A new generation of allergy immunotherapies
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About Circassia

- Founded 2006; listed on LSE (CIR.L) 18 March 2014
- Focused on development of novel immunotherapies for allergy
- Technology originated at Imperial College London
- Potential to revolutionise currently underserved multi-$Bn market
- Broad portfolio of seven product candidates
- Lead candidate in phase III; targets cat allergy (Cat-SPIRE)
- HDM-, ragweed- and grass-SPIREs clinically validated in phase IIb
- Strong IP to at least 2028; global commercial rights retained
- Fully-funded to bring first product to market (£192.5m cash\(^1\) at 30 Oct 2014)

1. Cash, cash equivalents and short-term bank deposits
Circassia’s strategy

*Building a successful specialty pharma company*

- Independently commercialise product candidates in N. America & major EU markets
  - Build or acquire sales and marketing infrastructure
- Establish commercialisation partnerships in other regions

Deliver the pipeline

Market novel products

Build broad & balanced portfolio
Allergic rhinitis is a global healthcare problem

Estimated 400 million sufferers worldwide

- Allergy is medical condition with greatest impact on work productivity in US
- Up to 57% adults and up to 88% children with allergy have sleep problems leading to daytime fatigue
- On any day ~10,000 children are absent from school in US because of allergic rhinitis
- Allergy is a precursor of asthma; treatment with immunotherapy halts “allergic march”

<table>
<thead>
<tr>
<th>USA</th>
<th>Skin prick test positive (%) Popn (million)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rank</td>
<td>Allergen</td>
</tr>
<tr>
<td>1</td>
<td>House dust mite</td>
</tr>
<tr>
<td>2</td>
<td>Perennial rye</td>
</tr>
<tr>
<td>3</td>
<td>Short ragweed</td>
</tr>
<tr>
<td>4</td>
<td>Cockroach</td>
</tr>
<tr>
<td>5</td>
<td>Bermuda grass</td>
</tr>
<tr>
<td>6</td>
<td>Cat</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>Europe</th>
<th>Skin prick test positive (%) Popn (million)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rank</td>
<td>Allergen</td>
</tr>
<tr>
<td>1</td>
<td>House dust mite</td>
</tr>
<tr>
<td>2</td>
<td>Grass pollen</td>
</tr>
<tr>
<td>3</td>
<td>Cat</td>
</tr>
<tr>
<td>4</td>
<td>Birch pollen</td>
</tr>
<tr>
<td>5</td>
<td>Mould</td>
</tr>
<tr>
<td>6</td>
<td>Olive pollen</td>
</tr>
</tbody>
</table>


Immunotherapy is the only way to treat the underlying disease

1. US Census Bureau, 2012
2. World Bank, 2012
3. Gemson & Eng, August 2004
Moderate to severe allergy is inadequately addressed by current therapies

- **Allergen avoidance:** not feasible in majority of cases
- **Symptomatic drugs:** (anti-histamines, nasal corticosteroids etc.) limited efficacy
  - Prescription market estimated at approximately $7bn\(^1\)

### Whole allergen immunotherapy
- Targets cause of allergy leading to tolerance of allergens
- Reduces “allergic march” to asthma

### Subcutaneous Immunotherapy (SCIT)
- Allergen injected
- Lengthy treatment 3 - 5yrs
- Poor patient adherence
- Non-standardised dosing
- High frequency of side effects incl. potential for anaphylaxis

**Total 5 year cost: ~$3,600 – $6,000\(^*\)**

### Sublingual Immunotherapy (SLIT)
- Allergen under the tongue
- Lengthy treatment 1 - 3yrs
- Low adherence (7% complete 3yrs\(^2\))
- US requires EpiPen prescription
- High frequency of side effects incl. potential for anaphylaxis

**Total 1 year cost: $1,400 - $2,700\(^**\)
**Total 3 year cost: ~$9,000\(^**\)

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1. Bloomberg Industries Tx Analysis

\(^*\) Based on Circassia’s estimates

\(^**\) Based on Merck/ALK and Stallergenes published US prices for SLIT treatments

Majority of allergic rhinitis patients consulting a GP have moderate to severe symptoms\(^3\)
Proprietary ToleroMune® technology

