BIOTECH AGORA

CONFÉRENCE ADOCIA

INNOVATIVE MEDICINE FOR EVERYONE, EVERYWHERE

Normandy Hotel, Paris

June 19, 2018

ADOCIA

innovative medicine
for everyone, everywhere

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Adocia's management and team

Gérard Soula PhD, MBA President & CEO Co-founder	Olivier Soula PhD, MBA Deputy General Manager, R&D Director Co-founder	Valérie Danaguezian Chief Financial Officer	Rémi Soula PhD, MBA Director of BD & Legal Co-founder	Steve Daly US General Manager
				

- Focused on **delivering advanced treatments** for diabetes and other metabolic diseases based on **innovative formulations**
- **Co-founded by G.Soula, O. Soula and R. Soula** in 2005
- Listed on **Euronext Paris** (FR0011184241 – ADOC) since 2012 ; Market Cap €121M[1]; Cash position €63M[2]
- **127 staff, of which 47 PhDs and MDs :** successful track-record **from discovery to Phase 3** in **protein and peptide formulation**
- **39 patent families** protecting BioChaperone platform technology and products, up to at least **2033**

[1]As of May 31, 2018; [2] As of April 30, 2018

2018

2018 sera une année charnière dans la vie d'Adocia

- **BC Lispro & BC Combo: un potentiel encore à réaliser sur les deux produits phare d'Adocia**
- Signature d'un deal avec Tonghua Dongbao:
  - 50 M$ d'upfront pour une valeur potentielle totale de 135 M$
  - Contrat limité au territoire chinois et quelques autres pays
  - Les frais de développement et d'enregistrement sont à la charge de Dongbao
- Préparation du lancement d'une étude clinique de phase 3 sur BC Lispro:
  - Sur personnes diabétiques de type 1
  - Aux US, Europe et Japon
  - En pompe à insuline
  - Deuxième partie de 2019
- Recherche active d'un partenaire pour les zones géographiques US, Europe et Japon

2018

Autres produits prometteurs

- Développement du produit BC Glucagon pour le traitement des hypoglycémies sévères, avec en parallèle la recherche d'un partenariat
- Développement du produit BC Pram Insulin, actuellement en étude clinique de phase ½ sur les personnes diabétiques de type 1 : résultats attendus au 3ème trimestre
- Extension de notre portefeuille à d'autre aires thérapeutiques:
  - Obésité avec BC Glucagon GLP-1
  - Short Bowel Syndrome avec BC GLP-2
- Promotion de notre plateforme BioChaperone auprès de pharmas

2018

Une situation financière favorable

- Position financière solide avec 63 M€ de trésorerie après l'accord signé avec Tonghua DongBao
- D'autres opportunités de partenariats :
  - BC Lispro et BC Combo pour les territoires libres de droit, USA, Europe et Japon entre autres
  - BC Glucagon
- Des produits en développement avec une preuve de concept à cours terme
  - BC Pram Insulin
- Premier arbitrage de notre litige avec Lilly portant sur environ 11 M$, attendu ce trimestre
- Deuxième arbitrage de notre litige avec Lilly en cours

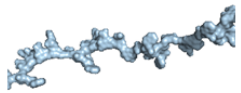
BIOCHAPERONE TECHNOLOGY

ADOCIA

BioChaperone® unlocks the potential of proteins and peptides and their combinations in a cost-effective way

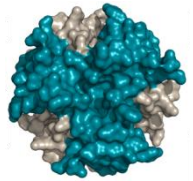
BioChaperone®

(library of molecules)

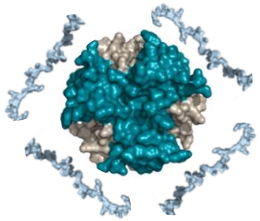


Proteins and peptides

(insulin, GLP-1 RA, pramlintide, glucagon, teduglutide…)



[BioChaperone® Protein] Complex



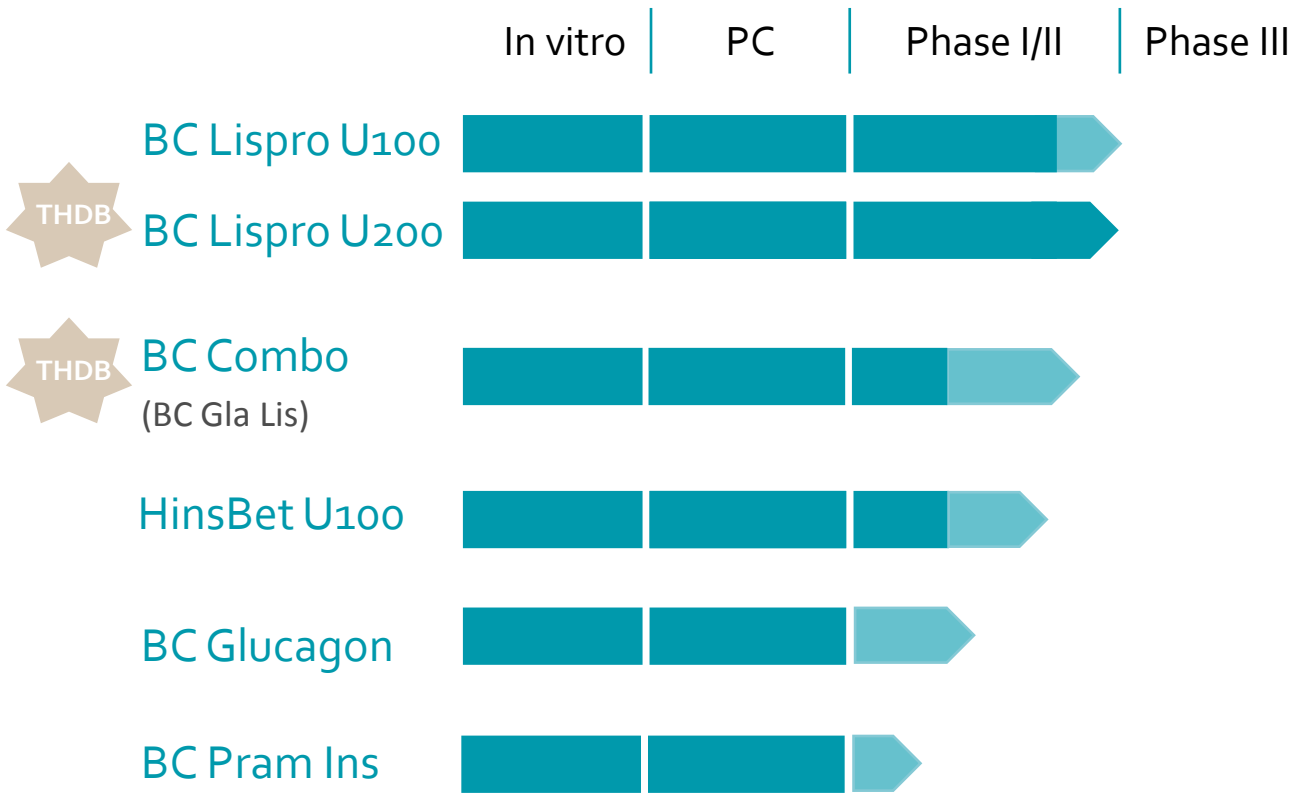
- ✓ Improved **solubility**
- ✓ Improved **stability**
- ✓ Accelerated **absorption**

Enabling **ready-to-use liquid formulations** and **combinations**

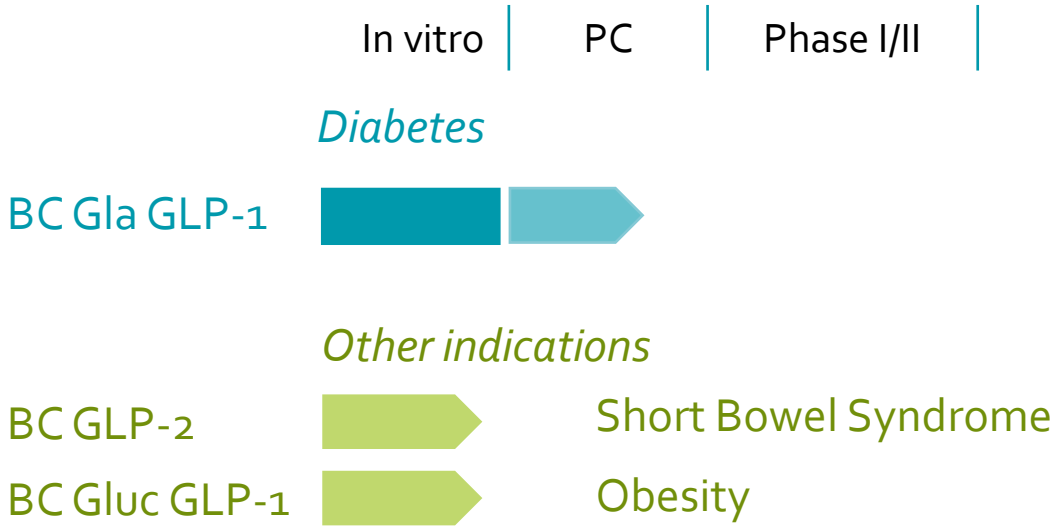
39 patent families on BC molecules and formulations: 1st expiry date 2033

BioChaperone-enabled innovation in diabetes and beyond

Diabetes clinical pipeline



Preclinical pipeline



BC: BioChaperone **; Gla**: glargine **; Lis**: lispro **; Pram**: pramlintide **; Ins**: recombinant human insulin; **GLP-1**: GLP-1 receptor agonist; **GLP-2**: GLP-2 receptor agonist; **Gluc**: Glucagon.

