

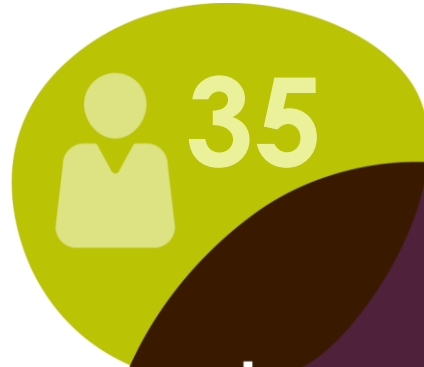


Agenda

- Who we are
- What we do, and how we do it
- What we look for in new staff
- Training and career opportunities ahead

Grey healthcare group aspires to be the most joined-up healthcare communications agency

Market access



Advertising



Medical education



health spoken here™

A global presence driven through regional hubs

New York

Kansas City, MO
Stamford, CT
Cincinnati, OH
Summit, NJ
Rio de Janeiro, Brazil

London

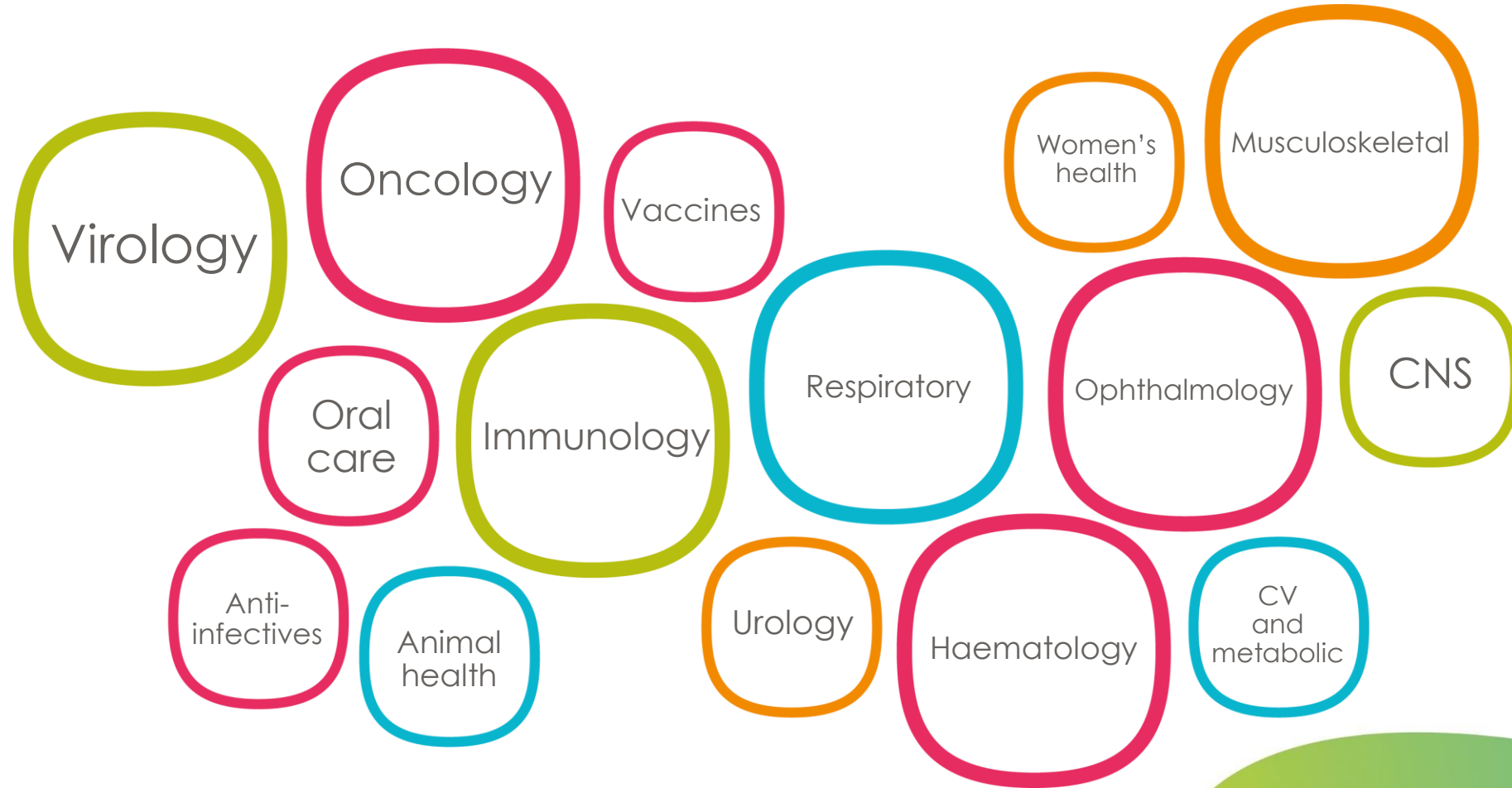
Oxford/ High Wycombe, UK
Madrid, Spain
Freiburg, Germany
Düsseldorf, Germany
Paris, France
Milan, Italy
Prague, Czech Republic
Sandton, South Africa

