

Science Backed Probiotics for New Applications in the Microbiome Era

November 2020





## **Today's Presenters**

For the First Time Together



Dr. Gregory Leyer Chief Scientific Officer, UAS Labs



Dr. Adam Baker Director of Science, Chr. Hansen UAS Labs was acquired by Chr. Hansen in July 2020.

Each with a history of success focused on science ...

We are now, Better Together





The Human Microbiome universe and the new narrative: Probiotics seed and are integral to support your microbiome ecosystem



### Your microbiome and your health are intimately connected



- The gut microbiome is established from birth and shaped during the first years of life
- How this microbiome develops effects our health as the infant microbiome coevolves with our immune, metabolic, and neurological programming
- Our everyday world introduces factors such as stress and antibiotic use that can affect our microbiome
- With the use of **probiotics** these effects may be reduced







## The Science Behind Probiotics Make the Connection





### We have a strain pipeline backed by strong science



#### In vitro



#### In vivo animal models



#### **Production and Pilot human trial**



Production of the B. breve clinical batch completed. - Parallel production is ongoing at CH and NIZO of B. adolescentis to mitigate the upscaling risk



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# Probiotics – The focus is on understanding how they work in the gastrointestinal system







## *In vitro* Screening to understand Probiotic **Mode of Action**







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# A state-of-the-art screening program was initiated to identify a bifidobacterium that could support the integrity of the intestinal tract

#### In vitro profiling

Bacteria

#### 127 bifidobacterial

- Acid tolerance
- Bile tolerance
- Intestinal permeability
- Mucus adhesion
- Immune modulation

#### Animal Study

#### **5 bifidobacterial**

 Chemically-induced inflammatory intestinal challenge model

#### Human Clinical Trials

- 1 bifidobacterium, Bif195
- Human gut permeability challenge model
- Human small intestinal ulceration challenge model





# The degree of small intestinal damage was asessed using video capsule endoscopy and calculating the Lewis Score

> The Pill cam was ingested at 6 different visits during the 8-week intervention period



> Example of ulcers observed in our video data:



## Lewis Score – An Estimate of Intestinal Damage

Reflects the severity of damage in the small intestinal wall

Calculated based on observations from the video material for the following parameters: villous oedema, ulcers and stenosis





### We have a strain pipeline backed by strong science



#### **Video material**

3-4 hours of video material for each subject was reviewed by 2 independent gastroenterologists





## The clinical trial met the primary endpoint



#### LEWIS SCORE:

*Reflects the severity of damage in the small intestinal wall.* 

MEAN LEWIS SCORE PER VISIT<sup>1</sup>

Calculated based on observations from the video material for the following parameters: villous oedema, ulcers and stenosis



#### MEAN LEWIS SCORE AUC ± SEM PER INTERVENTION ARM<sup>1</sup>

#### Conclusion

Area under-the-curve for the Lewis Score in the Bif195 group was significantly lower than in the placebo group

This demonstrates that supplementation with Bif195 safely reduces the risk of smallintestinal damage caused by acetylsalicylic acid



## The clinical trial also met the secondary endpoint



#### LEWIS SCORE:

*Reflects the severity of damage in the small intestinal wall.* 

Calculated based on observations from the video material for the following parameters: villous oedema, ulcers and stenosis

#### Conclusion

Area under-the-curve for the Lewis Score in the Bif195 group was significantly lower than in the placebo group

This demonstrates that supplementation with Bif195 safely reduces the risk of smallintestinal damage caused by acetylsalicylic acid





# The health state of the small intestine was improved for people receiving Bif195 versus placebo<sup>1</sup>

Aspirin + placebo



- Edema (red, swollen tissue, lack of villi)
- Ulcers (appearing as white spots)

Aspirin + Bif195



• Normal small intestine with villi

#### **Trial Conclusions<sup>1</sup>**

The Bif195 strain significantly reduces intestinal damage (Lewis Score)

Subjects taking Bif195 had significantly less intestinal ulcers than subjects taking placebo







## **The Science Behind Probiotics**

Back to the Basics







The emerging probiotic research areas offer exciting future health benefit targets

While probiotics for gut health is a more mature market, there is desperate need (>580 million global IBS sufferers) for gastrointestinal symptom relief backed by solid clinical evidence







## **Digestive Health Study Synopsis**

Randomized, double-blind, placebo-controlled (3-arm) Study

- Objective: To assess the effect of probiotics on symptomology in subjects with IBS including abdominal pain
- Subjects: 330 adults (ITT) with diagnosis of IBS (Rome IV criteria) and abdominal pain
- Probiotic Strains: L. acidophilus DDS<sup>®</sup>-1 or B. lactis UABla-12<sup>™</sup> at 10B CFU/day
- Site: India (12 sites)
- Duration: 2-week run-in and 6-week intervention period





