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Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Not applicable.

Trial Indication(s)

Amblyopia

Protocol Number

CDDO001F12201

Protocol Title

A 16 week randomized, single-masked, multicenter proof of concept study of binocular videogames versus patching for amblyopia in children 4-7 years of age with an open-label substudy of binocular videogames in children 8-12 years of age

Clinical Trial Phase

Phase 1

Phase of Drug Development

Not applicable.

Study Start/End Dates

Study Start Date: June 30, 2021 (Actual)
Primary Completion Date: August 03, 2022 (Actual)
Study Completion Date: August 03, 2022 (Actual)

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Reason for Termination (If applicable)

The study was terminated based upon the competitive landscape and strategic fit.

Study Design/Methodology

The clinical investigation consisted of 2 parts:

- Part A: a single-masked, randomized clinical investigation in subjects 4 to 7 years of age.
- Part B: an open-label, non-randomized sub-investigation in subjects 8 to 12 years of age.

Part A was a 16-week, prospective, randomized, single-masked, multicenter, controlled, 2-arm, parallel-group clinical investigation in subjects 4 to 7 years of age with amblyopia. Subjects were randomly assigned in a 1:1 ratio to either binocular videogame treatment for 8 to 12 weeks or patching treatment for 16 weeks. Randomization was stratified by severity of amblyopia in eligible subjects (moderate amblyopia with best-corrected visual acuity (BCVA) of the amblyopic eye of 20/100 or better, or severe amblyopia with BCVA of the amblyopic eye worse than 20/100).

Part B was a 16-week, open-label, single arm sub-investigation in subjects 8 to 12 years of age with amblyopia, in which selected sites could participate. Subjects received binocular videogame treatment for 8 weeks, followed by 8 weeks of follow-up.

Centers

8 centers in 3 countries: United States(5), Canada(2), Australia(1)

Objectives:

The primary effectiveness objective was to demonstrate the superiority of binocular videogames relative to patching of the fellow (sound) eye based on change from Baseline in the amblyopic eye BCVA after 8 weeks of treatment (Part A).

The secondary objectives of the clinical investigation were as follows:

- To evaluate the proportion of binocular videogame-treated subjects achieving BCVA of 0.1 logarithm of the minimum angle of resolution (logMAR) (20/25) or better in the amblyopic eye at Week 4, Week 8, Week 12, and Week 16 relative to patching (Part A).
- To evaluate change in stereoacuity from Baseline to Week 4, Week 8, Week 12, and Week 16 for binocular videogames relative to patching (Part A).
- To evaluate the proportion of binocular videogame-treated subjects achieving a 2-line or better improvement in the amblyopic eye at Week 4, Week 8, Week 12, and Week 16 relative to patching (Part A).
- To evaluate the change in BCVA in the amblyopic eye from Baseline to Week 4, Week 12, and Week 16 for binocular videogames relative to patching (Part A).
- To assess safety and tolerability of the binocular videogames (Part A and Part B).
- To assess compliance with treatment (Part A and Part B).

Test Product (s), Dose(s), and Mode(s) of Administration

Investigational treatment – Binocular videogames system:
The binocular videogames system composed of a computer tablet, a software with 2 interactive videogames (Dig Rush and Monster Burner) that were loaded on to the computer tablet, and a pair of 3D anaglyph glasses.
Subjects from Part A who were randomized to the binocular videogame treatment and all subjects from Part B were instructed to play 1 hour of binocular videogame of choice (Dig Rush and/or Monster Burner) a day 7 days a week for 8 weeks. At Week 8, subjects from Part A who did not reach 100% contrast in the fellow (sound) eye were instructed to continue playing the game(s) for additional 4 weeks until Week 12.
The 1 hour of active game play could be split into multiple intervals/sessions. The minimum session duration is 15 minutes without interruption.

Control treatment – Patching of the fellow (sound) eye:
Subjects from Part A who were randomized to the patching treatment were instructed to patch their fellow (sound) eye 2 hours a day 7 days a week for 16 weeks.