*Designed to treat underlying disease with minimal side-effects*

- **ToleroMune® identifies T cell epitopes**
  - Short linear stretches of amino acids in allergen sequence
  - Binds to antigen presenting cells to induce regulatory T cells
  - Identified from blood of allergic individuals

- **SPIREs – Synthetic Peptide Immuno-Regulatory Epitopes**

- **Short treatment provides efficacy without the safety issues**
  - Regulatory T cells down-regulate allergic response
  - Lack of B cell epitopes avoids cross-linking of mast cells eliminating early response / no need to dose escalate
  - Synthetic manufacture – no extraction from whole allergens

- **Broadly applicable across range of allergies**
  - Allergens already identified; no research required

- **Initial development of new SPIRE candidate takes ~18 months**

*Modern, synthetic, rationally-designed pharmaceuticals*
### Technology validated with clinical proof-of-concept in four programmes

<table>
<thead>
<tr>
<th></th>
<th>Development stage</th>
<th>Next milestone</th>
<th>Phase III data</th>
<th>Key findings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cat-SPIRE</strong></td>
<td>Phase III field study (n = 1,182)</td>
<td>Fully recruited Dec’14</td>
<td>H1’16</td>
<td>- Proof-of-concept in multiple products</td>
</tr>
<tr>
<td><strong>Ragweed-SPIRE</strong></td>
<td>Phase IIb study (n = 275)</td>
<td>Additional phase IIb study reports Q1’15</td>
<td>H1’17</td>
<td>- Short course treatment</td>
</tr>
<tr>
<td><strong>Grass-SPIRE</strong></td>
<td>Phase IIb study (n = 282)</td>
<td>Phase II asthmatic study reports H1’15</td>
<td>H2’17</td>
<td>- Efficacy persists over time</td>
</tr>
<tr>
<td><strong>House Dust Mite (HDM) - SPIRE</strong></td>
<td>Phase IIb study (n = 172)</td>
<td>Fully recruit phase IIb field study</td>
<td>H1’19</td>
<td>- Enhanced efficacy in more symptomatic subjects</td>
</tr>
</tbody>
</table>

Japanese Cedar-SPIRE, Birch-SPIRE and Alternaria-SPIRE in early stage development
Clinical trials in over 3,500 subjects
20 studies complete; 8 ongoing

<table>
<thead>
<tr>
<th>Year</th>
<th>Study</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>CP001: PhIIa / n=88 / dose finding</td>
<td></td>
</tr>
<tr>
<td>2009</td>
<td>CP003: PhII / n=48 / asthmatics</td>
<td></td>
</tr>
<tr>
<td>2010</td>
<td>CP005: PhIIb / n=202 / commercial formulation</td>
<td></td>
</tr>
<tr>
<td>2011</td>
<td>CP005A: 1-year follow-up</td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td>CP005B: 2-year follow-up</td>
<td></td>
</tr>
<tr>
<td>2013</td>
<td>CP009: PhIII / n ≥12 / Paediatric</td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td>CP007A: 2-5 year follow-up</td>
<td></td>
</tr>
</tbody>
</table>

**Cat-SPIRE**

<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>TH001: PhIIa / n=50 / dose finding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TH003: n=109 / observational study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TH002: PhIIb / n=172 / EEC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TH002A: 2 year follow-up</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**HDM-SPIRE**

<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR001: PhIIa / n=50 / dose finding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TR002: PhIIb / n=275 / EEC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TR002B: 1-year follow-up</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TR003: n=88 / observational study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TR006: Phase IIb/n=280 / EEC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TR007: Ph II / n=48-60 / asthma</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Ragweed-SPIRE**

<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>TG001: PhIIa / n=50 / dose finding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TG002: PhIIb / n=282 / EEC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TG002A: 2nd season follow-up</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Grass-SPIRE**

<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Note:** Excludes ongoing mechanistic studies (TR002A, RES-003, RES-004, CP007B, RES-008)
Cat-SPIRE phase IIb
Proof-of-concept

- Randomised, placebo-controlled parallel group chamber study
  - Commercial-scale room-temperature stable formulation
- 202 subjects randomised
  - 2 dosing regimens and placebo
- Primary objective: evaluate efficacy in cat allergic subjects following cat allergen challenge
- Subjects in chamber 3 hours per day for 4 days at baseline and at post-treatment challenge
  - Controlled levels of cat dander (similar to house that has a cat)
  - Symptoms recorded every 30 minutes
- Comparison of symptom scores at challenge 5 months after starting treatment to baseline