THDB **Products licensed to Tonghua Dongbao in China and other territories (*excluding* the US, EU & Japan)**

ADOCIA LEAD INSULIN PROGRAMS

BIOCHAPERONE LISPRO & BIOCHAPERONE COMBO

MARKET

People with diabetes require simpler, more physiologic treatments

415M[1] people with diabetes in **2015**

26M[2] on insulin

79%[3] live with **severe complications**

- **Despite 100 years of medical treatment, long-term consequences of diabetes remain a major issue**
- There is a need to address the **underlying complexity of diabetes**
  - **With more granularity**
  - **In a simple way** to ensure patient engagement
- Using **BioChaperone®**, Adocia is committed to developing **more physiologic, easy-to-use treatments to improve short and long-term outcomes in diabetes**

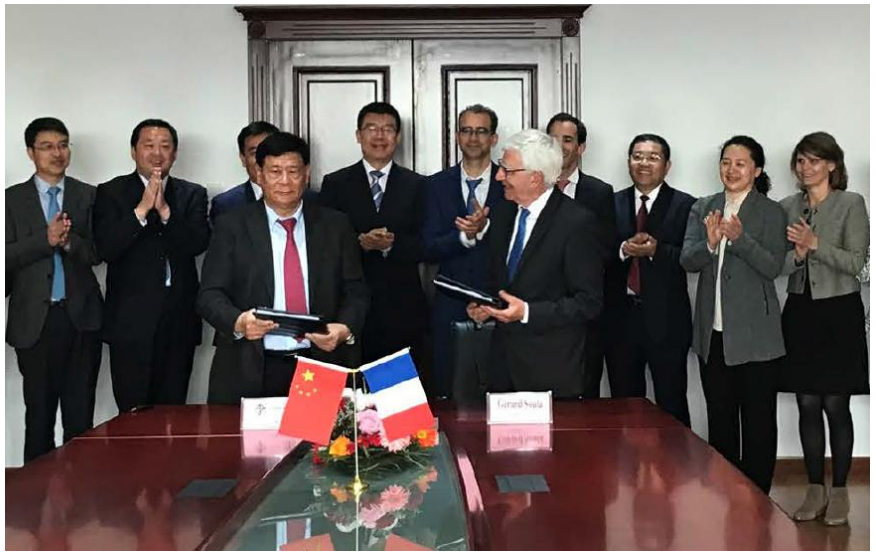
[1] International Diabetes Federation, 2017 ; [2] Estimate based on 25% of diabetes patients having access to care, of which ~25% use insulin, as per Novo Nordisk, Full Year 2014 Investor presentation [3]Hazel-Fernandez & al; Am J Manag Care. 2015

MARKET

BioChaperone Insulins formulations fit the need for innovation in a rapidly evolving insulin market

- **Diabetes injectable drugs market growth is driven by innovation**:
  - **Drugs:** ultra-rapid insulin, multi-agent combinations, co-agonists…
  - **Diabetes management**: development of **integrated solutions for diabetes care** combining **drugs, digital care and devices (smart pens, CGMs, pumps..)**
- **Cost control** is becoming the norm
  - **Biosimilar** analog insulins are set to continue to disrupt US & EU market dynamics
  - **New challengers with high manufacturing capacity and quality products** enter the market
- **BioChaperone Insulins are positioned to fit the strategy of biopharmaceutical companies poised to positively disrupt insulin therapy:**
  - **Best-in-class** injectable products
  - Potential to be **priced competitively** (based on biosimilar insulins)
  - **Long-lasting IP**

Adocia and Tonghua Dongbao entered a strategic alliance to develop best-in-class insulins



- Adocia and Tonghua Dongbao (THDB) strategic alliance:
  - ✓ **Licensing agreements for BioChaperone (BC) Lispro & BC Combo**
  - ✓ **Supply agreements** for insulins **glargine** and insulin **lispro**

- **THDB is the local leader in the Chinese insulin market**
  - Listed on Shanghai Stock exchange
  - **1st company to manufacture rHI in China** - **3 tons** manufacturing capacity
  - **Strategy to compete with global leaders in its markets**
    - **cGMP human insulin plant** (rHI in Phase 3 in Europe)
    - **Several insulin biosimilars in development** (including glargine; aspart; lispro; detemir..)
    - Focused on the **next generation** with BC Combo and BC Lispro

Key THDB financials

- $8bn Market cap. (May 2018)
- 78%[1] Of revenue from insulin
- 26%[2] Share of Chinese human insulin market
- 25%[1] YOY revenue growth

Source: [1] Company data ; [2] IQVIA data, volume, 2018.

TONGHUA DONGBAO

A short video of Tonghua Dongbao

LICENSE

Strategic licensing deals with THDB for BC Lispro & BC Combo on Chinese market

>100M[1]
People with diabetes in China

65%[2]
Of Chinese insulin market is premix

30M[3]
Treated in 2018

60M[3]
Treated in 2025

$135M
(+ Double digit Royalties) deal

- **Large and underserved Chinese insulin market features multiple drivers for growth**
  - **Rapidly growing (CAGR 12%)[2], with the number of treated patients set to double** in the next 7 years[3]
  - Better diagnosis, better reimbursement, stronger access in remote areas
- In April 2018, **Adocia and Tonghua Dongbao announced a strategic partnership to develop and commercialize BC Combo & BC Lispro in China** and other Asian and Middle East territories
  - **BioChaperone Combo is a key asset** in a predominantly **premix market**
    - **$40M** upfront **+ $50M** development milestones
  - **BioChaperone Lispro** offers the opportunity for a **best-in-class prandial analog insulin**
    - **$10M** upfront **+ $35M** development milestones
    - Analog insulins are becoming the norm in China, already reaching 50% market share[3]
  - **Adocia retains the rights in the US, Europe, Japan and Latin America**

Source: [1]IDF, 2017 ; [2] IQVIA data, volume, 2018; [3] Novo Nordisk market capital days 2017.

SUPPLY

Strategic supply agreement with THDB opens global opportunities for Adocia

- **With access to stable, high-quality insulin lispro and insulin glargine supplies, Adocia now gains full control over BC Lispro and BC Combo development**
  - **Partnering opportunities** are multiplied**:**
    - ✓ Companies **focused on diabetes but with no existing insulin manufacturing facilities**
    - ✓ **Drug or device companies** seeking to provide a **full solution** to patients
- **Adocia's Priorities**:
  - **Initiate bridging activities to launch a phase 3 clinical trial in pump setting**
  - **Accelerate efforts** in a sharply broadened potential partnership pool:
    - BC Lispro in the US, EU, Japan and other regions
    - BC Combo in the same regions and predominantly premix markets

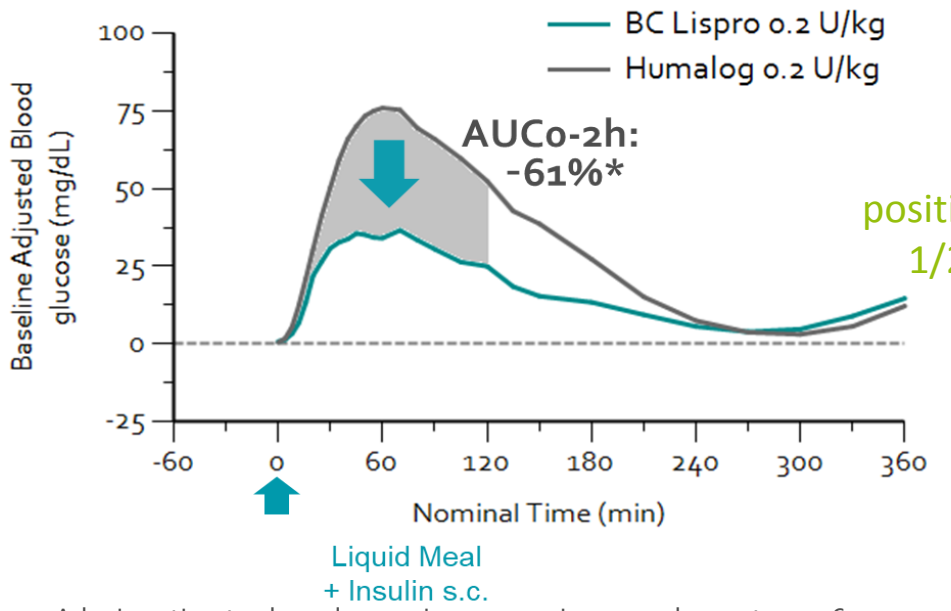
BC LISPRO

Licensed
to THDB in China

Ultra-rapid insulin with potential for best-in-class

$7B
Prandial insulin market (2016)[1]