Parent(s)/legal guardian(s) of the subjects were instructed that the 2 hours of daily patching should be completed in a single 2-hour session, but if this was not possible for any reason, the treatment could be divided into shorter sessions totaling 2 hours.

Statistical Methods

Due to the early termination of the clinical investigation, effectiveness analyses had been simplified and limited to descriptive statistics throughout. Observed data were used for all effectiveness analyses performed. No imputation for missing data was conducted. Effectiveness analyses were based on the full analysis set (FAS), defined as all enrolled subjects to whom clinical investigation treatment had been assigned.

Safety was monitored by assessing ophthalmic examination results and ocular alignment (strabismus), as well as collecting adverse events (AEs), adverse device effects (ADEs), and device deficiencies. Safety analyses were based on the safety set (SAF), defined as all enrolled subjects who used clinical investigation treatment at least once.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

1. Written informed consent must be signed by the parent(s) or legal guardian(s) prior to participation in the study.
2. Male or female children 4 to 7 years old at Screening (Part A) or 8 to 12 years old at Screening (Part B).
3. Diagnosis of amblyopia due to strabismus, anisometropia, or both.
4. Best corrected visual acuity (BCVA) of amblyopic eye (study eye) between 0.3 to 1.0 Logarithm of the Minimum Angle of Resolution (logMAR) (20/40 to 20/200 Snellen inclusive, 33 to 72 ETDRS letters inclusive) at Screening and Baseline.
5. BCVA of the sound eye (fellow eye) 0.1 logMAR (20/25 Snellen, 80 Early Treatment Diabetic Retinopathy Study (ETDRS) letters) or better in children 5 years of age and older or 0.2 logMAR (20/30 Snellen, 75 ETDRS letters) or better in children 4 years of age at Screening and Baseline.
6. Interocular difference of BCVA at least 0.3 logMAR (≥3 lines; ETDRS≥15 letters) at Baseline.
7. Patient is able to play the binocular game (Dig Rush and Monster Burner) on at least level 3 on the study tablet under binocular conditions (with red-green glasses).

Exclusion Criteria:

1. Treatment for amblyopia with patching, Bangerter filter, vision therapy, or binocular treatment in the past 1 week prior to Screening, or atropine in the past 4 weeks prior to Screening.
2. Treatment for amblyopia with patching, Bangerter filter, vision therapy, binocular treatment or atropine for more than 1 year prior to

screening cumulatively.
3. Myopia ≥ -6.00D spheric equivalent in either eye at Screening or Baseline.
4. Prior amblyopia treatment (patching, Bangerter filter, vision therapy, binocular treatment or atropine) for more than a year prior to screening cumulatively.

Participant Flow Table

Overall Study

	Binocular video games - Part A	Patching - Part A	Binocular video games - Part B	Total
Arm/Group Description	Binocular video games - patients will play 1 hour of binocular video game of choice (Dig Rush and/or Monster Burner) a day 7 days a week for 8 to 12 weeks.	Patching of the sound eye (fellow eye) - patients will have their sound eye (fellow eye) patched 2 hours per day 7 days a week for 16 weeks.	Part B was a 16-week, open-label, single arm sub investigation in subjects 8 to 12 years of age with amblyopia, in which selected sites could participate. Subjects received binocular videogame treatment for 8 weeks, followed by 8 weeks of follow-up.	
Started	6	6	15	27
Completed	4	6	3	13
Not Completed	2	0	12	14
Protocol Violation	1	0	0	1
Withdrawal by Subject	1	0	2	3
Study terminated by sponsor	0	0	10	10

