr Paul Edick was no longer considered by the Board to be independent. Mr Paul Edick resigned on 25 November 2014 and Dr Jean-Jacques Garaud was appointed in his place. From 25 November 2014 to 31 December 2014, all members of the Nomination Committee (excluding the Chairman) were considered by the Board to be independent. The Committee complied with the requirements of the Code for independence for the periods 21 February 2014 to 14 September 2014 and from 25 November 2014 following the resignation of Paul Edick and the appointment of Dr Jean-Jacques Garaud.

The Committee met three times during the year ended 31 December 2014 and all members were present at each meeting. A summary of the composition and attendance of the Committee is as follows:

Member	Date of appointment	Meetings attended (held)
Francesco Granata	21 February 2014	3 (3)
Tim Corn	21 February 2014	3 (3)
Paul Edick	21 February 2014	3 (3)

The Company Secretary acts as Secretary to the Committee. The Chief Executive Officer may attend meetings by invitation.

The Committee is empowered to obtain external professional advice to assist in the performance of its duties. During the year the Committee has retained the services of executive search firm Spencer Stuart as explained below.

### Activities

The principal activities during the year were:

- Review of the structure, size and composition of the Board (including skills, experience, independence, knowledge and diversity);
- Appointments of Board members and Committee members; and
- Annual performance evaluation of the Board, its members and its Committees.

The status of the Non-Executive Directors with respect to compliance with the independence requirements of the code is set out in the Corporate governance report.

During the year the Committee appointed the executive search firm Spencer Stuart to assist it in identifying a further independent Non-Executive Director and on 9 February 2015, Lota Zoth was appointed to the Board and on 27 February 2015 will be appointed as the new Chair of the Audit Committee.

### Appointment procedure

There is a formal and transparent procedure by which new Directors are appointed to the Board. Suitable candidates are proposed either by existing Board members or by an external search firm. The Committee will then assess whether the candidate has the requisite skills and experience for the role, sufficient time to perform it, and that their appointment will preserve or improve the balance of skills, experience and knowledge of the Board.

The Committee has worked closely with Spencer Stuart, a well-reputed executive search firm, in the course of the year in order to recruit an additional independent Non-Executive Director with financial experience who would be capable of chairing the Audit Committee. A list of candidates was prepared by the search firm and reviewed by the Committee. From this long list the Committee produced a short list of candidates for interview. At the conclusion of this process the Committee recommended to the Board that Lota Zoth be appointed.

Ms Zoth has been appointed under a service contract which provides for a notice period of three months.

### Diversity

The Company has an Equal Treatment, Equal Opportunities and Diversity policy which extends to the Board. The appointment procedure described above is carried out in full compliance with this policy.

### Chairman's commitments

In accordance with provision B.3.1 of the Code, it is confirmed that the Chairman's other significant commitments are as disclosed in the biography which appears in the Corporate governance report and that they have not changed in the course of the year.

### Committee evaluation

A review of the effectiveness of the Committee was carried out in November 2014 as part of the process of evaluating Board effectiveness.

### Dr Francesco Granata

Chairman of the Nomination Committee

26 February 2015

# Remuneration Committee report

## Annual statement

### Dear Shareholder

On behalf of the Board, I am pleased to present Circassia's Remuneration Committee report for the year ended 31 December 2014. This report will be presented for the consideration and approval of Shareholders at the Annual General Meeting on 20 May 2015.

This report complies with the regime set out in Part 4 to Schedule 8 of the Large and Medium-sized Companies and Groups (Accounts and Reports) (Amendment) Regulations 2013 (the Regulations), the UK Corporate Governance Code ('the Code') and the Listing Rules. Accordingly it consists of three parts: (i) an Annual statement which summarises the key issues and explains the business context in which the Committee's main decisions were taken; (ii) an unaudited Directors' remuneration policy report which describes the current and future executive remuneration policy, and which will be put to a binding Shareholder vote at the AGM on 20 May 2015; and (iii) the Annual report on remuneration which sets out details of and rationale for the remuneration provided to the Group's Directors during the 2014 financial year. This latter report is subject to an advisory vote at the AGM.

### Remuneration policy

The remuneration policy which has been put to Shareholders for approval, promotes the long-term sustainable success of the Group with the aim to reward Executive Directors for performance, and for delivery of Shareholder value judged against transparent and demanding criteria. As part of this policy a significant proportion of potential remuneration is linked to the achievement of corporate and individual performance indicators.

A new annual bonus plan was implemented for Executive Directors and management at Senior Vice President level for 2014, which in line with best practice included an element being deferred into shares for three years and subject to forfeiture.

Share incentive arrangements have been in effect since Admission which will closely align the interests of the Executive Directors with those of Shareholders. The earliest date of vesting under these schemes falls 3 years after grant subject to the achievement of performance conditions. Details of the awards made under these schemes to the Executive Directors are set out in the Annual report on remuneration.

In addition, shareholding guidelines have been introduced for the Executive Directors and management at Senior Vice President level.

The Committee believes that the emphasis on performance-related pay, the use of bonus deferral, annual long-term incentive awards and mandatory share ownership guidelines, creates a clear focus on sustainable performance, avoids paying more than is necessary and maintains an ongoing alignment between Executive Directors and Shareholders.

### Performance and reward

As described in the Strategic report, the Group has strengthened the human resources of the organisation and progressed its clinical programmes, with encouraging results noted to date.

The bonus arrangements consisted of an element of up to 100% of salary linked to the achievement of annual developmental and operational goals and an element of up to 50% of pre-IPO salaries linked to the success of the IPO. The strong operational developments since the Company's IPO in March 2014, were achieved at the same time as meeting pre-set financial targets. The overall performance assessment resulted in annual bonus payments of between 88% and 95% of salary for the Executive Directors. This has been paid in February as a mix of cash and deferred shares.

For the element of the bonus in relation to the IPO process, the Committee determined bonuses of between 23% and 50% of pre-IPO salary would be payable. These payments were made in cash in January 2015. The Committee is satisfied that the total variable pay outcome is a fair reflection of corporate and individual performance throughout 2014.

### Application of policy for 2015

The Remuneration policy set out in this report will be put to Shareholders for approval at the Annual General Meeting on 20 May 2015.

The salaries of the Executive Directors were reviewed with effect from 1 January 2015 and increased in line with increases to the general workforce of 3%.

We welcome Shareholder feedback on these matters and hope that you will be able to support our policy and its application at the forthcoming AGM.

### Jean-Jacques Garaud

Remuneration Committee Chairman

26 February 2015

## Directors' remuneration policy report (DRP)

This section of the Remuneration Committee sets out the remuneration policy for the Company and has been prepared in accordance with Part 4 of the Regulations. It also takes into account the provisions of the Code and the views of our major Shareholders. The policy report describes the policy which will be put to a binding Shareholder vote at the AGM on 20 May 2015. If approved, the Policy will formally take effect from that date and is expected to remain in force until the AGM in 2018.

### Remuneration philosophy

The potential levels of remuneration have been set so that they are competitive against those comparator companies from which the Group will compete for talented individuals.

The Committee's goal is to design and implement a remuneration policy which will support and reward Executive Directors for delivering the Group's strategic objectives and ultimately creating value to Shareholders, whilst adhering to good corporate governance and reflecting best practice. To achieve this, the balance of remuneration is focused on variable performance-related pay. In particular, to reflect the long-term nature of the Group's development pipeline, variable pay is more heavily weighted towards long-term sustainable value creation through the use of share incentive plans. When combined with significant levels of share ownership guidelines, this creates an alignment between Executive Directors and Shareholders with a longer term view.

The Committee annually reviews the operation of the variable incentive plans to ensure they are operating within an acceptable risk profile and that they do not inadvertently encourage any economic, social or governance issues.

### Remuneration policy

The total remuneration for each Executive Director is made up of the following elements:

- Salary;
- Benefits;
- Annual bonus;
- Long-term incentive awards; and
- Pension.

Recovery and withholding provisions will apply to the bonus and long-term incentive arrangements in specific circumstances as determined appropriate by the Remuneration Committee.



Salary	Benefits	Annual bonus
<b>Purpose and link to strategy</b> Provides fixed remuneration in-line with market rates that reflects the responsibilities of the role undertaken and the experience of the individual.	<b>Purpose and link to strategy</b> Provides market competitive, yet cost-effective employment benefits.	<b>Purpose and link to strategy</b> To incentivise and recognise execution of the business strategy and personal objectives on an annual basis.
<b>Operation</b> Set at an approximately mid-market level and reviewed annually taking into account individual responsibilities, performance, inflation, and market rates. The Committee will also consider the pay and employment conditions in the wider workforce when determining Executive Directors' salaries. Salary increases are normally effective from 1 January each year.  Salaries are periodically benchmarked against a relevant peer group of UK listed companies with similar market capitalisations and operations.	<b>Operation</b> For Executive Directors this includes private medical insurance, travel and life insurance.  Other employment benefits may be provided from time to time on similar terms as those of other employees.  If the Company introduces an all-employee share plan, Executive Directors will be eligible to participate on the same terms as other employees.  If an Executive Director is based outside the UK additional benefits and assistance with relocation may be provided which reflect local market norms or legislation.	<b>Operation</b> Annual bonus performance targets are set at the start of the year by the Board and performance against objectives is assessed by the Remuneration Committee.  Bonuses will be paid as a mix of cash and deferred shares. Until the share ownership guidelines are reached, the bonus will be payable as 50% cash and 50% shares. Thereafter, the bonus will be payable as 75% cash and 25% shares.  Bonus shares are deferred for three years from the date of the award and are subject to forfeiture.  Recovery and withholding provisions will apply in the event of mis-statement of results, error in performance calculation or gross misconduct  A dividend equivalent, if payable, will be payable in cash when the shares vest.
<b>Maximum potential value</b> The current base salaries are set out in the Implementation of policy section of the Annual report on remuneration.  There is no formal maximum limit, but increases are generally in line with those of the wider workforce.  Larger increases may be permitted to reflect a change in responsibilities or a significant increase in the scale or complexity of the role.	<b>Maximum potential value</b> There is no formal maximum limit as the value of insured benefits will vary from year to year based on the cost from third-party providers.	<b>Maximum potential value</b> The maximum payable for all Executive Directors is 100% of salary.
<b>Performance metrics</b> The overall performance of the individual and Company is a key determinant for salary increases.	<b>Performance metrics</b> None.	<b>Performance metrics</b> Research and development, business development, financial and operational targets are set at the start of the year by the Board. The weighting for each performance measure is determined by the Remuneration Committee and may vary for each Executive Director according to their role and reflecting their objectives for the year.  Details of the performance measures for the current year are provided in the Annual report on remuneration.

Performance share plan (PSP)	Pension
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## Remuneration Committee report continued

<p><b>Purpose and link to strategy</b> To align the interests of management with Shareholder interests and to enhance retention of staff.</p> <p>To incentivise and recognise achievement of longer term business objectives and sustained superior Shareholder value creation.</p>	<p><b>Purpose and link to strategy</b> To provide a competitive and cost-effective, level of retirement provision.</p>
<p><b>Operation</b> Conditional awards or options from the Performance Share Plan are granted annually. The awards vest provided certain performance conditions, which have been approved by the Board, are achieved over a period of at least three years.</p> <p>Performance targets are set at the start of each performance period.</p> <p>Recovery and withholding provisions apply for reasons of mis-statement of results, error in performance calculation or gross misconduct.</p>	<p><b>Operation</b> Executive Directors are eligible to join a defined contribution pension scheme.</p> <p>Alternatively a cash supplement (or a combination of contribution and cash) can be made.</p>
<p><b>Maximum potential value</b> Annual awards of up to the following each year are granted to Executive Directors:</p> <ul style="list-style-type: none"> <li>— CEO 150% of salary</li> <li>— Other 125% of salary</li> </ul> <p>In special circumstances (such as a recruitment) an award of up to 300% of salary is permitted.</p> <p>Dividend equivalents may be payable on vested awards.</p>	<p><b>Maximum potential value</b> The maximum contribution, cash supplement (or combination thereof) payable by the Company is 15% of salary.</p>
<p><b>Performance metrics</b> Awards are currently subject to a combination of relative Total Shareholder Return (TSR) and clinical progression timelines for Executive Directors.</p> <p>No more than 25% of the maximum award will vest for achieving the threshold performance level.</p> <p>The weighting of these performance measures, the choice of comparators for relative Total Shareholder Return (TSR) and/or the inclusion of additional performance measures will be reviewed annually by the Committee, reflecting the strategic objectives and priorities of the following three year performance period.</p> <p>If the Committee determines a material change to the performance measures used for future awards is required to reflect a change in strategy, this would only be made following appropriate dialogue with the Company's major Shareholders.</p>	<p><b>Performance metrics</b> None.</p>

<b>Share ownership guidelines</b>
<b>Purpose and link to strategy</b> To align Executives with Shareholders and provide an ongoing incentive for continued performance.
<b>Operation</b> Only shares which are fully owned with no outstanding vesting criteria count towards the shareholding guideline.  Executive Directors will be required to retain half of any post-tax awards which vest under long-term incentive plans, until the share ownership guideline has been satisfied.
<b>Maximum potential value</b> Executive Directors are required to build and maintain the following minimum level of shareholding: <ul style="list-style-type: none"> <li>— CEO 150% of salary</li> <li>— Other Executive Directors 100% of salary</li> </ul>
<b>Performance metrics</b> None.

The Committee operates the annual bonus and Performance Share Plan (PSP), in accordance with their rules, and where relevant, the Listing Rules. To maintain an efficient administrative process, the Committee retains the following discretions relating to remuneration:

- a. the eligibility to participate in the plans;
- b. the timing of grant of awards and any payments;
- c. the size of awards and payments (subject to the maximum limits set out in the policy table above and the respective plan rules);
- d. the determination of whether the performance conditions have been met;
- e. determining a good or bad leaver under the terms of the plan;
- f. dealing with a change of control or restructuring of the Group;
- g. adjustments required in certain capital events such as rights issues, corporate restructuring, events and special dividends; and
- h. the annual review of performance conditions for the annual bonus plan and PSP.

In certain exceptional circumstances, such as a material acquisition/divestment of a Group business, which mean the original performance conditions are no longer appropriate, the Committee may adjust the targets, alter weightings or set different measures as necessary, to ensure the conditions achieve their original purpose and are not materially less difficult to satisfy.

#### **Existing awards**

Awards which were granted prior to the Company's IPO are set out in the Annual report on remuneration (ARR).

These awards remain eligible to vest, based on their original terms and will be disclosed in the relevant ARR as required.

# Remuneration Committee report continued

## Performance measures

The rationale behind each performance measure currently used in the Performance Share Plan and how it is calculated is as follows:

Performance measure	Rationale
Relative TSR performance	<p><b>Recognises outperformance and delivery of relative value to Shareholders</b></p> <p>Relative total Shareholder return is currently measured against the FTSE 250 Index. This was chosen as a comparator group because it represents similar sized companies, is subject to less volatility than a smaller peer comparator group and is transparent for both Shareholders and participants.</p> <p>The Committee will review on an annual basis the continued appropriateness of the comparator group.</p>
Clinical and key strategic business objectives	<p><b>Recognises the importance of R&amp;D to future business growth</b></p> <p>The growth of the Company and therefore delivery of value to investors is dependent on achievement of certain key clinical timelines.</p>

The annual bonus is designed to drive the achievement of the Company's clinical and strategic business targets. These targets are agreed by the Board and selected because of their importance in value creation for Shareholders. Objectives are weighted for Executives in proportion to the degree of responsibility for control and achievement of that objective. The weightings are agreed by the Remuneration Committee.

## Remuneration on recruitment

The Remuneration Committee determines the remuneration package of new Executive Directors. Each element of an Executive Director's remuneration is set out below:

<b>Salary</b>	<p>Base salary will be determined based on the role, experience of the individual and the current market rate.</p> <p>It may be considered necessary to appoint a new Executive Director on a below market salary (e.g. to reflect limited plc board experience). In such circumstances phased increases above those of the wider workforce may be required over an appropriate time period, to bring the salary to the desired market level, subject to the continued development in the role.</p>
<b>Benefits</b>	<p>Benefits provided would be in line with those of current Executive Directors.</p> <p>Where required to meet business needs, reasonable relocation support will be provided.</p> <p>In addition if it becomes necessary to appoint a new Executive Director from outside the UK, additional benefits may be provided to reflect local market norms or legislation.</p>
<b>Annual bonus</b>	<p>The ongoing annual bonus maximum will be in line with that outlined in the policy table for existing Executive Directors, pro-rated to reflect the period of service.</p> <p>Depending on the timing or nature of an appointment it may be necessary to set different initial performance measures and targets for the first year of appointment.</p>
<b>Long-term incentive awards</b>	<p>PSP awards are granted in line with the policy outlined for existing Executives. Any ongoing annual award is limited to that of the current CEO.</p> <p>An award may be made shortly following an appointment (provided the Company is not in a prohibited period).</p> <p>For internal appointments, existing awards will continue on their original terms.</p>
<b>Pension</b>	<p>A company contribution or cash supplement up to the maximum as outlined for current Executive Directors.</p>
<b>Buy-out awards</b>	<p>To enable the recruitment of exceptional talent, the Committee may determine that the buy-out of remuneration forfeit from a prior employer is necessary. Where possible, any replacement remuneration will be offered on a like-for-like basis with the forfeited awards and may be in the form of cash or shares and depending whether the award forgone has similar performance conditions, may or may not be subject to performance conditions. The value of any buy-out will be limited to the value of remuneration forfeit. Where appropriate, such awards will be granted under existing share plans, however, the Remuneration Committee will have discretion to make use of the flexibility to make awards under exemptions in the Listing Rules.</p>

Fee levels for the Chairman and Non-Executive Directors will be set at a level that is consistent with those of existing Non-Executive Directors.

### Exit payment policy

The Group does not have a policy of fixed term employment contracts, however, all Directors put themselves forward for re-election at the Annual General Meeting. Notice periods for Executive Directors' employment contracts are 6 months and 3 months for the Chairman's and Non-Executive Directors' letters of appointment from either party.

The following policies and payments apply in the event that an Executive Director's employment is terminated.

Remuneration element	Exit payment policy
Current service contracts	Termination by notice: 6 months. Redundancy: 6 months annual salary payable (reduced accordingly if part of the notice period is worked). Retirement, death and ill-health, injury or disability: No termination payment.
Future service contracts	Termination by notice: up to 12 months' notice, with a provision to make a payment in lieu of notice for base salary and benefits only. Any payment will be phased on a monthly basis and would be subject to mitigation, whereby the payment made can be reduced (including to zero) if appropriate alternative employment is found. Redundancy: annual salary payable for the relevant notice period (reduced accordingly if part of the notice period is worked). Retirement, death and ill-health, injury or disability: No termination payment.
Long-term incentives and deferred bonuses	PSP awards are governed by the Plan Rules as approved by Shareholders. Likewise, the deferred bonus awards are subject to the same leaver provisions. These are summarised below. <b>Termination by notice:</b> Unvested awards lapse on cessation. <b>Redundancy, retirement, ill health, injury or disability, transfer of employment outside of the Group or change of control, or any other reason the Committee determines:</b> Unvested awards will vest either on the normal vesting date or if the Board decides, immediately on the participant ceasing to be in employment. Awards will vest subject to the extent the performance condition has been met, as determined by the Remuneration Committee. Awards will be pro-rated for time, unless the Committee determines otherwise. <b>Death:</b> Unvested awards will vest on the date of death. Awards will be pro-rated for time, unless the Committee determines otherwise. <b>Change of control:</b> Unvested awards will vest on the date of the takeover. Awards will vest subject to the extent the performance condition has been met, as determined by the Remuneration Committee. Awards will be pro-rated for time, unless the Committee determines otherwise.
Annual bonus	<b>Termination by notice by individual:</b> if an individual serves notice and the termination date falls before 31 December, the bonus is forfeited. If notice is served between 1 January following the year in which the bonus was earned and the payment date, the employee may (as determined by the Remuneration Committee) receive the entire bonus payable in cash, subject to malus and clawback provisions. <b>Redundancy, retirement, death and ill-health, or any other reason the Committee determines:</b> if the termination date falls during the financial year, pro-rated for service rendered and subject to performance. If it falls after the end of the financial year the bonus is payable in cash based on actual results on the normal bonus payment date. <b>Termination by notice:</b> Not normally paid, however, at the Committee's discretion, if the termination date falls during the financial year, a bonus may be paid pro-rata for service rendered and subject to performance over the full financial year and normally paid on the normal payment date. If it falls after the end of the financial year bonus is payable based on actual results on the normal bonus payment date.
Benefits	These will normally continue to apply until the termination date.
Pension	Contributions by the Company will normally continue to apply until the termination date.
Additional payments	The Committee will make payment of any statutory entitlements as necessary. In addition the Committee will retain the discretion to make settlement or to compromise a claim in connection with a termination of any Executive Directors as necessary. Reasonable legal and outplacement costs will be met if deemed necessary.

# Remuneration Committee report continued

## Service contracts

The following Executive Directors have service agreements with the Company which were effective from 18 March 2014 as follows:

Name	Position	Date of joining
Steven Harris	Chief Executive Officer	19 May 2006
Rod Hafner	Senior VP of R&D	1 March 2007
Julien Cotta	Chief Financial Officer	5 January 2012

The notice period for each Executive Director is 6 months and all Executive and Non-Executive Directors put themselves forward for re-election at the Annual General Meeting.

