



## Clinical trial results:

### An Open-Label, Multi-Center, Single-Dose Study to Assess the Safety, Tolerability, Pharmacodynamics, and Pharmacokinetics of Nasal Glucagon in Pediatric Patients with Type 1 Diabetes Aged 1 to <4 years

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2021-006088-61   |
| Trial protocol           | Outside EU/EEA   |
| Global end of trial date | 05 November 2023 |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 18 May 2024  |
| First version publication date | 18 May 2024  |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | I8R-MC-IGBO |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |                     |
|------------------------------------|---------------------|
| ISRCTN number                      | -                   |
| ClinicalTrials.gov id (NCT number) | NCT04992312         |
| WHO universal trial number (UTN)   | -                   |
| Other trial identifiers            | Trial Number: 17449 |

Notes:

##### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Eli Lilly and Company   |
| Sponsor organisation address | Lilly Corporate Center, Indianapolis, IN, United States, 46285            |
| Public contact               | Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877CTLilly, |
| Scientific contact           | Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 8772854559, |

Notes:

##### Paediatric regulatory details

|  |                     |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-001657-PIP01-14 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No                  |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes                 |

Notes:

## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 05 November 2023 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 05 November 2023 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

The main purpose of this study is to evaluate the safety and tolerability of a study drug called nasal glucagon (Baqsimi) in pediatric participants with type 1 diabetes (T1D) aged 1 to less than 4 years. Blood tests will be performed to check how much nasal glucagon gets into the bloodstream. Blood sugar will also be measured to understand the effect of the drug on blood sugar levels. The study consists of a screening period up to 35 days before dosing, 1 day when a dose of nasal glucagon will be given and then 2 telephone follow up calls; first follow-up call on the day after the nasal glucagon was given and second call about one week after nasal glucagon was given. The study will last up to 9 days, not including the screening period.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 24 March 2022 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | No            |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                  |
|--------------------------------------|------------------|
| Country: Number of subjects enrolled | United States: 7 |
| Worldwide total number of subjects   | 7                |
| EEA total number of subjects         | 0                |

Notes:

### Subjects enrolled per age group

|   |   |
|---|---|
| In utero                                  | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days)                      | 0 |
| Infants and toddlers (28 days-23 months)  | 1 |
| Children (2-11 years)                     | 6 |
| Adolescents (12-17 years)                 | 0 |

|                      |   |
|----------------------|---|
| Adults (18-64 years) | 0 |
| From 65 to 84 years  | 0 |
| 85 years and over    | 0 |

## Subject disposition

### Recruitment

Recruitment details:

No Text Available

### Pre-assignment

Screening details:

No Text Available

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Not applicable                 |
| Blinding used                | Not blinded                    |

### Arms

|                  |                                 |
|------------------|---------------------------------|
| <b>Arm title</b> | 3 milligram (mg) nasal glucagon |
|------------------|---------------------------------|

Arm description:

Participants received a single dose of 3 mg glucagon powder administered intranasally on day 1.

|  |                                       |
|--|---------------------------------------|
| Arm type                               | Experimental                          |
| Investigational medicinal product name | nasal glucagon                        |
| Investigational medicinal product code |                                       |
| Other name                             | Baqsimi                               |
| Pharmaceutical forms                   | Nasal powder in single-dose container |
| Routes of administration               | Intranasal use                        |

Dosage and administration details:

Participants received a single dose of 3 mg glucagon powder administered intranasally on day 1.

|  |                                    |
|--|------------------------------------|
| <b>Number of subjects in period 1</b>    | 3 milligram (mg)<br>nasal glucagon |
| Started                                  | 7                                  |
| received at least one dose of study drug | 7                                  |
| Completed                                | 7                                  |

## Baseline characteristics

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | Overall Study |
|-----------------------|---------------|