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Baseline Characteristics

	Binocular video games - Part A	Patching - Part A	Binocular video games - Part B	Total
Arm/Group Description	Binocular video games - patients will play 1 hour of binocular video game of choice (Dig Rush and/or Monster Burner) a day 7 days a week for 8 to 12 weeks.	Patching of the sound eye (fellow eye) - patients will have their sound eye (fellow eye) patched 2 hours per day 7 days a week for 16 weeks.	Part B was a 16-week, open-label, single arm sub investigation in subjects 8 to 12 years of age with amblyopia, in which selected sites could participate. Subjects received binocular videogame treatment for 8 weeks, followed by 8 weeks of follow-up.	
Number of Participants [units: participants]	6	6	15	27
Baseline Analysis Population Description				
Age Continuous (units: Years) Analysis Population Type: Participants Mean ± Standard Deviation				
	6.43±1.293	6.02±1.318	9.94±1.530	NA±NA[]
Sex: Female, Male (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)				
Female	1	3	6	10
Male	5	3	9	17
Race (NIH/OMB) (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)				

American Indian or Alaska Native	0	0	0	0
Asian	0	1	1	2
Native Hawaiian or Other Pacific Islander	0	0	0	0
Black or African American	0	0	1	1
White	6	5	12	23
More than one race	0	0	0	0
Unknown or Not Reported	0	0	1	1

Summary of Efficacy

Primary Outcome Result(s)

Change from Baseline at Week 8 in best corrected visual acuity (BCVA) in the amblyopic eye.

Description	Part A: Best corrected visual acuity (BCVA) in the amblyopic eye was measured via mixed model repeated measures (MMRM).
Time Frame	from Baseline to Week 8
Analysis Population Description	Full analysis set

	Binocular video games - Part A	Patching - Part A
Arm/Group Description	Binocular video games - patients will play 1 hour of binocular video game of choice (Dig Rush and/or Monster Burner) a day 7 days a week for 8 to 12 weeks.	Patching of the sound eye (fellow eye) - patients will have their sound eye (fellow eye) patched 2 hours per day 7 days a week for 16 weeks.
Number of Participants Analyzed [units: participants]	2	5

Change from Baseline at Week 8 in best corrected visual acuity (BCVA) in the amblyopic eye. (units: logMAR)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	−0.10 ± 0.141	−0.13 ± 0.118

Secondary Outcome Result(s)

Number of participants who attained BCVA of 0.1 logMAR or better in the amblyopic eye

Description	Part A: Best corrected visual acuity (BCVA) in the amblyopic eye was measured via mixed model repeated measures (MMRM).
Time Frame	at Week 4, Week 8, Week 12, and Week 16.
Analysis Population Description	Full analysis set

	Binocular video games - Part A	**Patching - Part A**
Arm/Group Description	Binocular video games - patients will play 1 hour of binocular video game of choice (Dig Rush and/or Monster Burner) a day 7 days a week for 8 to 12 weeks.	Patching of the sound eye (fellow eye) - patients will have their sound eye (fellow eye) patched 2 hours per day 7 days a week for 16 weeks.
Number of Participants Analyzed [units: participants]	6	6
Number of participants who attained BCVA of 0.1 logMAR or better in the amblyopic eye (units: Participants)	**Count of Participants (%)**	**Count of Participants (%)**
Baseline	0 (%)	0 (%)
Week 4	2 (33.33%)	0 (%)

Week 8	1 (50%)	0 (%)
Week 12	1 (50%)	0 (%)
Week 16	1 (20%)	1 (16.67%)

Change in stereoacuity or binocular video game relative to patching.

Description	Part A: Stereoacuity will be assessed at near using Randot Preschool Stereoacuity Test (Stereo Optical, Inc.). The test is performed using 3 stereotest booklets while wearing 3D glasses. In short, in each test booklet, the left-hand page shows two-dimensional black-and-white silhouettes of two sets (panels) of four test shapes. The right-hand page contains two sets of four random-dot patterns in different sequences that are on the left-hand page. In each set of random-dot patterns, one contains no test shape, while the remaining contains test shapes. The child must correctly identify at least two of the three test shapes at each disparity level.
Time Frame	from Baseline to Week 4, Week 8, Week 12, and Week 16.
Analysis Population Description	Full analysis set

Shifts in stereoacuity from Baseline to better post-baseline values in either treatment arm in Part A during the 16-week investigational period were reported as follows:

- Week 4: 1 subject (16.7%) had a shift from 800 arcsecs to 200 arcsecs and 1 subject (16.7%) had a shift from 200 arcsecs to 100 arcsecs in the game arm (n=6);
- Week 8: 1 subject (33.3%) had a shift from not scorable (Nil) to 800 arcsecs and 1 subject (33.3%) had a shift from 200 arcsecs to 100 arcsecs in the game arm (n=3), and 1 subject (20.0%) had a shift from 100 arcsecs to 60 arcsecs in the patch arm (n=5);
- Week 12: 1 subject (33.3%) had a shift from 800 arcsecs to 400 arcsecs and 1 subject (33.3%) had a shift from 200 arcsecs to 60 arcsecs in the game arm (n=3), and 1 subject (16.7%) had a shift from 100 arcsecs to 60 arcsecs in the patch arm (n=6);
- Week 16: 1 subject (20.0%) had a shift from not scorable (Nil) to 800 arcsecs, 1 subject (20.0%) had a shift from 400 arcsecs to 60 arcsecs, and 1 subject (20.0%) had a shift from 200 arcsecs to 100 arcsecs in the game arm (n=5), and 1 subject (16.7%) had a shift from not scorable (Nil) to 60 arcsecs in the patch arm (n=6).

Shifts in stereoacuity from baseline to worse post-baseline values in either treatment arm in Part A during the 16-week investigational period were reported as follows:

- Week 4: 1 subject (16.7%) had a shift from 400 arcsecs to 800 arcsecs in the game arm (n=6);
- Week 12: 1 subject (16.7%) had a shift from 400 arcsecs to not scorable (Nil), 1 subject (16.7%) had a shift form 200 arcsecs to 800 arcsecs, and 1 subject (16.7%) had a shift form 100 arcsecs to 400 arcsecs in the patch arm (n=6);
- Week 16: 1 subject (16.7%) had a shift from 100 arcsecs to 400 arcsecs in the patch arm (n=6).

Number of Participants who attained a 2-line or better improvement in BCVA in the amblyopic eye

Description	Part A: Best corrected visual acuity (BCVA) in the amblyopic eye will be measured via mixed model repeated measures (MMRM).
Time Frame	at Week 4, Week 8, Week 12, and Week 16.
Analysis Population Description	Full analysis set

	Binocular video games - Part A	**Patching - Part A**
Arm/Group Description	Binocular video games - patients will play 1 hour of binocular video game of choice (Dig Rush and/or Monster Burner) a day 7 days a week for 8 to 12 weeks.	Patching of the sound eye (fellow eye) - patients will have their sound eye (fellow eye) patched 2 hours per day 7 days a week for 16 weeks.
Number of Participants Analyzed [units: participants]	6	6
Number of Participants who attained a 2-line or better improvement in BCVA in the amblyopic eye (units: Participants)	**Count of Participants (%)**	**Count of Participants (%)**
Week 4	2 (33.33%)	2 (40%)
Week 8	1 (50%)	3 (60%)

Week 12	1 (50%)	4 (66.67%)
Week 16	1 (20%)	3 (50%)

Change in BCVA in the amblyopic eye

Description	Part A: Best corrected visual acuity (BCVA) in the amblyopic eye will be measured via mixed model repeated measures (MMRM).
Time Frame	from Baseline to Week 4, Week 12, and Week 16.
Analysis Population Description	Full analysis set

	Binocular video games - Part A	**Patching - Part A**
Arm/Group Description	Binocular video games - patients will play 1 hour of binocular video game of choice (Dig Rush and/or Monster Burner) a day 7 days a week for 8 to 12 weeks.	Patching of the sound eye (fellow eye) - patients will have their sound eye (fellow eye) patched 2 hours per day 7 days a week for 16 weeks.
Number of Participants Analyzed [units: participants]	6	6
Change in BCVA in the amblyopic eye (units: logMAR)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
Week 4	−0.07 ± 0.180	−0.11 ± 0.099
Week 8	−0.10 ± 0.141	−0.13 ± 0.118
Week 12	−0.10 ± 0.283	−0.15 ± 0.091
Week 16	−0.09 ± 0.091	−0.16 ± 0.142

Frequency of treatment-emergent Adverse Events - Part A

Description	Part A and B: An adverse event (AE) is any untoward medical occurrence (e.g. any unfavorable and unintended sign [including abnormal laboratory findings], symptom or disease) in a clinical study subject, user or other person, after providing written informed consent for

participation in the study. Therefore, an AE may or may not be temporally or causally associated with the use of the study device, i.e., videogame system (tablet, software, 3D glasses) or patch.