Singapore

Tokyo, Japan
Kuala Lumpur, Malaysia
Sydney, Australia
Shanghai, China
Hong Kong, China
Auckland, New Zealand



Our experience



Integrated service offering



Strategic support



Publications planning



Thought leader engagement



Scientific events



Medical support



Promotional marketing



Integrated digital solutions



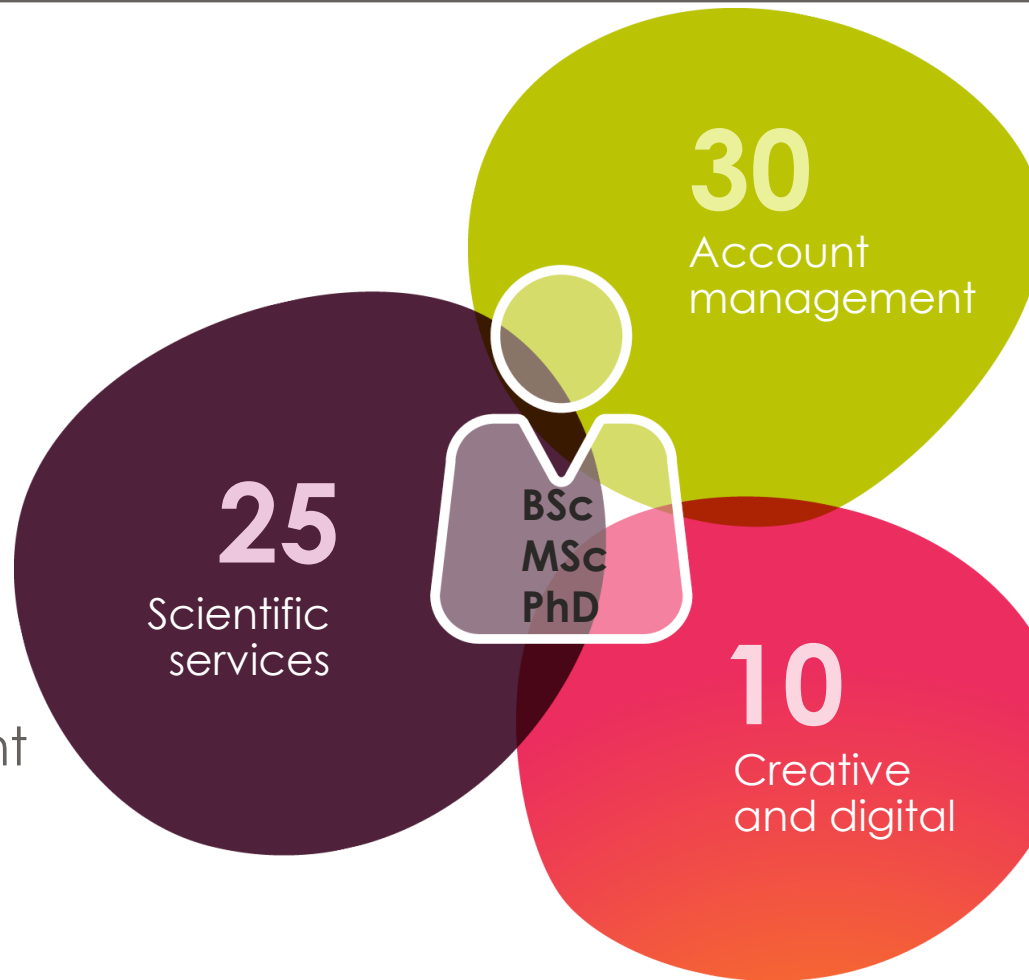
Training programmes



Internal communications

A high-performing medical education team of 65 experts with over 400 years of healthcare experience between them