Post-meal glycaemia in T1D



Ready for
Phase 3

9
positive Phase 1/2 trials

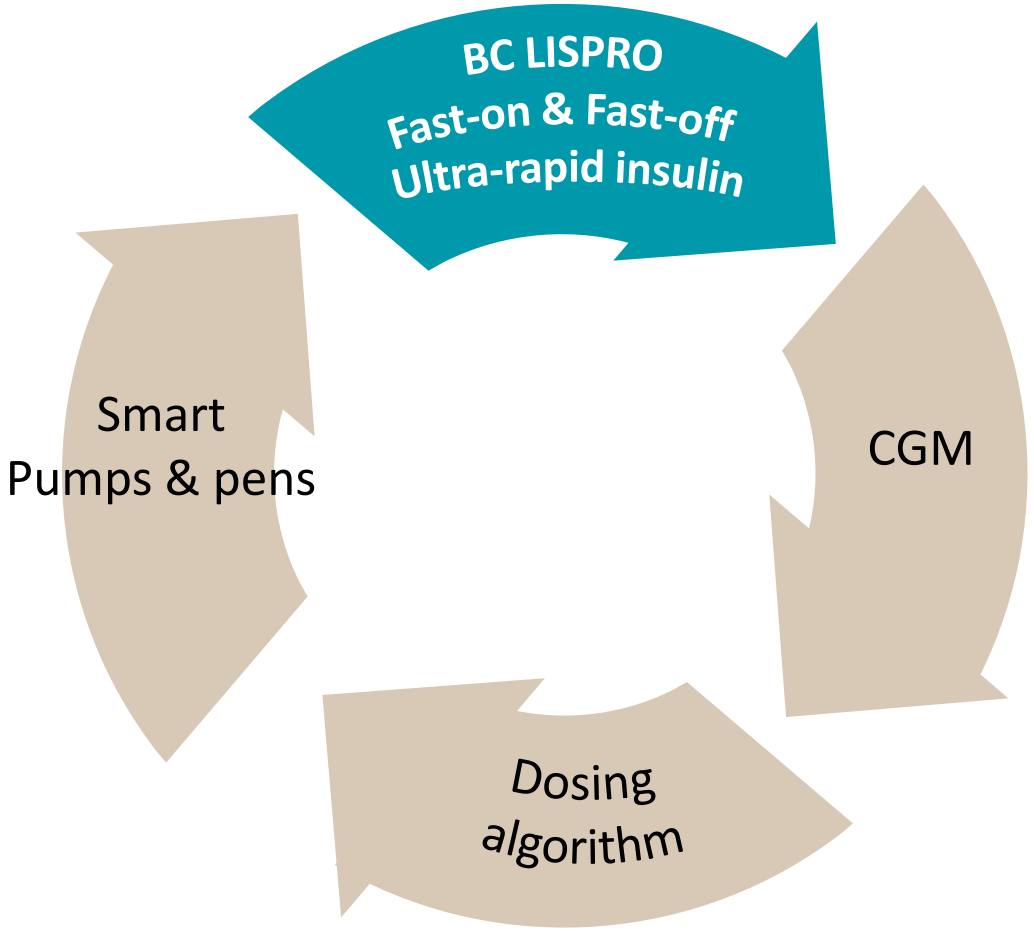
- **BioChaperone® Lispro could be a differentiated competitor to Fiasp®** (1st approved ultra-rapid insulin, Novo Nordisk).
  - **Consistently faster-on and faster-off metabolic effect vs. Humalog® & Novolog® in 252 people with T1D & T2D,** using syringes or insulin pumps
  - **Significantly faster-off effect** and **similar fast-on** effect **vs. Fiasp®** in a Phase 1 head-to-head trial (T1D, insulin pumps)
    - **Faster-off** is considered a key feature to enable "**closing the loop"** in an artificial pancreas setting
  - Concentrated, **bioequivalent BC Lispro U200**

Actively seeking partners for the US, Europe and Japan

[1] Source: Adocia estimates based on major companies annual reports, 2016

BC LISPRO

Ultra-rapid insulin with fast-on and fast-off profile is a key element to « close the loop »



Adocia intends to initiate its first Phase 3 trial in the insulin pump setting

Licensed
to THDB in China

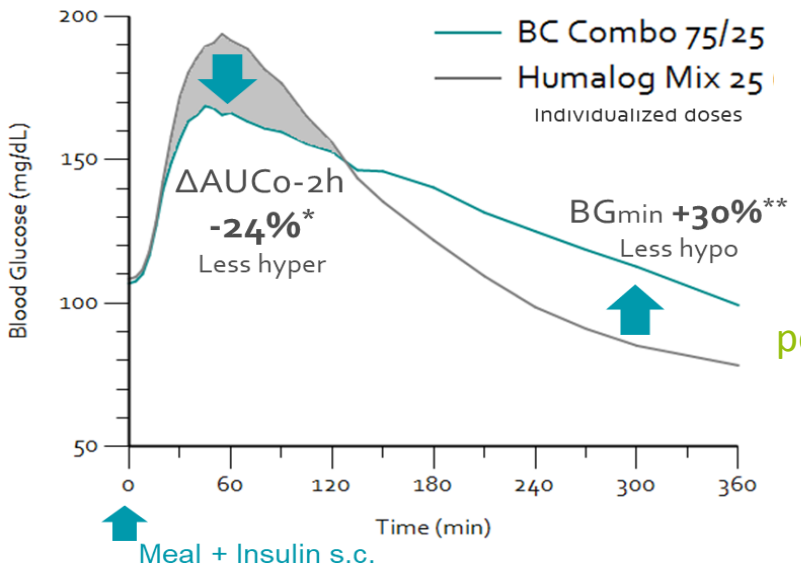
BC COMBO

A safer and more efficient alternative to premix insulin for the treatment of type 2 diabetes

$5B
Premix insulin market (2016)[1]

- **Premix products are easier to use** than basal-bolus regimens but present **inferior prandial coverage** and a **higher risk of hypoglycemia**
- **As a true basal/prandial insulins combination, BioChaperone® Combo could be highly differentiated vs. premix insulins:**
  - **Stronger postprandial control vs. Humalog® Mix25** in people with T1D & T2D (3,4)
  - **Similar performance to separate injections** of Lantus® and Humalog® in people with T2D (4)
  - Potential pricing advantage vs. Ryzodeg® (Novo Nordisk, only approved basal/prandial insulins combination)

Post-meal glycemia in T1D



5
positive Phase 1/2 trials

Actively seeking partners for the US, Europe, Japan, and other premix markets

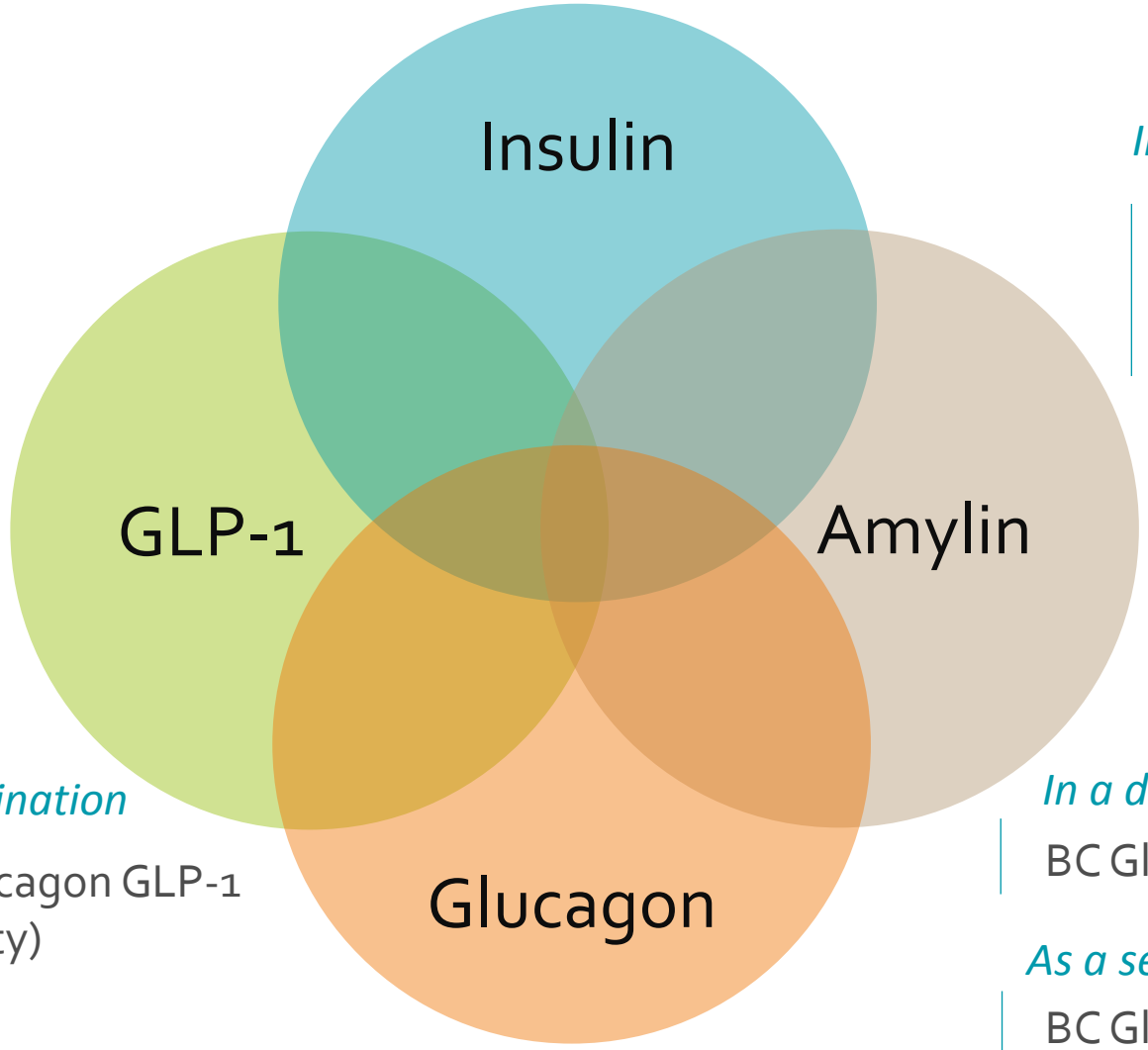
[1] Source: Adocia estimates based on major companies annual reports, 2016 ; [2] IQVIA data 2017, [3] T1D: NCT#01981031 & NCT#02514954 ; [2]T2D: NCT#02514850 ; NCT#02915250; NCT#03180710.

MULTIHORMONAL TREATMENTS FOR DIABETES

NEXT GENERATION OF CARE FOR BETTER OUTCOMES

RATIONALE

Innovative multi-hormonal approaches aim to improve diabetes and obesity management



In combination

- BC Glargine GLP-1 (T2D)
- BC Pramlintide rhIns (T1D & T2D)

In combination

- BC Glucagon GLP-1 (Obesity)

In a dual-chamber pump

- BC Glucagon with Insulin (T1D)

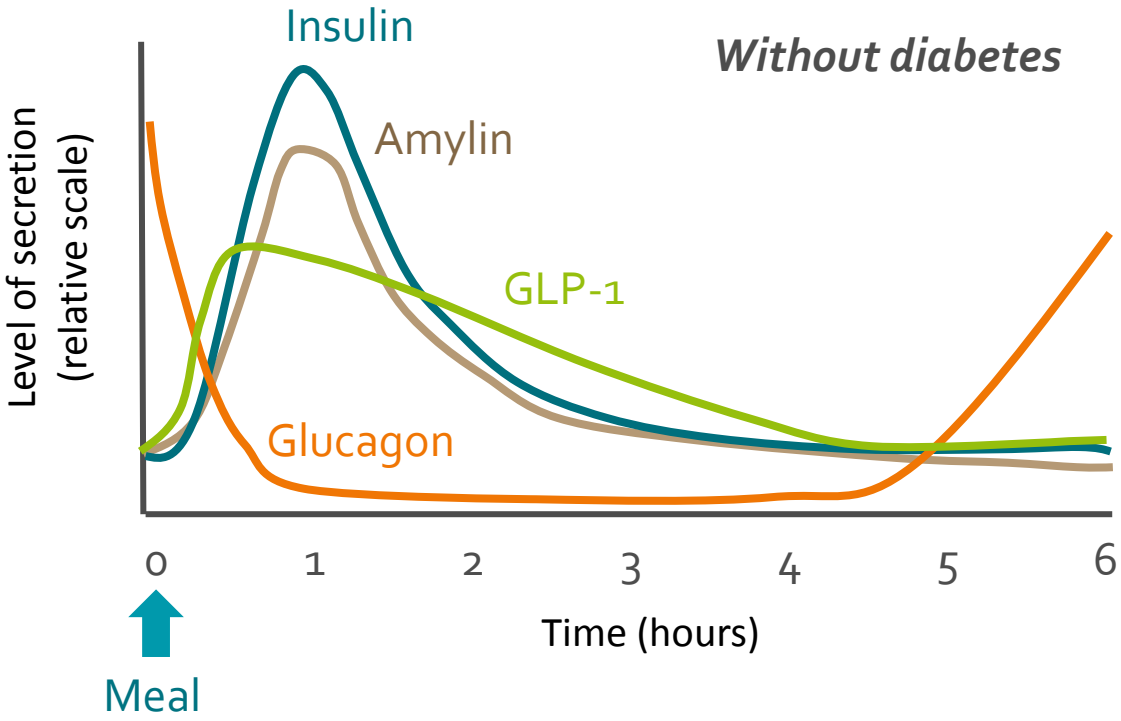
As a severe hypoglycemia rescue treatment

- BC Glucagon (T1D & T2D)

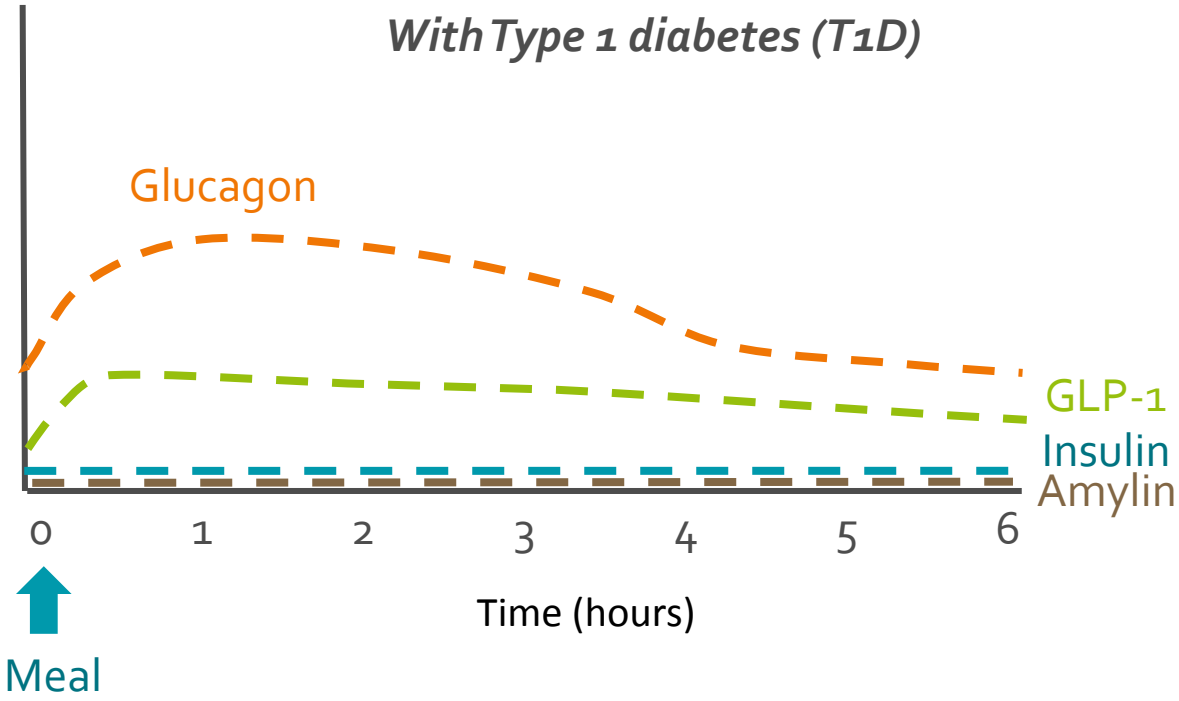
DIABETES

In non-diabetic people, a time-sensitive hormonal pattern maintains normo-glycemia

Schematic representation of hormonal pattern[1]



Without diabetes



With Type 1 diabetes (T1D)

[1] Source: Adapted from Toff-Neilsen et al, J. Clin Endocrinol Metab 2001;86:3717-3723; Cummings DE et al, Diabetes 2001;50:1714-1719; Aronoff SL et al , Diabetes Spectrum 2004; 17(3): 183-190

BC PRAM INSULIN

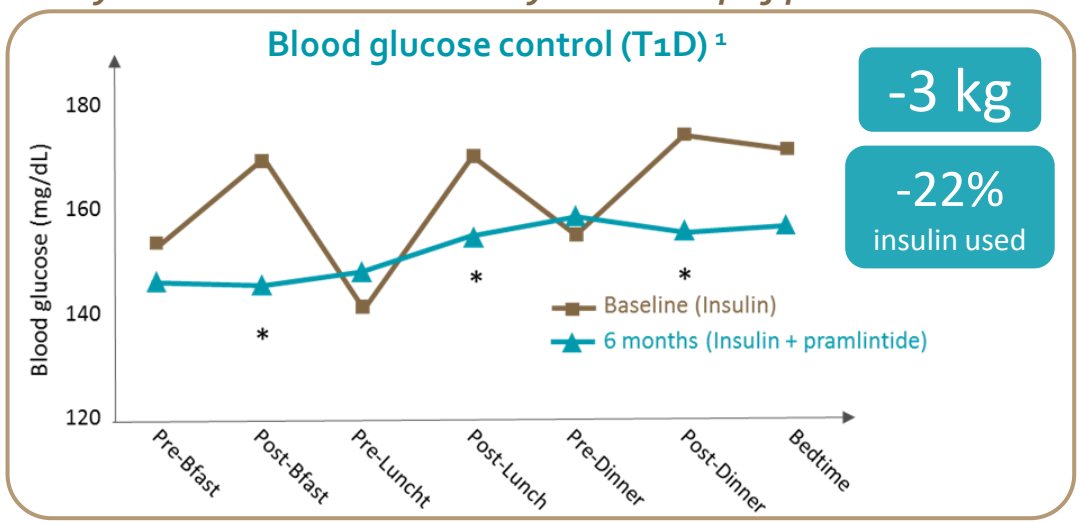
Next generation of prandial treatment to improve long-term outcomes in T1D

79%[2]
Of diabetics live with **severe complications**

65%[3]
of US adults with T1D are overweight or obese

- **BioChaperone Pramlintide Insulin exceptionally tight prandial control**[1,2,3], potentially lowering the risk of long-term severe complications
- **Multiple hormonal combinations could be the next generation of T1D treatment**
  - **Pramlintide** (amylin analog) is the only hormone approved and marketed for T1D on top of insulin, but nearly doubles the injection burden up to 7+/day (incl. insulin)
  - Pramlintide 3x daily has demonstrated real-world synergistic benefits when administered on top of an insulin regimen[1]
- **BioChaperone® enables the combination of prandial insulin with pramlintide**

Amylin Pharmaceutical data: Symlin® on top of prandial insulin



1
Ongoing clinical trial

Expected results from ongoing FIH Study of BioChaperone Pramlintide Insulin: Q3 18