The key terms for the Letters of Appointment for Non-Executive Directors are set out below:

Name	Notice period	Date of joining
Dr Francesco Granata	3 months	1 September 2013
Dr Tim Corn	3 months	1 August 2006
Russell Cummings	3 months	25 January 2007
Paul Edick	3 months	3 April 2013
Dr Jean-Jacques Garaud	3 months	1 November 2012
Cathrin Petty	3 months	8 March 2010
Charles Swingland	3 months	31 May 2006
Lota Zoth	3 months	9 February 2015

Copies of the service contracts and letters of appointment are available for inspection at the registered office.

## Statement of consideration of employees' pay and remuneration conditions elsewhere in the Group

The Company does not formally consult with employees on the matters of Executive Director remuneration. However, the Committee is made aware of employment conditions in the wider Group.

The same broad principles apply to the remuneration policy for both Executive Directors and the wider employee population. However, the remuneration for Executive Directors has a stronger emphasis on performance-related pay than for other employees. In particular the following approach is used:

- Salaries, benefits and pensions are compared to appropriate market rates and set at approximately mid-market level with allowance for role, responsibilities and experience.
- When setting salary levels for the Executive Directors, the Committee considers the salary increases provided to other employees and in particular those based in the UK.
- An annual bonus plan is available to all employees and is based on business and individual performance.
- Awards from the Performance Share Plan are made to all current employees including Executive Directors.

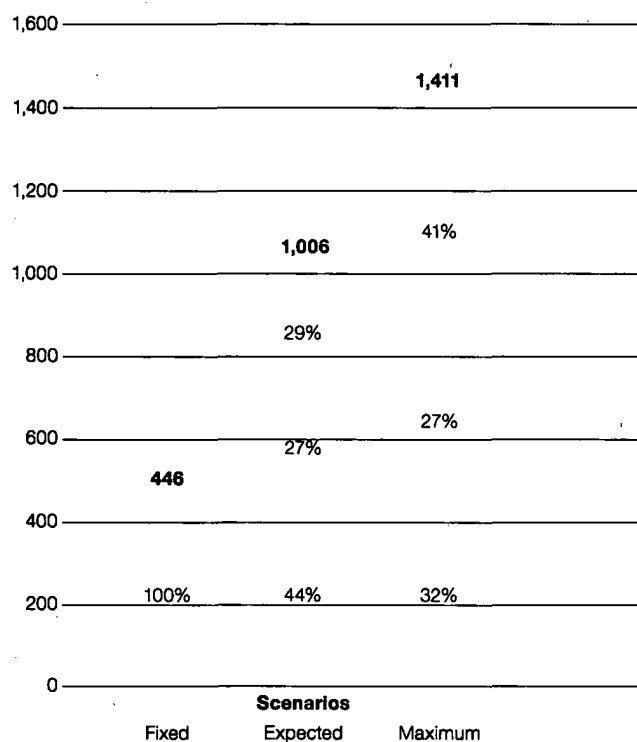
## Scenarios

The charts set out for illustrative purposes only, what annual remuneration the Company expects the Directors to obtain if performance levels are below threshold, meet expectations or exceed the maximum targets.

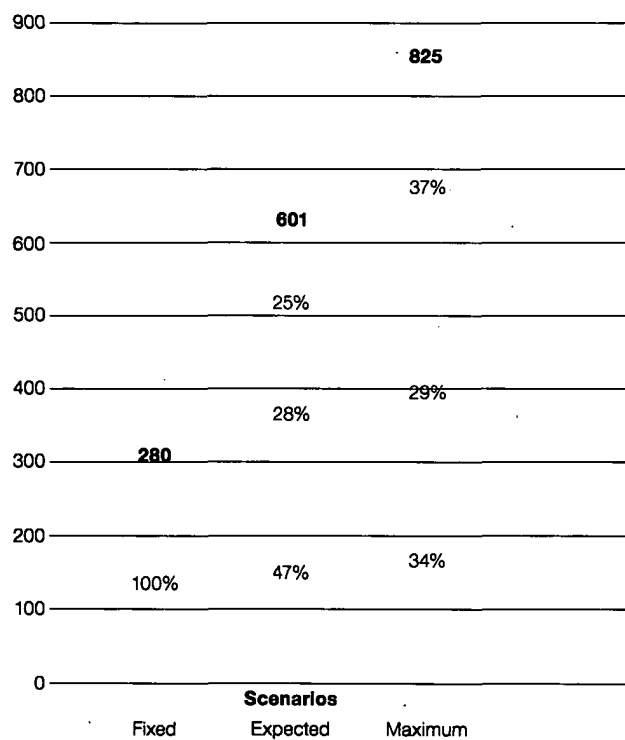
The assumptions used in the calculations are set out below:

- Fixed pay: this includes salary, pension and benefits.
- Base salary effective 1 January 2015 and expected pension contribution has been used.
- The actual monetary value of benefits received in 2014 have been used.
- Expected: this includes salary, pension, benefits, annual bonus and PSP. This assumes that 70% of the annual bonus maximum will be payable for each of the Directors and 50% of PSP awards will vest.
- Maximum: It is assumed that the maximum annual bonus would be payable and that the awards under the PSP vest in full.
- No share price growth has been assumed.

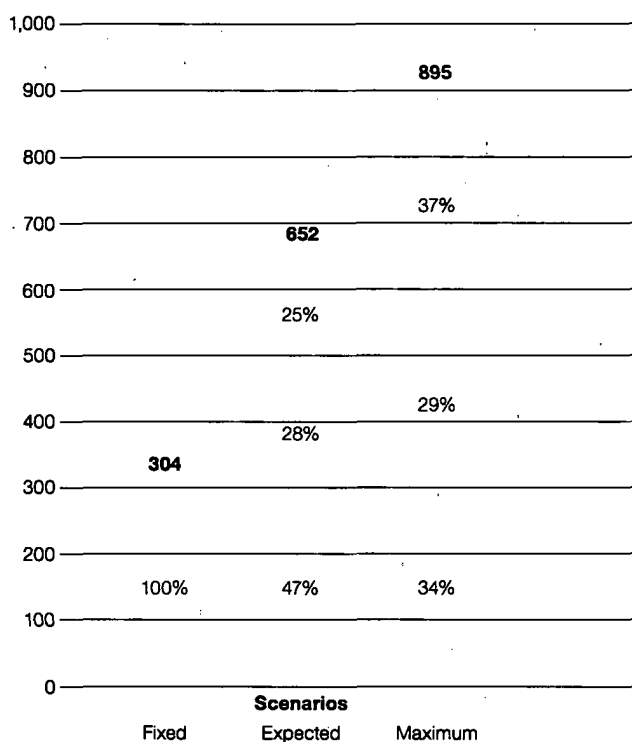
**CEO**  
£'000



**CFO**  
£'000



**Senior VP R&D**  
£'000



Fixed  
Annual bonus  
Long-term variable remuneration

# Remuneration Committee report continued

## Remuneration policy for Non-Executive Directors

The Remuneration Committee is responsible for evaluating and making recommendations to the Board on fees payable to the Chairman. The Chairman does not participate in discussions in respect of fees. The Chairman and CEO are responsible for evaluating and making recommendations to the Board on the fees payable to the Company's Non-Executive Directors.

Remuneration element	Purpose and link to strategy	Operation and maximum
Chairman's fee	To attract and retain a high calibre individual with the requisite experience and knowledge.	<p>The current fee is set out in the Implementation of policy section of the Annual report on remuneration. There is no formal maximum.</p> <p>Fees are reviewed on a periodic basis against those in similar sized companies to ensure they remain competitive and adequately reflect the time commitments and scope of the role.</p> <p>Any increase in fee levels may be above that of the wider workforce in a particular year to reflect the periodic nature of any review and/or any change in responsibilities/ time commitments.</p> <p>The Chairman may also receive limited travel and/or hospitality related benefits in connection with the role.</p>
Non-Executive Director fee	To attract and retain high calibre individuals with the requisite experience and knowledge.	<p>The current fee levels are set out in the Implementation of policy section of the Annual report on remuneration. There is no formal maximum.</p> <p>Fees are reviewed on a periodic basis against those in similar sized companies to ensure they remain competitive and adequately reflect the time commitments and scope of the role.</p> <p>A Board fee is paid to each Non-Executive Director. Supplemental fees are paid to the Senior Independent Director and for the Chairing and membership of Committees to recognise the additional time commitments and responsibilities of these roles.</p> <p>Any increase in fee levels may be above that of the wider workforce in a particular year to reflect the periodic nature of any review and/or any change in responsibilities/time commitments.</p> <p>Non-Executive Directors may also receive limited travel and/or hospitality related benefits in connection with the role.</p>



### Statement of consideration of Shareholders' views

The Remuneration Committee will consider any Shareholder feedback received at the AGM and at meetings throughout the year, when reviewing the overall remuneration policy each year. The guidance from shareholder representative bodies is also considered on an ongoing basis.

More specifically the Committee will consult with major Shareholders when proposing any significant changes to the policy in the future.

### Annual report on remuneration

This section of the Remuneration Committee report has been prepared in accordance with Part 3 of the Regulations as amended, and 9.8.6R of the Listing Rules. The Annual report on remuneration will be put to an advisory Shareholder vote at the AGM on 20 May 2015.

### Composition

The Committee consisted entirely of independent Non-Executive Directors in accordance with the recommendations of the UK Corporate Governance Code (the "Code") from 1 January to 14 September 2014. From 15 September 2014, Paul Edick was considered by the Board to be no longer independent. On 9 February 2015 Mr Edick stood down from the Committee and was replaced by Ms Lota Zoth who is an independent Non-Executive Director. The composition of the Committee did not therefore comply with the recommendations of the Code for the period from 15 September 2014 to 9 February 2015. The terms of reference of the Committee appear on the Company's website. Its members for the year ended 31 December 2014 were Dr Jean-Jacques Garaud, Dr Tim Corn, and Mr Paul R Edick. The Committee met four times during the year ended 31 December 2014. All three members attended all four meetings.

### Responsibilities

The Committee is responsible for the following matters:

- setting a remuneration strategy which is designed to promote the long-term success of the Company;
- ensuring that the remuneration of the Executive Directors and senior employees reflects performance and delivery of Shareholder value;
- agreeing the design and targets of share incentive plans which require Shareholder approval and monitoring the achievement of those targets;
- deciding on the remuneration of the Executive Directors and senior employees, including any specific recruitment or retention terms;
- making a recommendation to the Board in relation to the Chairman's fees;
- appointing external advisers where necessary.

### Activities

A summary of the matters considered by the Committee in the course of the year ended 31 December 2014 is as follows:

Meeting	Agenda items
January	Review and approval of the new share incentive arrangements to be adopted on the day prior to Admission: the Circassia Pharmaceuticals plc Performance Share Plan (the "PSP").
January	Review of the salary levels and annual bonus plan for the Executive Directors. Review of remuneration for the Non-Executive Directors and the Chairman.
April	Approval of IPO bonus and option awards for new employees.
September & November	Review and approval of shareholding policy for Executive Directors and senior employees.
September & November	Review and approval of policy and scheme rules for the annual bonus plan and deferred bonus shares for Executive Directors and senior employees.
September & November	Review and approval of the Directors' remuneration policy report.
September & November	Approval of the Employee Benefit Trust Deed.

### Advisers

The Committee appointed New Bridge Street (NBS) (a trading name of Aon Hewitt Limited, part of Aon plc) to advise it on the formulation of the Group's remuneration policy. NBS is a signatory to the Remuneration Consultants' Group Code of Conduct which sets out guidelines to ensure that its advice is independent and free from undue influence. The fees to NBS in 2014 were £26,940, which were charged on the basis of a negotiated fixed fee. The Committee intends to review the performance and independence of its advisers on an annual basis.

# Remuneration Committee report continued

## Committee evaluation

A review of the effectiveness of the Committee was carried out in November 2014 as part of the process of evaluating Board effectiveness.

## Audited information

### Total remuneration – year ended 31 December 2014

The total remuneration of the individual Directors who served during the year is set out in the table below. Total remuneration is the sum of emoluments plus pension contributions and the value of long-term incentive awards vesting by reference to performance in the year ended 31 December 2014.

		Salary or fees <sup>6</sup> £'000	Benefits <sup>7</sup> £'000	Bonus <sup>8</sup> £'000	Long-term incentives <sup>9</sup> £'000	Pension <sup>10</sup> £'000	Total remuneration £'000
<b>Executive Directors</b>							
Steve Harris	2014	375	2	420	675	56	1,528
	2013	284	2	124	–	62	472
Julien Cotta	2014	235	2	313	–	35	585
	2013 <sup>1</sup>	15	–	27	–	4	46
Rod Hafner	2014	255	2	272	658	38	1,225
	2013	195	2	98	–	10	305
<b>Non-Executive Directors</b>							
Francesco Granata	2014	133	–	–	–	–	133
	2013 <sup>2</sup>	22	–	–	–	–	22
Tim Corn	2014	55	–	–	–	–	55
	2013	25	–	–	–	–	25
Russell Cummings	2014	38	–	–	–	–	38
	2013 <sup>3</sup>	27	–	–	–	–	27
Paul R Edick	2014	50	–	–	–	–	50
	2013 <sup>4</sup>	22	–	–	–	–	22
Jean-Jacques Garaud	2014	62	–	–	–	–	62
	2013	25	–	–	–	–	25
Cathrin Petty	2014	51	–	–	–	–	51
	2013	25	–	–	–	–	25
Charles Swingland	2014 <sup>5</sup>	84	–	–	675	6	765
	2013	247	6	62	–	30	345
<b>Total 2014</b>		<b>1,338</b>	<b>6</b>	<b>1,005</b>	<b>2,008</b>	<b>135</b>	<b>4,492</b>
<b>Total 2013</b>		<b>887</b>	<b>10</b>	<b>311</b>	<b>–</b>	<b>106</b>	<b>1,314</b>

<sup>1</sup> For the period 26 November 2013 to 31 December 2013 as a Director of the Company

<sup>2</sup> For the period 1 September 2013 to 31 December 2013

<sup>3</sup> All fees for Russell Cummings are paid to Imperial Innovations Limited

<sup>4</sup> For the period from 3 April 2013 to 31 December 2013

<sup>5</sup> For the period from 1 January to 18 March 2014 as an Executive Director and thereafter as a Non-Executive Director

<sup>6</sup> This is the amount earned as salary or fees in the financial year

<sup>7</sup> This is the taxable value of benefits paid in respect of the financial year. These benefits typically relate to medical insurance and life assurance

<sup>8</sup> This is the value of the total bonus earned during the financial year and includes the annual bonus paid in respect of performance against goals for 2014 and the IPO bonus paid for performance in ensuring an orderly and efficient IPO. Where the requisite shareholding requirement has not been met by an Executive Director then 50% of the annual bonus will be paid in shares. Where the requirement has been met then 25% will be paid in shares. The IPO bonus was paid fully in cash.

<sup>9</sup> The amount shown relates to the gain, being the market value on date of exercise less exercise price, on EMI share option awards that vested during the year

<sup>10</sup> UK tax legislation imposes penalty taxes on annual pension contributions where prescribed maximum limits are exceeded. The Committee has previously determined that Executive Directors affected by this legislation would receive pension benefits limited by the prescribed maximum amounts and an additional taxable supplementary cash payment equal to the cost to the Company of the benefit foregone. The amount of this supplementary allowance is set so that there is no additional cost to the Company as a result of the implementation of this arrangement

### Annual bonus for the year to 31 December 2014

For the year ended 31 December 2014 the bonus consisted of two elements. For performance against annual operational and development goals bonuses up to a maximum of 100% of base salary for Executive Directors and senior vice presidents could be earned. As disclosed in the IPO prospectus, for performance in ensuring an orderly and efficient IPO, cash bonuses of up to 50% of pre-IPO salary could also be paid to Executive Directors.

Performance objectives are agreed by the Board at the beginning of the year and the Remuneration Committee determines the proportion of bonus payable to each Director and senior vice president in the event that the objective is achieved. The Remuneration Committee determines at the beginning of the year following the bonus year, the extent to which the objective has been achieved and the proportion of the bonus earned. The bonus is calculated on base salary.

The annual performance objectives agreed for 2014 together with proportions payable to each Executive Director are set out below.

Objective	Target date	Potential bonuses (as % of salary)			Awarded bonuses (as % of salary)			Commentary
		S Harris	R Hafner	J Cotta	S Harris	R Hafner	J Cotta	
1 Complete recruitment in Cat-SPIRE phase III study. All subjects to have passed visit 1B/C.	31 Dec 14	20%	25%	15%	20%	25%	15%	Study recruitment completed on 31 December 2014 with 1,409 subjects randomised.
2 Initiate HDM-SPIRE phase II — First regulatory and IRB approval by 30 September 2014 — Start screening by 30 November 2014	30 Sept 14 30 Sept 14 30 Nov 14	15%	20%	15%	15%	20%	15%	First regulatory and IRB approval received on 5 August 2014 and screening began on 24 September 2014.
3 Be ready for FDA End of Phase II meeting for Ragweed-SPIRE. — Complete Ragweed-SPIRE phase II — Request FDA end phase II meeting	31 Jan 15 31 Mar 15	15%	20%	15%	11%	15%	11%	Ragweed-SPIRE phase II exposure chamber and controlled asthmatics studies completed and announcement to the market of top line results for exposure chamber study TR006 made on 8 December 2014.  Master File in IND format submitted to FDA in September 2014 to update FDA on status of programme in readiness for submission of end of phase II meeting request.  All work in respect of completion of Ragweed-SPIRE phase II substantially complete.  Following sight of exposure chamber study results request for end of phase II meeting will not be submitted.
4 Prepare Japanese Cedar-SPIRE for clinical trial. — Complete epitope work — Ready to start toxicological studies	31 Mar 15	—	5%	—	—	—	—	Not completed.
5 Identify strategic growth opportunities and bring at least one to Board for approval.	31 Dec 14	20%	5%	10%	20%	5%	10%	Strategy for establishment of commercial infrastructure brought to Board and approved.

## Remuneration Committee report continued

Objective	Target date	Potential bonuses (as % of salary)			Awarded bonuses (as % of salary)			Commentary
		S Harris	R Hafner	J Cotta	S Harris	R Hafner	J Cotta	
6 Ensure orderly disposal of shares from any Shareholders who wish to sell once the lock ups have expired	31 Dec 14	5%	5%	10%	5%	5%	10%	Completed.
7 Operate within budget	31 Dec 14	5%	5%	10%	5%	5%	10%	Achieved.
8 Recruit staff as per plan	31 Dec 14	5%	5%	5%	4%	4%	4%	94% achievement against target
9 Ensure that Circassia's patents are secured <ul style="list-style-type: none"> <li>— Prepare robust responses to oppositions to ensure that we get valuable (protective) claims</li> <li>— Win any oppositions that occur such that Circassia maintains valuable (protective) claims</li> </ul>	31 Dec 14	5%	5%	20%	5%	5%	20%	Robust responses have been prepared during the year to the oppositions filed against Circassia.  In November 2014, Circassia was successful at a European Patent Office opposition hearing, at which the Opposition Division upheld the validity of Circassia's patent covering Ragweed-SPIRE.
10 Prepare Circassia for the launch of Cat-SPIRE <ul style="list-style-type: none"> <li>— Have approved pre-launch plans (strategy, objectives and activities), in place by Q4 2014 including: Commercial, Market access, Communications, Distribution</li> <li>— Conduct US and EU payer advisory boards</li> <li>— Understand Japanese IT market by conducting qualitative interviews with key opinion leaders and quantitative market research with allergists</li> </ul>	31 Dec 14 31 Dec 14 31 Dec 14 31 Dec 14	5%	—	—	4%	—	—	Pre-launch plans were presented to the Board and approved.  12 EU interviews and 5 US interviews completed.  7 interviews with Japanese key opinion leaders completed in May. Quantitative research with 135 allergists has been started and was completed by end January. In addition, quantitative research with 1,000 patients was carried out and completed. The work with patients was in addition to the original objective.