## **Digestive Health Study Synopsis**

#### Primary Outcome Measure:

• Abdominal Pain Severity Numeric Rating Scale (APS-NRS)

#### Secondary Outcome Measures:

- Global assessment of digestive symptoms
- Bowel habits and stool consistency
- IBS-QOL questionnaire
- Bloating

#### **Clinical Research Organization (CRO):**

 Vedic Life Sciences, a GCP and ISO compliant CRO based in Mumbai, India with over 400 clinical and preclinical studies to their name





<b>Visit 1</b> Screen Day -18	Visit 2 Baseline Day 0	Visit 3 Midpoint Day 21	Visi Fina Day
Screen Placebo Run-In (1	4 Days)	Intervention (42 Day	s)
Visit 1	Visit 2	Visit 3	Visit 4
Primary Inclusion - M/F 18-70 yo - IBS via Rome IV - Max abdominal pain severity ( ≥ 4 on 10 ) confirmed at Visits 1 & 2	Primary - APS-NRS Secondary - IBS-SSS - Bowel Habits	<b>Secondary</b> - APS-NRS - IBS-SSS - Bowel Habits - IBS-QoL	Primary - APS-NRS Secondary - IBS-SSS - Bowel Habits
	- IBS-QoL Other - PSS - IP tolerability - Rescue Rx	Other - PSS - IP tolerability - Rescue Rx - Compliance - Safety	- IBS-QoL Other - PSS - IP tolerability - Rescue Rx

#### Legend

Abdominal pain severity – Numeric rating scale (APS-NRS), IBS Severity Scoring System (IBS-SSS), IBS-QoL (IBS-Quality of Life), PSS (Perceived Stress Scale)





### **Primary Outcome Measure**

DDS subjects experienced a mean 36.1% reduction in

their abdominal pain severity after 6 weeks

Abdominal Pain Severity Numeric Rating Scale (APS-NRS)

While there are multiple symptoms of IBS, abdominal pain independently drives health related quality of life (HRQOL) and is the principal driver of patient reported symptom severity

- Abdominal pain is measured on an 11-point scale known as the Abdominal Pain Severity Numeric Rating Scale (APS-NRS)



\*p=0.018; \*\*\*p<0.001 between treatment and placebo (based on Mann-Whitney U test)

## **B.** *lactis* subjects experienced a 21.6% reduction in their abdominal pain severity after 6 weeks



\*\*\*p<0.001 between treatment and placebo (based on Mann-Whitney U test)



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## **Secondary Outcome: Digestive Symptomology**

It's been suggested that a minimum reduction of 95 points is needed to show a clinically relevant change in symptoms<sup>1</sup>



\*\*\* Change in Mean Total Score vs Placebo: P-value < 0.001

#### Conclusion

Both probiotic groups showed significant improvements:

B. lactis decrease of 104 points

*L. acidophilus* decrease of 132 points





### **Secondary Outcome: Stool Normalization**



#### Conclusion

Probiotic consumption improved the number of subjects reporting normal stool consistency and improved regularity (Bristol Stool 3 - 5)



\*p<0.022; \*\*p=0.002 between treatment and placebo (based on Pearson Chi Square test)



% categorization

## **Clinical Trial Takeaways**

- ✓ Both probiotic strains (*L. acidophilus* DDS<sup>®</sup>-1 and *B. lactis* UABla-12<sup>™</sup>) achieved the primary objective of significantly decreasing abdominal pain vs. placebo after 6 weeks of intervention
- Several secondary objectives also achieved, including improvements in digestive symptomology, bloating, quality of life, and normalization of stool patterns
- Both probiotic strains shown to be safe and well tolerated



MDPI

#### 🕎 nutrients

#### Article

Lactobacillus acidophilus DDS-1 and Bifidobacterium lactis UABla-12 Improve Abdominal Pain Severity and Symptomology in Irritable Bowel Syndrome: Randomized Controlled Trial

Christopher J. Martoni <sup>1</sup>, Shalini Srivastava <sup>2</sup> and Gregory J. Leyer <sup>1,\*</sup>

Details of the study can be found in the publication - Martoni et al. Nutrients. 2020;12(2):363





# In Conclusion



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### We continuously expand our science ...



Expand within the infant space

Enter new ventures into microbiome adjacencies and lifestages: \*Healthy Aging \*Heart Health

# Thank You! Dr. Adam Baker and Dr. Gregory Leyer

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