Time Frame: from Baseline to week 16

Analysis Population Description: Safety set

	Binocular video games - Part A	Patching - Part A
Arm/Group Description	Binocular video games - patients will play 1 hour of binocular video game of choice (Dig Rush and/or Monster Burner) a day 7 days a week for 8 to 12 weeks.	Patching of the sound eye (fellow eye) - patients will have their sound eye (fellow eye) patched 2 hours per day 7 days a week for 16 weeks.
Number of Participants Analyzed [units: participants]	6	6
Frequency of treatment-emergent Adverse Events - Part A (units: Participants)	**Count of Participants (%)**	**Count of Participants (%)**
Number of subjects with any Treatment-emergent adverse event (TEAE)	1 (16.67%)	0 (%)
Number of subjects with any serious TEAE	0 (%)	0 (%)
Number of subjects with any severe TEAE	0 (%)	0 (%)
Number of subjects with any TEAE leading to treatment discontinuation	0 (%)	0 (%)
No. w/ any TEAE leading to treatment interruption/reduced daily duration of treatment	0 (%)	0 (%)
Number of subjects with any TEAE of potential relevance to the treatment of amblyopia	1 (16.67%)	0 (%)
Number of subjects with any Adverse device effect (ADE)	1 (16.67%)	0 (%)
Number of subjects with any study treatment-related TEAE	1 (16.67%)	0 (%)

Number of subjects with any study procedure-related TEAE	1 (16.67%)	0 (%)
Number of subjects with any Serious adverse device effect (SADE)	0 (%)	0 (%)

Frequency of treatment-emergent Adverse Events - Part B

Description	Part A and B: An adverse event (AE) is any untoward medical occurrence (e.g. any unfavorable and unintended sign [including abnormal laboratory findings], symptom or disease) in a clinical study subject, user or other person, after providing written informed consent for participation in the study. Therefore, an AE may or may not be temporally or causally associated with the use of the study device, i.e., videogame system (tablet, software, 3D glasses) or patch.
Time Frame	from Baseline to week 16
Analysis Population Description	Safety set

	Binocular video games - Part B
Arm/Group Description	Part B was a 16-week, open-label, single arm sub investigation in subjects 8 to 12 years of age with amblyopia, in which selected sites could participate. Subjects received binocular videogame treatment for 8 weeks, followed by 8 weeks of follow-up.
Number of Participants Analyzed [units: participants]	15
Frequency of treatment-emergent Adverse Events - Part B (units: Participants)	**Count of Participants** **(%)**
Number of subjects with any Treatment-emergent adverse event (TEAE)	4 (26.67%)
Number of subjects with any serious TEAE	0 (%)
Number of subjects with any severe TEAE	1 (6.67%)

Number of subjects with any TEAE leading to treatment discontinuation	0 (%)
No. w/ any TEAE leading to treatment interruption/reduced daily duration of treatment	0 (%)
Number of subjects with any TEAE of potential relevance to the treatment of amblyopia	1 (6.67%)
Number of subjects with any Adverse device effect (ADE)	1 (6.67%)
Number of subjects with any study treatment-related TEAE	1 (6.67%)
Number of subjects with any study procedure-related TEAE	0 (%)
Number of subjects with any Serious adverse device effect (SADE)	0 (%)

Time played and time patched as recorded in the diary

Description	Part A: To assess compliance with treatment
Time Frame	from Baseline to week 12
Analysis Population Description	Time patched as recorded in the diary

	Binocular video games - Part A	**Patching - Part A**
Arm/Group Description	Binocular video games - patients will play 1 hour of binocular video game of choice (Dig Rush and/or Monster Burner) a day 7 days a week for 8 to 12 weeks.	Patching of the sound eye (fellow eye) - patients will have their sound eye (fellow eye) patched 2 hours per day 7 days a week for 16 weeks.
Number of Participants Analyzed [units: participants]	5	5
Time played and time patched as recorded in the diary (units: Hours)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**

Week 1	4.39 ± 2.929	8.13 ± 4.684
Week 2	4.94 ± 3.460	12.81 ± 1.908
Week 3	4.37 ± 3.293	11.00 ± 2.000
Week 4	3.51 ± 3.431	9.60 ± 4.561
Week 5	4.70 ± 3.410	9.00 ± 3.606
Week 6	4.26 ± 3.011	7.50 ± 3.969
Week 7	3.36 ± 3.323	10.40 ± 4.336
Week 8	3.80 ± 2.949	13.72 ± 9.660
Week 9	2.58 ± 2.959	10.00 ± 3.742
Week 10	2.58 ± 2.003	9.33 ± 4.619
Week 11	3.63 ± 3.359	8.00 ± 5.888
Week 12	1.00	6.50 ± 5.260
Week 13		8.50 ± 5.635
Week 14		7.33 ± 2.309
Week 15		9.06 ± 4.656
Week 16		7.50 ± 3.536

Time played as recorded in the video game system - Part A

Description	Part A: To assess compliance with treatment
Time Frame	from Baseline to week 12
Analysis Population Description	Time patched as recorded in the diary

Binocular video games - Part A

Arm/Group Description	Binocular video games - patients will play 1 hour of binocular video game of choice (Dig Rush and/or Monster Burner) a day 7 days a week for 8 to 12 weeks.
Number of Participants Analyzed [units: participants]	6
Time played as recorded in the video game system - Part A (units: Hours)	**Mean ± Standard Deviation**
Week 1	6.39 ± 0.610
Week 2	6.02 ± 1.124
Week 3	5.40 ± 2.292
Week 4	4.92 ± 2.432
Week 5	5.18 ± 1.860
Week 6	5.29 ± 2.083
Week 7	3.83 ± 3.199
Week 8	4.03 ± 2.720
Week 9	2.52 ± 1.986
Week 10	0.40 ± 0.566
Week 11	0.47 ± 0.670
Week 12	0.63 ± 0.886

Time played as recorded in the video game system - Part B

Description	Part B: To assess compliance with treatment
Time Frame	from Baseline to week 12
Analysis Population Description	Time patched as recorded in the diary

Binocular video games - Part B

Arm/Group Description	Part B was a 16-week, open-label, single arm sub investigation in subjects 8 to 12 years of age with amblyopia, in which selected sites could participate. Subjects received binocular videogame treatment for 8 weeks, followed by 8 weeks of follow-up.
Number of Participants Analyzed [units: participants]	15
Time played as recorded in the video game system - Part B (units: Hours)	**Mean ± Standard Deviation**
Week 1	4.94 ± 1.575
Week 2	4.78 ± 2.284
Week 3	4.68 ± 2.524
Week 4	4.31 ± 2.625
Week 5	4.81 ± 2.293
Week 6	4.88 ± 2.276
Week 7	4.32 ± 2.439
Week 8	3.71 ± 2.877

Percentage of participants who complete at least 75% of prescribed game play as recorded in the videogame system by weekly intervals - Part A

Description	Part A: To assess compliance with treatment
Time Frame	from Baseline to Week 12
Analysis Population Description	Full Analysis Set