Skin prick +ve Cat:
US: 17%\(^1\) (53m)
EU: 8-10%\(^2\) (30-37m)

Cat-SPIRE phase IIb (n=202)
Confirmed efficacy

- Total Rhinoconjunctivitis Symptoms Score ("TRSS")
- Patient self-rated scores used as primary efficacy measure
- Scoring system required by regulators
  - Used for approval of intranasal steroids, antihistamines etc.
- Scores measured on 4-point rating scale
  - 0: absent
  - 1: mild, barely noticeable
  - 2: moderate, annoying / troublesome
  - 3: severe, incapacitating
- SPIRE studies use 8 symptoms = 24-point scale; Cat-SPIRE used sneezing & runny / blocked / itchy nose & itchy / watery / red / sore eyes

- TRSS score of 8 could be 8 “mild / barely noticeable scores”
- TRSS score of 12 could be 4 “mild / barely noticeable” and 4 “moderate / annoying” scores

Note: Based on non-asthmatic subjects
Cat-SPIRE phase IIb
Sustained benefit at 1 and 2 years with no additional dosing

1 year follow-up study: Efficacy enhanced over time

2 years follow-up study: Efficacy persists at 2 years

Mean change in TRSS (Baseline minus follow-up)

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>4 x 6nmol</td>
<td>Placebo</td>
<td>4 x 6nmol</td>
</tr>
</tbody>
</table>

Overall TRSS improvement of 3.9 vs. placebo (p = 0.01)

Overall TRSS improvement of 3.9 vs. placebo (p=0.13)

Secondary endpoint: TRSS improvement at end of day 4: 5.1 vs. placebo (p=0.02)

Tolerance persists at least 2 years without further dosing

**Cat-SPIRE represents therapeutic step change**

*More effective and more convenient*

<table>
<thead>
<tr>
<th>Product/Study</th>
<th>Treatment</th>
<th>Difference Active vs. Placebo TRSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat-SPIRE chamber study</td>
<td>4 doses 4 weeks apart</td>
<td>3.9</td>
</tr>
<tr>
<td>ALK-Abelló Grazax® pivotal field study (licensed in Europe) SLIT tablets</td>
<td>Daily 16 weeks before and during season</td>
<td>1.0</td>
</tr>
<tr>
<td>Stallergenes Oralair® grass field study (licensed in Europe) SLIT tablets</td>
<td>Daily 16 weeks before and during season</td>
<td>1.4</td>
</tr>
<tr>
<td>Allergy Therapeutics Pollinex® Quattro grass field study (filed Germany in 2009, not yet approved) adjuvanted whole allergen IT</td>
<td>4 administrations 1 week apart</td>
<td>1.1</td>
</tr>
<tr>
<td>GSK fluticasone furoate perennial rhinitis field study intranasal steroid</td>
<td>Once daily for 4 weeks</td>
<td>0.86</td>
</tr>
<tr>
<td>Sanofi fexofenadine cat chamber study antihistamine</td>
<td>180 mg 2 hours before chamber (ie pre-symptoms)</td>
<td>1.3</td>
</tr>
</tbody>
</table>

1. Based on the 4 x 6 nmol dose of Cat-SPIRE in CP005A
3. TRSS scoring ranges from 16 – 24 points for these studies
Increasing symptom severity

The more symptomatic the subjects the better the result

TRSS score of 12 is modest threshold

Important for future pricing and reimbursement

1 year follow-up study

Mean change in TRSS (Baseline minus follow-up)
Superior safety profile in all programmes
Approved patient-friendly delivery

Superior safety profile

- Adverse events no different to placebo\(^1\)
  - No evidence of asthma exacerbation
  - No increase in infections / infestations (no non-specific immunosuppression)

- Excellent local tolerability
  - Far exceeds conventional and adjuvant short course immunotherapy and SLIT
  - Avoids oral pruritus, mouth oedema and ear pruritus reported for SLIT
  - In Grazax SLIT trial 67% of patients had adverse events vs 8% on placebo\(^2\)

Safety profile comparable to placebo – clearly superior to current immunotherapy

Patient-friendly MicronJet™

- Single use device
- Mounted on standard syringe
- Approved in EU and US
- Included in ragweed, house dust mite and grass chamber studies and cat phase III