Objective	Target date	Potential bonuses (as % of salary)			Awarded bonuses (as % of salary)			Commentary
		S Harris	R Hafner	J Cotta	S Harris	R Hafner	J Cotta	
11 Complete all necessary CMC activities required to support the goals of the business including: <ul style="list-style-type: none"> <li>– Complete manufacture and testing of Cat-SPIRE validation batches at Patheon and Bachem</li> <li>– Establish lyophilisation manufacturing process for HDM-SPIRE 120µM and 200µM and validate methods for both dose strengths</li> <li>– Establish potency assay for HDM-SPIRE and Ragweed-SPIRE</li> <li>– Develop formulations and analytical methods to release materials for toxicological studies of Birch-SPIRE and Japanese Cedar-SPIRE</li> <li>– Prepare CMC sections of CTA/IND applications for HDM-SPIRE, Ragweed-SPIRE, Grass-SPIRE</li> </ul>	31 Dec 14	5%	5%	–	4%	4%	–	<p>Patheon completed the manufacture of the fourth drug product validation batch on 27th October 2014. Batch analysis (UPLC) complete in November 2014; potency assay testing completed in January 2015.</p> <p>Manufacture of 3rd set of validation batches at Bachem has been completed. These were released and shipped on 30 June 2014 and placed on stability in August 2014.</p> <p>HDM-SPIRE Lyo process established for both dose strengths, methods validated and batches manufactured for HDM-SPIRE phase II study, packed and released to study sites November 2014</p> <p>Potency assay for HDM-SPIRE established and qualified in May 2014.</p> <p>Ragweed-SPIRE potency assay not complete. Target date for completion Q1 2015.</p> <p>Development of an alternative assay has been initiated with EpiVax and ProImmune respectively.</p> <p>Birch-SPIRE: Manufacture of tox material completed by 2nd July. Release testing at Hologic completed 25th July with reported data available 7th Aug 2014. Materials released and toxicity study commenced on 28th August 2014.</p> <p>Japanese Cedar-SPIRE: Target date for completion of formulation development for toxicity studies H1 2015 following selection of epitopes.</p>
<b>Total</b>		<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>93%</b>	<b>88%</b>	<b>95%</b>	
<b>Immediate payment in cash as % of salary</b>		<b>–</b>	<b>–</b>	<b>–</b>	<b>75%</b>	<b>75%</b>	<b>50%</b>	
<b>Deferred payment in shares as % of salary</b>		<b>–</b>	<b>–</b>	<b>–</b>	<b>25%</b>	<b>25%</b>	<b>50%</b>	

## Remuneration Committee report continued

The Remuneration Committee is able to determine the final outcome of the Bonus Award upwards or downwards where exceptional events occur which are outside the control of the Executive Directors and which materially affect the calculation. No such events occurred in the year to 31 December 2014.

Deferred share bonus awards are structured as conditional awards over shares which vest after three years. The level of deferral is linked to the achievement of the Company's shareholding guidelines as set out in the policy report. Where the guidelines have been met in full, 75% of bonuses are paid in cash and 25% in shares. Both Steve Harris and Rod Hafner have met their shareholding guidelines and therefore 75% of their 2014 bonus was paid in cash. Julien Cotta has not yet met the shareholding guidelines and so 50% of his bonus was paid in cash and 50% in shares.

In relation to the element of the bonus that was subject to a successful IPO process:

Objective	Target date	Potential bonuses (as % of pre-IPO salary)			Awarded bonuses (as % of pre-IPO salary)			Commentary
		S Harris	R Hafner	J Cotta	S Harris	R Hafner	J Cotta	
Support an orderly and efficient IPO process	March 14	25%	25%	50%	23%	24%	50%	Performance assessment reflects the level of involvement and additional time commitments required to deliver a successful IPO on a timely basis.

In total the annual bonus payments opportunity for 2014 was greater than the ongoing level of bonus opportunity which Shareholders will be asked to approve in the Directors' remuneration policy report. The Committee considers that the higher opportunity for 2014 was necessary to recognise the efforts of the Executive Directors in achieving the strong operational results at the same time as managing an orderly IPO process to very short deadlines. The bonus maximum will be 100% of salary for 2015 and future years.

### Long-term incentive plan (LTIP) awards made during the year

On 12 March 2014 the following awards under the Circassia Pharmaceuticals plc Performance Share Plan (the "PSP") were made to the Executive Directors.

Executive Director	Type of award	Basis of award granted	Share price at date of grant	Number of shares over which award was granted	% of shares granted that vest at threshold performance	Face value of shares over which award originally granted £'000	Vesting determined by performance over
Steve Harris	Nil cost option	208% of salary of £375,000	£3.10	251,125	25%	£778	3 years to 31 Dec. 2016
Julien Cotta	Nil cost option	173% of salary of £235,000	£3.10	131,125	25%	£406	3 years to 31 Dec. 2016
Rod Hafner	Nil cost option	249% of salary of £255,000	£3.10	204,750	25%	£635	3 years to 31 Dec. 2016

The award level for 2014 was greater than the ongoing award limit which Shareholders will be asked to approve in the policy report. The Committee considered that the higher opportunity for this first award was necessary to fully support retention and incentivisation over a critical period of the Company's development.

The number of options in the 2014 PSP that ultimately vest will be determined according to the following performance criteria:

**Criterion 1: Relative TSR**

For options granted in 2014, up to 70% of the total award will vest subject to achievement of the performance criterion.

% vesting of the total award	Relative TSR ranking against the FTSE 250 Index (as at 12 March 2014) for the period 12 March 2014 to 12 March 2017. <sup>1</sup>
0%	Below median
25%	Median
70%	Upper quartile

<sup>1</sup> In respect of criterion 1, vesting occurs on a straight line basis between the median and upper quartile points

**Criterion 2: Clinical and strategic business objectives**

For options granted in 2014, up to 30% of the total award will vest subject to achievement of the performance criterion.

The clinical and strategic business objectives referred to in criterion 2 are as follows. Percentages in brackets relate to the percentage of the total award:

- Cat-SPIRE phase III results (CP007) by 30 Sept 2016 (9%);
- Ragweed-SPIRE Phase II results (TR006) by 31 December 2015 (3%);
- Ragweed-SPIRE regulatory and IRB approval for commencement of Phase III by 31 March 2016 (3%);
- HDM-SPIRE phase II fully recruited by 31 March 2016 (6%);
- Grass-SPIRE end of phase II meeting by 31 December 2015 (3%);
- Regulatory and IRB approval for commencement of new clinical programme by 31 March 2017 (3%);
- Signed agreement for out-licensing deal/partnership for development and commercialisation by end 31 December 2016 (3%); and
- Achievement against objectives results in proportionate vesting.

**Directors' pensions**

For the financial year ended 31 December 2014 the Company contributed £135,871 to defined contribution money purchase pension schemes for the Directors. As was explained in the remuneration table, Executive Directors may also receive a supplementary cash payment in lieu of pension contributions where statutory limits have been exceeded. No supplementary payments were made in the financial year.

**Statement of Directors' shareholding and share interests (audited information)**

The Directors who have held office during the year ended 31 December 2014 and their interests (in respect of which transactions must be notified to the Company) in the share capital of the Company are shown in the following tables.

There was no change in the Directors' interests between 31 December 2014 and the date of this report.

Directors holding office at 31 December 2014 with LTIP awards and options outstanding over Ordinary shares of 0.08p were as follows:

# Remuneration Committee report continued

Plan	Date of grant	Awards granted and options held as at 1 January 2014 <sup>1</sup>	Awards and options granted (exercised, lapsed, or cancelled) during year	Awards and options held at 31 December 2014 and at the date of this report
<b>Executive Directors</b>				
<b>S Harris</b>				
2007 EMI Scheme	2 August 2007	317,500	–	317,500
2007 EMI Scheme	15 August 2011	217,875	–	217,875
2014 PSP	12 March 2014	–	251,125	251,125
<b>Total</b>		<b>535,375</b>	<b>251,125</b>	<b>786,500</b>
<b>J Cotta</b>				
2013 Unapproved Scheme	22 October 2013	149,250	–	149,250
2014 PSP	12 March 2014	–	131,125	131,125
<b>Total</b>		<b>149,250</b>	<b>131,125</b>	<b>280,375</b>
<b>R Hafner</b>				
2007 EMI Scheme	3 July 2008	125,000	(125,000)	–
2007 EMI Scheme	18 March 2009	62,500	(62,500)	–
2007 EMI Scheme	22 January 2010	312,500	(312,500)	–
2007 EMI Scheme	15 August 2011	212,375	(212,375)	–
2014 PSP	12 March 2014	–	204,750	204,750
<b>Total</b>		<b>712,375</b>	<b>(507,625)</b>	<b>204,750</b>
<b>Non-Executive Directors</b>				
<b>T Corn</b>				
2007 Unapproved Scheme	23 February 2010	62,500	–	62,500
2007 Unapproved Scheme	15 August 2011	16,750	–	16,750
<b>Total</b>		<b>79,250</b>	<b>–</b>	<b>79,250</b>
<b>P Edick</b>				
2007 Unapproved Scheme	3 April 2013	156,250	–	156,250
<b>JJ Garaud</b>				
2007 Unapproved Scheme	12 November 2012	77,500	–	77,500
<b>C Petty</b>				
2007 Unapproved Scheme	15 August 2011	16,250	–	16,250
<b>C Swingland</b>				
2007 EMI Scheme	2 August 2007	317,500	(317,500)	–
2007 Unapproved Scheme	15 August 2011	217,875	(217,875)	–
<b>Total</b>		<b>535,375</b>	<b>(535,375)</b>	<b>–</b>

<sup>1</sup> The awards granted and options held as at 1 January 2014 have been re-stated to reflect the capital re-organisation which took place prior to the IPO

Each 10p Ordinary share prior to the re-organisation converted to 125 new Ordinary shares of 0.08 pence each



Vesting during year	Vested as at year end	Unvested as at year end	Exercise price (p)	Date from which first exercisable	Expiry date
-	317,500	-	0.08	2 August 2010	1 August 2017
217,875	217,875	-	0.08	18 March 2014	14 August 2021
-	-	251,125	nil	12 March 2017	11 March 2024
<b>217,875</b>	<b>535,375</b>	<b>251,125</b>			
-	-	149,250	242	22 October 2016	21 October 2023
-	-	131,125	nil	12 March 2017	11 March 2024
-	-	<b>280,375</b>			
-	-	-	0.08	3 July 2011	2 July 2018
-	-	-	0.08	18 March 2012	17 March 2019
-	-	-	0.08	22 January 2013	21 January 2020
212,375	-	-	0.08	18 March 2014	14 August 2021
-	-	204,750	nil	12 March 2017	11 March 2024
<b>212,375</b>	<b>-</b>	<b>204,750</b>			
-	62,500	-	0.08	23 February 2013	22 February 2020
16,750	16,750	-	0.08	15 August 2014	14 August 2021
<b>16,750</b>	<b>79,250</b>	<b>-</b>			
-	-	156,250	0.08	3 April 2016	2 April 2023
-	-	77,500	0.08	12 November 2015	11 November 2022
16,250	16,250	-	0.08	15 August 2014	14 August 2021
-	-	-	0.08	2 August 2010	1 August 2017
217,875	-	-	0.08	15 August 2014	14 August 2021
<b>217,875</b>	<b>-</b>	<b>-</b>			

# Remuneration Committee report continued

With regard to the PSP, the number of shares released to Directors at the end of the three year performance period is dependent upon satisfying the criteria relating to TSR and clinical and strategic milestones which are set out in the section of this report relating to the LTIP.

Executive Directors hold options under the Circassia Holdings Limited EMI Share Option Scheme 2007 (the "EMI Scheme"); the Circassia Holdings Limited Unapproved Share Option Scheme 2007 (the "2007 Unapproved Scheme"); and the Circassia Holdings Limited Unapproved Share Option Scheme 2013 (the "2013 Unapproved Scheme"). Historically, no performance conditions have been attached to the options granted under these schemes. The exercise price is equal to the market value of the Company's shares at the time the options are granted.

It was explained in the Corporate governance section of this report that the Group granted certain Non-Executive Directors share options in the past, when it was a private company. No further options have been granted since Admission and no awards will be made in the future.

## Gain on exercise of share options

Executive Directors	Date of exercise	Number of options exercised	Exercise price (p)	Market value at date of exercise (p)	Gain on exercise of share options (£)
Dr Rod Hafner <sup>1</sup>	24 February 2014	500,000	0.08p	0.08p <sup>1</sup>	nil
	27 March 2014	212,375	0.08p	295.25	626,867
Charles Swingland <sup>1</sup>	27 March 2014	535,375	0.08p	295.25	1,580,266

<sup>1</sup> Rod Hafner exercised 500,000 share options on 24 February 2014 at an exercise price of 10p (converted into 0.08p shares post IPO). On this date, the market value of the share capital of the Company was 10p. A proportion of these shares were sold on 18 March 2014 at a price of 310p each. The gain shown above is the notional gain on exercise of options exercised during the year. In total, Rod Hafner exercised 712,375 options and of this total he sold 322,581 shares to cover the cost of the exercise and the associated tax liabilities and Charles Swingland exercised 535,375 options and did not sell any of these shares.

## Directors' interests in shares (including shares held as Restricted shares)

As was noted earlier in this report, the Company has implemented guidelines which require the Executive Directors and key senior employees to build up and maintain an interest in the Ordinary shares of the Company which is equal in value to their annual base salary. For the purpose of assessing compliance with these guidelines, the value of the shareholding is calculated using the higher of the share price on 31 December 2014 (279p) and the acquisition price of the shares. The value as a percentage of salary has been calculated using base salary as at 31 December 2014.

The following table shows the number of Ordinary shares beneficially owned by the Directors who served during the financial year which are not subject to any restrictions on transfer or to forfeiture.

	Shares beneficially owned as at 31 December 2014	Value of owned shares as a % of salary	Shareholding requirement met
<b>Executive Directors</b>			
S Harris	5,048,677	3756%	Yes
J Cotta	—	—	No
R Hafner	389,794	426%	Yes
<b>Non-Executive Directors</b>			
F Granata	19,354	n/a	n/a
T Corn	62,500	n/a	n/a
C Petty	188,875	n/a	n/a
C Swingland	5,584,177	n/a	n/a

The following table shows the interests in Restricted shares of the Directors who served during the year. These are subject to restrictions on transfer or to forfeiture.

	Date of grant of Restricted shares	b/f as at 1 January 2014	Additions, exercises or lapses during year	c/f as at 31 December 2014	Value of owned shares as a % of salary
<b>Executive Directors</b>					
S Harris	6 February 2013	250,000		250,000	279%
	7 March 2013	125,000		125,000	
J Cotta	6 February 2013	25,000		25,000	56%
	7 March 2013	12,500		12,500	
	4 March 2014		9,375	9,375	
R Hafner	6 February 2013	125,000		125,000	251%
	7 March 2013	75,000		75,000	
	4 March 2014		29,500	29,500	
<b>Non-Executive Directors</b>					
F Granata	1 September 2013	312,500	–	312,500	649%
C Swingland	20 December 2012	62,500		62,500	913%
	7 March 2013	75,000		75,000	

The table below sets out further information for those shares awarded in the year.

Executive Director	Type of award	Basis of award granted	Share price at date of grant	Number of shares over which award was granted	Face value of shares over which award originally granted £	Vesting determined by time
<b>Julien Cotta</b>	Restricted share award	Awards to a number of key employees pre-IPO to incentivise and aid retention	0.08 pence	9,375	£7.50	3 years to 4 March 2017
<b>Rod Hafner</b>	Restricted share award	Awards to a number of key employees pre-IPO to incentivise and aid retention	0.08 pence	29,500	£23.60	3 years to 4 March 2017

Restricted shares have been subscribed for or purchased at a price of 10p per Ordinary share and, under the terms of their acquisition, are subject to certain restrictions on transfer and forfeiture. The restrictions lift on the earlier of a sale of the Company and the expiry of a vesting period of between two and three years (depending on the date of award of the Restricted shares). The Ordinary shares may be forfeited if the participant ceases to be employed or be an officer of the Company prior to the vesting of the shares other than by reason of: death; resignation; permanent incapacity; redundancy; retirement; non-renewal of a fixed term contract or consultancy.

Directors are not permitted to hold their shares in hedging arrangements or as collateral for loans without the express permission of the Board. None of the Directors currently holds or has held their shares in such an arrangement.

# Remuneration Committee report continued

## Unaudited information

### Percentage increase in the remuneration of the CEO

	% change between 31 December 2013 and 31 December 2014
<b>CEO</b>	
Salary <sup>1</sup>	21% increase
Benefits	1% increase
Bonus	240% increase
<b>Average per employee</b>	
Salary	31% increase
Benefits	1% increase
Bonus	46% increase

<sup>1</sup> Salary includes £25,000, which was salary sacrificed as pension contribution

The salary of the CEO and other Executive Directors was recalibrated as part of the IPO process. The increase indicated above has brought Mr Harris' salary, in the Committee's view, to a roughly mid-market level when compared with other companies at a similar stage of their development and in the same sector.

### Total shareholder return

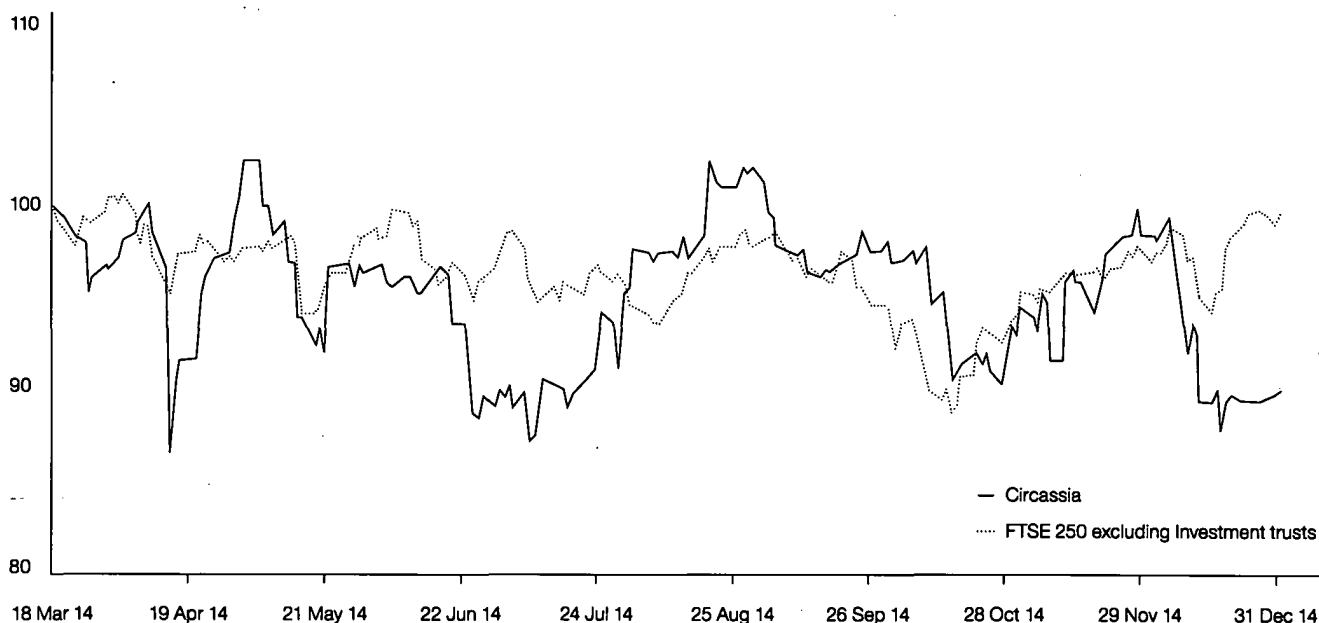
The performance of the Company's Ordinary shares compared with the FTSE 250 (excluding Investment trusts) (the "Index") for the period from Admission on 18 March 2014 to 31 December 2014 is shown in the graph below:

The Company has chosen the Index as its benchmark of share price performance as it believes that this gives Shareholders a reasonable comparison with the total shareholder return of other equity investments in companies of a broadly similar size across all sectors. The TSR performance has been measured by JPMorgan Cazenove.

The mid-market price of an Ordinary share on 31 December 2014 was £2.79p. From 18 March 2014 to 31 December 2014 the share price ranged from a high of £3.18p to a low of £2.68p.

### Total shareholder return

18 March 2014 – 31 December 2014



### Total remuneration for the CEO over time

Description	2014
Total remuneration (£'000)	1,528
Bonus awarded (%)	93%
LTIP vesting (%)	100%

The table above shows the total remuneration of the Chief Executive Officer during the financial years in which the Company has been constituted as a public company. The total remuneration figure includes the annual bonus and LTIP awards which vested based on performance during those years. The annual bonus and LTIP percentages show the amount paid out for each year as a percentage of the maximum.

### Relative importance of expenditure on pay

The table below shows the expenditure by the Company on remuneration paid to all employees of the Group and distributions to Shareholders for the financial period.

	2014 £m
Overall expenditure on pay	6.1
Dividend plus share buyback	Nil

### Application of remuneration policy to 2015 salary review

The Executive Directors' salaries were reviewed in January 2014 as part of the IPO process and were set at a level which the Committee regarded as broadly mid-market when compared with other companies of a similar size operating within the same sector. New Bridge Street provided advice to the Committee on this process. A further salary review took place on 9 February 2015 and a 3% increase was applied effective 1 January 2015. This increase is equal to the average salary increase provided to UK employees.

	Salary as at 1 January 2015	Salary as at 1 January 2014	% Increase
Steve Harris	386,000	375,000	3
Julien Cotta	242,000	235,000	3
Rod Hafner	262,500	255,000	3

### Performance targets for 2015 bonus and LTIP awards

For the financial year 2015, the annual bonus will continue to be based on corporate objectives analogous to those set out in the Remuneration Policy. The maximum bonus opportunity will be 100% of salary for Executive Directors in line with the ongoing remuneration policy.

The Committee has decided not to disclose the detailed nature of these performance targets as they comprise commercially sensitive information. Retrospective disclosure of the targets and performance against them will be made in the 2015 Remuneration Committee report.

The measures applicable to awards made under the Performance Share Plan will be as disclosed in the table in the section 'LTIP Awards made during the year' except that the percentage weighting ascribed to relative TSR versus the FTSE 250 Index and clinical and strategic objectives shall be adjusted so that each accounts for 50% of the total awards available. The clinical and strategic objectives will be set in accordance with the achievement of certain key timelines which the Committee will approve prior to grant of the award and will be fully disclosed in the 2015 Remuneration report.

Award levels for 2015 will be in accordance with the remuneration policy.

## Remuneration Committee report continued

### Non-Executive Director remuneration

The fees for the Chairman and Non-Executive Directors have been increased by 3% effective 1 January 2015. This increase is in line with the average increases awarded to employees. The fees paid to the Non-Executive Directors in 2014 and the fees proposed to be paid in 2015 are set out below:

	From 1 January 2014 (£)	From 1 January 2015 (£)	Increase %
Chairman	126,800	130,500	3
Non-Executive Director	42,000	43,250	3
Senior Independent Non-Executive Director Fee	48,500	49,950	3
Remuneration and Audit Committee Chairmanship Fee	10,000	10,300	3
Nomination Committee Chair	7,500	7,725	3
Committee Memberships	5,000	5,150	3

### Shareholder voting at the Annual General Meeting

At last year's AGM held on 21 February 2014, as the Company was private, no Remuneration Committee report was presented to the Shareholders.

### Approval

This report was approved by the Board on 26 February 2015.

### Dr Jean-Jacques Garaud

Chairman of the Remuneration Committee

# Directors' report

## Directors' report

In accordance with the Companies Act 2006, the Directors present their report together with the financial statements and the Independent Auditors' report for the year ended 31 December 2014.

## Principal activity

The principal activity of the Company undertaken during the year was the development and commercialisation of a range of immunotherapy products for the treatment of allergies.

## Review of business

The Strategic report on pages 01 to 33 comprises a review of the Company's performance during the year, its corporate objectives, an overview of the market, a review of the Company's risk management processes, issues relating to corporate citizenship, and a financial review. Key events are described in the Chairman's statement and the Chief Executive's review. Progress against key performance indicators are provided throughout the Strategic report and in particular in the section 'Strategy and progress against objectives'. Information relating to the environment, employees and stakeholders, health and safety, ethical considerations and political and charitable donations is also set out in the Strategic report as well as the Board's assessment of the key risks and uncertainties facing the business. The Chairman's introduction in relation to corporate governance appears at the beginning of the Corporate governance report. It is followed by the Audit Committee report, the Nomination Committee report, and the Remuneration Committee report.

These various reports form part of this Directors' report by reference and should be read as part of it. The consolidated income statement for the year ended 31 December 2014 is set out in the financial statements.

## Results and dividend

The results for the year and the financial position as at 31 December 2014 are shown in the Consolidated statement of comprehensive income and the Consolidated statement of financial position. The results of the Group are explained in more detail in the Financial review.

The Directors do not recommend the payment of a dividend for the year to 31 December 2014 (2013: £nil).

## Directors and Directors' interests

The Directors of the Company at the date of this report, together with their biographical details and dates of appointment are set out in the Corporate governance report and the Board of Directors section.

The Directors served throughout the year with the exception of Lota Zoth who served from 9 February 2015. Charles Swingland served as an Executive Director from 1 January 2014 to 18 March 2014 and as a Non-Executive Director for the remainder of the year.

The Board confirms that each of the Directors who served during the year has been formally appraised during this period. In accordance with the Code, all Directors of the Company will stand for re-election on an annual basis.

Information on the Directors' remuneration and their interests in the share capital of the Company are set out in the Remuneration report. None of the Directors has a commercial interest in any material contract entered into by the Company.

As is permitted by sections 232 to 235 Companies Act 2006, and consistent with the Company's Articles of Association, the Company has maintained insurance cover for its Directors and Officers under a Directors and Officers Liability Policy. Further, the Company has granted an indemnity to its Directors against liability which arises due to claims brought by third parties.

The Directors may exercise their powers pursuant to the Articles of Association, the Companies Act 2006 and related legislation, and any resolution of the Shareholders. The Articles are available for review at the registered office.

## Share capital and Shareholders

### Share capital

At 18 February 2015 the Company had a total of 125 Ordinary Shareholders and 189,419,634 Ordinary shares in issue.

During the year the share capital of the Company increased by 64,516,129 Ordinary shares as a result of the Initial Public Offering which took place on 18 March 2014 and by a further 1,363,875 Ordinary shares due to the vesting and exercise of share awards. On 11 April 2014, a further 633,380 Ordinary shares from the Over-Allotment Option were issued. Details of the movements in the Company's share capital are shown in note 21 to the financial statements.

Following the reorganisation of the share capital which occurred immediately prior to the Initial Public Offering, the Company has only one class of shares which carry no right to fixed income. Each share carries the right to one vote at general meetings of the Company. There are no restrictions on voting rights or on the holding or transfer of these securities.

Details of employee share schemes are set out in note 22. Shares held by the Circassia Pharmaceuticals plc Employee Benefit Trust abstain from voting. No shares were held in the Employee Benefit Trust during the year (2013: Nil).

Pursuant to the Articles of Association the Company has been granted authority to allot up to 5% of its issued Ordinary share capital on a non-pre-emptive basis. No such allotments were made during the year.

### Lock up arrangements

The Company and the Directors agreed certain lock-up arrangements in advance of the IPO of the Company.

Pursuant to the Underwriting Agreement which was made between the Company, the Directors, the Selling Shareholders, and the Banks, the Company agreed that, subject to certain exceptions, for a period of six months from the date of Admission, it would not without prior consent of the Joint Bookrunners, issue, offer, sell or contract to sell or otherwise dispose of any Ordinary shares. This obligation expired on 17 September 2014.

Also pursuant to the Underwriting Agreement, each of the Directors agreed that, subject to certain exceptions, during the period of 12 months following Admission, they would not without prior consent of the Joint Bookrunners, offer, sell or contract to sell or otherwise dispose of any Ordinary shares. This obligation expires on 17 March 2015.

Finally, pursuant to the Lock-up Agreement, which was put in place between Invesco, Imperial Innovations, Lansdownie and the Banks, the Locked-up Shareholders agreed that, subject to certain exceptions, for a period of six months from the date of Admission, they would not without prior consent of the Banks, offer, sell or contract to sell or otherwise dispose of any Ordinary shares which they held prior to the IPO. This obligation expired on 17 September 2014.

## Directors' report continued

### Share price

The mid-market share price ranged from £2.68p to £3.18p during the period from 18 March 2014 to 31 December 2014. The average price for the period was £2.93p. The mid-market price of an Ordinary share on 31 December 2014 was £2.79p.

### Significant shareholdings

As at 18 February 2015 the Company had been notified of the following interests, held, directly or indirectly, in 3% or more of the Company's issued share capital.

	Number of shares	% of shares
The Bank of New York (Nominees) Limited	77,566,867	40.95
PH Nominees Limited	28,214,229	14.90
Chase Nominees Limited	18,399,221	9.71
State Street Nominees Limited	8,997,808	4.75
Nortrust Limited	7,561,524	3.99
Chase (GA Group) Nominees Limited	7,188,634	3.80
HSBC Client Holdings Nominee (UK) Limited	6,947,305	3.67
Lynchwood Nominees Limited	6,291,955	3.32
Mr Charles Swingland	5,721,677	3.02



The Board confirms that, in accordance with LR 9.2.2AR(2)(a) Relationship Agreements were put in place on 12 March 2014 between the Company and Invesco Asset Management Limited, and the Company and Imperial Innovations LLP and their affiliates. Invesco holds more than 20% of the voting rights attached to the issued share capital of Imperial Innovations and accordingly there is a presumption (which has not been rebutted) that Invesco and Imperial Innovations are acting in concert in relation to their shareholdings in the Company. At the date of this report, Invesco and Imperial Innovations together held 49.3% of the voting rights attached to the issued share capital of the Company.

#### **Invesco relationship agreement**

The principal purpose of the relationship agreement is to ensure that the Company will be capable of carrying on its business independently of Invesco for so long as Invesco, together with its concert parties, holds a controlling interest.

Pursuant to these agreements, and for so long as Invesco holds a controlling interest:

- The parties shall procure that all transactions and relationships between the Company and any other member of the Group and Invesco (or any of its associates) are conducted at arms-length and on normal commercial terms; and
- Invesco shall (and shall procure that each of its associates shall) not take any action that would prevent the Company from complying with its obligations under the Listing Rules and shall not propose or procure the proposal of any Shareholder resolution which is intended to or appears to be intended to circumvent the proper application of the Listing Rules.

#### **Imperial Innovations relationship agreement**

The principal purpose of the Relationship Agreement is to ensure that the Company will be capable of carrying on its business independently of Imperial Innovations for so long as Imperial Innovations with its concert parties, holds a controlling interest.

Pursuant to these agreements, and for so long as Imperial Innovations together with Invesco holds a controlling interest:

- The parties shall procure that all transactions and relationships between the Company and any other member of the Group and Imperial Innovations (or any of its associates) are conducted at arms-length and on normal commercial terms; and
- Imperial Innovations shall (and shall procure that each of its associates shall) not take any action that would prevent the Company from complying with its obligations under the Listing Rules and shall not propose or procure the proposal of any Shareholder resolution which is intended to or appears to be intended to circumvent the proper application of the Listing Rules.

The Board confirms that the Company has complied with the independence provisions under LR 9.2.2AR(2)(a) referred to above and, that so far as it is aware, the controlling Shareholders have complied with the independence provisions and, so far as it is aware, the controlling Shareholders have complied with the procurement obligation.

#### **Treasury management**

The Company's policy on the use of financial instruments and the management of financial risks is set out in note 2 to the financial statements.

#### **Going concern**

The accounts have been prepared on a going concern basis. Budgets are prepared on a rolling three year basis each year. These are built from the bottom up and presented to the Board each year for review and approval. The Directors have reviewed the current and projected financial position of the Company, taking into account existing cash balances and available financial facilities. On the basis of this review, the Directors have a reasonable expectation that the Company has adequate resources to continue to operate - for the foreseeable future.

#### **Employment and environment**

The Company's policies on health and safety, the environment, and employee-related matters are disclosed in the Strategic review. Greenhouse gas emissions have been calculated as carbon dioxide equivalents.

#### **Political and charitable donations**

There were no charitable or political donations in the year to 31 December 2014.

#### **Auditor**

PricewaterhouseCoopers LLP has expressed its willingness to continue in office as Auditor and a resolution to re-appoint PwC will be put to the members at the forthcoming Annual General Meeting.

The Directors who held office at the date of approval of this report confirm that, so far as they are each aware, there is no relevant audit information of which the Company's Auditor is unaware, and each Director has taken all the steps a Director ought to have taken to make themselves aware of relevant audit information and to establish that the Auditor is aware of that information. This confirmation is given in accordance with section 418 Companies Act 2006.

#### **Annual General Meeting**

The Annual General Meeting will be held at the offices of Circassia Pharmaceuticals plc on 20 May 2015 at 10a.m. Details of the business to be transacted at the forthcoming AGM will be given in a separate circular to Shareholders.

By order of the Board

#### **Julien Cotta**

Company Secretary

26 February 2015

# Statement of Directors' responsibilities

## **In respect of the Annual report and accounts and financial statements for the year ended 31 December 2014**

The Directors are responsible for preparing the Annual report and the financial statements in accordance with applicable law and regulations.

Company law requires the Directors to prepare Group and parent Company financial statements for each financial year. Under that law the Directors are required to prepare the Group financial statements in accordance with International Financial Reporting Standards (IFRSs) as adopted by the European Union and Article 4 of the IAS Regulation and have also chosen to prepare the parent Company financial statements under IFRSs as adopted by the European Union. Under company law the Directors must not approve the accounts unless they are satisfied that they give a true and fair view of the state of affairs of the Company and of the profit or loss of the Company for that period. In preparing these financial statements, International Accounting Standard 1 requires that Directors:

- properly select and apply accounting policies;
- present information, including accounting policies, in a manner that provides relevant, reliable, comparable and understandable information;
- provide additional disclosures when compliance with the specific requirements in IFRSs are insufficient to enable users to understand the impact of any particular transactions, other events and conditions on the entity's financial position and financial performance; and
- make an assessment of the Company's ability to continue as a going concern.

The Directors are responsible for keeping adequate accounting records that are sufficient to show and explain the Company's transactions and disclose with reasonable accuracy at any time the financial position of the Company and enable them to ensure that the financial statements comply with the Companies Act 2006. They are also responsible for safeguarding the assets of the Company and for taking reasonable steps to prevent and detect fraud and other irregularities.

The Directors are responsible for the maintenance and integrity of the corporate and financial information included on the website. Legislation in the United Kingdom governing the preparation and dissemination of financial statements may differ from legislation in other jurisdictions.

## **Directors' responsibility statement**

We confirm that to the best of our knowledge:

- the financial statements, prepared in accordance with International Financial Reporting Standards as adopted by the European Union, give a true and fair view of the assets, liabilities, financial position and profit or loss of the Company and the undertakings included in the consolidation taken as a whole;
- the Strategic report includes a fair review of the development and performance of the business and the position of the Company and the undertakings included in the consolidation taken as a whole, together with a description of the principal risks and uncertainties which they face; and
- the Annual report and the financial statements, taken as a whole, are fair, balanced and understandable and provide the information necessary for Shareholders to assess the Company's performance, business model and strategy.

**Julien Cotta**

Director

26 February 2015



# Independent Auditors' report to the members of Circassia Pharmaceuticals plc

## Report on the financial statements

### Our opinion

In our opinion:

- Circassia Pharmaceuticals plc's Group financial statements and parent Company financial statements (the "financial statements") give a true and fair view of the state of the Group's and of the parent Company's affairs as at 31 December 2014 and of the Group's loss and the Group's and the parent Company's cash flows for the year then ended;
- the Group financial statements have been properly prepared in accordance with International Financial Reporting Standards ("IFRSs") as adopted by the European Union;
- the parent Company financial statements have been properly prepared in accordance with International Financial Reporting Standards ("IFRSs") as adopted by the European Union and as applied in accordance with the provisions of the Companies Act 2006; and
- the financial statements have been prepared in accordance with the requirements of the Companies Act 2006 and, as regards the Group financial statements, Article 4 of the IAS Regulation.

### What we have audited

Circassia Pharmaceuticals plc's financial statements comprise:

- the Consolidated statement of financial position as at 31 December 2014;
- the Parent Company statement of financial position as at 31 December 2014;
- the Consolidated statement of comprehensive income for the year then ended;
- the Group and parent Company statement of cash flows for the year then ended;
- the Group and parent Company statement of changes in equity for the year then ended; and
- the notes to the financial statements, which include a summary of significant accounting policies and other explanatory information.

Certain required disclosures have been presented elsewhere in the Annual report, rather than in the notes to the financial statements. These are cross-referenced from the financial statements and are identified as audited.

The financial reporting framework that has been applied in the preparation of the financial statements is applicable law and IFRSs as adopted by the European Union and, as regards the parent Company financial statements, as applied in accordance with the provisions of the Companies Act 2006.

## Our audit approach

### Overview

#### Materiality:

Overall Group materiality: £463k which represents 1% of total group expenses.

#### Audit scope:

- We conducted audit work in one location. All entities are managed from Oxford, and the vast majority of the Group's transactions and balances are recorded in one UK subsidiary.
- We paid particular attention to the Initial Public Offering ('IPO') and admission to the Official List of the UK Listing Authority which occurred in March 2014. This impacted on a number of areas in the financial statements including the equity structure of the parent and the treatment of IPO costs.
- Taken together, the entities on which we performed our audit work accounted for 98% of Group expenses and 98% of Group loss before tax.

#### Areas of focus:

- Completeness of Research and Development accruals.
- Measuring the fair value of awards under new share options schemes and the related accounting treatment.
- Accounting for IPO costs.
- Accounting for the changes in the capital structure as a result of the IPO.

### The scope of our audit and our areas of focus

We conducted our audit in accordance with International Standards on Auditing (UK and Ireland) ("ISAs (UK & Ireland)").

We designed our audit by determining materiality and assessing the risks of material misstatement in the financial statements. In particular, we looked at where the Directors made subjective judgements, for example in respect of significant accounting estimates that involved making assumptions and considering future events that are inherently uncertain. As in all of our audits, we also addressed the risk of management override of internal controls, including evaluating whether there was evidence of bias by the Directors that represented a risk of material misstatement due to fraud.

The risks of material misstatement that had the greatest effect on our audit, including the allocation of our resources and effort, are identified as "areas of focus" in the table below. We have also set out how we tailored our audit to address these specific areas in order to provide an opinion on the financial statements as a whole, and any comments we make on the results of our procedures should be read in this context. This is not a complete list of all risks identified by our audit.

# Independent Auditors' report to the members of Circassia Pharmaceuticals plc continued

Area of focus	How our audit addressed the area of focus
<p><b>Accounting for the changes in the capital structure as a result of the IPO</b></p> <p>Immediately prior to the admission of shares onto the main market for listed securities of the London Stock Exchange, the Company converted Preference shares into Ordinary shares and issued liquidation shares to the Preference Shareholders. Loan notes were also converted into Ordinary shares.</p> <p>On 18 March 2014 each 10p Ordinary share was subdivided into 125 0.08p Ordinary shares. In addition, new Ordinary shares were issued as part of the admission onto the London Stock Exchange on 18 March.</p> <p>Share options have also been exercised by employees during the year under the EMI option scheme.</p> <p>As a result of these transactions, the capital structure of the Company has been significantly altered. There is a risk that the accounting and disclosure implications of these agreements have not been correctly reflected in the financial statements.</p>	<p>We have examined the underlying documentation and associated accounting treatment for each of the transactions as follows:</p> <ul style="list-style-type: none"> <li>— For the conversion of Preference shares into Ordinary shares and the liquidation shares issued, we considered the terms of the shares in the articles of association to ensure their appropriate classification within equity.</li> <li>— We agreed the share movements in the year to the board meeting minutes and regulatory news service announcements and traced cash received for each issue of new shares to bank statements.</li> <li>— We inspected board approval for the share options exercised during March 2014.</li> <li>— The appropriate split between share capital and share premium was recalculated and confirmed as appropriate.</li> </ul> <p>Based on the procedures performed we agreed with management's classification, disclosure and presentation of the revised capital structure.</p>
<p><b>Accounting for IPO costs</b></p> <p>The Group incurred £9.6m of costs in completing the IPO in March 2014. Incremental costs that are directly attributable to the equity transaction are accounted for through equity, with the remaining costs through the income statement. There is an element of judgement and allocation in this treatment in order to determine what costs are directly attributable to a new equity issue.</p> <p>Management performed an allocation of the IPO transaction costs by considering the type of expenditure incurred and whether it meets the criteria to be considered directly attributable to the issue of shares. From this determination, £9.4m was attributed to equity. There is a risk that these costs do not qualify as directly attributable to the equity transaction and, as such, should have been recorded in the income statement.</p>	<p>We obtained a sample of IPO cost invoices and considered whether management's assessment of whether legal and professional fees incurred were directly attributable to the IPO was supportable.</p> <p>Having tested the appropriateness of the split in expenditure, we then traced the amounts into the financial statements and tested they were appropriately included and disclosed.</p> <p>As a result, we agreed with management's allocation of the costs to equity and that the appropriate accounting treatment and disclosures were applied.</p>

**Measuring the fair value of awards under new share options schemes and the related accounting treatment**

The accounting treatment for share options can be complex and involves judgement regarding identifying the underlying assumptions and the appropriate model. Prior to the IPO, Circassia had a small number of share options under EMI approved schemes which gave rise to a charge of £98k in FY13. Following the IPO a further 2,206,611 share options were issued under a new Performance Share Scheme.

The newly granted share options were valued under the Black Scholes model or Monte Carlo model dependent on the performance vesting conditions.

The fair value determined drives the charge recognised by the Company.

The value of the shares in the Group used in the share options calculation has increased and therefore the share options charge has also increased. As a result the risk of a material error or misstatement is higher. In addition the new scheme includes market vesting performance conditions for some of the options grant which makes the fair value calculation more complex.

As a result there is a risk that the fair value of options could be measured incorrectly.

We obtained the grant award details and reviewed the performance conditions considering the reasonableness of the judgements made by management in determining the relevant assumptions utilised in determining the fair value of the options. We reviewed the fair value using a Monte Carlo method for all options issued with market vesting performance conditions and Black Scholes for any with non-market vesting conditions to test the accuracy of the calculation.

Our approach was underpinned by the following testing:

- Assumed volatility was compared to the historical share price volatility of the Company since listing and also benchmarked against other companies in similar industries.
- The dividend rate was reviewed against the Group's dividend history and management's assessment that no dividends will be declared in the foreseeable future.
- The exercise price was agreed to the Group share option award agreements and the board meeting minutes approving the transaction.
- The interest rate was compared to the UK 10 year Gilt rate at the date of issue for a comparable period and found to be materially similar.
- The share price at grant date was compared to the listed share price on the day of grant.

In light of the above, we found that the method of calculating the fair value of share options has been applied consistently and with reasonable assumptions. The charge booked was not materially sensitive to what we considered to be a range of realistically possible alternative outcomes as to the levels of performance attained.

**Completeness of research and development accruals**

The Group is a clinical-stage speciality biopharmaceutical group focused on the development and commercialisation of a range of immunotherapy products for the treatment of allergies.

The research operations of the Group are outsourced to Clinical Research Organisations (CROs) who submit applications for payment at regular intervals throughout the clinical trials.

During the year research and development costs for the Group totalled £38.6m of which £4.5m was accrued at year end in relation to invoices not yet received.

The appropriate timing and accuracy of these costs between financial periods requires close monitoring. Submissions for payment by suppliers do not always correspond to the periods in which the underlying activities occurred, making the underlying calculations for the accruals more complex.

We performed substantive procedures to identify liabilities which were not recorded at the year end. This included testing a sample of invoices received after the year end and post year-end payments to confirm that they were recorded in the correct period.

We compared the level of expenses incurred to the previous year and to budget in order to identify any areas of apparent underspend where accruals may be required.

We further tested a sample of accruals to subsequent invoices received from suppliers to identify any significant differences.

From our procedures in relation to Research and Development accruals, there were no significant matters arising. We identified no material errors in the timing and accuracy of costs and their recognition in the correct period.

**How we tailored the audit scope**

We tailored the scope of our audit to ensure that we performed enough work to be able to give an opinion on the financial statements as a whole, taking into account the geographic structure of the Group, the accounting processes and controls, and the industry in which the Group operates.

The Group consists of four entities which are consolidated into the Group financial statements along with an equity investment in a joint venture. The majority of the Group's operations are managed from the UK along with all associated books and records. A US subsidiary was created during the year which currently pays US employees. The joint venture is based in Canada but is immaterial to the Group. The costs incurred in the US are not significant to the Group.

The most significant Group entity (Circassia Limited) was identified as requiring an audit of its complete financial information because its activity constituted the majority of the Group's trading activity. In addition one further entity required an audit of certain balances based on its level of contribution to the Group's overall results.

This work, all of which was carried out by the Group audit team, together with additional procedures performed on the consolidation, gave us sufficient appropriate audit evidence for our opinion on the Group financial statements as a whole.

# Independent Auditors' report to the members of Circassia Pharmaceuticals plc continued

## Materiality

The scope of our audit was influenced by our application of materiality. We set certain quantitative thresholds for materiality. These, together with qualitative considerations, helped us to determine the scope of our audit and the nature, timing and extent

of our audit procedures and to evaluate the effect of misstatements, both individually and on the financial statements as a whole.

Based on our professional judgement, we determined materiality for the financial statements as a whole as follows:

Overall Group materiality	£463k (2013: £245k).
How we determined it	1% of total Group expenses.
Rationale for benchmark applied	The Group is currently at the research & development stage and therefore generates no revenue. As a result, business performance is monitored by investors as the level of spend for the year, which equates to total Group expenses.

We agreed with the Audit Committee that we would report to them misstatements identified during our audit above £23k (2013: £12k) as well as misstatements below that amount that, in our view, warranted reporting for qualitative reasons.

## Going concern

Under the Listing Rules we are required to review the Directors' statement, set out on page 72, in relation to going concern. We have nothing to report having performed our review.

As noted in the Directors' statement, the Directors have concluded that it is appropriate to prepare the financial statements using the going concern basis of accounting. The going concern basis presumes that the Group and parent Company have adequate resources to remain in operation, and that the Directors intend them to do so, for at least one year from the date the financial statements were signed. As part of our audit we have concluded that the Directors' use of the going concern basis is appropriate.

However, because not all future events or conditions can be predicted, these statements are not a guarantee as to the Group's and parent Company's ability to continue as a going concern.

## Other required reporting

### Consistency of other information

Companies Act 2006 opinions

In our opinion:

- the information given in the Strategic report and the Directors' report for the financial year for which the financial statements are prepared is consistent with the financial statements; and
- the information given in the Corporate governance statement set out on pages 36 to 41 with respect to internal control and risk management systems and the information about share capital structures are in the Directors' report on pages 69 to 71, consistent with the financial statements.

## Under ISAs (UK & Ireland) reporting

Under ISAs (UK & Ireland) we are required to report to you if, in our opinion:

<ul style="list-style-type: none"> <li>— information in the Annual report is: <ul style="list-style-type: none"> <li>— materially inconsistent with the information in the audited financial statements; or</li> <li>— apparently materially incorrect based on, or materially inconsistent with, our knowledge of the Group and parent Company acquired in the course of performing our audit; or</li> <li>— otherwise misleading.</li> </ul> </li> </ul>	We have no exceptions to report arising from this responsibility.
<ul style="list-style-type: none"> <li>— the statement given by the Directors on page 40, in accordance with provision C.1.1 of the UK Corporate Governance Code ("the Code"), that they consider the Annual report taken as a whole to be fair, balanced and understandable and provides the information necessary for members to assess the Group's and parent Company's performance, business model and strategy is materially inconsistent with our knowledge of the Group and parent Company acquired in the course of performing our audit.</li> </ul>	We have no exceptions to report arising from this responsibility.
<ul style="list-style-type: none"> <li>— the section of the Annual report on page 42, as required by provision C.3.8 of the Code, describing the work of the Audit Committee does not appropriately address matters communicated by us to the Audit Committee.</li> </ul>	We have no exceptions to report arising from this responsibility.

### **Adequacy of accounting records and information and explanations received**

Under the Companies Act 2006 we are required to report to you if, in our opinion:

- we have not received all the information and explanations we require for our audit; or
- adequate accounting records have not been kept by the parent Company, or returns adequate for our audit have not been received from branches not visited by us; or
- the parent Company financial statements and the part of the Directors' Remuneration report to be audited are not in agreement with the accounting records and returns.

We have no exceptions to report arising from this responsibility.

### **Directors' remuneration**

Directors' remuneration report – Companies Act 2006 opinion  
In our opinion, the part of the Directors' remuneration report to be audited has been properly prepared in accordance with the Companies Act 2006.

### **Other Companies Act 2006 reporting**

Under the Companies Act 2006 we are required to report to you if, in our opinion, certain disclosures of Directors' remuneration specified by law are not made. We have no exceptions to report arising from this responsibility.

### **Corporate governance statement**

Under the Companies Act 2006 we are required to report to you if, in our opinion, a corporate governance statement has not been prepared by the parent Company. We have no exceptions to report arising from this responsibility.

Under the Listing Rules we are required to review the part of the Corporate Governance Statement relating to the parent Company's compliance with nine provisions of the UK Corporate Governance Code. We have nothing to report having performed our review.

### **Responsibilities for the financial statements and the audit Our responsibilities and those of the Directors**

As explained more fully in the Directors' Responsibilities Statement set out on page 72, the Directors are responsible for the preparation of the financial statements and for being satisfied that they give a true and fair view.

Our responsibility is to audit and express an opinion on the financial statements in accordance with applicable law and ISAs (UK & Ireland). Those standards require us to comply with the Auditing Practices Board's Ethical Standards for Auditors.

This report, including the opinions, has been prepared for and only for the Company's members as a body in accordance with Chapter 3 of Part 16 of the Companies Act 2006 and for no other purpose. We do not, in giving these opinions, accept or assume responsibility for any other purpose or to any other person to whom this report is shown or into whose hands it may come save where expressly agreed by our prior consent in writing.

### **What an audit of financial statements involves**

An audit involves obtaining evidence about the amounts and disclosures in the financial statements sufficient to give reasonable assurance that the financial statements are free from material misstatement, whether caused by fraud or error. This includes an assessment of:

- whether the accounting policies are appropriate to the Group's and the parent Company's circumstances and have been consistently applied and adequately disclosed;
- the reasonableness of significant accounting estimates made by the Directors; and
- the overall presentation of the financial statements.

We primarily focus our work in these areas by assessing the Directors' judgements against available evidence, forming our own judgements, and evaluating the disclosures in the financial statements.

We test and examine information, using sampling and other auditing techniques, to the extent we consider necessary to provide a reasonable basis for us to draw conclusions. We obtain audit evidence through testing the effectiveness of controls, substantive procedures or a combination of both.

In addition, we read all the financial and non-financial information in the Annual report to identify material inconsistencies with the audited financial statements and to identify any information that is apparently materially incorrect based on, or materially inconsistent with, the knowledge acquired by us in the course of performing the audit. If we become aware of any apparent material misstatements or inconsistencies we consider the implications for our report.

### **Simon Ormiston (Senior Statutory Auditor)**

for and on behalf of PricewaterhouseCoopers LLP  
Chartered Accountants and Statutory Auditors  
London, Embankment Place

26 February 2015

# Consolidated statement of comprehensive income

For the year ended 31 December 2014

	Notes	2014 £'000	2013 £'000
Research and development costs		(38,574)	(21,101)
Administrative expenses		(7,239)	(3,817)
Other gains	8	–	393
<b>Operating loss</b>	6	<b>(45,813)</b>	<b>(24,525)</b>
Finance costs	5	(18)	(21)
Finance income	5	1,924	606
<b>Finance income – net</b>		<b>1,906</b>	<b>585</b>
Share of (loss)/profit of joint venture	14	(82)	46
<b>Loss before tax</b>		<b>(43,989)</b>	<b>(23,894)</b>
Taxation	9	8,881	3,913
<b>Loss for the financial year attributable to owners of the parent</b>		<b>(35,108)</b>	<b>(19,981)</b>
Other comprehensive expense			
Items that may be subsequently reclassified to profit or loss:			
Share of other comprehensive expense of joint venture	14	(10)	(18)
Currency translation differences	24	(6)	–
<b>Total other comprehensive expense for the year, net of tax</b>		<b>(16)</b>	<b>(18)</b>
<b>Total comprehensive expense for the year</b>		<b>(35,124)</b>	<b>(19,999)</b>

## Loss per share attributable to owners of the parent during the year (expressed in £ per share)

	£	£
<b>Basic and diluted loss per share</b>		
Loss per share from continuing operations	(0.21)	(1.26)

The results for the financial years above are derived entirely from continuing operations.

The Company has elected to take the exemption under section 408 of the Companies Act 2006 not to present the parent Company profit and loss account.

The profit for the parent Company for the year was £467k (2013: £57k).

The notes on pages 84 to 105 are an integral part of these consolidated financial statements.



# Consolidated statement of financial position

as at 31 December 2014

	Notes	2014 £'000	2013 £'000
<b>Assets</b>			
<b>Non-current assets</b>			
Property, plant & equipment	11	309	–
Intangible assets	12	2,050	2,012
Investment in joint venture	14	103	195
		<b>2,462</b>	<b>2,207</b>
<b>Current assets</b>			
Other receivables	15	2,649	1,215
Current tax assets	9	8,824	3,995
Short-term bank deposits	16	156,874	7,047
Cash and cash equivalents	16	29,716	23,568
		<b>198,063</b>	<b>35,825</b>
<b>Total assets</b>		<b>200,525</b>	<b>38,032</b>
<b>Equity and liabilities</b>			
<b>Equity attributable to the owners of the parent Company</b>			
Ordinary shares	21	152	13
Preference shares	21	–	52
Share premium	23	297,938	103,403
Share option reserve	25	1,305	56
Translation reserve	24	(6)	–
Accumulated losses	25	(108,630)	(73,479)
<b>Total equity</b>		<b>190,759</b>	<b>30,045</b>
<b>Liabilities</b>			
<b>Current liabilities</b>			
Trade and other payables	17	9,766	5,975
Financial liabilities	18	–	2,012
<b>Total liabilities</b>		<b>9,766</b>	<b>7,987</b>
<b>Total equity and liabilities</b>		<b>200,525</b>	<b>38,032</b>

The notes on pages 84 to 105 are an integral part of these consolidated financial statements.


The financial statements on pages 78 to 105 were authorised for issue by the Board of Directors on 26 February 2015 and were signed on its behalf by

**Steven Harris**  
Chief Executive Officer  
Circassia Pharmaceuticals plc

Registered number: 05822706



**Julien Cotta**  
Chief Financial Officer  
Circassia Pharmaceuticals plc



# Parent Company statement of financial position

as at 31 December 2014

	Notes	2014 £'000	2013 £'000
<b>Assets</b>			
<b>Non-current assets</b>			
Investments in subsidiaries	13	3,035	1,780
		<b>3,035</b>	<b>1,780</b>
<b>Current assets</b>			
Other receivables	15	122,583	94,157
Short-term bank deposits	16	156,874	7,047
Cash and cash equivalents	16	18,754	3,839
		<b>298,211</b>	<b>105,043</b>
<b>Total assets</b>		<b>301,246</b>	<b>106,823</b>
<b>Equity and liabilities</b>			
<b>Equity attributable to the owners of the Company.</b>			
Ordinary shares	21	152	13
Preference shares	21	–	52
Share premium account	23	297,938	103,403
Share option reserve	25	1,305	56
Retained earnings	25	1,198	764
<b>Total equity</b>		<b>300,593</b>	<b>104,288</b>
<b>Liabilities</b>			
<b>Current liabilities</b>			
Trade and other payables	17	653	523
Financial liabilities	18	–	2,012
		<b>653</b>	<b>2,535</b>
<b>Total equity and liabilities</b>		<b>301,246</b>	<b>106,823</b>

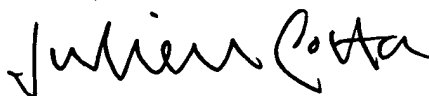
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**Steven Harris**  
Chief Executive Officer  
Circassia Pharmaceuticals plc

**Julien Cotta**  
Chief Financial Officer  
Circassia Pharmaceuticals plc

Registered number: 05822706

# Group and parent Company statement of cash flows

For the year ended 31 December 2014

		<b>Group</b>		<b>Company</b>	
	<b>Notes</b>	<b>2014</b>	<b>2013</b>	<b>2014</b>	<b>2013</b>
		<b>£'000</b>	<b>£'000</b>	<b>£'000</b>	<b>£'000</b>
<b>Cash flows from operating activities</b>					
Cash used in operations	26	(41,010)	(22,168)	(28,695)	(6,199)
Interest received		246	1,279	208	366
Interest paid		(15)	(11)	(7)	–
Tax credit received		4,052	3,019	–	–
<b>Net cash used in operating activities</b>		<b>(36,727)</b>	<b>(17,881)</b>	<b>(28,496)</b>	<b>(5,833)</b>
<b>Cash flows from investing activities</b>					
Investment in subsidiary		–	–	(6)	–
Purchases of intangibles		(38)	–	–	–
Purchases of property, plant & equipment		(333)	–	–	–
(Increase)/decrease in short-term bank deposits		(149,827)	27,179	(149,827)	4,184
<b>Net cash (used in)/from investing activities</b>		<b>(150,198)</b>	<b>27,179</b>	<b>(149,833)</b>	<b>4,184</b>
<b>Cash flows from financing activities</b>					
Proceeds from issue of Ordinary shares		192,574	2	192,574	2
<b>Net cash from financing activities</b>		<b>192,574</b>	<b>2</b>	<b>192,574</b>	<b>2</b>
<b>Net increase/(decrease) in cash and cash equivalents</b>		<b>5,649</b>	<b>9,300</b>	<b>14,245</b>	<b>(1,647)</b>
Cash and cash equivalents 1 January	16	23,568	13,981	3,839	5,621
Exchange gains/(losses) on cash and cash equivalents		499	287	670	(135)
<b>Cash and cash equivalents at 31 December</b>	<b>16</b>	<b>29,716</b>	<b>23,568</b>	<b>18,754</b>	<b>3,839</b>

The notes on pages 84 to 105 are an integral part of these consolidated financial statements.

# Group statement of changes in equity

For the year ended 31 December 2014

	Notes	Share capital £'000	Share premium £'000	Share option reserve £'000	Translation reserve £'000	Accumulated losses £'000	Total equity £'000
<b>At 1 January 2013</b>	21, 23, 25	63	103,403	1	–	(53,480)	49,987
Comprehensive expense:							
Loss for the financial year		–	–	–	–	(19,981)	(19,981)
Other comprehensive expense:							
Share of other comprehensive expense of joint venture		–	–	–	–	(18)	(18)
<b>Total comprehensive expense</b>	25	–	–	–	–	(19,999)	(19,999)
Transactions with owners:							
Issue of Ordinary shares	21	2	–	–	–	–	2
Employee share option scheme	25	–	–	55	–	–	55
<b>At 31 December 2013</b>	21, 23, 25	65	103,403	56	–	(73,479)	30,045
<b>At 1 January 2014</b>	21, 23, 25	65	103,403	56	–	(73,479)	30,045
Comprehensive expense:							
Loss for the financial year		–	–	–	–	(35,108)	(35,108)
Other comprehensive expense:							
Share of other comprehensive expense of joint venture		–	–	–	–	(10)	(10)
Currency translation differences		–	–	–	(6)	–	(6)
<b>Total comprehensive expense</b>	24, 25	–	–	–	(6)	(35,118)	(35,124)
Transactions with owners:							
Issue of Ordinary shares	21	54	194,535	–	–	–	194,589
Capitalised reserves of bonus shares at IPO	25	33	–	–	–	(33)	–
Employee share option scheme	25	–	–	1,249	–	–	1,249
<b>At 31 December 2014</b>	21, 23, 24, 25	<b>152</b>	<b>297,938</b>	<b>1,305</b>	<b>(6)</b>	<b>(108,630)</b>	<b>190,759</b>

The notes on pages 84 to 105 are an integral part of these consolidated financial statements.

# Parent Company statement of changes in equity

For the year ended 31 December 2014

	Notes	Share capital £'000	Share premium £'000	Share option reserve £'000	Retained earnings £'000	Total equity £'000
<b>At 1 January 2013</b>	21, 23, 25	63	103,403	1	707	104,174
Profit and total comprehensive income	25	–	–	–	57	57
Transactions with owners:						
Issue of Ordinary shares	21	2	–	–	–	2
Employee share option scheme	25	–	–	55	–	55
<b>At 31 December 2013</b>	21, 23, 25	65	103,403	56	764	104,288
<b>At 1 January 2014</b>	21, 23, 25	65	103,403	56	764	104,288
Profit and total comprehensive income	25	–	–	–	467	467
Transactions with owners:						
Issue of Ordinary shares	21	54	194,535	–	–	194,589
Capitalised reserves of bonus shares at IPO	25	33	–	–	(33)	–
Employee share option scheme	25	–	–	1,249	–	1,249
<b>At 31 December 2014</b>	21, 23, 25	<b>152</b>	<b>297,938</b>	<b>1,305</b>	<b>1,198</b>	<b>300,593</b>

The notes on pages 84 to 105 are an integral part of these financial statements.

# Notes to the financial statements

## 1. Summary of significant accounting policies

### General information

The Group is a clinical-stage specialty biopharmaceutical group focused on the development and commercialisation of a range of immunotherapy products for the treatment of allergy. These product candidates were developed using the Company's innovative technology, Toleromune® which was initially developed at Imperial College, London by Mark Larché and Barry Kay and acquired by the co-founders of the Company, Steve Harris and Charles Swingland in 2006.

Circassia Pharmaceuticals plc is a public limited company which is listed on the London Stock Exchange and incorporated and domiciled in England and Wales. The Company is resident in England and the registered office is The Magdalen Centre, Robert Robinson Avenue, Oxford Science Park, Oxford, Oxfordshire, England, OX4 4GA.

The principal accounting policies adopted in the preparation of this financial information are set out below. These policies have been consistently applied to all the financial years presented, unless otherwise stated.

### Basis of preparation

The financial information has been prepared in accordance with International Financial Reporting Standards as adopted by the European Union ('IFRS'), International Financial Reporting Interpretations Committee ('IFRIC') interpretations endorsed by the European Union and with those parts of the Companies Act 2006 applicable to companies reporting under IFRS. The financial information is prepared on the going concern basis and in accordance with the historical cost convention as modified by revaluation of financial liabilities (including derivative instruments) at fair value through profit or loss.

### Going concern

Though the Group continues to make losses, the Directors believe it is appropriate to prepare the financial information on the going concern basis. This is because the Group's research into new products continues to progress according to plan and the additional funding secured in March 2014 when the Company successfully completed its IPO, will allow the Group to meet its liabilities as they fall due for the foreseeable future.

### Changes in accounting policy and disclosures

#### a) New and amended standards adopted by the Group

No new or amended standards were adopted during the year.

The following standards had previously been early adopted and applied consistently in the years ended 31 December 2013 and 2014 (effective 1 January 2014 and early adopted from 1 January 2013):

- IFRS 10 'Consolidated financial statements';
- IFRS 11 'Joint arrangements';
- IFRS 12 'Disclosure of interests in other entities';
- IAS 27 (revised 2011), 'Separate financial statements';
- IAS 28 (revised 2011), 'Investments in associates and joint ventures';
- IAS 32 (amendment), 'Financial instruments – Presentation' on asset and liability offsetting;
- Amendments to IFRS 10, IFRS 11 and IFRS 12; and
- Amendments to IAS 36, 'Impairment of assets'.