Binocular video games - Part A

Arm/Group Description	Binocular video games - patients will play 1 hour of binocular video game of choice (Dig Rush and/or Monster Burner) a day 7 days a week for 8 to 12 weeks.
Number of Participants Analyzed [units: participants]	6
Percentage of participants who complete at least 75% of prescribed game play as recorded in the videogame system by weekly intervals - Part A (units: Participants)	**Count of Participants (%)**
Week 1- Compliance > 125% : 6	0 (%)
Week 1 - Compliance > 75% : 6	3 (50%)
Week 2- Compliance > 125% : 6	0 (%)
Week 2 - Compliance > 75% : 6	2 (33.33%)
Week 3 - Compliance > 125% : 6	0 (%)
Week 3- Compliance > 75% : 6	2 (33.33%)
Week 4 - Compliance > 125% : 6	0 (%)
Week 4 - Compliance > 75% : 6	2 (33.33%)
Week 5 - Compliance > 125% : 6	0 (%)
Week 5 - Compliance > 75% : 6	1 (16.67%)
Week 6 - Compliance > 125% : 6	0 (%)
Week 6 - Compliance > 75% : 6	2 (33.33%)
Week 7 - Compliance > 125% : 6	0 (%)

Week 7 - Compliance > 75% : 6	1 (16.67%)
Week 8 - Compliance > 125% : 6	0 (%)
Week 8 - Compliance > 75% : 6	1 (16.67%)
Week 9 - Compliance > 125% : 6	0 (%)
Week 9 - Compliance > 75% : 6	0 (%)
Week 10 - Compliance > 125% : 6	0 (%)
Week 10 - Compliance > 75% : 6	0 (%)
Week 11 - Compliance > 125% : 6	0 (%)
Week 11 - Compliance > 75% : 6	0 (%)
Week 12 - Compliance > 125% : 6	0 (%)
Week 12 - Compliance > 75% : 6	0 (%)

Percentage of participants who complete at least 75% of prescribed game play as recorded in the videogame system by weekly intervals - Part B

Description	Part B: To assess compliance with treatment
Time Frame	from Baseline to Week 12
Analysis Population Description	Full Analysis Set

	Binocular video games - Part B
Arm/Group Description	Part B was a 16-week, open-label, single arm sub investigation in subjects 8 to 12 years of age with amblyopia, in which selected sites could participate. Subjects received binocular videogame treatment for 8 weeks, followed by 8 weeks of follow-up.
Number of Participants Analyzed [units: participants]	15
Percentage of participants who complete at least 75% of prescribed game play as recorded in the videogame system by weekly intervals - Part B (units: Participants)	**Count of Participants (%)**
Week 1- Compliance > 125% : 15	0 (%)
Week 1 - Compliance > 75% : 15	3 (20%)
Week 2- Compliance > 125% : 15	0 (%)
Week 2 - Compliance > 75% : 15	3 (20%)
Week 3 - Compliance > 125% : 15	0 (%)
Week 3- Compliance > 75% : 15	3 (20%)
Week 4 - Compliance > 125% : 15	0 (%)
Week 4 - Compliance > 75% : 15	3 (20%)
Week 5 - Compliance > 125% : 15	0 (%)
Week 5 - Compliance > 75% : 15	4 (26.67%)
Week 6 - Compliance > 125% : 15	0 (%)

Week 6 - Compliance > 75% : 15	3 (20%)
Week 7 - Compliance > 125% : 15	0 (%)
Week 7 - Compliance > 75% : 15	2 (13.33%)
Week 8 - Compliance > 125% : 15	0 (%)
Week 8 - Compliance > 75% : 15	3 (20%)

Summary of Safety

Safety Results

Time Frame	Adverse events were reported from start of treatment (gaming or patching) until end of study treatment, up to a maximum timeframe of 16 weeks.
Source Vocabulary for Table Default	MedDRA (25.0)
Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	Binocular video games - Part A N = 6	Patching - Part A N = 6	Binocular video games - Part B N = 15	Overall N = 27
Arm/Group Description	Binocular video games - patients will play 1 hour of binocular video game of choice (Dig Rush and/or Monster Burner) a day 7 days a week for 8 to 12 weeks.	Patching of the sound eye (fellow eye) - patients will have their sound eye (fellow eye) patched 2 hours per day 7 days a week for 16 weeks.	Part B was a 16-week, open-label, single arm sub investigation in subjects 8 to 12 years of age with amblyopia, in which selected sites could participate. Subjects received binocular videogame treatment for 8 weeks, followed by 8 weeks of follow-up.	Overall
Total Number Affected	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Total Number At Risk	6	6	15	27