Consistent patient-friendly intra-dermal administration

Cat-SPIRE phase III
Single phase III & supporting studies sufficient for registration

1,182 cat-allergic subjects living with cat(s) in the home

Baseline TRSS ≥10

Includes adolescents and controlled asthmatics

Primary endpoint measured 1 year after start dosing
  - Designed with 99% power vs placebo
  - Treatment effect assumed 25% (vs 40% on Day 4 in phase IIb)
  - Variability assumed 50% greater than in observational field study

On track to recruit all subjects by year-end 2014
  - Results expected H1 2016

Observational study and formal regulatory feedback support development plan

Observational study in 105 subjects with cat at home
  - Validation of subject population for phase III with TRSS consistent with phase IIb
  - Informed design and powering of phase III
  - Confirmed importance of ocular symptoms

Regulatory pathway
  - EMA formal Scientific Advice completed
  - End of Phase II meeting with FDA
  - Pre-CTA meeting with Health Canada
  - Clinical trial authorisation in Russia
  - Paediatric Investigation Plan approved by EMA

1,112 phase III subjects (94%) randomised (11 November 2014)
HDM-SPIRE phase IIb (n=172)

Efficacy demonstrated at 1 year

Overall TRSS improvement of 2.8 vs. placebo (p = 0.02) at one year

Mean change in TRSS (Baseline minus follow-up)

Day 1  Day 2  Day 3

Placebo  4 x 12 nmol

Increasing symptom severity

Treatment effect maintained in more symptomatic subjects

Excellent data – similar to Cat-SPIRE at 1 year

Selected for oral presentation at AAAAI 2014

Skin prick +ve HDM:
US: 28%\(^1\) (86m)
EU: 22%\(^2\) (82m)
HDM-SPIRE phase IIb 2 year follow-up study

*Improvement maintained; enhanced effect in more symptomatic*

**Matched subjects at year 1 and 2**

- Overall TRSS improvement of 1.4 vs placebo at two years

**Subjects with baseline TRSS >12**

- Overall TRSS improvement of 3.0 vs placebo

Symptom improvement sustained at same level in same patients
HDM-SPIRE phase IIb field study

Initiated Q3 2014

◆ Randomised, double-blind, placebo-controlled, multi-centre field study
  – Study centres in USA, Canada, France, Germany, Italy, Netherlands, Spain and South Africa

◆ Safety, tolerability and efficacy of 3 treatment regimens
  – 4 x 12 nmol, 8 x 12 nmol, 4 x 20 nmol
  – Comparing optimal course from previous study vs double course vs higher dose

◆ 660 subjects (165 per treatment group)
  – Aged 18-65 years old

◆ Efficacy evaluations include
  – Symptom reduction and use of rescue medication
  – Effect on quality of life and sleep quality

◆ Status
  – Enrolment ongoing
Ragweed-SPIRE phase IIb (n=275)

Proof-of-concept demonstrated

Subjects with mean baseline TRSS ≥8

Overall TRSS improvement of 1.7 vs. placebo (p = 0.066)

Subjects with mean baseline TRSS ≥12

Overall TRSS improvement of 2.9 vs. placebo (p = 0.044)

Skin prick +ve Ragweed: US: 26%¹ (82m)

Stronger efficacy in more symptomatic subjects

Ragweed-SPIRE phase IIb chamber study

*Fully-recruited: 280 subjects randomised*

- Randomised, double-blind, placebo-controlled, phase II chamber study
  - Baseline and dosing pre-ragweed season with challenge after

- Safety, tolerability and efficacy of 3 different dose regimens
  - 8 x 12 nmol, 4 x 6 nmol, 8 x 6 nmol
  - Including best performing regimen from previous study

- 280 subjects (70 per treatment group)

- Efficacy evaluations include
  - Reduction in symptom scores 6 months after dosing

- Status
  - Fully-recruited all subjects randomised
  - Data expected H1 2015
Grass-SPIRE phase IIb (n=282)

*Efficacy demonstrated after first grass season*

### Subjects with mean baseline TRSS ≥8

![Graph showing mean change in TRSS for different days and treatment groups.](image)

**Overall TRSS improvement of 1.6 vs. placebo (p = 0.035)**

### Subjects with mean baseline TRSS ≥12

![Graph showing mean change in TRSS for different days and treatment groups.](image)