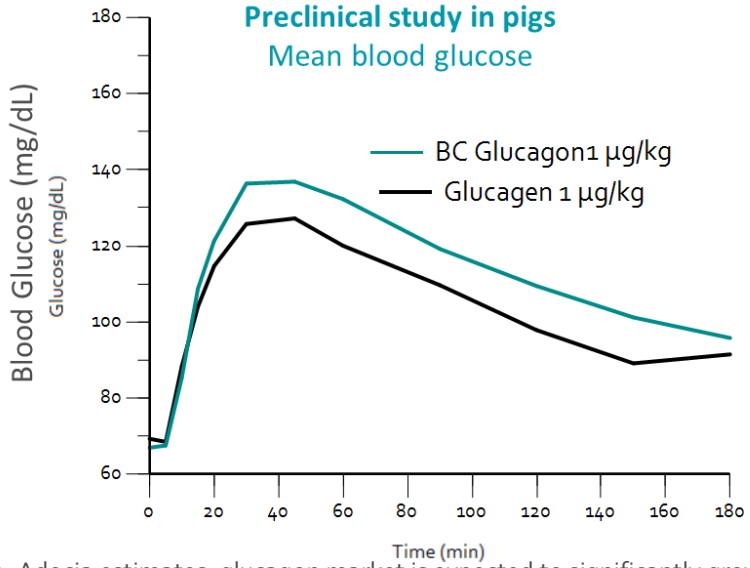
[1] Guthrie R et al *Diabetes* 2005, 54(Suppl 1):A118 T1D, after 6 mo, *P <.05. See also Pullman J et al Vasc Health Risk Manag. 2006, 2 (3), 203-212 and in T2D : Karl D, et al. *Diabetes Technol Ther* 2007; 9(2):191-199 ; [2]Hazel-Fernandez & al; Am J Manag Care. 2015; [3] Conway et al, Diabetes Med 2010 April; 27(4):398-404. BMI>25, Data for 2004-2007 period.

BC GLUCAGON

A ready-to-use aqueous formulation of human glucagon for acute and chronic use

$400M
Forecasted market in 2025[1]

Preclinical study in pigs
Mean blood glucose



- **BioChaperone Glucagon is a ready-to-use aqueous formulation of human glucagon supporting:**
  - **Rescue treatment of severe hypoglycemia in a ready-to-use autoinjector:** current glucagon reconstitution kits suffer from poor usability[1]
  - **Chronic use:** dual hormone artificial pancreas and rare diseases due to dysfunctional glucagonemia
- In a FIH study in people with T1D, BC Glucagon (1mg) for rescue[2]:
  - Was safe and well tolerated
  - Efficiently rescued **100% participants** from medically-induced hypoglycemia in a median time of **11 minutes**

1
Positive clinical trial

Adocia plans to initiate a Phase 1/2 trial in Q4 2018. This is expected to be the final trial before Phase 3

[1] Source: Adocia estimates; glucagon market is expected to significantly grow following the introduction of ready-to-use rescue products. [2] Yale JF, *Diabetes Technol Ther* 2017 Jul 1; 19(7): 423–432. [3] Detailed results under embargo until submission for publication at a major diabetes congress

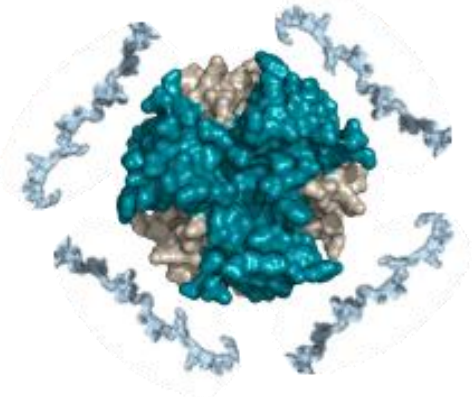
EXPANDING THE PORTFOLIO

LEVERAGING BIOCHAPERONE TRACK-RECORD AND VERSATILITY TO ADDRESS NEW THERAPEUTIC TARGETS

BC PLATFORM

BioChaperone can be used to improve both approved or NCE proteins and peptides

BioChaperone/Protein complex



Multi-agent combinations

Ready-to-use injectables

- **Leveraging Adocia core competencies in protein and peptide formulation** to fit partner's needs
  - More than **20 clinical trials (Phase 1-3)** to date on **6 different pharmaceutical products based on BioChaperone**
  - **39** patent families worldwide
  - **500+** screenable compounds in the BioChaperone® library
- **Commitment to excellence and building long-term relationships with partners**

PIPELINE EXPANSION

Expanding the use of BioChaperone platform

36.5%[1] of US adults are obese

- **BioChaperone Glucagon GLP-1 for the treatment of obesity**
  - **Obesity prevalence has tripled** from 1975 to 2016 globally[2], triggering the development of more aggressive treatment regimens:
  - Based on BC Glucagon, Adocia develops **injectable combinations of glucagon and GLP-1**:
    - Flexibility in glucagon/GLP-1 ratio selection for optimized effect
    - Cost-effective approach that could compare favorably to dual-agonists NCEs

20,000[3] People w/ SBS require parenteral nutrition

- **BioChaperone GLP-2 for short bowel syndrome (SBS)**
  - **Gattex®** (teduglutide, Shire) **is the only approved treatment** for patients with severe SBS requiring parenteral nutrition
    - $336 M sales in 2017 (+53% YOY)
    - Requires reconstitution prior to daily injection: 6 stages, two syringes, long process
  - BioChaperone solubilizes and stabilizes teduglutide in a **ready-to-use formulation**

Adocia plans to enter clinical testing with these programs in H1 19

[1] Conway et al, Diabetes Med 2010 April; 27(4):398-404. BMI>25, Data for 2004-2007 period ; [2] WHO, 2016 ; [3] US & EU only: Jeppesen PB, J Parenter Enteral Nutr. 2014 May;38(1 Suppl):8S-13S.

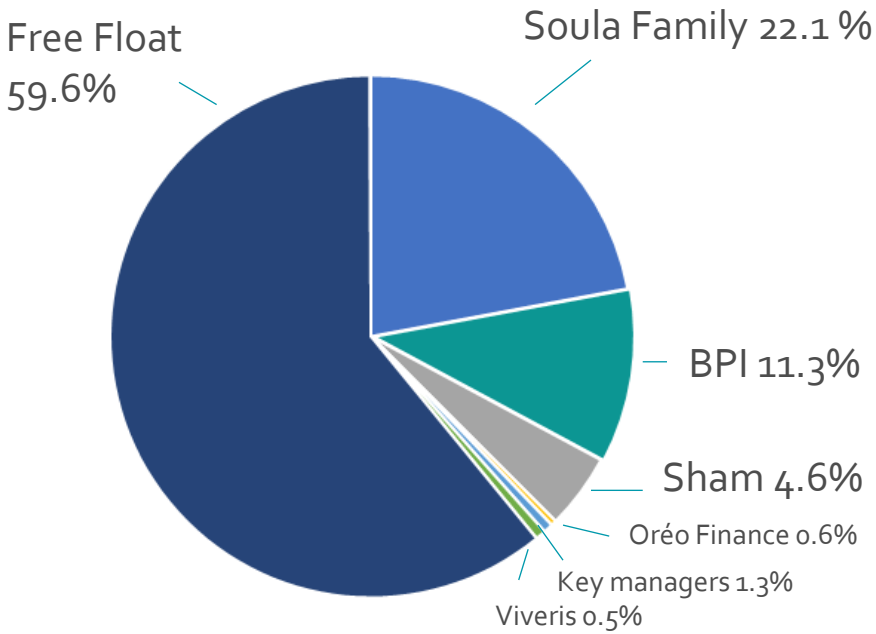
ADOCIA

Key financial elements

Financial summary

- **Listed on Euronext Paris** (ADOC)
  - 6.9M shares outstanding
  - ADR program in the US (ADOCY)
- **Cash position: €63M** (April 2018)
- **€85M raised** since inception
- **Financial debt:**
  - €0.7M loan from BPI France (refundable in case of success)
  - €5.3M bank loan for purchase of Lyon headquarters building
  - €0.6M lease back
  - €2M credit line

Shareholders' equity (May 2018)



Analysts

- Jefferies (Peter Welford)
- Kepler Market (Arsène Guekam)
- Oddo (Sébastien Malafosse – Pierre Corby)
- Louis Capital Partners (Pierre Vaurice)

RÉSULTATS FINANCIERS 2017

VALERIE DANAGUEZIAN

DIRECTEUR FINANCIER

FINANCE

Compte de résultat 2017

En milliers d'euros	Exercice 2017 (12 mois)	Exercice 2016 (12 mois)
Chiffres d'affaires	19 469	22 488
Autres produits opérationnels	7 708	7 966
Produits opérationnels	**27 177**	**30 454**
Dépenses de recherche et de développement	(27 074)	(30 971)
Frais généraux	(8 284)	(7 484)
Charges opérationnelles	**(35 358)**	**(38 455)**
RESULTAT OPERATIONNEL (PERTE)	**(8 180)**	**(8 001)**
RESULTAT FINANCIER NET	**(335)**	**181**
Charge d'impôt	(35)	(72)
RESULTAT NET (PERTE)	**(8 550)**	**(7 892)**