Reporting group description: -

| Reporting group values | Overall Study | Total |  |
|------------------------|---------------|-------|--|
| Number of subjects     | 7             | 7     |  |
| Age categorical        |               |       |  |
| Units: Subjects        |               |       |  |

|   |        |   |  |
|---|--------|---|--|
| Age continuous                            |        |   |  |
| Units: years                              |        |   |  |
| arithmetic mean                           | 2.98   |   |  |
| standard deviation                        | ± 0.82 | - |  |
| Gender categorical                        |        |   |  |
| Units: Subjects                           |        |   |  |
| Female                                    | 3      | 3 |  |
| Male                                      | 4      | 4 |  |
| Ethnicity (NIH/OMB)                       |        |   |  |
| Units: Subjects                           |        |   |  |
| Hispanic or Latino                        | 1      | 1 |  |
| Not Hispanic or Latino                    | 6      | 6 |  |
| Unknown or Not Reported                   | 0      | 0 |  |
| Race (NIH/OMB)                            |        |   |  |
| Units: Subjects                           |        |   |  |
| American Indian or Alaska Native          | 0      | 0 |  |
| Asian                                     | 0      | 0 |  |
| Native Hawaiian or Other Pacific Islander | 0      | 0 |  |
| Black or African American                 | 0      | 0 |  |
| White                                     | 7      | 7 |  |
| More than one race                        | 0      | 0 |  |
| Unknown or Not Reported                   | 0      | 0 |  |
| Region of Enrollment                      |        |   |  |
| Units: Subjects                           |        |   |  |
| United States                             | 7      | 7 |  |

### Subject analysis sets

|                            |                     |
|----------------------------|---------------------|
| Subject analysis set title | 3 mg nasal glucagon |
|----------------------------|---------------------|

|                           |              |
|---------------------------|--------------|
| Subject analysis set type | Per protocol |
|---------------------------|--------------|

Subject analysis set description:

Participants received a single dose of 3 mg glucagon powder administered intranasally on day 1.

| Reporting group values | 3 mg nasal glucagon |  |  |
|------------------------|---------------------|--|--|
| Number of subjects     | 7                   |  |  |

|   |                |  |  |
|---|----------------|--|--|
| Age categorical<br>Units: Subjects                                      |                |  |  |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 2.98<br>± 0.82 |  |  |
| Gender categorical<br>Units: Subjects                                   |                |  |  |
| Female  | 3              |  |  |
| Male  | 4              |  |  |
| Ethnicity (NIH/OMB)<br>Units: Subjects                                  |                |  |  |
| Hispanic or Latino  | 1              |  |  |
| Not Hispanic or Latino  | 6              |  |  |
| Unknown or Not Reported   | 0              |  |  |
| Race (NIH/OMB)<br>Units: Subjects                                       |                |  |  |
| American Indian or Alaska Native  | 0              |  |  |
| Asian   | 0              |  |  |
| Native Hawaiian or Other Pacific Islander                               | 0              |  |  |
| Black or African American   | 0              |  |  |
| White   | 7              |  |  |
| More than one race  | 0              |  |  |
| Unknown or Not Reported   | 0              |  |  |
| Region of Enrollment<br>Units: Subjects                                 |                |  |  |
| United States   | 7              |  |  |

## End points

### End points reporting groups

|   |                                 |
|---|---------------------------------|
| Reporting group title   | 3 milligram (mg) nasal glucagon |
| Reporting group description:  |                                 |
| Participants received a single dose of 3 mg glucagon powder administered intranasally on day 1. |                                 |
| Subject analysis set title  | 3 mg nasal glucagon             |
| Subject analysis set type   | Per protocol                    |
| Subject analysis set description:   |                                 |
| Participants received a single dose of 3 mg glucagon powder administered intranasally on day 1. |                                 |

### Primary: Number of Participants with One or More Treatment-Emergent Adverse Event(s) (TEAEs) and Serious Adverse Event(s) (SAEs) Considered by the Investigator to be Related to Study Drug Administration

|                 |  |
|-----------------|--|
| End point title | Number of Participants with One or More Treatment-Emergent Adverse Event(s) (TEAEs) and Serious Adverse Event(s) (SAEs) Considered by the Investigator to be Related to Study Drug Administration <sup>[1]</sup> |
|-----------------|--|

#### End point description:

A TEAE is defined as an adverse event which occurs post-dose or which is present prior to dosing and becomes more severe post-dose. An SAE is any AE from the study that results in 1 of the following: Death, initial or prolonged inpatient hospitalization, a life-threatening experience (i.e., immediate risk of dying), persistent or significant disability/incapacity, congenital anomaly/birth defect, important medical events that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the subject or may require intervention to prevent 1 of the other outcomes listed in the definition above. The number of participants with one or more TEAEs, SAEs considered by the investigator to be related to study drug administration is reported here. A summary of SAEs and other non-serious AEs, regardless of causality is located in the Reported Adverse Events section of this record.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