**Overall TRSS improvement of 1.9 vs. placebo (p=0.034)**

**Increasing treatment effect over time**

**Enhanced efficacy in the more symptomatic**

Grass-SPIRE phase IIb long-term follow-up studies

Symptom improvement confirmed in same subjects

Initial treatment effect maintained after three grass pollen seasons despite no further doses
Earlier-stage programmes

Broadening the portfolio

◆ Novel product candidate for Birch allergy
  – Toxicology programme to commence H2 2014
  – Recruitment into first-in-man study expected 2015

◆ Novel product candidates for Japanese cedar and Alternaria allergies
  – Candidate epitopes identified
  – Pre-clinical studies ongoing to confirm do not cause histamine release

<table>
<thead>
<tr>
<th>EUROPE</th>
<th>Skin prick test positive</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(% Popln)</td>
</tr>
<tr>
<td>Birch*</td>
<td>6</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>(% Popln)</th>
<th>(million)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Japanese cedar**</td>
<td>56</td>
<td>71.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>US Prevalence (% Popln)</th>
<th>EU Prevalence (% Popln)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alternaria*</td>
<td>13</td>
<td>3.3</td>
</tr>
</tbody>
</table>

# Potential to revolutionise immunotherapy market

<table>
<thead>
<tr>
<th>Key characteristics</th>
<th>Current immunotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Subcutaneous</td>
</tr>
<tr>
<td><strong>Short course immunotherapy giving clearly superior efficacy</strong></td>
<td>✓</td>
</tr>
<tr>
<td>- Efficacy for at least a year with single course</td>
<td></td>
</tr>
<tr>
<td>- Two year follow-up data encouraging¹</td>
<td></td>
</tr>
<tr>
<td><strong>Excellent safety and well-tolerated</strong></td>
<td>✓</td>
</tr>
<tr>
<td>- Safety profile comparable to placebo</td>
<td></td>
</tr>
<tr>
<td>- No anaphylaxis</td>
<td></td>
</tr>
<tr>
<td><strong>Standardised dose</strong></td>
<td>✓</td>
</tr>
<tr>
<td>- No need for dose escalation</td>
<td></td>
</tr>
<tr>
<td>- No need for doses tailored to individual patients</td>
<td></td>
</tr>
<tr>
<td><strong>State-of-the-art synthetic production process</strong></td>
<td>✓</td>
</tr>
<tr>
<td>- No natural whole allergen</td>
<td></td>
</tr>
<tr>
<td>- No potency variation between vials</td>
<td></td>
</tr>
<tr>
<td><strong>Patient-friendly administration</strong></td>
<td>✓</td>
</tr>
</tbody>
</table>

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1. Demonstrated for Cat-SPiRE and HDM-SPiRE, study ongoing for Grass-SPiRE
### Selected sizing and pricing studies

- **US market research for Cat-SPIRE (Kantar / 2010)**
  - 93 allergists, 82 PCPs, 8 payers
  - **US opportunity $0.5-1.0 billion peak annual sales**

- **US pricing research for Cat-SPIRE (Bridgehead / 2011)**
  - 101 allergists, 105 patients, 35 payers
  - **Supports pricing of $2,000-3,000**

- **EU market and pricing research for Cat-SPIRE (PRMA / 2011)**
  - 27 specialists, 28 PCPs, 27 payers
  - **Supports Grazax as the likely benchmark**

- **US market overview for 4 lead SPIRE products (LEK / 2009)**
  - **$2.6bn opportunity in US**

- **US and European research for 4 lead SPIREs (GfK / 2013)**
  - **$2,600 pricing in US**

### Opportunity for Cat-SPIRE

**Illustrative peak sales of c.$500-700mm** for US and EU

- **US:**
  - 200,000 x $2,600 = $520mm
  - **US pricing:** Supported by third party research
  - Equals 5 of 34 new cat allergy patients / month already coming to allergist

- **EU:**
  - 50,000 x $1,500 (€1,100) = $75mm
  - **EU pricing:** Discount to Grazax cost of €2.5-5.3k over 3+ years
  - 1.5 million patients in EU already on allergy immunotherapy

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**Consistent assessment of commercial opportunity**
US market gathering momentum