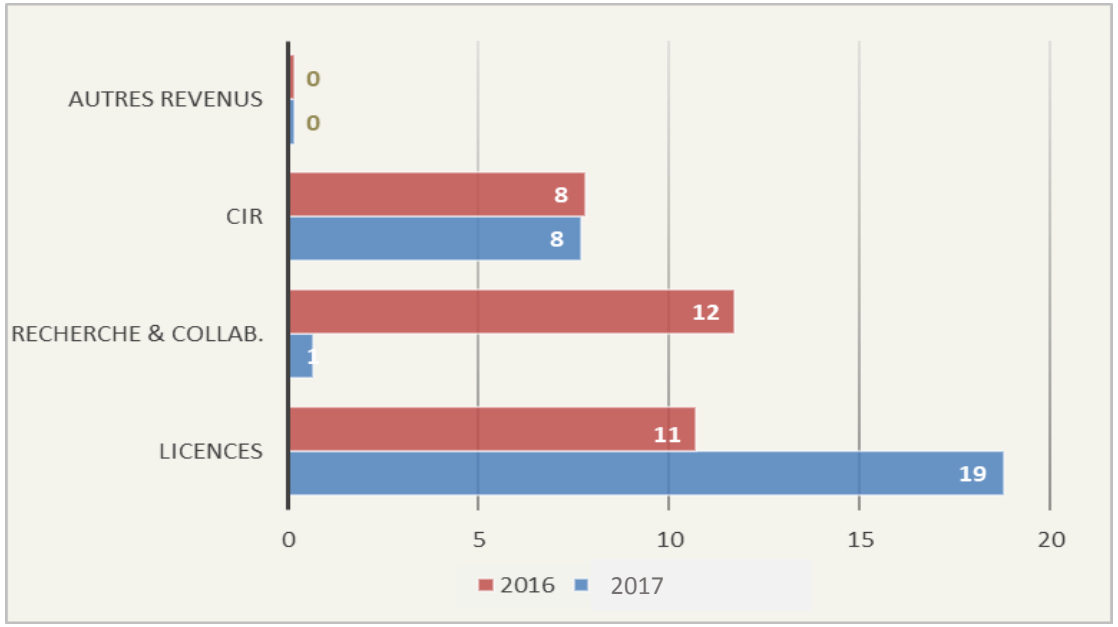
- Un chiffre d'affaires de 19,5M€ issu de la fin de la collaboration avec Lilly
- Des charges opérationnelles de 35,3M€ constituées près de 77% de dépenses de R&D
- Une perte nette de 8,6M€

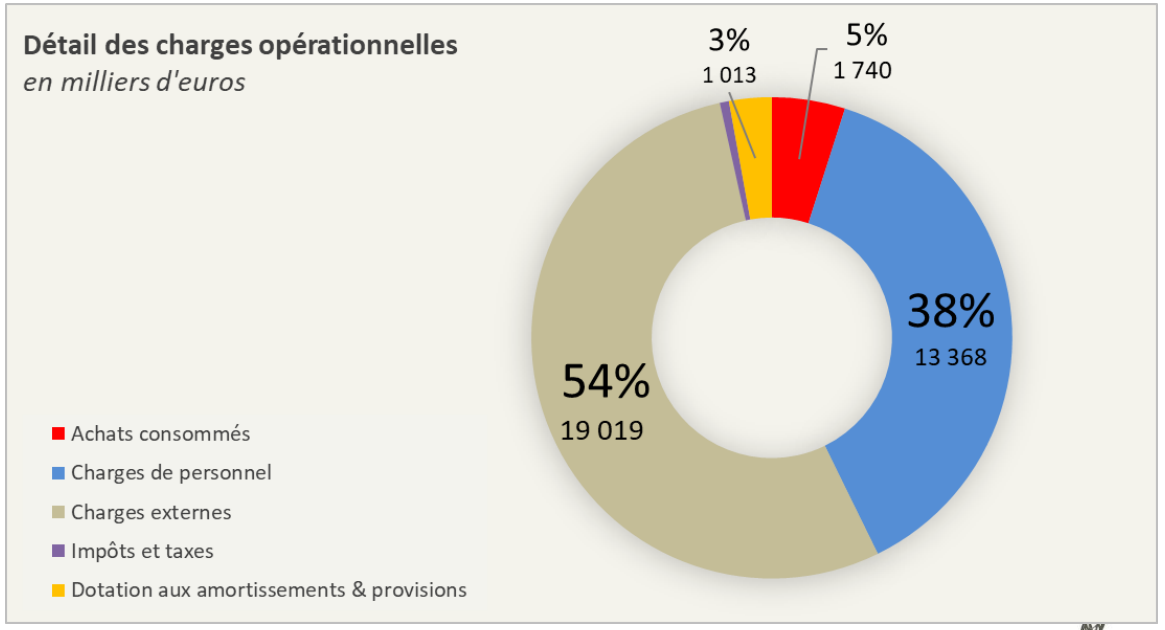
FINANCE

Détail du résultat opérationnel 2017

- Des revenus essentiellement lié au contrat avec Lilly
- Un montant de CIR de 7,8M€ en ligne avec l'an dernier

- Des charges opérationnelles de près de 35,3M€ en baisse de 3M€ (8%) par rapport à 2016 constituées de :
  - 54% des charges externes
  - 38% de dépenses de personnel



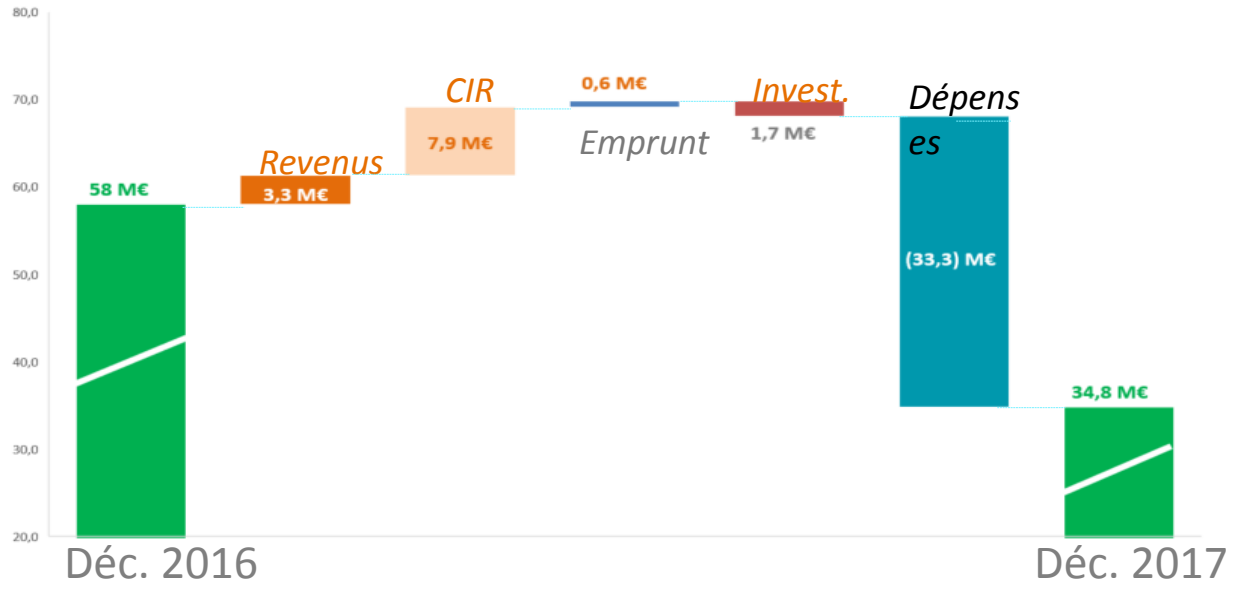


FINANCE

Bilan et Cash flow 2017

	Exercice 2017 (12 mois)
Immobilisations	9 069
Autres actifs courants	9 914
Trésorerie	34 778
TOTAL ACTIF	**53 761**

	Exercice 2017 (12 mois)
Capitaux propres	36 857
Provision LT	2 241
Dettes	7 336
Autres passifs courants	7 327
TOTAL PASSIF	**53 761**



ADOCIA

Expected News Flow

Pipeline

- **BC HUMAN GLUCAGON**
  - Phase 1/2 expected to **launch in H2 18**
- **BC PRAMLINTIDE INSULIN**
  - Results of first-in-man study **expected Q3 18**
- **BC GLUCAGON GLP-1 & BC GLP-2**
  - First-in-man study planned in **H1 19**

Legal

- Adocia expects conclusion of ongoing arbitration with Eli Lilly relative to previous collaborations:
  - First claim: **Q2 18**
  - Additional claims: **Q4 18**

Conferences

Adocia will present at the **American Diabetes Association 78th Scientific Sessions in Orlando, Florida, June 22nd-June 26th:**

- **2 oral presentations**
  - BioChaperone Pramlintide Insulin (Mon Jun 25; 349-OR)
  - BioChaperone Glucagon (Mon, Jun 25; 305-OR)
- **2 poster presentations with moderated discussions**
  - BioChaperone Lispro (Sat Jun 23; 998-P)
  - BioChaperone Combo (Sat Jun 23; 1001-P)
- **2 poster presentations**:
  - BC 222 absorption and excretion (Sat Jun 23; 1024-P)
  - BioChaperone Lispro (Sat Jun 23; 1035-P)

THANK YOU FOR YOUR KIND INTEREST

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ADOCIA

innovative medicine
for everyone, everywhere

APPENDIX

ADOCIA

Adocia is supported by a top-tier Medical Advisory Board

- **Dr. Jay Skyler**, MD, **Chairman,** University of Miami (US)
- **Dr. Vanita Aroda**, MD, MedStar Health Research Institute (US)
- **Dr. Bruce Bode**, MD, Emory University (US)
- **Dr. John Buse**, MD, PhD, University of North Carolina (US)
- **Dr. Eda Cengiz**, MD, Yale School of Medicine (US)
- **Dr. Steven V. Edelman**, MD, University of California at San Diego (US)
- **Dr. Dan Einhorn**, MD, University of California at San Diego (US)
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- **Dr. Thomas Pieber**, MD, Medical University of Graz (Austria)
- **Prof. Denis Raccah**, MD, PhD, APHM (France)

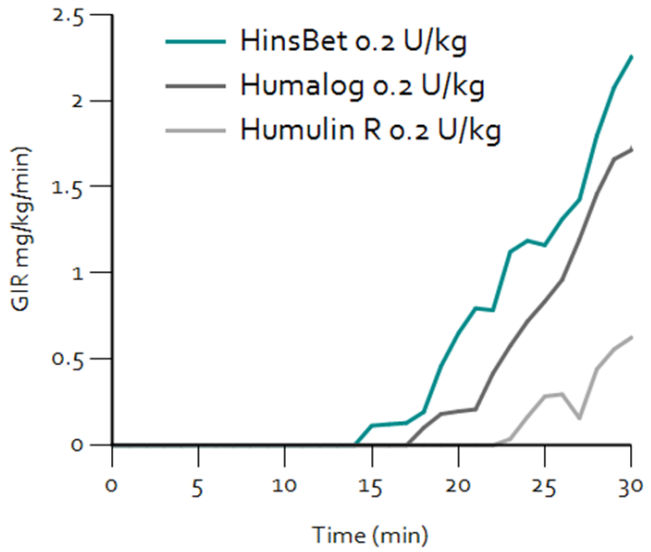
HINSBET

Affordable prandial insulin for price-sensitive populations

$1B
Human prandial insulin market (2016)[1]

77%
of diabetics live in low/middle-income countries

Early Glucose Infusion Rate (U100)[1]



[1]PK/PD clinical trial in 36 subjects with type 1 diabetes (NCT#02213146).

2
Positive Phase 1/2 trials

- **HinsBet is a formulation of human insulin designed to act as rapidly as an insulin analog**
  - Human insulin is the most common prandial insulin choice in low-income countries, but diffuses more slowly than insulin analogs
- **HinsBet could be an affordable prandial treatment option in markets dominated by human insulin**
  - May provide better control and more flexibility at competitive pricing level
- **Meal-test study in 36 T1D confirmed PD profile in first hour[2]** (Oct 2016)
  - Significantly reduced glucose excursion vs. Humulin® (p=0.0002)
  - Was not significantly different from Humalog® (p=0.5373)

[2]Meal-test study in 36 subjects with type 1 diabetes (NCT#02739906). Subjects received individualized single doses of HinsBet, regular human insulin (Humulin) and rapid-acting analog insulin lispro (Humalog) immediately before ingesting a standardized mixed meal. Detailed results remain under embargo until publication at a major diabetes conference.

Actively seeking partners in emerging markets

[1] Source: Adocia estimates based on major companies annual reports, 2016

BC
GLAR GLP-1

Efficient and affordable intensification options over basal insulin for T2D

$2.2B[1]
2023 Forecast Basal-GLP1 market

- **Combinations of basal insulin and GLP-1 are a new class of treatment for T2D**
  - 50% patients are not controlled on basal insulin alone[2]
  - **2 products recently approved in EU & US for T2D**: Xultophy® (IDegLira, Novo Nordisk) & Suliqua®/Soliqua® (IGlarLixi, Sanofi).
    - 1 daily injection
    - Lower HbA1c, weight neutrality / weight loss, less nausea than GLP-1 alone, lower hypoglycemia risk than basal insulin alone
- **BioChaperone Glargine GLP-1 candidates leverage the established safety and efficacy profiles of gold standards glargine, liraglutide & dulaglutide**
  - BioChaperone technology enables combination by solubilizing glargine at neutral pH

[1] Source: Consensus forecast, Clarivate Analytics (2017) ; [2] Sanofi, JP Morgan Healthcare Conference Presentation , San Francisco, January 12, 2015.

BC LISPRO

Results summary compared to Humalog U100 in T1DM subjects

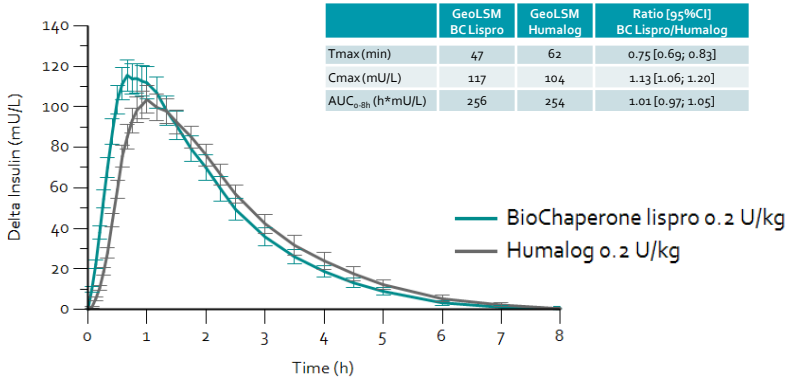
294-OR in Novel Therapeutics in T1D, June 13, 2016, 76th ADA Scientific Sessions

- **BioChaperone Lispro in comparison with Humalog showed:**
  - Faster absorption
    - Faster-in (Early $t_{[50\%max]}$, t_{max}, $AUC_{0\text{-}30min}$)
    - Faster-out (Late $t_{[50\%max]}$, $AUC_{2\text{-}8h}$)
  - Similar total exposure
- **Reduced post prandial glucose excursions**
  - 61% PPG reduction over the first two hours
  - Reduction of blood glucose by 42 mg/dL at 1 hour
- Similar safety profile at single dose conditions based on local tolerance and number of hypoglycemic events

Comprehensive work to further evaluate BioChaperone Lispro ongoing, including a concentrated U200 formulation

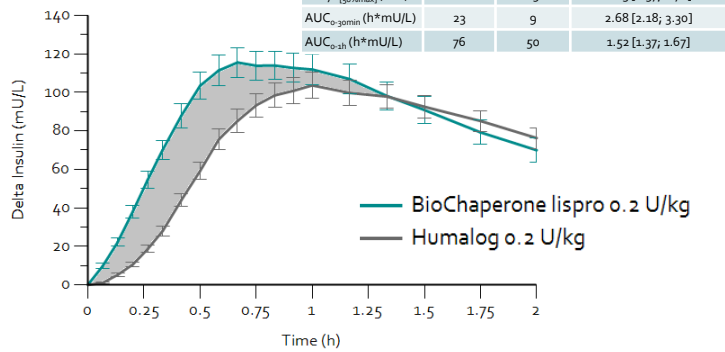
Biochaperone Lispro: Shorter TMAX, Higher CMAX and Similar Exposure

	GeoLSM BC Lispro	GeoLSM Humalog	Ratio [95%CI] BC Lispro/Humalog
Tmax (min)	47	62	0.75 [0.69; 0.83]
Cmax (mU/L)	117	104	1.13 [1.06; 1.20]
$AUC_{0\text{-}8h}$ (h*mU/L)	256	254	1.01 [0.97; 1.05]



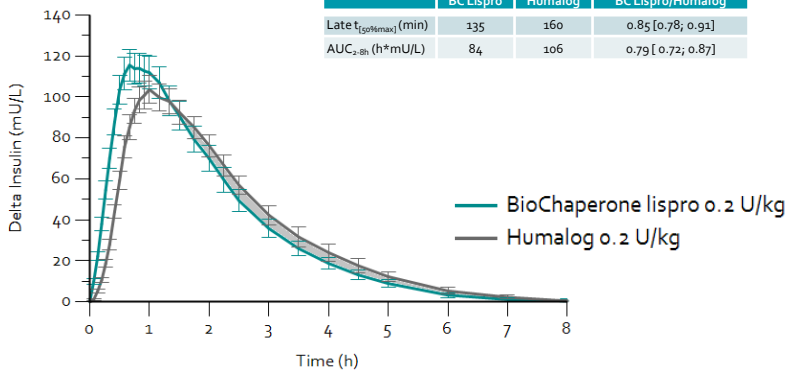
Greater Earlier Exposure: Faster In

	GeoLSM BC Lispro	GeoLSM Humalog	Ratio [95%CI] BC Lispro/Humalog
Early $t_{[50\%max]}$ (min)	18	29	0.63 [0.57; 0.70]
$AUC_{0\text{-}30min}$ (h*mU/L)	23	9	2.68 [2.18; 3.30]
$AUC_{0\text{-}1h}$ (h*mU/L)	76	50	1.52 [1.37; 1.67]



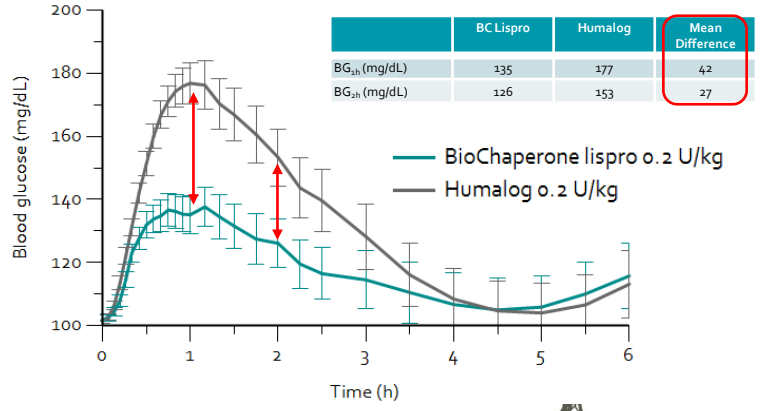
Lower Late Exposure: Faster Out

	GeoLSM BC Lispro	GeoLSM Humalog	Ratio [95%CI] BC Lispro/Humalog
Late $t_{[50\%max]}$ (min)	135	160	0.85 [0.78; 0.91]
$AUC_{2\text{-}8h}$ (h*mU/L)	84	106	0.79 [0.72; 0.87]