#### b) Standards, amendments and interpretations to existing standards that are not yet effective and have not been early adopted by the Group

IFRS 9 'Financial instruments', on 'Classification and measurement' (effective 1 January 2015). This is the first part of a new standard on classification and measurement of financial assets that will replace IAS 39. IFRS 9 has two measurement categories: amortised cost and fair value. All equity instruments are measured at fair value. A debt instrument is at amortised cost only if the entity is holding it to collect contractual cash flows and the cash flows represent principal and interest. Otherwise it is at fair value through profit or loss. Amortised cost accounting will also be applicable for most financial liabilities, with bifurcation of embedded derivatives. The main change is that in cases where the fair value option is taken for financial liabilities, the part of a fair value change due to an entity's own credit risk is recorded in other comprehensive income rather than the income statement, unless this creates an accounting mismatch. The Group is yet to assess the impact of IFRS 9 on its financial information. The Group will also consider the impact of the remaining phases of IFRS 9.

IFRS 15 'Revenue from contract with customers' (effective from 1 January 2017), IFRIC 21 'Leases' (effective from 1 January), and IFRS 14 'Regulatory deferral accounts' (effective from 1 January 2016) will have no impact on the Group.

There are no other IFRSs or IFRIC interpretations that are not yet effective that would be expected to have a material impact on the Group.

### Use of estimates and assumptions

The preparation of financial information in conformity with IFRS requires the use of certain critical accounting estimates and assumptions that affect the reported amounts of assets and liabilities at the date of the financial information and the reported amounts of revenues and expenses during the reporting period. Estimates and judgements are continually made and are based on historic experience and other factors, including expectations of future events that are believed to be reasonable in the circumstances.

#### Critical accounting estimates and assumptions

Where the Group makes estimates and assumptions concerning the future, the resulting accounting estimates will seldom exactly match actual results. The estimates and assumptions that have a significant risk of causing a material adjustment to the carrying amounts of assets and liabilities within the next financial year are addressed below.

#### Clinical study accruals

Due to the amounts involved, the estimates and assumptions regarding the amounts accrued for clinical study costs have a greater risk of causing a material adjustment to the carrying amounts of assets and liabilities.

#### Intangible assets

The Group tests annually whether goodwill has suffered any impairment. The key assumptions used for the value in use calculations are given in note 12 and in particular the anticipated launch date. If the Company is unable to obtain regulatory approval or to commercialise its product candidates, or experiences significant delays in doing so, this could result in an impairment of the related goodwill and intellectual property rights.

#### Share based payments

Options were valued using the Black Scholes option pricing model or the Monte Carlo Simulation depending on the type of option issued. For each relevant option grant, individual valuation assumptions were assessed based upon conditions at the date of grant. The range of assumptions in the calculation of share based payments is given in note 22.

#### Classification of IPO costs

Due to the nature of an initial public offering (IPO), new shares are issued to investors to raise additional capital and, along with existing shares, subsequently become listed on a stock exchange. Judgement is required in assessing whether the associated expenditure is directly attributable to the issue of shares and whether it meets the criteria to be offset against the share premium account.

### Consolidation

#### (a) Subsidiaries

Subsidiaries are all entities (including structured entities) over which the Group has control. The Group controls an entity when the Group is exposed to, or has rights to, variable returns from its involvement with the entity and has the ability to affect those returns through its power over the entity. Subsidiaries are fully consolidated from the date on which control is transferred to the Group. They are de-consolidated from the date that control ceases.

Inter-company transactions, balances and unrealised gains on transactions between Group companies are eliminated. Accounting policies of subsidiaries are consistent with the policies adopted by the Group.

#### (b) Joint arrangements

The Group has applied IFRS 11 to all joint arrangements since 1 January 2013. Under IFRS 11 investments in joint arrangements are classified as either joint operations or joint ventures depending on the contractual rights and obligations of each investor. Circassia Pharmaceuticals plc has assessed the nature of its joint arrangements and determined them to be joint ventures. Joint ventures are accounted for using the equity method.

Under the equity method of accounting, interests in joint ventures are initially recognised at cost and adjusted thereafter to recognise the Group's share of the post-acquisition profits or losses and movements in other comprehensive income. When the Group's share of losses in a joint venture equals or exceeds its interests in the joint ventures (which includes any long-term interests that, in substance, form part of the Group's net investment in the joint ventures), the Group does not recognise further losses, unless it has incurred obligations or made payments on behalf of the joint ventures.

Unrealised gains on transactions between the Group and its joint ventures are eliminated to the extent of the Group's interest in the joint ventures. Unrealised losses are also eliminated unless the transaction provides evidence of an impairment of the asset transferred. Accounting policies of the joint ventures have been changed where necessary to ensure consistency with the policies adopted by the Group.

### Segmental reporting

The Group has one single business segment, based upon its proprietary technology, operated out of a single geographical location. This is consistent with the internal reporting provided to the chief operating decision-maker. The chief operating decision-maker, who is responsible for allocating resources and assessing performance, has been identified as the Executive Directors, who make strategic decisions.

### Clinical study expenses

Where payments to clinical study sites are made in advance for the purchase of stocks of materials for use in clinical studies, the relevant costs are included in receivables as prepaid clinical study expenses. Expenses are charged to the statement of comprehensive income as clinical study services are carried out by third-party suppliers, or clinical study materials are received.

# Notes to the financial statements continued

## Financial instruments

The Group's financial instruments comprise cash and cash equivalents, short-term bank deposits, debtors and creditors arising directly from operations.

Cash and cash equivalents comprise cash in hand and short-term deposits which have an original maturity of three months or less and are readily convertible into known amounts of cash. Such assets are classified as current, where management intend to dispose of the asset within twelve months of the end of the reporting period. Bank deposits with maturity of more than twelve months after the end of the reporting period are classified as non-current assets.

The Group previously held derivatives in 2013 which comprised solely of forward rate foreign exchange contracts and were categorised as financial liabilities through profit or loss. Where derivatives exist in the financial year, they are initially recognised at fair value on the date a derivative contract is entered into and are subsequently re-measured at their fair value at each reporting date, with any resulting gain or loss recognised through profit or loss. With the exception of the loan notes in 2013, the Group does not have any committed borrowing facilities, as its cash, cash equivalents and short-term deposits are sufficient to finance its current operations. Cash balances are mainly held on short and medium term deposits with quality financial institutions, in line with the Group's policy to minimise the risk of loss. The main risks associated with the Group's financial instruments relate to interest rate risk and foreign currency risk (note 2).

The Group had in issue loan notes which were convertible into fully paid Ordinary shares at any time and could be redeemed, if they have not previously been converted, on 31 March 2016. The loan notes were recognised initially at fair value, net of transaction costs incurred and subsequently carried at amortised cost. The loan notes were classified as current liabilities as the Group did not have an unconditional right to defer settlement for at least 12 months after the end of the reporting period. As part of the capital reorganisation and prior to the IPO, loan notes were converted into equity shares. Borrowing costs were recognised in profit or loss in the period in which they were incurred. See note 21 for details on the conversion of the loan notes in 2014.

## Leases

Leases in which a significant portion of the risks and rewards of ownership are retained by the lessor are classified as operating leases. Payments made under operating leases (net of any incentives received from the lessor) are charged to the statement of comprehensive income on a straight line basis over the period of the lease.

## Intangible assets

Intangible fixed assets, relating to goodwill and intellectual property rights acquired through licensing or assigning patents and know-how are carried at historic cost, less accumulated amortisation, where the useful economic life of the asset is finite and the asset will probably generate economic benefits exceeding costs. Where a finite useful life of the acquired intangible asset cannot be determined, the asset is tested annually for impairment by allocating the assets to the cash generating units to which they relate. Amortisation would commence when product candidates underpinned by the intellectual property rights become available for commercial use. Amortisation would be calculated on a straight line basis over the shorter of the remaining useful life of the intellectual property or the estimated sales life of the product candidates. No amortisation has been charged to date, as the product candidates underpinned by the intellectual property rights are not yet available for commercial use.

Expenditure on product development is capitalised as an intangible asset and amortised over the expected useful economic life of the product candidate concerned. Capitalisation commences from the point at which technical feasibility and commercial viability of the product candidate can be demonstrated and the Group is satisfied that it is probable that future economic benefits will result from the product candidate once completed. Capitalisation ceases when the product candidate receives regulatory approval for launch. No such costs have been capitalised to date.

Expenditure on research and development activities that do not meet the above criteria, including ongoing costs associated with acquired intellectual property rights and intellectual property rights generated internally by the Group, is charged to the statement of comprehensive income as incurred. Intellectual property and in-process research and development from acquisitions are recognised as intangible assets at fair value. Any residual excess of consideration over the fair value of net assets in an acquisition is recognised as goodwill in the financial statements.

Expenditure on software costs are capitalised as an intangible asset and amortised over the expected useful economic life of the software. Until such an asset is fully developed, the costs are capitalised and classified within intangibles assets as 'Software in development'. These costs are not amortised until the software has been fully developed and operational, at which point the total cost of the software development is amortised over its estimated useful life.

## Impairment of non-financial assets

Assets that have an indefinite useful life, for example goodwill or intangible assets not ready for use, are not subject to amortisation and are tested annually for impairment. Assets that are subject to amortisation are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount may not be recoverable. An impairment loss is recognised for the amount by which the asset's carrying amount exceeds its recoverable amount. The recoverable amount is the higher of an asset's fair value less costs to sell and value in use. For the purposes of assessing impairment, assets are grouped at the lowest levels for which there are separately identifiable cash flows (cash-generating units). Non-financial assets other than goodwill that suffered an impairment are reviewed for possible reversal of the impairment at each reporting date. Charges or credits for impairment are passed through the statement of comprehensive income.

## Property, plant and equipment

Property, plant and equipment is stated at historical cost less depreciation. Historical cost includes expenditure that is directly attributable to the acquisition of the items. Subsequent costs are included in the asset's carrying amount or recognised as a separate asset, as appropriate, only when it is probable that future economic benefits associated with the item will flow to the Group and the cost of the item can be measured reliably. The carrying amount of replaced parts is derecognised. All other repairs and maintenance are charged to the income statement during the financial period in which they are incurred.



Depreciation is calculated using the straight line method to allocate the cost of assets over their estimated useful lives, as follows:

#### Leasehold improvements

Over the life of the unbreakable portion of the lease	43%
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Individually significant tangible assets that are intended to be held by the Group for use in the production or supply of goods and services or for administrative purposes and that are expected to provide economic benefit for more than one year are capitalised. All other assets of insignificant value are charged to the income statement in the year of acquisition.

#### Other receivables

Other receivables are recognised initially at fair value and subsequently measured at amortised cost, using the effective interest method, less provision for impairment. A provision for impairment of other receivables is established when there is objective evidence that the Group will not be able to collect all amounts due according to the original terms of the receivables.

#### Trade payables

Trade payables are obligations to pay for goods or services that have been acquired in the ordinary course of business from suppliers. They are initially recognised at fair value and subsequently held at amortised cost. Accounts payable are classified as current liabilities if payment is due within one year or less. If not, they are presented as non-current liabilities.

#### Cash and cash equivalents

In the consolidated statement of cash flows, cash and cash equivalents include cash in hand, deposits held on call with banks, and other short-term highly liquid investments with original maturities of three months or less from the date of original investment.

#### Share capital

Ordinary shares and Preference shares are classified as equity. All shares are classified as equity as there are no mandatorily redeemable shares in the Company. Incremental costs directly attributable to the issue of new shares or options are shown in equity as a deduction, net of tax, from the proceeds.

#### Employee benefit costs

The Group makes contributions to defined contribution personal pension schemes for its Directors and employees. The pension cost charge recognised in the year represents amounts payable by the Group to the funds. The Group has no further payment obligations once the contributions have been paid. The contributions are recognised as employee benefit expense when they are due.

#### Share based payments

The Group operates a number of equity-settled, share based compensation plans, under which the entity receives services from employees as consideration for equity instruments (options) of the Group. The fair value of the employee services received in exchange for the grant of the options is recognised as an expense. The total amount to be expensed is determined by reference to the fair value of the options granted:

- including the effect of any market performance conditions (for example, an entity's share price);
- excluding the impact of any service and non-market performance vesting conditions (for example, profitability, sales growth targets and remaining an employee of the entity over a specified time period); and
- including the impact of any non-vesting conditions (for example, the requirement for employees to save).

Non-market performance and service conditions are included in assumptions about the number of options that are expected to vest. The total expense is recognised over the vesting period, which is the period over which all of the specified vesting conditions are to be satisfied.

At the end of each reporting period, the Group revises its estimates of the number of options that are expected to vest based on the non-market vesting conditions. It recognises the impact of the revision to original estimates, if any, in the income statement, with a corresponding adjustment to equity.

When the options are exercised, the Company issues new shares. The proceeds received net of any directly attributable transaction costs are credited to share capital (nominal value) and share premium.

The grant by the Company of options over its equity instruments to the employees of subsidiary undertakings in the Group is treated as a capital contribution. The fair value of employee services received, measured by reference to the grant date fair value, is recognised over the vesting period as an increase to investment in subsidiary undertakings, with a corresponding credit to equity in the parent entity financial statements.

The Group's employees participate in various share option schemes as disclosed in note 22. Equity settled share based payments are measured at fair value at the date of grant and expensed on a straight line basis over the vesting period of the award. At the end of each reporting period the Group revises its estimate of the number of options that are expected to become exercisable. The financial consequences of revisions to the original estimates, if any, are recognised in the statement of comprehensive income, with a corresponding adjustment to equity.

The fair value of share options is measured using either the Black Scholes option pricing model or the Monte Carlo Simulation. This is dependent on the conditions attached to each of the issued options. Where conditions are non-market based the Black Scholes option pricing model is used. Where market based conditions are attached to options, the fair value is determined using the Monte Carlo Simulation.

# Notes to the financial statements continued

## Other employee benefits

The expected cost of compensated short-term absence (e.g. holidays) is recognised when employees render services that increased their entitlement. An accrual is made for holidays earned but not taken, and prepayments recognised for holidays taken in excess of days earned.

## Foreign currency translation

Monetary assets and liabilities in foreign currencies are translated into Sterling at the rates of exchange ruling at the end of the financial year. Transactions in foreign currencies are translated into Sterling at the rates of exchange ruling at the date of the transaction. Foreign exchange differences are taken to the statement of comprehensive income in the year in which they arise and presented within 'Finance costs or income'.

Foreign exchange differences on translation of foreign operations into the Group presentational currency, are recognised as a separate element of other comprehensive income. Cumulative exchange differences are presented in a separate component of equity entitled translation reserve.

## Taxation including deferred tax

The charge for current tax is based on the results for the year, adjusted for items which are non-assessable or disallowed. It is calculated using tax rates that have been enacted or substantively enacted at the end of each reporting period.

The Group is entitled to claim tax credits in the United Kingdom for certain research and development expenditure. The amount included in the financial statements at the year end represents the credit receivable by the Group for the year and adjustments to prior years.

Deferred tax is accounted for using the liability method in respect of temporary differences arising from differences between the carrying amount of assets and liabilities in the financial information and the corresponding tax bases used in the computation of taxable profit. In principle, deferred tax liabilities are recognised for all taxable temporary differences and deferred tax assets are recognised to the extent that it is probable that taxable profits will be available against which deductible temporary differences can be utilised.

Deferred tax liabilities are recognised for taxable temporary differences arising on investments in subsidiaries and joint ventures, except where the Group is able to control the reversal of the temporary difference and it is probable that the temporary difference will not reverse in the foreseeable future.

Deferred tax is calculated at the average tax rates that are expected to apply to the period when the asset is realised or the liability is settled. Deferred tax is charged or credited in the statement of comprehensive income, except when it relates to items credited or charged directly to equity, in which case the deferred tax is also dealt with in equity.

## 2. Financial and capital risk management

### Capital risk management

The Group's objectives when managing capital are to safeguard the ability to continue as a going concern and ensure that sufficient capital is in place to fund the Group's research activities. The Group's principal method of adjusting the capital available is through issuing new shares. The Group's share capital and share premium are disclosed in notes 21 and 23 respectively. The Group monitors the availability of capital with regard to its forecast future expenditure on an ongoing basis. The Group has extinguished its liability instruments (loan notes) through the issue of equity instruments during the year.

## Financial risk factors

The Group's simple structure, operating from a single location in the United Kingdom, and the lack of external debt financing reduces the range of financial risks to which it is exposed. Monitoring of financial risk is part of the Board's ongoing risk management, the effectiveness of which is reviewed annually. The Group's agreed policies are implemented by the Chief Executive Officer, who submits periodic reports to the Board.

### a) Foreign exchange risk

The Group currently has no revenue. The majority of operating costs are denominated in Sterling, United States dollars, Canadian dollars, Euro or Swiss francs. Foreign exchange risk arises from future commercial transactions and recognised assets and liabilities.

In relation to foreign currency risk, the Group's policy is to hold the majority of its funds in Sterling, and to use short – medium term currency purchase options (including spot purchases and forward contracts) and interest-bearing foreign currency deposits to manage short – medium term fluctuations in exchange rates.

The Group sometimes uses short-term currency purchase options and interest-bearing deposits of Swiss francs and Euros to manage short-term fluctuations in exchange rates. The Group uses foreign currency forward contracts to manage medium term fluctuations in Canadian and United States dollars exchange rates.

At 31 December 2014, if the Euro had weakened/strengthened by 5% against Sterling with all other variables held constant, the post tax loss for the year would have been £5,595 (2013: £709) lower/higher, as a result of net foreign exchange gains/losses on translation of Euro-denominated payables and foreign exchange losses/gains on translation of Euro-denominated bank balances.

The impact on post tax loss at 31 December 2014 of a 5% weakening/strengthening of the US Dollar against Sterling with all other variables held constant would have been a decrease/increase of £30,304 (2013: £38,509).

The impact on post tax loss at 31 December 2014 of a 5% weakening/strengthening of the Canadian dollar against Sterling with all other variables held constant would have been a decrease/increase of £23,713 (2013: £4,627).

The impact on post tax loss at 31 December 2014 of a 15% weakening/strengthening of the Swiss franc against Sterling with all other variables held constant would have been a decrease/increase of £129,561 (2013: based on 5% £4,984).

The change in foreign exchange rates that is assessed to be reasonably likely for each currency except Swiss francs in 2014 is 5%. As the Swiss franc strengthened by 15% after the year end, this has been used as the basis for assessment in determining the impact on post tax loss.

### b) Interest rate risk

The Group's policy in relation to interest rate risk is to monitor short and medium term interest rates and to place cash on deposit for periods that optimise the amount of interest earned while maintaining access to sufficient funds to meet day to day cash requirements.

The Group does not have any committed external borrowing facilities, as its cash and cash equivalents and short-term deposit balances are sufficient to finance its current operations. Consequently, there is no material exposure to interest rate risk in respect of interest payable.

If interest rates had been 10 basis points higher/lower the impact on net loss in 2014 would have been an increase/decrease of £169,105 (2013: £39,800) due to changes in the amount of interest receivable.

**c) Credit risks**

The Group's policy following Admission to the London Stock Exchange is to place funds with financial institutions which have a minimum credit rating with Fitch IBCA of A-long term/F1 short term. During 2014 the Group placed funds on deposit with 12 banks (2013: nine banks). The Group does not allocate a quota to individual institutions but seeks to diversify its investments, where this is consistent with achieving competitive rates of return. It is the Group's policy to place not more than £35 million (or the equivalent in other currencies) with any one counterparty.

The value of financial instruments held represents the maximum exposure that the Group has to them. There is no collateral held for this type of credit risk. No credit limits were exceeded during any of the periods reported, and management does not expect any material losses from non-performance by these counterparties.

**d) Cash flow and liquidity risk**

Funds are generally placed on deposit with the maturity profile of investments being structured to ensure that sufficient liquid funds are available to meet operating requirements. The Directors do not consider that there is presently a material cash flow or liquidity risk.

The table below analyses the Group's financial liabilities into relevant maturity groupings based on the remaining period at the balance sheet date to the contractual maturity date. There were no financial liabilities outstanding for periods greater than one year. The amounts disclosed in the table are the contracted undiscounted cash flows:

	Less than 1 year 2014 £'000	Less than 1 year 2013 £'000
<b>At 31 December</b>		
Trade and other payables	9,766	5,975
Financial liabilities (convertible loan notes)	-	2,012
<b>Total</b>	<b>9,766</b>	<b>7,987</b>

**Derivative financial instruments and hedging**

There were no derivatives at 31 December 2014 or 31 December 2013. Hedge accounting was not used.

**Fair value estimates**

There were no financial liabilities at fair value through profit or loss at 31 December 2014 or 31 December 2013.

# Notes to the financial statements continued

## 3. Principal activity analysis

The Group's loss on ordinary activities before taxation is derived entirely from its one business segment, pharmaceutical research and development, which is carried out at a single site. All costs of acquisition of intangible assets borne by the Group, relate to this one segment. In addition, all other non-cash expenses incurred by the Group relate to this one segment.

## 4. Employees and Directors

The average monthly number of persons (including Executive Directors) employed by the Group during the year was:

By activity	2014 Number	2013 Number
Office and management	15	6
Research and development	34	14
<b>Total average headcount</b>	<b>49</b>	<b>20</b>

### Company

The average number of administration staff employed by the Company during the year, including Executive Directors was 2 (2013: nil).

	Group		Company	
	2014 £'000	2013 £'000	2014 £'000	2013 £'000
<b>Employee benefit costs</b>				
Wages and salaries	6,128	2,744	1,788	–
Social security costs	762	331	183	–
Pension costs	358	215	91	–
Share options expense	1,249	55	–	–
<b>Total employee benefit costs</b>	<b>8,497</b>	<b>3,345</b>	<b>2,062</b>	<b>–</b>

The Group contributes to defined contribution pension schemes for its Executive Directors and employees. Contributions of £29,876 (included in other payables) were payable to the funds at the year end (2013: £8,768).