**Recent approvals to open market to new approaches**

<table>
<thead>
<tr>
<th>Prescribing information</th>
<th>Grastek/Grazax</th>
<th>Ragwitek</th>
<th>Oralair</th>
</tr>
</thead>
<tbody>
<tr>
<td>◆ Initiate <strong>daily</strong> treatment 12 weeks before each grass pollen season</td>
<td>◆ Initiate <strong>daily</strong> treatment 12 weeks before ragweed pollen season</td>
<td>◆ Initiate <strong>daily</strong> treatment 4 months before grass pollen season</td>
<td></td>
</tr>
<tr>
<td>◆ Continue treatment through season</td>
<td>◆ Continue through season</td>
<td>◆ Maintain throughout season</td>
<td></td>
</tr>
<tr>
<td>◆ Grastek may be taken daily for three years (including between seasons)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily cost of treatment</td>
<td>$8.25</td>
<td>$8.25</td>
<td>$10.00</td>
</tr>
<tr>
<td>All require EpiPen to be prescribed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average duration during season (incl. pre-treatment)*</td>
<td>234 days</td>
<td>174 days</td>
<td>270 days</td>
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<tr>
<td>Total pollen season treatment cost</td>
<td>$1,930</td>
<td>$1,435</td>
<td>$2,700</td>
</tr>
<tr>
<td>Example: total cost for 3 pollen seasons</td>
<td>$5,791</td>
<td>$4,306</td>
<td>$8,100</td>
</tr>
<tr>
<td>Duration of 3 years continuous daily treatment</td>
<td>1,095 days</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total 3 years treatment cost</td>
<td>$9,033</td>
<td>-</td>
<td>-</td>
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</tbody>
</table>

*US SLIT costs suggest potential for pricing above $2,600 / course for SPIREs*

*Assumes US & EU grass pollen seasons are: April-August*

*Assumes US ragweed pollen season is: August-end of October.*
Driving incremental revenues for allergists

**Targeting patients already in the office**

No change to market structure

- **Primary focus on eligible patients who decline current IT**
  - Avoids cannibalisation

- **New treatment option for patients already in the allergists’ office**
  - Eligible patients not offered IT
  - Those who decline IT
  - Those who do not finish IT

- **Patients remain with allergist**
  - Patients not lost to PCPs

- **Incremental revenue for allergist**

**US target population for Cat-SPIRE**

<table>
<thead>
<tr>
<th>Cat-allergic individuals</th>
<th>~24 million¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consulting an allergist / specialist</td>
<td>~1.3 million</td>
</tr>
<tr>
<td>Offered IT</td>
<td>~1.0 million</td>
</tr>
<tr>
<td>Accept IT (~378k)</td>
<td></td>
</tr>
<tr>
<td>Complete IT (~60k)</td>
<td></td>
</tr>
</tbody>
</table>

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¹. Kantar Health Quantitative Cat Allergy Report 2010

**Notes**

- **Primary Circassia focus**
  Patients not offered IT

- **Secondary Circassia focus**
  Patients declining IT

- **Secondary Circassia focus**
  Patients failing to complete IT
Full commercial rights retained
Establish direct sales in North America & major EU markets

- Set up / acquire commercial infrastructure
  - Actively evaluating options
  - Potential to license / acquire complementary products

- Anticipated sales force
  - 100 in N America targeting all allergists
  - 90 in EU targeting high prescribers

- Subsequently target other IT high-prescribers
  - Selected ear nose and throat physicians
  - Primary care physicians