Serious Adverse Events

Time Frame	Adverse events were reported from start of treatment (gaming or patching) until end of study treatment, up to a maximum timeframe of 16 weeks.
Source Vocabulary for Table Default	MedDRA (25.0)
Collection Approach for Table Default	Systematic Assessment

	Binocular video games - Part A N = 6	Patching - Part A N = 6	Binocular video games - Part B N = 15	Overall N = 27

Arm/Group Description	Binocular video games - patients will play 1 hour of binocular video game of choice (Dig Rush and/or Monster Burner) a day 7 days a week for 8 to 12 weeks.	Patching of the sound eye (fellow eye) - patients will have their sound eye (fellow eye) patched 2 hours per day 7 days a week for 16 weeks.	Part B was a 16-week, open-label, single arm sub investigation in subjects 8 to 12 years of age with amblyopia, in which selected sites could participate. Subjects received binocular videogame treatment for 8 weeks, followed by 8 weeks of follow-up.	Overall
Total Number Affected	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Total Number At Risk	6	6	15	27

Other (Not Including Serious) Adverse Events

Time Frame	Adverse events were reported from start of treatment (gaming or patching) until end of study treatment, up to a maximum timeframe of 16 weeks.
Source Vocabulary for Table Default	MedDRA (25.0)
Collection Approach for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	0%

	Binocular video games - Part A N = 6	Patching - Part A N = 6	Binocular video games - Part B N = 15	Overall N = 27
Arm/Group Description	Binocular video games - patients will play 1 hour of binocular video game of choice (Dig Rush and/or Monster Burner) a day 7 days a week for 8 to 12 weeks.	Patching of the sound eye (fellow eye) - patients will have their sound eye (fellow eye) patched 2 hours per day 7 days a week for 16 weeks.	Part B was a 16-week, open-label, single arm sub investigation in subjects 8 to 12 years of age with amblyopia, in which selected sites could participate. Subjects received binocular videogame treatment for 8 weeks, followed by 8 weeks of follow-up.	Overall
Total # Affected by any Other Adverse Event	1 (16.67%)	0 (0%)	4 (26.67%)	5 (18.52%)
Total # at Risk by any Other Adverse Event	6	6	15	27
Eye disorders				
Asthenopia	1 (16.67%)	0 (0.00%)	0 (0.00%)	1 (3.70%)
Eye pain	0 (0.00%)	0 (0.00%)	1 (6.67%)	1 (3.70%)
Gastrointestinal disorders				
Dental caries	0 (0.00%)	0 (0.00%)	1 (6.67%)	1 (3.70%)
General disorders and administration site conditions				
Influenza like illness	0 (0.00%)	0 (0.00%)	1 (6.67%)	1 (3.70%)
Infections and infestations				
COVID-19	0 (0.00%)	0 (0.00%)	1 (6.67%)	1 (3.70%)
Sinusitis	0 (0.00%)	0 (0.00%)	1 (6.67%)	1 (3.70%)

Injury, poisoning and procedural complications				
Head injury	0 (0.00%)	0 (0.00%)	1 (6.67%)	1 (3.70%)
Nervous system disorders				
Headache	1 (16.67%)	0 (0.00%)	1 (6.67%)	2 (7.41%)
Respiratory, thoracic and mediastinal disorders				
Tonsillar hypertrophy	0 (0.00%)	0 (0.00%)	1 (6.67%)	1 (3.70%)

Other Relevant Findings

Not Applicable.

Conclusion:

- The decision to discontinue the development of DDO001F1 digital therapeutic and by that the DDO001F12201 study in amblyopia is based on the competitive landscape and strategic fit.
- No conclusion can be drawn from this clinical investigation, given the early closure with only a limited number of subjects enrolled, and the consequent simplification of the planned analyses.
- Safety evaluation did not show any safety signal.

Date of Clinical Trial Report

28 Feb 2023