#### End point timeframe:

Baseline to Day 9

#### Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No inferential statistics were planned for this endpoint.

| End point values            | 3 mg nasal glucagon  |  |  |  |
|-----------------------------|----------------------|--|--|--|
| Subject group type          | Subject analysis set |  |  |  |
| Number of subjects analysed | 7 <sup>[2]</sup>     |  |  |  |
| Units: participants         |                      |  |  |  |
| TEAEs                       | 5                    |  |  |  |
| SAEs                        | 0                    |  |  |  |

#### Notes:

[2] - All participants who received at least one dose of study drug.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacodynamics (PD): Change From Baseline in Maximum Observed Blood Glucose (BG<sub>max</sub>)

|                 |  |
|-----------------|--|
| End point title | Pharmacodynamics (PD): Change From Baseline in Maximum |
|-----------------|--|

## End point description:

Change from baseline in BGmax was measured to investigate the PD effect of nasal glucagon on blood glucose level following 3 mg nasal glucagon administration on day 1. Baseline is defined as Day 1 pre-dose. The BGmax on Day 1 was determined using plasma samples collected pre-dose, 10, 30, 60, and 90 minutes post nasal glucagon dose.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

Baseline, Day 1 (pre-dose, 10, 30, 60, 90 minutes post-dose)

| End point values                        | 3 mg nasal glucagon  |  |  |  |
|---|----------------------|--|--|--|
| Subject group type                      | Subject analysis set |  |  |  |
| Number of subjects analysed             | 7 <sup>[3]</sup>     |  |  |  |
| Units: milligrams per deciliter (mg/dL) |                      |  |  |  |
| arithmetic mean (standard deviation)    | 132.4 (± 52.4)       |  |  |  |

## Notes:

[3] - All participants who received at least one dose of study drug and had evaluable PD data.

### Statistical analyses

No statistical analyses for this end point

### Secondary: PD: Absolute BGmax of Nasal Glucagon

|                 |                                      |
|-----------------|--------------------------------------|
| End point title | PD: Absolute BGmax of Nasal Glucagon |
|-----------------|--------------------------------------|

## End point description:

PD: Absolute BGmax of Nasal Glucagon

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

Day 1 (Pre-dose, 10, 30, 60, 90 minutes post-dose)

| End point values                     | 3 mg nasal glucagon  |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| Subject group type                   | Subject analysis set |  |  |  |
| Number of subjects analysed          | 7 <sup>[4]</sup>     |  |  |  |
| Units: mg/dL                         |                      |  |  |  |
| arithmetic mean (standard deviation) | 242.1 (± 46)         |  |  |  |

## Notes:

[4] - All participants who received at least one dose of study drug and had evaluable PD data.

### Statistical analyses

No statistical analyses for this end point

### Secondary: PD: Time of Maximum Observed Blood Glucose (TBGmax) of Nasal Glucagon



|  |   |
|--|---|
| End point title  | PD: Time of Maximum Observed Blood Glucose (TBGmax) of Nasal Glucagon |
| End point description:<br>PD: TBGmax of Nasal Glucagon                     |   |
| End point type   | Secondary   |
| End point timeframe:<br>Day 1 (Pre-dose, 10, 30, 60, 90 minutes post-dose) |   |

|                                      |                      |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| <b>End point values</b>              | 3 mg nasal glucagon  |  |  |  |
| Subject group type                   | Subject analysis set |  |  |  |
| Number of subjects analysed          | 7 <sup>[5]</sup>     |  |  |  |
| Units: minutes                       |                      |  |  |  |
| arithmetic mean (standard deviation) | 55.6 (± 20.9)        |  |  |  |

Notes:

[5] - All participants who received at least one dose of study drug and had evaluable PD data.