- Medical experts
- Scientific strategy
- Content development
- Editorial



- Scientifically qualified
- Brand strategy
- Project management

- Healthcare experts
- Print, interactive and video
- Mobile, web and tablet
- Medical animation

Examples of deliverables

- Meetings
 - Advisory boards
 - Symposia
 - Standalone meetings
 - Workshops

Atlantic
Alliance for EAME Ophthalmologists
Managing Dry Eye Disease – challenges and advances

The Atlantic Meeting
5–6 July 2014
Hilton Diagonal Mar
Barcelona, Spain

Established and funded by
ALLERGAN
ophthalmology

Two cyclosporine-based treatments for dry eye disease have significant differences in composition and physicochemical properties
A. Gove,¹ M. Attar,¹ L. Grobolski¹ and C. Pujana¹
¹Allergan, Inc., Irvine, CA, USA; ²Allergan, Inc., Seattle, WA, USA

BACKGROUND
Dry eye disease (DED) is a serious disorder that, if left untreated or undertreated, progressively damages the ocular surface and can lead to vision loss. Inflammation is a key mediator in the vicious cycle of DED pathogenesis, and is triggered by tear film instability, tear film hypoxemia and apoptosis. Cyclosporine A (CsA) (0.05% RESTASIS[®], Allergan, Inc., Irvine, CA, USA) was the first prescription treatment for DED that was approved in the US and in several other countries.

Allergan's formulation of CsA is a complex, oil-in-water, ophthalmic emulsion that delivers the topical immunosuppressive CsA to the surface of the eye for absorption and therapeutic effect. The emulsion allows CsA to penetrate directly into the ocular tissues in therapeutic amounts and over the requisite time course, with minimal systemic absorption.

In patients with DED, Allergan's formulation of CsA was associated with decreases in markers of inflammation,^{1,2} and improvements in objective measures (eg, Schirmer test score and corneal staining) and some subjective measures of DED (eg, blurred vision and the need for concomitant artificial tears) compared with vehicle alone.³ Long-term therapy was generally well-tolerated, with no systemic adverse events reported.⁴

There are currently no generic equivalents to Allergan's formulation of CsA approved in the US. A generic drug product is usually not required to be evaluated in clinical trials, but in most cases must be shown to be bioequivalent to the original. Demonstrating the bioequivalence of two topical ophthalmic formulations is problematic: the eye drop, in spite of the small volume, is often administered within 5 minutes after administration, and only a small fraction (< 1%) of the active substance is delivered to the tear film and/or is absorbed and becomes bioavailable in ocular tissues. The required amount of drug in individual eye diseases are not known, and even if they were, local drug concentrations cannot be measured directly.

In some markets outside of the US, emulsion products containing CsA are marketed as generic versions of Allergan's formulation. Given the differences described above in demonstrating the bioequivalence of generic CsA (G-CsA) products with the original, clinically proven product, the purpose of this analysis was to compare Allergan's formulation of CsA and a G-CsA in terms of composition and physicochemical characteristics.

METHODS
Information on product composition was obtained from package inserts. Tests were conducted on three lots of Allergan's formulation of CsA and two lots of G-CsA (Table 1). Comodity and pH were measured using standard tests recommended by the United States Pharmacopoeia and the European Pharmacopoeia. Data potential, a measure of electrical charge on the surface of emulsion globules, was measured in triplicate at 25 ± 1 °C using a Malvern Zetasizer 2000 (effective under the emulsion droplets: 1–4); viscosity of the dispersant (0.887).

RESULTS
Composition
Both Allergan's formulation of CsA and G-CsA contained CsA 0.5 mg/mL, castor oil (1.25% and 0.525% in Allergan's formulation of CsA and G-CsA, respectively), polyoxylamine 60, an emulsion stabilizer to control polymer coagulation.

Physicochemical properties and data potential

Parameter	Allergan's formulation of CsA ¹	G-CsA ²
Mean pH	7.4 (n=3)	6.4 (n=3)
Mean viscosity (mPa·s)	307 (n=3)	304 (n=3)
Mean potential (mV)	-23.0 (n=3)	-33.2 (n=3)

For each lot, 100 µL of 0.05% CsA was emulsified and analyzed. CsA, cyclosporine A; G-CsA, generic cyclosporine A; CsA, cyclosporine A.

DISCUSSION
Castor oil content
Differences in castor oil content can influence bioavailability. In a phase II clinical study, a formulation with CsA 0.05% and castor oil 0.25% showed a lower increase in Schirmer test score and a lower decrease in corneal staining compared with a CsA 0.1% and castor oil 1.25% formulation. In two phase III clinical studies, a formulation with CsA 0.05% and 1.25% castor oil (Allergan's formulation) showed an equal or better increase in Schirmer test score and decrease in corneal staining compared with a CsA 0.1% and castor oil 1.25% formulation (Figure 1). This suggests that G-CsAs, which has a lower castor oil content, may not exhibit similar efficacy in key objective measures of efficacy in DED.

Data potential
In general, emulsions with a higher zeta potential (> 30 mV) are electrostatically stable (Figure 2).⁵ The change on the globules stabilizes the emulsion droplets by preventing the oil globules from coalescing by charge-charge repulsion of droplets. The charge on the globules may also play a role in the spreading of emulsion on the ocular surface and binding to the ocular tissue. The difference in zeta potential between G-CsA and Allergan's formulation of CsA (Table 2) suggests that the emulsion in G-CsA may be less stable, have larger globule sizes and different spreading characteristics compared with Allergan's formulation of CsA. In shape, this could affect the dissolution rates and bioavailability.

CONCLUSIONS
The in vitro differences between Allergan's formulation of CsA and G-CsA may affect the delivery of CsA to the eye. Further studies are required to assess the clinical relevance.

CONFLICTS OF INTEREST
Allergan, Inc. and CP are employees and shareholders of Allergan.

ACKNOWLEDGMENTS
Danish Regulatory Communications provided medical writing and editorial assistance for production of this poster, which was funded by Allergan, Inc.

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2. Lefkowitz et al. *J Clin Ocul Pharmacol Ther* 2013; 33: 100–10.
3. Lefkowitz et al. *J Clin Ocul Pharmacol Ther* 2013; 33: 100–10.
4. Lefkowitz et al. *J Clin Ocul Pharmacol Ther* 2013; 33: 100–10.
5. *Colloid and Interface Science* 2012; 382: 100–10.
6. *Colloid and Interface Science* 2012; 382: 100–10.

Examples of deliverables

• Publications

- Manuscripts
- Review papers
- Abstracts/posters/oral presentations
- Publications plan
- Objection handlers

Two cyclosporine-based treatments for dry eye disease have significant differences in composition and physicochemical properties

A. Gora, M. Atasu, I. Groshar and C. Pujari
Optometry, 2016, 87(10), 62-69

BACKGROUND
Dry eye disease (DED) is a painful disorder that, if left untreated or undertreated, progressively damages the ocular surface and can lead to vision loss. Inflammation is a key mediator in the vicious cycle of DED pathogenesis, and is triggered by tear film instability, tear film hyperosmolality and apoptosis.¹ Cyclosporine A (CsA; 0.05%, RESTOR, Allergan Inc., Irvine, CA, US) was the first prescription treatment for DED that was approved in the US and in several other countries.

Allergan's formulation of CsA is a complex, oil-in-water, synthetic emulsion that delivers the lipophilic immunosuppressant CsA to the surface of the eye for absorption and therapeutic effect. The emulsion allows CsA to penetrate directly into the ocular tissues in therapeutic amounts and over the requisite time course, with minimal systemic absorption.²

In patients with DED, Allergan's formulation of CsA was associated with decreases in markers of inflammation^{3,4} and improvement in objective measures (eg, Schirmer test score and corneal staining) and some subjective measures (DEDQ) (eg, blurred vision and the need for concurrent artificial tears) compared with vehicle alone.⁵ Long-term therapy was generally well tolerated, with no systemic adverse events reported.⁶

There are currently no generic equivalents to Allergan's formulation of CsA approved in the US. A generic drug product is usually not required to be evaluated in clinical trials, but in most cases must be shown to be bioequivalent to the original. Demonstrating the bioequivalence of two topical ophthalmic formulations is problematic: the eye drop, irrespective of the instilled volume, is often administered within 5 minutes after administration, and only a small fraction (< 1%) of the active substance is delivered to the tear film and/or is absorbed and becomes bioavailable in ocular tissues. The required amount of drug in individual eye tissues are not known, and even if they were, local drug concentrations cannot be measured directly.