- Partner in other markets worldwide

License rights or collaboration

Japan and key RoW markets
### Key upcoming clinical milestones

*Four studies to report* by end H1 2015

<table>
<thead>
<tr>
<th>Programme</th>
<th>Date*</th>
<th>Subjects</th>
<th>Description</th>
<th>Ref.</th>
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</thead>
<tbody>
<tr>
<td>HDM-SPIRE</td>
<td>19 May ‘14</td>
<td>109</td>
<td>Observational study reports</td>
<td>TH003</td>
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<tr>
<td>HDM-SPIRE</td>
<td>13 June ‘14</td>
<td>72</td>
<td>Phase IIb 2 year follow-up reports</td>
<td>TH002A</td>
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<td>HDM-SPIRE</td>
<td>11 Nov ‘14</td>
<td>30</td>
<td>Phase II controlled asthmatic study reports</td>
<td>TH004</td>
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<tr>
<td>HDM-SPIRE</td>
<td>11 Nov ‘14</td>
<td>660</td>
<td>Initiate phase IIb field study</td>
<td>TH005</td>
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<tr>
<td>Grass-SPIRE</td>
<td>11 Nov ‘14</td>
<td>85</td>
<td>Phase IIb third season follow-up reports</td>
<td>TG002B</td>
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<tr>
<td>Ragweed-SPIRE</td>
<td>Q4’14</td>
<td>48-60</td>
<td>Phase II controlled asthmatic study reports</td>
<td>TR007</td>
</tr>
<tr>
<td>Cat-SPIRE</td>
<td>Q4’14</td>
<td>1,182</td>
<td>Complete phase III recruitment</td>
<td>CP007</td>
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<tr>
<td>Ragweed-SPIRE</td>
<td>Q1’15</td>
<td>280</td>
<td>Phase IIb chamber study reports</td>
<td>TR006</td>
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<tr>
<td>Grass-SPIRE</td>
<td>H1’15</td>
<td>Up to 120</td>
<td>Observational study reports</td>
<td>TG003</td>
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<tr>
<td>Grass-SPIRE</td>
<td>H1’15</td>
<td>48-60</td>
<td>Phase II controlled asthmatic study reports</td>
<td>TG004</td>
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<tr>
<td>Cat-SPIRE</td>
<td>H2’15</td>
<td>At least 12</td>
<td>Pilot paediatric safety study reports</td>
<td>CP009</td>
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<tr>
<td>Ragweed-SPIRE</td>
<td>H2’15</td>
<td>-</td>
<td>Enrolment into phase III field study</td>
<td>-</td>
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<tr>
<td>Cat-SPIRE</td>
<td>H1’16</td>
<td>At least 1,182</td>
<td>Phase III study reports</td>
<td>CP007</td>
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<tr>
<td>Grass-SPIRE</td>
<td>H1’16</td>
<td>-</td>
<td>Enrolment into phase III field study</td>
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<tr>
<td>Cat-SPIRE</td>
<td>H2’16</td>
<td>-</td>
<td>File for marketing approval</td>
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*To be included in announcements as appropriate and in-line with financial calendar incl. IMS, half-year/full-year results.*
Summary

◆ **New generation of allergy immunotherapies**
  – Robust long-lasting efficacy after as few as four doses
  – Excellent safety profile with patient-friendly delivery technology
  – Lead product (Cat-SPIRE) in single registration phase III study
  – Three other programmes achieved clinical proof-of-concept in phase IIb

◆ **Large market with significant unmet medical need**
  – Potential to overcome limitations of current treatments
  – Offering allergists additional treatment option

◆ **Ideally-positioned to exploit opportunity**
  – Commercial rights retained; targeting direct sales in N America and key EU markets
  – Commercial scale manufacturing for Cat- and Ragweed-SPIREs
  – Strong IP; multiples layers of protection to at least 2028; potential to add up to 5 yrs
  – Fully funded to bring lead product to market (£192.5m cash\(^1\) at 30 October 2014)

◆ **Experienced management team with proven track record of value creation**

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1. Cash, cash equivalents and short-term bank deposits
<table>
<thead>
<tr>
<th><strong>Contact us:</strong></th>
<th><strong>Investors</strong></th>
<th><strong>Financial and Corporate Communications</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Circassia Ltd</td>
<td>Steven Harris, CEO</td>
<td>FTI Consulting</td>
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<tr>
<td>Northbrook House</td>
<td>Julien Cotta, CFO</td>
<td>200 Aldersgate</td>
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<td>Aldersgate Street</td>
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<tr>
<td>The Oxford Science Park</td>
<td></td>
<td>London EC1A 4HD</td>
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<tr>
<td>Oxford, OX4 4GA</td>
<td>w: <a href="http://www.circassia.co.uk">www.circassia.co.uk</a></td>
<td>t: +44 (0) 20 7831 3113</td>
</tr>
<tr>
<td></td>
<td>e: <a href="mailto:info@circassia.co.uk">info@circassia.co.uk</a></td>
<td>e: <a href="mailto:circassia@FTIConsulting.com">circassia@FTIConsulting.com</a></td>
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