Better Post Prandial Glucose Control

	BC Lispro	Humalog	Mean Difference
BG_{1h} (mg/dL)	135	177	42
BG_{2h} (mg/dL)	126	153	27



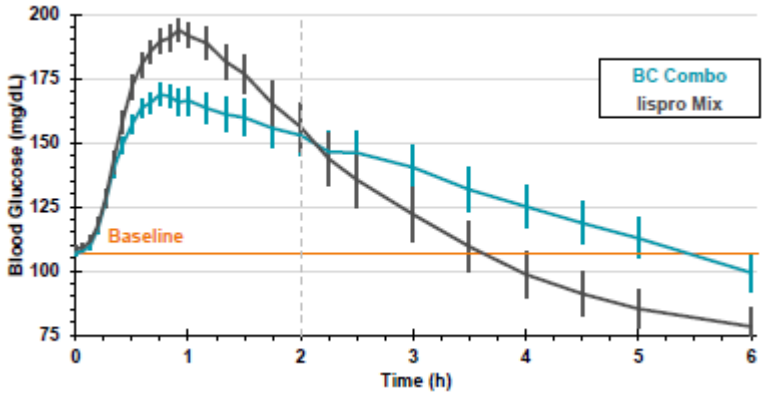
BC COMBO

Results summary compared to Conventional Lispro Mix 75/25 in T1DM subjects

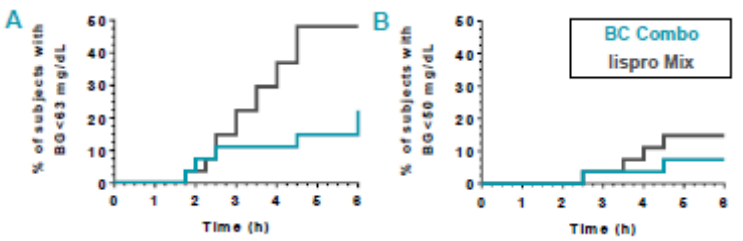
295-OR in Novel Therapeutics in T1D, June 13, 2016, 76th ADA Scientific Sessions

- **In this solid mixed meal study, BC Combo achieved more effective PPG control than lispro Mix:**
  - ✓ **Improved post-prandial blood glucose control**
    - 24% reduction in ΔAUCBG_0-2h
    - 23 mg/dL decrease in maximum BG
    - 24 mg/dL mean BG reduction at 1hr
  - ✓ **Lower risk for delayed prandial hypoglycaemia**
    - Less subjects with low BG < 63 mg/dL and 50 mg/dL
    - Less time spent in hypoglycaemia and more time spent in target glycaemia
- **Potential of BC Combo to improve post-prandial glucose control and lower risk of both hyperglycaemic and hypoglycaemic excursions will be investigated in further clinical studies**

Mean Unadjusted BG Profiles ± SEM Over 6hr After s.c. Administration of Individualised Doses of BC Combo and Lispro Mix



Cumulative Percentage of Subjects With BG Values < 63 mg/dL (A) or < 50 mg/mL (B) Over the Course of the Meal Test



Demographic and Baseline Characteristics of the Study Population

Parameter	Mean ± SD	Parameter	Mean ± SD
Sex	Female: n-6 (21.4%) Male: n-22 (78.6%)	Diabetes Duration (years)	27.2 ± 11.5
Race	White 100%	BMI (kg/m²)	24.2 ± 2.1
Age (years)	45.9 ± 11.2	C-Peptide (nmol/L)	0
Height (cm)	177 ± 8	HbA_{1c} (%)	7.33 ± 0.80
Weight (kg)	76 ± 10		

30 subjects screened, 28 randomised, 28 received lisproMix – 27 received BC Combo
Full analysis set n=28: 27 BC Combo – 27 lispro Mix (1 exclusion due to wrong dosing)

Hypoglycaemic events

Parameter	BC Combo	Lispro Mix	P-value
Subjects with at least one hypoglycaemic event	7 / 27	15 / 28	0.0364[1]
Number of hypoglycaemic events	12	29	0.0079[1]
Number of hypoglycaemic event per subject	0[2]	1[2]	0.0151[3]

1 Chi-Square test 2 Median 3 Wilcoxon Signed Rank test

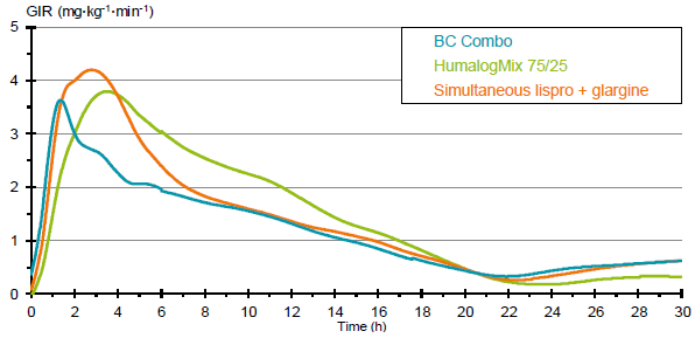
BC COMBO

Results summary compared to Humalog 75/25 in T2DM subjects

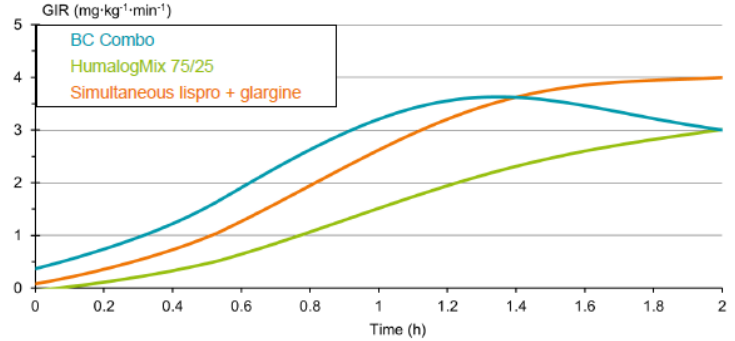
942-P in 12-B Clinical Therapeutics/ New Technology-Insulins, June 11, 2016, 76th ADA Scientific Sessions

- **In this study, BC Combo demonstrated:**
  - ✓ Greater early glucodynamic effect in first hour post dosing and faster time to maximum blood glucose lowering which is essential to achieve better post prandial blood glucose control
  - ✓ Lower late post prandial effect in comparison to Humalog Mix 75/25 which may reduce the risk of delayed post-prandial hypoglycaemia as shown in a meal test study in subjects with T1DM (ADA2016 OR-295)
  - ✓ Higher late basal effect than Humalog Mix 75/25, similar to the separate injections, indicating that BC Combo could adequately provide both basal and prandial insulin requirements for a meal with only one injection per day
  - ✓ The results obtained in T2DM subjects replicate our findings in subjects with T1DM by demonstrating BC Combo's favorable time-action profile over Humalog Mix 75/25

Smoothed GIR Profiles (0-30h) of 0.8 U/kg BioChaperone Combo, 0.8 U/kg HumalogMix 75/25 and Separate Injections of 0.2 U/kg Lispro + 0.6 U/kg Glargine



Smoothed GIR Profiles (0-2h) of 0.8 U/kg BioChaperone Combo, 0.8 U/kg HumalogMix 75/25 and Separate Injections of 0.2 U/kg Lispro + 0.6 U/kg Glargine



PD Parameters Based on Glucose Infusion Rate

	BC Combo	Humalog Mix 75/25	P-value vs. BC Combo	Lispro _ glargine	P-value vs. BC Combo
Pramdial Phase (0.6h)					
$AUC_{GIR\ 0\text{-}1h}$ [mg/kg]	88 (74)	29 (34)	<0.0001	58 (48)	0.0087
$AUC_{GIR\ 0\text{-}2h}$ [mg/kg]	294 (227)	174 (126)	0.0001	277 (184)	0.5227
$AUC_{GIR\ 0\text{-}6h}$ [mg/kg]	860 (536)	1011 (535)	0.0335	1121 (556)	0.0003
$TGIR_{max}$ [h]	1.3 [1.2;5.1]	3.8 [1.8;6.0]	<0.0001	2.9 [1.4;4.9]	0.0057
Prandial – Basal Transition (6-12h)					
$AUC_{GIR\ 6\text{-}12h}$ [mg/kg]	589 (275)	870 (501)	0.0002	630 (211)	0.3420
$AUC_{GIR\ 6\text{-}24h}$ [mg/kg]	1075 (615)	1481 (911)	0.0001	1156 (551)	0.4522
Basal Phase (12-30h)					
$AUC_{GIR\ 12\text{-}18h}$ [mg/kg]	342 (225)	473 (354)	0.0063	382 (221)	0.2156
$AUC_{GIR\ 24\text{-}30h}$ [mg/kg]	186 (133)	99 (102)	0.0105	174 (139)	0.6747
Overall					
$AUC_{GIR\ 0\text{-}30h}$ [mg/kg]	2122 (1184)	2590 (1368)	0.0103	2451 (1071)	0.0124

Table shows arithmetic means (SD) except median [min;max] for $TGIR_{max}$
P-value from Hodges and Lehmann Estimates or (for $AUC_{GIR\ 0\text{-}6h}$ and $AUC_{GIR\ 0\text{-}30h}$) from LS Means

THANK YOU FOR YOUR KIND INTEREST

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