The details of Directors of the Group who received emoluments from the Group during the year are shown in the Annual report on remuneration in the Remuneration Committee report.

### Key management personnel

Key management includes Directors (Executive and Non-Executive), the VP of Commercial Operations, the Senior VP of Corporate Development, the Chief Commercial Officer (start date 15 September 2014), the General Counsel (start date 7 July 2014), VP of Human Resources (start date 4 June 2014), the Chief Medical Officer (start date 6 January 2014) and the VP of Investor Relations (start date 20 January 2014, leave date 5 August 2014). The compensation paid or payable to key management is set out below.

	2014 £'000	2013 £'000
Salaries and fees	2,048	1,318
Benefits in kind	15	13
Pension contributions to money purchase schemes	208	130
Share based payments	815	55
Bonus	1,221	347
<b>Total</b>	<b>4,307</b>	<b>1,863</b>

## 5. Finance income and costs

	2014 £'000	2013 £'000
<b>Finance costs:</b>		
Bank charges payable	(16)	(11)
Interest payable on loan notes	(2)	(10)
<b>Total finance costs</b>	<b>(18)</b>	<b>(21)</b>
<b>Finance income:</b>		
Bank interest receivable	1,746	606
Net gain on foreign exchange	178	-
<b>Total finance income</b>	<b>1,924</b>	<b>606</b>
<b>Net finance income</b>	<b>1,906</b>	<b>585</b>

Translational foreign exchange gains and losses relating to cash and cash equivalents and short-term deposits have been reallocated from 'Administrative expenses' to 'Finance costs' in 2014.

## 6. Operating loss

	2014 £'000	2013 £'000
Employee benefit costs (note 4)	8,497	3,345
Externally contracted research & development	33,419	19,080
Legal and professional fees including patent costs	1,763	707
Net loss on foreign exchange <sup>1</sup>	-	480
Foreign exchange forward contract derivative (profit) (note 8)	-	(393)
Operating lease expense	330	89
Depreciation	24	-
Impairment	-	122
Other expenses	1,780	1,095
<b>Total operating loss</b>	<b>45,813</b>	<b>24,525</b>

<sup>1</sup> As explained in note 5, translational foreign exchange gains and losses on cash and cash equivalents and short-term deposits have been reallocated from 'Administrative expenses' to 'Finance costs' in 2014 on the face of the income statement. Translational foreign exchange gains and losses on cash and cash equivalents and short-term deposits are disclosed in 'Administrative expenses' in 2013

## 7. Auditors' remuneration

### Services provided by the Group's Auditor and its associates

During the year the Group obtained services from the Auditor as detailed below:

Group	2014 £'000	2013 £'000
Fees payable to the Company's Auditor and its associates for the audit of the parent Company and consolidated financial statements	50	16
Fees payable to the Company's Auditor and its associates for other services:		
The audit of the Company's subsidiaries	5	-
Audit related assurance services	5	-
Tax compliance services	5	5
Other assurance services	235	235
Other	10	-
<b>Total</b>	<b>310</b>	<b>256</b>

# Notes to the financial statements continued

## 8. Other gains

	2014 £'000	2013 £'000
Foreign exchange forward contract derivative gain	–	393

## 9. Taxation

The Group is entitled to claim tax credits in the United Kingdom for certain research and development expenditure. The amount included in the financial statements for the years ended 31 December 2014 and 2013 represents the credit receivable by the Group for the year and adjustments to prior years. The 2014 amounts have not yet been agreed with the relevant tax authorities.

	2014 £'000	2013 £'000
<b>Continuing operations</b>		
United Kingdom corporation tax research and development credit	(8,824)	(3,995)
Adjustments in respect of prior year	(57)	82
<b>Income tax credit</b>	<b>(8,881)</b>	<b>(3,913)</b>

The tax credit for the year is lower (2013: lower) than the standard rate of corporation tax in the UK of 21.5% (2013: 23.25%). The differences are explained below:

	2014 £'000	2013 £'000
<b>Loss on ordinary activities before tax</b>	<b>(43,989)</b>	<b>(23,894)</b>
Loss on ordinary activities before tax multiplied by the standard rate of corporation tax in the UK of 21.5% (2013: 23.25%)	(9,471)	(5,555)
Expenses not deductible for tax purposes (permanent differences)	(937)	12
Temporary timing differences	(43)	–
Research & development relief 100%/125% mark-up on expenses	(7,572)	(4,691)
Surrender of losses for research & development tax credit refund	5,118	4,449
Adjustments in respect of prior year	(57)	82
Tax losses carried forward to future periods	4,081	1,790
<b>Current tax credit for the year</b>	<b>(8,881)</b>	<b>(3,913)</b>

At 31 December 2014, the Group had tax losses to be carried forward of approximately £76.4m (2013: £58.0m).

At 31 December 2014, the Group has current tax assets arising from tax credits in the United Kingdom for certain research and development expenditure of £8.8m (2013: £3.9m).

No deferred tax assets are recognised. See note 20 for more details.

## 10. Loss per share

Basic loss per share is calculated by dividing the loss attributable to Ordinary equity holders of the Company by the weighted average number of Ordinary shares in issue during the year.

	2014	2013
Loss from continuing operations attributable to Ordinary equity owners of the parent Company (£'000)	(35,108)	(19,981)
Weighted average number of Ordinary shares in issue (Number <sup>1</sup> )	169,118,824	15,812,679
<b>Loss per share</b>	<b>(£0.21)</b>	<b>(£1.26)</b>

As net losses from continuing operations were recorded in 2014 and 2013, the dilutive potential shares are anti-dilutive for the earnings per share calculation.

<sup>1</sup> Please refer to called-up share capital note (see note 21) regarding the change in the number of shares. Pursuant to IAS 33.26, the weighted average number of Ordinary shares outstanding during the year and for all years presented have been adjusted for the subdivision of each 10p Ordinary share into 125 Ordinary shares of 0.08p

The additional Ordinary shares issued in respect of the above events have been treated as if the events had occurred at the beginning of the earliest year reported

## 11. Property, plant & equipment

Group	Leasehold Improvements £'000
<b>Cost</b>	
At 1 January and 31 December 2013	–
Additions	333
<b>As at 31 December 2014</b>	<b>333</b>
<b>Accumulated depreciation</b>	
At 1 January and 31 December 2013	–
Depreciation charge	(24)
<b>As at 31 December 2014</b>	<b>(24)</b>
Net book value at 31 December 2013	–
<b>Net book value at 31 December 2014</b>	<b>309</b>

All of the above assets are wholly owned and not pledged as security against any of the Group's liabilities.

## 12. Intangible assets

Group	Goodwill £'000	Intellectual property rights £'000	Software in development £'000	Total £'000
<b>Cost</b>				
At 1 January 2013	1,835	437	–	2,272
Additions	–	–	–	–
As at 31 December 2013	1,835	437	–	2,272
Additions	–	–	38	38
<b>As at 31 December 2014</b>	<b>1,835</b>	<b>437</b>	<b>38</b>	<b>2,310</b>
<b>Accumulated amortisation and impairment</b>				
At 1 January 2013	–	(138)	–	(138)
Impairment charge	–	(122)	–	(122)
As at 31 December 2013	–	(260)	–	(260)
Impairment charge	–	–	–	–
<b>As at 31 December 2014</b>	<b>–</b>	<b>(260)</b>	<b>–</b>	<b>(260)</b>
Net book value at 31 December 2013	1,835	177	–	2,012
<b>Net book value at 31 December 2014</b>	<b>1,835</b>	<b>177</b>	<b>38</b>	<b>2,050</b>

Impairment charges are included within research and development costs in the Consolidated statement of comprehensive income. An impairment test is performed annually based on the value in use of the intangible assets.

The cumulative impairment charge at 1 January 2013 arose in 2008 when the results of a clinical study for dopexamine indicated that one licence agreement should be fully impaired.

## Notes to the financial statements continued

In 2013, the results of the clinical study for the Company's psoriasis product indicated that this licence be fully impaired. In addition, a full impairment charge has been taken on a licence relating to a peanut product.

The goodwill arose on the purchase of 100% of the share capital of Circassia Limited from Imperial Innovations Businesses LLP on 17 July 2006. The goodwill represents the excess of cost over the fair value of assets acquired.

The Group tests annually whether goodwill and intangible assets have suffered any impairment and tests more frequently when events or circumstances indicate that the current carrying value may not be recoverable. No such adverse events or circumstances have arisen in the year and the market capitalisation of the Group at the year end is substantially in excess of the carrying value of the Group's net assets. The Directors consider there to be one cash-generating unit and have determined the recoverable amount based on value in use calculations, which require the use of estimates and assumptions.

The calculations use pre-tax cash flow projections. In light of the stage of development of the product candidates these cover a ten year period. Cash flows beyond the ten year period are extrapolated using the estimated growth rates stated below. The growth rates do not exceed the long-term average growth rate for the business. The discount rate used is pre-tax and reflects specific risks relating to the Group and uncertainties surrounding the cash flow projections, particularly in relation to the assumed successful launch of the Group's products in the expected timeframe and the resulting sales.

The key assumptions used for the value in use calculations for 2013 and 2014 are as follows:

Anticipated launch date	Cat-SPIRE	2017
	Tier 2 product candidates (House Dust Mite-SPIRE, Grass-SPIRE, Ragweed-SPIRE)	2018 – 2020
	Remaining pipeline	2020 – 2022
Research and development costs	Based on management forecasts of clinical study costs for its product candidates, as well as related expenses associated with the regulatory approval process and commercialisation.	
Sales value and volume	Estimates of sales value and volume are internal forecasts based on both internal and external market information and market research commissioned by the Company.	
Advertising and promotion investment	Based on management forecasts of advertising and promotion required in the key territories.	
Profit margins	Margins reflect management's forecasts of sales values and costs of manufacture adjusted for its expectations of market developments.	
Period of specified projected cash flows	10 years	
Terminal growth rate	Terminal growth rates based on management's estimate of future long-term average growth rate: 2014 0% 2013 0%	
Discount rate	Discount rates based on Group WACC, adjusted where appropriate: 2014 20% 2013 20%	

In each case the valuations indicate sufficient headroom such that a change to key assumptions that are reasonably possible is unlikely to result in an impairment of the related goodwill. Therefore, the Group did not take a goodwill impairment charge for the years ended 31 December 2014 and 2013.

Software in development relates to the development of a new financial reporting software platform that was not yet complete at year end. Once this is complete and the system fully operational, it will be reviewed for impairment on a regular basis.



### 13. Investments in subsidiaries

	2014 £'000	2013 £'000
Investments in subsidiaries at 1 January	1,780	1,725
Investment in Circassia Pharmaceuticals Inc	6	–
Equity settled instruments granted to employees of subsidiaries	1,249	55
<b>Investments in subsidiaries at 31 December</b>	<b>3,035</b>	<b>1,780</b>

The capital contribution relating to share based payment is for 3,165,857 (2013: 3,010,375) 0.08p share options granted by the Company to employees of subsidiary undertakings in the Group. Further details on the Group's share option schemes can be found in note 22.

Details of the Company's subsidiaries are provided below. All subsidiaries are included in the consolidation and the Directors believe that the fair value of all subsidiaries exceeds their carrying values.

Name	Country of Incorporation	Nature of business	Proportion of Ordinary shares held
Circassia Limited	UK	Pharmaceutical research	100%
Circassia Pharma Limited	UK	Pharmaceutical research	100%
Circassia Pharmaceuticals Inc	USA	Pharmaceutical research	100%

### 14. Investment in joint venture

	2014 £'000	2013 £'000
<b>At 1 January</b>	<b>195</b>	<b>167</b>
Share of (loss)/profit	(82)	46
Foreign exchange loss on consolidation	(10)	(18)
<b>At 31 December</b>	<b>103</b>	<b>195</b>

The joint venture listed below has share capital consisting solely of Ordinary shares, which are held directly by the Group.

#### Nature of investment in joint venture 2014 and 2013

Name of entity	Place of business/ country of Incorporation	% of ownership interest	Nature of the relationship	Measurement method
Adiga Life Sciences	Canada	50	Note 1	Equity

**Note 1** Adiga Life Sciences ("Adiga") is a joint venture with McMaster University in Canada for early epitope and mechanistic clinical studies. Adiga is a private company and there is no quoted market price available for its shares. There are no contingent liabilities or commitments relating to the Group's interest in the joint venture.

#### Summarised financial information for joint venture

Set out below is the summarised financial information for Adiga which is accounted for using the equity method.

Summarised statement of financial position at 31 December	2014 £'000	2013 £'000
<b>Current assets</b>		
Trade and other receivables	116	436
Cash	695	644
	<b>811</b>	<b>1,080</b>
<b>Current liabilities</b>		
Trade payables	(518)	(600)
Other payables	(88)	(91)
	<b>(606)</b>	<b>(691)</b>
<b>Net assets</b>	<b>205</b>	<b>389</b>

## Notes to the financial statements continued

Summarised statement of comprehensive income for the year ended 31 December	2014 £'000	2013 £'000
Revenue	4,893	4,257
Research & development costs	(5,830)	(5,245)
Administration expense	(28)	(36)
Interest income	2	4
Interest expense	(2)	(2)
Loss from continuing operations	(965)	(1,022)
Income tax income	801	1,114
Post tax (loss)/profit from continuing operations	(164)	92
Other comprehensive expense	(20)	(37)
Total comprehensive (expense)/income	(184)	55

The information above reflects the amounts presented in the financial statements of the joint venture adjusted for differences in accounting policies between the Group and the joint venture (and not Circassia Pharmaceuticals plc's share of those amounts).

### Reconciliation of summarised financial information

Reconciliation of the summarised financial information presented to the carrying amount of the Company's interest in the joint venture.

Summarised financial information	2014 £'000	2013 £'000
Opening net assets 1 January	389	334
(Loss)/profit for the year	(164)	92
Other comprehensive expense	(20)	(37)
Closing net assets	205	389
Interest in joint venture @ 50%	103	195
Carrying value	103	195

### 15. Other receivables

	Group		Company	
	2014 £'000	2013 £'000	2014 £'000	2013 £'000
Other receivables	700	717	64	90
Prepayments and accrued interest	1,949	498	1,530	449
Receivables from subsidiary undertakings	-	-	120,989	93,618
<b>Total trade and other receivables</b>	<b>2,649</b>	<b>1,215</b>	<b>122,583</b>	<b>94,157</b>

The fair value of other receivables are their current book values.

Receivables from subsidiary undertakings are amounts provided by the Company to its subsidiaries in order to undertake studies.

The receivable is unsecured, interest free and has no fixed date of repayment. Recoverability of the amount is dependent on the success of those studies.

The carrying amounts of the Group and Company other receivables, excluding prepayments and recoverable taxes, are denominated in the following currencies:

	Group		Company	
	2014 £'000	2013 £'000	2014 £'000	2013 £'000
UK pounds	1,552	1,205	122,494	94,148
United States dollar	-	7	-	7
Canadian dollar	14	2	14	2
Other currencies	-	1	-	-
	<b>1,566</b>	<b>1,215</b>	<b>122,508</b>	<b>94,157</b>

## 16. Cash and cash equivalents and short-term bank deposits

	Group		Company	
	2014 £'000	2013 £'000	2014 £'000	2013 £'000
Short-term bank deposit, with original maturity: More than 3 months	156,874	7,047	156,874	7,047
<b>Total short-term bank deposits</b>	<b>156,874</b>	<b>7,047</b>	<b>156,874</b>	<b>7,047</b>
Cash and cash equivalents:				
Cash at bank and in hand	29,716	23,568	18,754	3,839
<b>Total cash and cash equivalents</b>	<b>29,716</b>	<b>23,568</b>	<b>18,754</b>	<b>3,839</b>

The Group and Company cash and cash equivalents and short-term deposits are held with institutions with the following Fitch IBCA long-term rating:

	Group		Company	
	2014 £'000	2013 £'000	2014 £'000	2013 £'000
AA-	51,446	12,641	40,593	-
A+	35,000	-	35,000	-
A	92,114	7,858	92,005	770
A-	8,030	-	8,030	-
BBB-	-	10,116	-	10,116
	<b>186,590</b>	<b>30,615</b>	<b>175,628</b>	<b>10,886</b>

The Group and Company cash and cash equivalents and short-term deposits are held in the following currencies at 31 December:

	Group		Company	
	2014 £'000	2013 £'000	2014 £'000	2013 £'000
UK pounds	157,899	13,255	154,437	3,270
United States dollar	11,683	14,532	11,321	6,197
Canadian dollar	9,462	1,489	8,030	1,419
Euro	1,979	48	1,840	-
Swiss franc	5,567	1,291	-	-
	<b>186,590</b>	<b>30,615</b>	<b>175,628</b>	<b>10,886</b>

## 17. Trade and other payables

	Group		Company	
	2014 £'000	2013 £'000	2014 £'000	2013 £'000
Trade payables	2,746	3,461	321	523
Social security and other taxes	199	104	-	-
Other payables	40	19	-	-
Accruals	6,781	2,391	332	-
<b>Total trade and other payables</b>	<b>9,766</b>	<b>5,975</b>	<b>653</b>	<b>523</b>

# Notes to the financial statements continued

## 18. Financial liabilities

	<b>Group</b>		<b>Company</b>	
	<b>2014</b>	<b>2013</b>	<b>2014</b>	<b>2013</b>
	<b>£'000</b>	<b>£'000</b>	<b>£'000</b>	<b>£'000</b>
Convertible loan notes	-	2,012	-	2,012
<b>Financial liabilities</b>	<b>-</b>	<b>2,012</b>	<b>-</b>	<b>2,012</b>

The Group had in issue nil (2013: 115) convertible loan notes which accrued interest at the daily Libor rate and were convertible into fully paid Ordinary shares at the option of the holder at any time and were to be redeemed, if they had not previously been converted, on 31 March 2016. The loan notes were classified as current liabilities as the Group did not have an unconditional right to defer settlement for at least 12 months after the end of the reporting period. Borrowing costs were recognised in profit or loss in the period in which they were incurred.

As part of the capital reorganisation in 2014, the 115 loan notes and accrued interest were converted into 7,155 Ordinary shares (note 21).

Included in current financial liabilities is accrued interest of £nil (2013: £0.3m).

## 19. Financial instruments

The Group's financial instruments comprise cash and cash equivalents, derivatives, convertible loan notes, short-term bank deposits, other receivables and trade and other payables. Additional disclosures are set out in the accounting policies relating to risk management (note 2).

The Group had the following financial instruments at 31 December each year:

	<b>2014</b>	<b>2013</b>
	<b>£'000</b>	<b>£'000</b>
<b>Assets</b>		
Cash and cash equivalents	29,716	23,568
Short-term bank deposits	156,874	7,047
Other receivables	1,566	1,215
<b>Loans and receivables</b>	<b>188,156</b>	<b>31,830</b>
	<b>2014</b>	<b>2013</b>
	<b>£'000</b>	<b>£'000</b>
<b>Liabilities</b>		
Trade and other payables – current	9,766	5,975
Financial liabilities	-	2,012
<b>Financial liabilities at amortised cost</b>	<b>9,766</b>	<b>7,987</b>

The Company had the following financial instruments at 31 December each year:

	2014 £'000	2013 £'000
<b>Assets</b>		
Cash and cash equivalents	18,754	3,839
Short-term bank deposits	156,874	7,047
Other receivables	1,519	539
Receivable from subsidiary undertaking	120,989	93,618
<b>Loans and receivables</b>	<b>298,136</b>	<b>105,043</b>

	2014 £'000	2013 £'000
<b>Liabilities</b>		
Trade and other payables – current	653	523
Financial liabilities	-	2,012
<b>Financial liabilities at amortised cost</b>	<b>653</b>	<b>2,535</b>

Cash balances comprise floating rate instant access deposits earning interest at prevailing bank rates. Short-term deposits bear interest at fixed rates.

In accordance with IAS 39 'Financial instruments Recognition and Measurement' the Group has reviewed all contracts for embedded derivatives that are required to be separately accounted for if they do not meet certain requirements set out in the standard. There were no such derivatives identified at 31 December 2014 or 31 December 2013.

#### Fair value

The Directors consider that the fair values of the Group's financial instruments do not differ significantly from their book values.

## 20. Deferred taxation

The Group has no recognised deferred tax assets or liabilities at 31 December 2014 (2013: £nil). The Group has an unrecognised deferred tax asset in respect of:

	2014 £'000	2013 £'000
Losses	15,323	11,652
Accelerated capital allowances	43	-
Other	1,337	1
<b>Total unrecognised deferred tax asset</b>	<b>16,703</b>	<b>11,653</b>

In light of the continuing losses, recovery of the deferred tax asset is not sufficiently certain, and therefore no asset has been recognised.

# Notes to the financial statements continued

## 21. Share capital

	2014 £'000	2013 £'000
<b>Authorised, called up and fully paid<sup>1</sup></b>		
189,419,634 (2013: 80,548,375) Ordinary shares of 0.08p each	152	65

<sup>1</sup> All numbers of Ordinary shares in the 2013 column above were updated retrospectively to give effect to the capital reorganisation which occurred on 18 March 2014

The change in the number of shares in 2013 is reconciled below:

2013 Share capital pre and post capital reorganisation	Post capital reorganisation Number	Capital <sup>2</sup> reorganisation Number	Pre capital reorganisation Number
Ordinary shares of 10p	-	-	129,489
A Preference shares of 10p	-	-	147,932
B Preference shares of 10p	-	-	366,967
Conversion and subdivision of 10p Ordinary shares into 0.08p Ordinary shares	-	79,903,987	-
<b>Ordinary shares</b>	<b>80,548,375</b>	<b>79,903,987</b>	<b>644,388</b>

<sup>2</sup> See note 21 (a) and (d). The Preference A and B shares were converted into 10p Ordinary shares and all 10p Ordinary shares were subsequently subdivided into 0.08p Ordinary shares

On 24 February 2014, a Director of the Company, exercised 4,000 EMI share options, which resulted in 4,000 Ordinary shares of 10p (equivalent to 500,000 Ordinary shares of 0.08p) being issued, with proceeds on exercise of £400.

Immediately prior to admission of the Company's shares on the London Stock Exchange, the Company effected a capital reorganisation, which resulted in the following:

### a) Conversion of Preference shares to Ordinary shares

There were 514,898 Preference shares all of which converted automatically into Ordinary shares at a conversion rate of one Ordinary share for each Preference share held.

### b) Issue of liquidation Preference shares

Each holder of Preference shares was issued additional Ordinary shares (Liquidation Preference shares) by the Company. This was by way of capitalisation of reserves and resulted in the issue of 327,708 additional 10p Ordinary shares.

### c) Conversion of loan notes

As part of the capital reorganisation, the 115 loan notes were converted into 7,155 Ordinary shares of 10p in the Company.

### d) Initial Public Offering

On 18 March 2014, the Company subdivided each 10p Ordinary share held (983,250) into 125 Ordinary shares of 0.08p (122,906,250). In addition, 64,516,129 new Ordinary shares of 0.08p were issued, raising gross proceeds of £200 million.

On 20, 22, 24 and 27 March 2014, a number of employees exercised their EMI options, which resulted in 1,363,875 shares being issued, with exercise proceeds of £1,091.10.

On 11 April 2014, 633,380 Ordinary shares of 0.08p from the Over-Allotment Option were issued, raising gross proceeds of approximately £2 million.

## 22. Share based payments

### Share options

Options have been awarded under the Circassia PSP Share Option Scheme ("the PSP Scheme"), the Circassia EMI Share Option Scheme ("the EMI Scheme") and the Circassia Unapproved Share Option Scheme ("the Unapproved Scheme").

The share options outstanding can be summarised as follows:

	2014 Number of Ordinary shares ('000)	2013 <sup>1</sup> Number of Ordinary shares ('000)
PSP Scheme <sup>(i)</sup>	1,969	–
EMI Scheme <sup>(ii)</sup>	535	2,399
Unapproved Scheme <sup>(iii)</sup>	661	611
	<b>3,165</b>	<b>3,010</b>

The contractual life of all options is 10 years and the options cannot normally be exercised before the third anniversary of the date of grant.

- (i) All employees of the Group are eligible for options over 0.08p Ordinary shares in the Company. Options granted under the PSP Scheme do not have a fixed exercise price and are subject to additional vesting performance conditions. The performance conditions state that 70% of an award shall vest subject to the Company Total Shareholder Return (TSR) ranking against the Comparator Index TSR and the remaining 30% of an award shall vest subject to the meeting of certain strategic Company objectives.
- (ii) Options granted under the EMI Scheme have a fixed exercise price based on the market price at the date of grant.
- (iii) Options granted under the Unapproved Scheme also have a fixed exercise price based on the market price at the date of grant.
- (iv) All numbers of Ordinary shares in the 2013 column above were updated retrospectively to give effect to the capital reorganisation which occurred on 18 March 2014.

The movement in share options outstanding is summarised in the following table:

	2014		2013 <sup>1</sup>	
	Number ('000)	Weighted average exercise price (£)	Number ('000)	Weighted average exercise price (£)
Outstanding at 1 January	3,010	0.23	2,949	0.0008
Granted	2,439	0.23	438	1.55
Expired	–	n/a	–	n/a
Forfeited	(420)	1.05	–	n/a
Exercised	(1,864)	0.0008	(377)	0.0008
<b>Outstanding at 31 December</b>	<b>3,165</b>	<b>0.25</b>	<b>3,010</b>	<b>0.23</b>
<b>Exercisable at 31 December</b>	<b>631</b>	<b>0.0008</b>	<b>1,598</b>	<b>0.0008</b>

<sup>1</sup> See note 21. The 2013 numbers were updated retrospectively to give effect to the capital reorganisation which occurred on 18 March 2014

The options exercised in 2014 resulted in 1.9m shares (2013: 0.4m shares) being issued at a weighted average price of £0.0008 each (2013: £0.0008 each). The related weighted average share price at the time of exercise was £2.23 (2013: £0.0008) per share.

### Valuation models

The fair value of PSP share options granted during the period was determined using the Monte Carlo Simulation model or Black Scholes model dependent on the performance vesting conditions. All other options granted during the year and in previous years were valued using the Black Scholes valuation model.

The weighted average fair value of options granted during the period determined using the Monte Carlo Simulation model at the grant date was £1.39 per option (2013: £nil).

The weighted average fair value of options granted during the period determined using the Black Scholes valuation model at the grant date was £1.57 per option (2013: £2.16).

## Notes to the financial statements continued

The following weighted average assumptions were used in the Black Scholes model in calculating the fair value of the options granted during the year:

	2014	2013
Share price	£3.19	£2.88
Exercise price	£0.23	£1.55
Expected volatility	50%	50%
Expected life	10 years	10 years
Expected dividends	0%	0%
Risk free interest rate	3%	3%

For the options using the Monte Carlo Simulation, a 50% probability was applied to the number of options likely to vest. Expected volatility is based on historical volatility for a period the same length as the expected option life ending on the date of grant. The risk free rate of return is the yield on zero-coupon UK government bonds of a term consistent with the expected option life. Expected life was based on the contractual life of the options.

### Restricted shares

The Company previously made awards of Ordinary shares to employees and Non-Executive Directors by entering into a form of Restricted share agreement with each participant, under which the participant subscribed for or purchased Ordinary shares in the Company at 10p per Ordinary share (converted into 0.08p shares post capital reorganisation). These shares are subject to certain restrictions on transfer and forfeiture, as set out in the Restricted share agreement. The restrictions lift on the earlier of a sale of the Company and the expiry of a vesting period of between two and three years (depending on the date of award of the Restricted shares).

There were 1.8m Ordinary shares of 0.08p (2013: 1.8m Ordinary shares of 0.08p) in issue at 31 December 2014 and 46,875 Ordinary shares were forfeited during the year (2013: nil).

### Income statement

See note 4 for the total expense recognised in the income statement in respect of the above equity settled instruments granted to Directors and employees.

### 23. Share premium

Group and Company	2014 £'000	2013 £'000
At 1 January	103,403	103,403
Conversion of loan notes into Ordinary shares	2,014	–
Issue of new shares	201,911	–
Expenses relating to share issue	(9,390)	–
<b>At 31 December</b>	<b>297,938</b>	<b>103,403</b>

### 24. Translation reserve

Group	2014 £'000	2013 £'000
At 1 January	–	–
Currency translation differences	(6)	–
<b>At 31 December</b>	<b>(6)</b>	<b>–</b>



## 25. Deficit on reserves

Group	Share option reserve		Accumulated losses	
	2014 £'000	2013 £'000	2014 £'000	2013 £'000
At 1 January (deficit)	56	1	(73,479)	(53,480)
Total comprehensive expense	-	-	(35,118)	(19,999)
Capitalised reserves – bonus shares for Preference shares	-	-	(33)	-
Employee share option scheme	1,249	55	-	-
<b>At 31 December (deficit)</b>	<b>1,305</b>	<b>56</b>	<b>(108,630)</b>	<b>(73,479)</b>

Company	Share option reserve		Retained earnings	
	2014 £'000	2013 £'000	2014 £'000	2013 £'000
At 1 January	56	1	764	707
Total comprehensive income	-	-	467	57
Capitalised reserves – bonus shares for Preference shares	-	-	(33)	-
Employee share option scheme	1,249	55	-	-
<b>At 31 December</b>	<b>1,305</b>	<b>56</b>	<b>1,198</b>	<b>764</b>

## 26. Cash used in operations

### Reconciliation of (loss)/profit before tax to net cash used in operations

	Group		Company	
	2014 £'000	2013 £'000	2014 £'000	2013 £'000
<b>Continuing operations</b>				
(Loss)/profit before tax	(43,989)	(23,894)	467	57
Adjustment for: <sup>1</sup>				
Interest income	(1,746)	(606)	(1,709)	(158)
Interest expense	18	21	9	10
Impairment	-	122	-	-
Depreciation	24	-	-	-
Share of joint venture loss/(profit)	82	(46)	-	-
Fair value loss on derivative	-	(393)	-	(393)
Share based payment charge	1,249	55	-	-
Exchange movements	(6)	-	-	-
Foreign exchange on non-operating cash flows	(499)	8	(670)	430
Changes in working capital:				
Decrease/(increase) in trade and other receivables	65	(492)	(26,922)	(6,668)
Increase in trade and other payables	3,792	3,057	130	523
<b>Net cash used in operations</b>	<b>(41,010)</b>	<b>(22,168)</b>	<b>(28,695)</b>	<b>(6,199)</b>

<sup>1</sup> The conversion of the loan notes is a non-cash item

# Notes to the financial statements continued

## 27. Contingent liabilities

There were no contingent liabilities at 31 December 2014 or at 31 December 2013.

## 28. Operating lease commitments

The total of future minimum lease payments payable under the entity's non-cancellable operating lease for each of the following periods is as follows:

	2014 £'000	2013 £'000
Due within one year	282	17
Due between one and five years	329	–
Due after five years	–	–

The Company operates out of two leased buildings. The operating lease commitment above relates to the lease of the Oxford premises John Eccles House. The second lease currently held does not constitute a commitment due to the existence of an annual break clause.

## 29. Capital commitments

The Group had no capital commitments as at 31 December 2014 (2013: £nil).

## 30. Related party transactions

### Group

There is no ultimate controlling party of the Group as ownership is split between the Company's Shareholders. The most significant Shareholders as at 31 December 2014 are as follows: Invesco Asset Management (35.30% of total voting rights); Imperial Innovations Businesses LLP (13.99% of total voting rights); Oppenheimer Funds Inc (9.23% of total voting rights), Odey Asset Management (7.96% of total voting rights) and Lansdowne Partners Limited (6.10% of total voting rights).

Transactions with related parties during the year and balances with related parties at 31 December are as follows:

Related party	2014 Purchases £'000	2013 Purchases £'000	2014 Payables £'000	2013 Payables £'000
Adiga Life Sciences (Joint venture)	4,920	4,202	–	113
Key management personnel	–	8	–	–
Imperial Innovations Businesses LLP <sup>1,2</sup>	38	27	–	1,487
Steven Harris <sup>2</sup>	–	–	–	262
Charles Swingland <sup>2</sup>	–	–	–	262

<sup>1</sup> 'Purchases' includes compensation paid or payable in respect of services provided by Russ Cummings as Non-Executive Director of the Company

<sup>2</sup> 'Payables' represents the amounts due on the convertible loan notes including accrued interest to 31 December 2013 (see note 18)

Disclosure of compensation provided to Directors is given in the Annual report on remuneration and in note 4 for key management. Included within key management personnel is Chief Commercial Officer (start date 15 September 2014) Linda Szyper. Linda is the spouse of Paul Edick, a Non-Executive Director of the Company. The compensation paid or payable to Linda is shown below:

	2014 £'000	2013 £'000
<b>Key management compensation</b>		
<b>Linda Szyper:</b>		
Short-term employee benefits (including bonus)	147	–
Post-employment benefits	11	–
Share based payments	8	–
<b>Total</b>	<b>166</b>	<b>–</b>

#### Company

The following transactions with subsidiaries occurred in the year:

	<b>Circassia Limited</b>	
	2014 £'000	2013 £'000
<b>Related party</b>		
Rendering of services to Circassia Limited <sup>1</sup>	1,622	(41)
Settlement of liabilities on behalf of the Company	(2,955)	(16)
Net transfer of funds to Circassia Limited	28,704	6,202
	<b>27,371</b>	<b>6,145</b>

<sup>1</sup> Remuneration costs (excluding share options charges) relating to Steven Harris and Julien Cotta in respect of services rendered to Circassia Limited

	2014 £'000	2013 £'000
<b>Balances with subsidiary companies</b>		
<b>Payable:</b>		
Circassia Limited	120,989	93,618

The amount due is unsecured, interest free and has no fixed date of repayment.

#### Employee benefit trust

During the year the Company set up an Employee benefit trust for the purposes of buying and selling shares on the employees' behalf. A total of £5,100 of funding was paid into the Trust by the Company during the year ended 31 December 2014 (2013: £nil). This balance has been included in the Company financial statements on the grounds that the Trust is controlled by the Company.

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# Glossary

**Allergen**

A substance causing an allergic reaction or allergy

**Allergic rhinitis/allergic rhinoconjunctivitis**

An allergic inflammation of the eyes, nasopharynx and nasal airways

**Allergist**

A physician specialising in the diagnosis and treatment of allergies

**Allergy**

An inappropriate immune response by the body to an allergen i.e. a substance (for example a particular food, pollen, animal or plant protein) to which the body has become hypersensitive

**Alternaria**

A genus of ascomycete fungi, otherwise known as a type of mould

**Antibody**

A large protein produced by B-cells that is used by the immune system to identify and neutralise foreign objects such as bacteria and viruses

**Antigen**

The part of the allergen to which antibodies bind

**Asthma**

A common chronic inflammatory disease of the airways characterised by variable and recurring symptoms, reversible airflow obstruction and bronchospasm (which is a sudden constriction of the muscles in the walls of the bronchioles – part of the lungs)

**B-cells**

Part of a group of white blood cells (lymphocytes) which forms part of the immune system. The principal functions of B-cells are to make antibodies against antigens

**Bermuda grass**

Bermuda grass (*Cynodon dactylon*), a grass native to north and east Africa, Asia, Australia and southern Europe

**Birch**

A broad-leaved deciduous hardwood tree of the genus *Betula*

**Cat dander**

A material shed from the body of a cat comprised of skin cells

**Double-blind**

Neither the participants nor the researchers know which participants receive the placebo or the study drug

**Eczema**

A form of chronic inflammation of the skin

**Efficacy**

The ability of an intervention or drug to produce a desired effect

**Environmental exposure chamber (EEC)**

Controlled indoor environment into which controlled amounts of substance can be released

**Epitope**

The part of an antigen that is recognised by the immune system, specifically by antibodies, B-cells, or T-cells

**Fill finish**

Filling and closure of the primary drug container and conduct of post-filling processes, e.g. sealing and inspection, resulting in a product that is suitable for commercial or investigational use following appropriate labelling and packaging

**House dust mite (HDM)**

A small translucent organism belonging to the arachnid class commonly found in mattresses or pillows of beds, sofas and carpets

**Immune cells**

Cells relating to the immune system

**Immunoglobulin**

Antibody

**Immunoglobulin E (IgE)**

A class of antibody specifically involved in triggering the early phase of allergic reactions

**Inflammatory mediators**

Soluble, diffusible molecules that act locally at the site of tissue damage and infection, and at more distant sites

**Japanese cedar**

An evergreen tree also known as *Cryptomeria*, a monotypic genus of conifer in the cypress family *Cupressaceae*

**Lyophilisation**

A dehydration process typically used to preserve a perishable material or make the material more convenient for transport

**Mast cells**

A resident cell of several types of tissues and contains many granules rich in histamine and heparin. It binds IgE and degranulates on exposure to allergen to trigger allergic reactions

**Peptides**

Molecules that are comprised of a series of amino acids

**Perennial Rye**

*Lolium perenne*, a grass from the family *Poaceae* native to Europe, Asia and northern Africa and used worldwide in agriculture

## **Phase II**

In a phase II study, a new product candidate is studied in trials in a relatively homogenous population of subjects who have the relevant allergy. These studies are undertaken to identify possible adverse effects and safety risks, and to explore the preliminary or potential efficacy of the product candidate, as well as dosage tolerance and the optimal effective dose

## **Phase IIb**

Phase II studies are sometimes further divided into two phases: phase IIa trials are designed to assess dosage (how much product candidate subjects should be given); and phase IIb trials are specifically designed to study efficacy (how well the product candidate works at a prescribed dose). Often phase II trials are designed as randomised clinical studies, where some subjects receive the product candidate and others receive a placebo/standard treatment. Randomised phase II trials typically have fewer subjects than randomised phase III trials

## **Phase III**

When phase II trials demonstrate that a specific dosage range of the product candidate is likely to be effective and has an acceptable safety profile, confirmatory phase III trials are undertaken. These studies are intended to provide an adequate basis for establishing the benefit/risk ratio for a subsequent application for marketing approval. Therefore, a sufficiently high number of subjects must be enrolled and exposed to the product candidate for a duration which will provide adequate efficacy and safety data for the envisaged clinical use. The studies must be controlled, i.e. compare the product candidate to placebo and/or to active treatment depending on the medical condition and the product candidate under investigation. Confirmatory phase III trials on specific immunotherapy for the treatment of allergic diseases should be performed using a randomised placebo-controlled double-blind design

## **Placebo**

A sham or simulated medical treatment or procedure

## **Placebo controlled**

A way of testing a medical therapy in which, in addition to a group of subjects that receives the treatment to be evaluated, a separate control group receives a placebo treatment which is specifically designed to have no real effect

## **Pollen**

Fine to coarse powder containing the microgametophytes of seed plants, which produce the male gametes

## **Proof-of-concept**

Early clinical drug development (typically in phase I and phase II) conducted to provide first evidence that a product candidate may be an effective treatment of a certain indication

## **Randomised**

The process of allocating subjects to active drug or placebo in a clinical study

## **Rhinoconjunctivitis**

Irritation and inflammation of the mucous membrane inside the nose and eyes

## **Safety profile**

The known information about how safe a medicine is

## **Seasonal allergy**

An allergy where symptoms are only experienced at certain times of the year

## **Short ragweed**

Ambrosia artemisiifolia, a type of flowering plant common in North America

## **Synthetic peptide immuno-regulatory epitopes (SPIREs)**

Short amino acid sequences that contain the T-cell epitope, and intended to elicit a T-reg response to an allergen identified using the Company's ToleroMune® technology

## **T-cell epitope**

Epitope that is recognised by a T-cell

## **TH2 response**

The defensive response of the immune system response to an allergen, triggered by TH2 cells

## **T-Helper cells class 2 (TH2 cells)**

A sub-group of lymphocytes (a type of white blood cell)

## **Total rhinoconjunctivitis symptom score (TRSS)**

Scoring system used to track the severity of symptoms of rhinoconjunctivitis

## **T-regulatory cells (T-regs)**

A component of the immune system that suppresses immune responses of other cells in the immune system

## **T-regulatory response**

Reaction of T-regs which is to control immune responses

## **Whole allergen immunotherapy**

A process of administering allergenic extracts to allergic subjects to decrease the degree of hypersensitivity and symptoms by reducing immunologic responses to allergens

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## Advisors and contact details

### Financial calendar

- Annual General Meeting: 20 May 2015
- Interim results for the six months ending 30 June 2015: Q3 2015

### Registrars

All administrative enquiries relating to shareholdings and requests to receive corporate documents by email should, in the first instance, be directed to Equiniti. Shareview is Equiniti's shareholder portal offering access to services and information to help manage your shareholdings and inform your important investment decisions.

### Shareview Portfolio

Shareview Portfolio is an online portfolio management tool which enables you to view and manage all the shareholdings you have, where Equiniti is the Registrar, in one place. It is free to use and provides access to a wide range of market information and investment services. Please visit [www.shareview.co.uk](http://www.shareview.co.uk).

This is not a recommendation to buy or sell shares. The price of shares can go down as well as up, and you are not guaranteed to get back the amount that you originally invested.

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### **Forward-looking statements**

This Annual report and accounts contains certain projections and other forward-looking statements with respect to the financial condition, results of operations, businesses and prospects of Circassia. The use of terms such as "may", "will", "should", "expect", "anticipate", "project", "estimate", "intend", "continue", "target" or "believe" and similar expressions (or the negatives thereof) are generally intended to identify forward-looking statements.

These statements are based on current expectations and involve risk and uncertainty because they relate to events and depend upon circumstances that may or may not occur in the future. There are a number of factors that could cause actual results or developments to differ materially from those expressed or implied by these forward-looking statements. Any of the assumptions underlying these forward-looking statements could prove inaccurate or incorrect and therefore any results contemplated in the forward-looking statements may not actually be achieved. Nothing contained in this Annual report and accounts should be construed as a profit forecast or profit estimate. Investors or other recipients are cautioned not to place undue reliance on any forward-looking statements contained herein. Circassia undertakes no obligation to update or revise (publicly or otherwise) any forward-looking statement, whether as a result of new information, future events or other circumstances.

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