METHODS
Information on product composition was obtained from package inserts. Tests were conducted to compare the Allergan's formulation of CsA and two lots of GsCaA (Table 1). Conductivity and pH were measured using standard tests as recommended by the United States Pharmacopoeia and the European Pharmacopoeia. Data presented: a measure of electric charge on the surface of emulsion globules, was measured at 25 ± 1 °C using a Malvern Zetasizer ZS90 (refractive index for the emulsion droplets 1.48, viscosity of the dispersant 0.887).

RESULTS
Composition
Both Allergan's formulation of CsA and GsCaA contained CsA. Lot 0190, lot 0219 and lot 0236 in Allergan's formulation of CsA and GsCaA, respectively, poly(2-vinylpyrrolidone) emulsion stabilizer (VCO) 2% polymer copolymer

DISCUSSION
Carboxyl end content
Differences in carboxyl end content can influence bioavailability in a phase II clinical study, a formulation with CsA 0.05% and carboxyl end content of 0.05% showed a lower increase in Schirmer test score and a lower decrease in corneal staining compared with a CsA 0.05% formulation with carboxyl end content of 1.25%. In two phase II clinical studies, a formulation with CsA 0.05% and 1.25% carboxyl end content (Allergan's formulation) showed an equal or better increase in Schirmer test score and decrease in corneal staining compared with a CsA 0.1% and carboxyl end 0.25% formulation (Figure 1). This suggests that GsCaA, which has a lower carboxyl end content, may not exhibit similar efficacy in key objective measures of efficacy in DED.

CONCLUSIONS
There are differences between Allergan's formulation of CsA and GsCaA that may affect the delivery of CsA to the eye. Further studies are required to assess the clinical relevance.

REFERENCES

1. Burstein H, et al. *Invest Ophthalmol Vis Sci* 2010;51(12):6988-96.
2. Allergan Inc. *RESTOR (Cyclosporine) Ophthalmic Emulsion*. Allergan Inc, Irvine, CA, USA; 2011.
3. Groshar I, et al. *Invest Ophthalmol Vis Sci* 2012;53(12):7263-72.
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5. Groshar I, et al. *Invest Ophthalmol Vis Sci* 2013;54(12):7146-54.
6. Groshar I, et al. *Invest Ophthalmol Vis Sci* 2013;54(12):7146-54.

Examples of deliverables

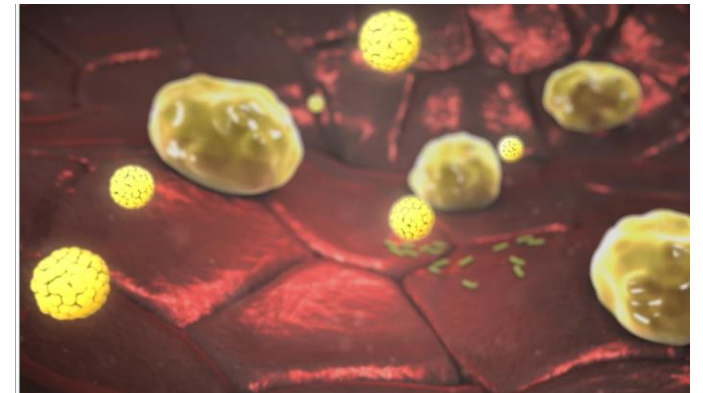
- **Digital**

- MOA videos
- Patient videos
- Website



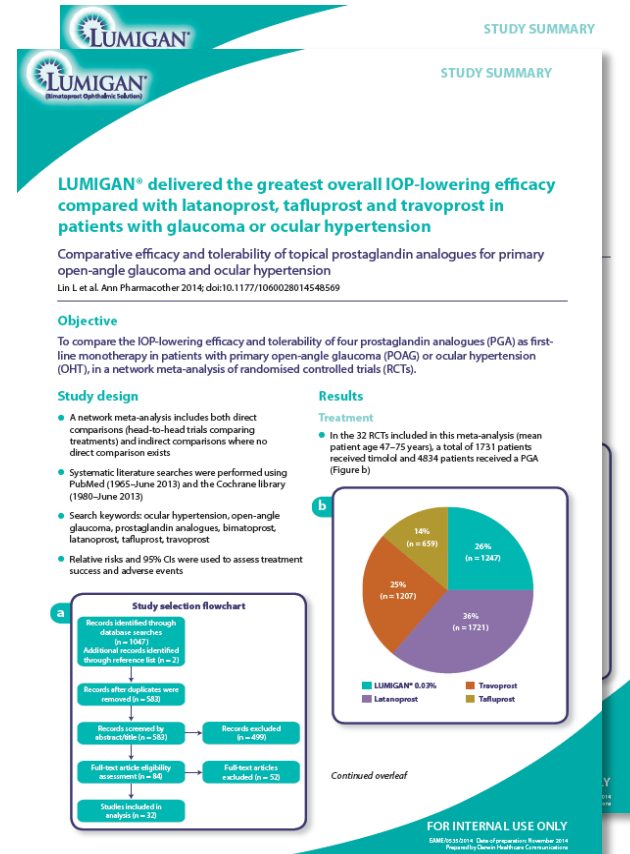
- **Other materials**

- Training materials (slide decks/manuals)
- Newsletters
- Competitor intelligence report



Examples of deliverables

- Other materials
 - Training materials (slide decks/manuals)
 - Newsletters
 - Competitor intelligence report



Examples of deliverables

- **Meetings**

- Advisory boards
- Symposia
- Standalone meetings
- Workshops

- **Publications**

- Manuscripts
- Review papers
- Abstracts/posters/oral presentations
- Publications plan
- Objection handlers

- **Digital**

- MOA videos
- Patient videos
- Website

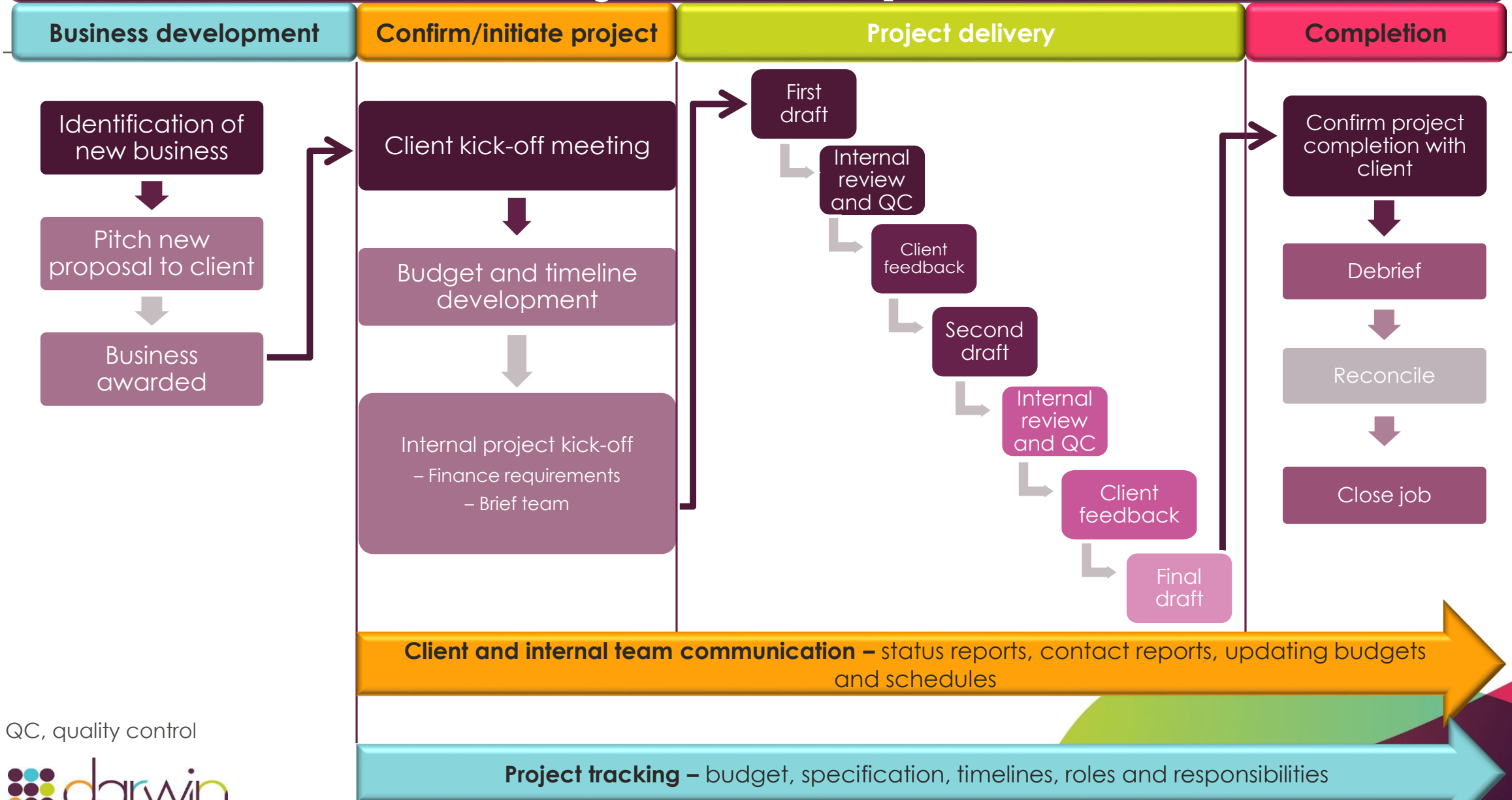
- **Other materials**

- Training materials (slide decks/manuals)
- Newsletters
- Competitor intelligence report

- In a crowded, competitive and ever-evolving market place, clients are constantly asking us for suggestions that show creativity and innovation

- As a company, it is therefore imperative that we keep up to date with new products, technology and processes that affect the pharmaceutical industry

Project lifecycle



QC, quality control

Account management

My background

- Scientific background (BSc and MSc)
- Joined Darwin Healthcare Communications in June 2014

My role at Darwin

- Account Manager with 3 years of experience
- Day-to-day management of accounts
 - Budgets and timelines
 - Internal and external liaison on project delivery
 - Mentoring and training junior members
 - Involvement in business development (organic growth and new business)
- Working on a range of projects including standalones, symposia, advisory boards, publications, MoA videos and training materials across a variety of therapy areas, such as rare diseases, hepatitis C infection, ophthalmology, and animal health

Medical writing

Background

- Scientific background (PhD)
- Darwin is my first agency 😊

My role at Darwin

- Dedicated writer on two accounts and work on a variety of therapy areas (urology, chronic migraine and ophthalmology)
- Communicating science in a succinct, engaging way and tailoring the style to the target audience (patients, HCPs etc.)
- Responsible for writing a variety of materials, including educational slide decks, newsletters and website content, to name but a few
- Work closely with account management/editorial/creative to ensure that content is aligned with messaging and is scientifically robust

Interested in medical communications?

- Prospect of working across a variety of therapy areas and tactics (no 2 days are the same!)
- Enjoy the thought of consultancy and customer service
- Lots of travel
- Fast-paced
- Progression

Account management vs medical writing?

Account management

- You enjoy organising, planning and working with people
- Enjoy science and are able to pick things up quickly
- Good communicator (written and verbal)
- Enjoy providing excellent customer service

Medical writing

- You love writing! If you don't – medical writing is not for you
- Good multitasker, can rapidly assimilate new information
- Have the 'knack' of making complex data look simple ;-)
- Want to stay close to the science

Training at Darwin

- **On-the-job training**
- **Mentors and buddies**
- **Opportunities to be involved in variety of therapy areas**
- **Opportunities to develop business acumen**
 - Marketing
 - Business development
 - Company Website
- **Regular company-wide training**
 - Training on guidelines such as GPP and ABPI
 - Communication
 - Finance

Why choose Darwin?

Dynamic
Friendly
Energy Competitive
State-of-the-art Engaging
Professional Innovative Bold
Leaders

- Excellent team support
- Good structure
- Wider opportunities
- Good work–life balance
- Great social activities!

Thank you for listening!



Our mission

Darwin is proud to be an agency bursting with **talented, creative** and **principled** individuals

Communicating science with **passion, flair** and **integrity**, we create high-science solutions across all media that inform and persuade, surpassing expectations every step of the way

Our solutions are complemented by **innovative thinking** from our creative advertising, digital and access partners, creating truly **joined-up** brand thinking

We at Darwin are your natural selection