### Statistical analyses

No statistical analyses for this end point

### Secondary: PD: Area Under the Concentration Versus Time Curve (AUC) of Blood Glucose

|  |   |
|--|---|
| End point title  | PD: Area Under the Concentration Versus Time Curve (AUC) of Blood Glucose |
| End point description:<br>AUC from time 0 to the last measured concentration of blood glucose at 90 minutes [AUC(0-90)] is reported. |   |
| End point type   | Secondary   |
| End point timeframe:<br>Day 1 (Pre-dose, 10, 30, 60, 90 minutes post-dose)   |   |

|   |                      |  |  |  |
|---|----------------------|--|--|--|
| <b>End point values</b>                         | 3 mg nasal glucagon  |  |  |  |
| Subject group type                              | Subject analysis set |  |  |  |
| Number of subjects analysed                     | 7 <sup>[6]</sup>     |  |  |  |
| Units: milligram*minute per deciliter (mg*m/dL) |                      |  |  |  |
| arithmetic mean (standard deviation)            | 18200 (± 3000)       |  |  |  |

Notes:

[6] - All participants who received at least one dose of study drug and had evaluable PD data.

### Statistical analyses

No statistical analyses for this end point

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**Secondary: Pharmacokinetics (PK): AUC of Nasal Glucagon**

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|                 |  |
|-----------------|--|
| End point title | Pharmacokinetics (PK): AUC of Nasal Glucagon |
|-----------------|--|

End point description:

Geometric coefficient of variation value given in percentage.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 1 (10, 30, 60 min post-dose)

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| End point values                                    | 3 mg nasal glucagon  |  |  |  |
|---|----------------------|--|--|--|
| Subject group type                                  | Subject analysis set |  |  |  |
| Number of subjects analysed                         | 7 <sup>[7]</sup>     |  |  |  |
| Units: picogram*hour per milliliter (pg*hr/mL)      |                      |  |  |  |
| geometric mean (geometric coefficient of variation) | 1560 ( $\pm$ 25.3)   |  |  |  |

Notes:

[7] - All participants who received at least one dose of study drug and had evaluable PK data.

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**Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline to Day 9

Adverse event reporting additional description:

All participants who received at least one dose of study drug.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 24.0 |
|--------------------|------|

### Reporting groups

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | 3 mg nasal glucagon |
|-----------------------|---------------------|

Reporting group description:

Participants received a single dose of 3 mg glucagon powder administered intranasally on day 1.

| Serious adverse events                            | 3 mg nasal glucagon |  |  |
|---|---------------------|--|--|
| Total subjects affected by serious adverse events |                     |  |  |
| subjects affected / exposed                       | 0 / 7 (0.00%)       |  |  |
| number of deaths (all causes)                     | 0                   |  |  |
| number of deaths resulting from adverse events    |                     |  |  |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events                            | 3 mg nasal glucagon |  |  |
|---|---------------------|--|--|
| Total subjects affected by non-serious adverse events |                     |  |  |
| subjects affected / exposed                           | 5 / 7 (71.43%)      |  |  |
| Eye disorders   |                     |  |  |
| eye pruritus  |                     |  |  |
| alternative dictionary used: MedDRA 24.0              |                     |  |  |
| subjects affected / exposed                           | 1 / 7 (14.29%)      |  |  |
| occurrences (all)                                     | 1                   |  |  |
| Gastrointestinal disorders                            |                     |  |  |
| abdominal discomfort                                  |                     |  |  |
| alternative dictionary used: MedDRA 24.0              |                     |  |  |
| subjects affected / exposed                           | 1 / 7 (14.29%)      |  |  |
| occurrences (all)                                     | 1                   |  |  |
| vomiting  |                     |  |  |

|   |                                |  |  |
|---|--------------------------------|--|--|
| <p>alternative dictionary used:<br/>MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>1 / 7 (14.29%)</p> <p>1</p> |  |  |
| <p>nausea</p> <p>alternative dictionary used:<br/>MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>1 / 7 (14.29%)</p> <p>1</p> |  |  |
| <p>post-tussive vomiting</p> <p>alternative dictionary used:<br/>MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>1 / 7 (14.29%)</p> <p>1</p> |  |  |
| <p>dyspepsia</p> <p>alternative dictionary used:<br/>MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>1 / 7 (14.29%)</p> <p>1</p> |  |  |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>epistaxis</p> <p>alternative dictionary used:<br/>MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 7 (14.29%)</p> <p>1</p> |  |  |
| <p>sneezing</p> <p>alternative dictionary used:<br/>MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>1 / 7 (14.29%)</p> <p>1</p> |  |  |
| <p>nasal discomfort</p> <p>alternative dictionary used:<br/>MedDRA 24.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>1 / 7 (14.29%)</p> <p>1</p> |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported