2022 Full-year results and business update

PRESS RELEASE

Positive data on key clinical candidates delivered in 2022 – Promising outlook for 2023 as industry interest in therapeutic cancer vaccines and oncolytic viruses gains significant momentum

- ***TG4050:*** *New Phase I data confirm the strong clinical and commercial potential of this highly innovative personalized immunotherapy. Preparing for a Phase II trial in head and neck cancer, which purpose is to provide data for a potential registration.*
- ***TG4001:*** *Positive interim analysis supports continuation of the ongoing randomized Phase II clinical trial. Final results to be reported in 2024. Transgene is preparing for a registration targeting study.*
- ***Oncolytic viruses:*** *New clinical data confirm the potential for Invir.IO® oncolytic viruses to be given via intravenous administration. Launch of the new multi-armed TG6050 aimed at a major solid tumor indication.*
- ***€26.8 million in cash and cash equivalents*** *as of December 31, 2022 – Financial visibility until early 2024.*

Conference call in English scheduled today at 6:00 p.m. CET (details at the end of the release)

Strasbourg, France, March 16, 2023, 5:45 p.m. CET – **Transgene (Euronext Paris: TNG), a biotech company that designs and develops virus-based immunotherapies for the treatment of cancer,** today publishes its financial results for 2022 and provides an update on its product pipeline.

Hedi Ben Brahim, CEO of Transgene, commented: "*I am extremely happy with the multiple positive milestones that Transgene has delivered in 2022 and I would like to thank all our employees and partners for their commitment and support. We also are very encouraged by the growing industry interest in therapeutic cancer vaccines and oncolytic viruses that have the potential to become new standards of care for the treatment of solid tumors. This trend backs us in our strategy and validates our technological and medical choices. I am confident that Transgene is at the forefront of helping to realize the potential of these exciting treatment modalities.*

"With regard to our therapeutic cancer vaccine pipeline, we presented new Phase I results for TG4050 demonstrating the full clinical and commercial potential of this highly innovative neoantigen vaccine in patients with head and neck cancer. These very encouraging data have led us to start the planning of Phase II trial. Positive data from this Phase II trial could be used for a potential registration of TG4050. For TG4001, our most advanced product, the positive outcome of the interim analysis of the Phase II trial in HPV-positive cancers has allowed us to reduce the total number of patients to be randomized in the ongoing study.

"Turning to the oncolytic virus platform, we have achieved two important milestones. We presented new positive data from the Phase I trial evaluating our oncolytic virus TG6002 administered intravenously, showing in all patients its ability to reach the tumor, multiply and express its payload. The ability to administer our oncolytic viruses intravenously significantly expands the range of solid tumors they can be used to treat and the market opportunity they can access. In addition, we announced the launch of a new oncolytic virus, TG6050. This multi-armed oncolytic virus has been designed to address major solid tumor indications, such as lung cancer, and will begin a Phase I in the months ahead.

"The progress we have made in 2022 has positioned Transgene to deliver multiple major milestones in the next 18 months, including launching potentially registrational trials for our two most advanced therapeutic vaccine candidates, as well as a Phase I study with our high-potential oncolytic virus, TG6050, given by intravenous administration.

"Based on the potential of TG4050, TG4001 and TG6050, I believe that Transgene has a very exciting future and is well positioned to deliver for all of its key stakeholders."

Key achievements in 2022 and expected near-term news flow

Therapeutic Cancer Vaccines

TG4001: Positive result from interim analysis of randomized Phase II trial in HPV-positive anogenital cancers

With TG4001, Transgene aims to bring a new solution to patients with HPV-positive anogenital cancers who currently have very limited second-line treatment options.

In November 2022, Transgene announced that following a prespecified interim analysis of its randomized, Phase II clinical study comparing TG4001 in combination with avelumab vs avelumab alone in patients with HPV16-positive anogenital tumors (NCT: 03260023), **the Independent Data Monitoring Committee (IDMC) has recommended the study continue**. **Based on progression-free survival (PFS) and positive efficacy signals** observed in the interim analysis, the trial is now expected to enroll **a total of 120 patients** compared to the initial forecast of 150 patients.

Transgene anticipates the last patient to be randomized in the trial in the first half of 2024, and final results to be communicated in 2024.

Based on **the positive outcome of the interim analysis,** we are already working on the initial design of a potentially registrational trial to further confirm the benefit of this therapeutic vaccine.

TG4050: Strong clinical and commercial potential confirmed by initial data from the two ongoing Phase I trials – Transgene is preparing a Phase II trial in head and neck cancers

The personalized therapeutic vaccine TG4050 is intended to extend the remission of patients at high risk of relapse.

In the randomized Phase I trial in head and neck patients, following surgery and radio-chemotherapy, the latest data reported was as of the end of August 2022, when **20 of the 30 planned patients had been randomized.**

All 10 evaluable patients who were vaccinated with TG4050 remained stable and in complete response at the cutoff date. This contrasts with the control group where **2 out of the 10 patients, who did not receive the vaccine, have relapsed.** Transgene expects treatment start of the last patient in this Phase I trial in the first half of 2023.

In the current Phase I ovarian cancer trial (n=5), one patient treated after an elevation of CA-125 experienced a normalization of CA-125 without clinical progression for nine months until death from an unrelated chronic illness. Another patient was treated upon onset of radiological evidence of relapse and remained stable for 11.4 months. Although enrollment in this trial has been completed, treatment of patients is significantly delayed by the recent registration of PARP inhibitors, extending the time to relapse, which is required before they can receive treatment with TG4050.

Transgene has also produced data on circulating tumor DNA (ctDNA); signals of this increasingly validated surrogate marker of efficacy are particularly encouraging. **Combined with the first signs of clinical activity, these results suggest that the individualized TG4050 vaccine has the potential to extend the period of remission, potentially offering a new treatment option for cancer patients.**

In the two clinical studies, enrollment has been completed. To date, TG4050 vaccine has been well tolerated and no related Serious Adverse Events have been reported.

The Company is preparing a Phase II trial in head and neck cancers. Positive data from this upcoming trial could be used for a potential registration of TG4050.

Further information on our development plans for TG4050 will be communicated following the presentation of a poster at the American Association for Cancer Research (AACR) Annual Meeting (April 2023).

Oncolytic Viruses

TG6002: New data support the potential of intravenous administration of Invir.IO®-based oncolytic viruses – Key competitive advantage

Clinical data generated with TG6002, has enabled Transgene to confirm the mechanism of action, competitive advantages and safety of our Invir.IO® based oncolytic viruses.

Data generated on 37 patients treated in the Phase I study assessing its intravenous administration (IV) have been presented at the European Society for Medical Oncology (ESMO) Annual Congress (September 2022).

These findings support the potential of IV administration of Invir.IO®-based oncolytic viruses, extending the use of these therapies to a much broader range of solid tumors. At present the use of oncolytic viruses is limited by their intratumoral administration.

Additional data will be produced from the Phase I program and will be presented at AACR (April 2023).

BT-001: Positive initial clinical data in monotherapy

In June 2022, Transgene and BioInvent released positive progress and safety data in the ongoing Phase I/IIa trial evaluating BT-001 in patients with solid tumors. The initial data generated in the Part A of the Phase I trial demonstrated that BT-001 alone is well tolerated, with first signs of anti-tumor activity in a hard-to-treat population and confirmed the mechanism of action of BT-001 as a single agent.

A clinical collaboration and supply agreement for KEYTRUDA® (pembrolizumab) was signed with MSD (Merck & Co) at the end of June 2022. The Part B of the Phase I trial (in combination with pembrolizumab) is expected to start in the second half of 2023.

TG6050: Novel Invir.IO® candidate designed to express IL-12 and be administered IV to enter the clinic

In early 2023, Transgene announced the regulatory approval to initiate a clinical trial of TG6050, a novel oncolytic virus from its Invir.IO® platform. This innovative candidate has been designed to express human IL-12, a cytokine known to trigger a potent anti-tumor immune response, and a full-length anti-CTLA4 antibody.

The Delivir trial will evaluate TG6050 in patients with advanced non-small cell lung cancer who have failed treatment with an anti-PD1 agent.
The first patient will be enrolled in the first half of 2023. With TG6050, Transgene seeks to capitalize on the attractiveness of IL-12, while limiting exposure to its systemic toxicity through the selectivity of Invir.IO® oncolytic viruses.

Collaboration with AstraZeneca

The research collaboration with AstraZeneca on viruses derived from the Invir.IO® platform continues to move forward.

Key scientific advisors

In March 2023, Transgene appointed Dr. John C. Bell and Dr. Pedro Romero as key scientific advisors. These key opinion leaders in cancer immunotherapy bring considerable expertise to Transgene.

Summary of key ongoing clinical trials

TG4001
+ avelumab
Phase II
NCT03260023

Targets: HPV16 E6 and E7 oncoproteins

Recurrent/metastatic anogenital HPV16-positive — 1st (patients ineligible for chemotherapy) and 2nd lines

- ✓ Randomized Phase II trial comparing the combination of TG4001 with avelumab versus avelumab alone
- ✓ Ongoing patient enrollment in Europe (France and Spain) and in the USA
- ✓ Positive result of interim analysis, allowing trial to continue. Total number of patients to be randomized reduced from 150 to 120
- ➲ **Last patient expected to be randomized in H1 2024**
- ➲ **Final results to be communicated in 2024**
- ➲ **Registration targeting trial being prepared**

myvac®

TG4050
Phase I
NCT04183166

Targets: tumor neoantigens

- ✓ Codeveloped with NEC
- ✓ Positive initial data demonstrating the immunogenicity of the vaccine as well as first signs of clinical activity
- ➲ **Additional data expected in H1 2023 (AACR)**

HPV-negative head and neck cancers — after surgery and adjuvant therapy

- ✓ Trial ongoing in the UK and in France
- ✓ Patient enrollment completed
- ✓ Treatment start of last patient expected in H1 2023
- ➲ **Preparation of registration targeting Phase II trial**

TG4050
Phase I
NCT03839524

Ovarian cancer — after surgery and first-line chemotherapy

- ✓ Trial ongoing in the USA and in France
- ✓ Patient enrollment completed

TG6002 Phase I/IIa NCT03724071	**Payload: FCU1 for the local production of a 5-FU chemotherapy** ➲ **Additional data to be presented at AACR (April 2023)** *Advanced gastro-intestinal cancer — Intravenous (IV) administration* ✓ Multicenter trial – France, Belgium and Spain ✓ **Data confirming the potential of the IV administration presented at ESMO 2022 (Sept. 2022)** ✓ Patient enrollment completed in Phase I part
TG6002 Phase I/IIa NCT04194034	*Colorectal cancer with liver metastasis — Intrahepatic artery (IHA) administration* ✓ Multicenter trial – UK and France ✓ Patient enrollment completed in Phase I part
Invir.IO® **BT-001** Phase I/IIa NCT04725331	**Payload: anti-CTLA4 antibody and GM-CSF cytokine** *Solid tumors* ✓ Co-development with BioInvent ✓ Collaboration agreement with MSD, supplying pembrolizumab for the trial ✓ Trial ongoing in France, Belgium and approved in the USA ✓ Initial data showing safety and first signs of clinical activity ➲ **Part A data to be communicated in H1 2023** ➲ **Start of part B of the Phase I trial in H2 2023**
Invir.IO® **TG6050** Phase I (Delivir)	**Payload: interleukin-12 (IL-12) and anti-CTLA4 antibody** *Non-Small Cell Lung Cancer (NSCLC) – Intravenous (IV) administration* ✓ Promising preclinical results to be presented at AACR (April 2023) ✓ Multicenter trial ➲ **First patient to be enrolled in H1 2023**

Key financials for 2022

- **Operating income of €10.3 million in 2022**, compared to €17.4 million in 2021.
  R&D services for third parties amounted to €3.1 million in 2022 (€10.0 million in 2021), mainly due to the collaboration with AstraZeneca. In 2021, AstraZeneca exercised the first license option for an oncolytic virus developed by Transgene. This option exercise led to Transgene receiving a €7.1 million payment.
  Research tax credit amounted to €6.8 million in 2022 (€7.0 million in 2021).
- **Net operating expenses of €40.2 million in 2022,** compared to €40.9 million in 2021.
  R&D expenses were €32.2 million in 2022 (€32.9 million in 2021).
  General and administrative expenses amounted to €7.9 million in 2022 (€7.4 million in 2021).
- **Financial loss of €2.9 million in 2022**, compared to an income of €4.0 million in 2021.
- **Net loss of €32.8 million in 2022,** compared to a net loss of €19.5 million in 2021.
- **Net cash burn of €22.8 million in 2022,** compared to €10.0 million in 2021 (excluding capital increase).
- **Cash available at year-end 2022: €26.8 million**, compared to €49.6 million at the end of 2021. In addition, Transgene still holds Tasly BioPharmaceuticals shares reevaluated at €14.3 million at the end of December 2022. The Company is expecting to sell its shareholding in Tasly BioPharmaceuticals in mid-2023.
- **Transgene has a financial visibility until early 2024.**

The financial statements for 2022 as well as management's discussion and analysis are attached to this press release (Appendices A and B).

The Board of Directors of Transgene met on March 16, 2023, under the chairmanship of Dr. Alessandro Riva and closed the 2022 financial statements. Audit procedures have been performed by the statutory auditors and the delivery of the auditors' report is ongoing.

The Company's universal registration document, which includes the annual financial report, will be available early April 2023 on Transgene's website, www.transgene.fr.

A conference call **in English** is scheduled today on **March 16, 2023, at 6:00 p.m. CET (12:00 p.m. ET)**.

Webcast link to English language conference call:
https://channel.royalcast.com/landingpage/transgene/20230316_1/

Participant telephone numbers:
France: +33 (0) 1 7037 7166 Confirmation code: Transgene
United Kingdom: +44 (0) 33 0551 0200
United States: +1 786 697 3501

A replay of the call will be available on the Transgene website (www.transgene.fr) following the live event.

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About Transgene
Transgene (Euronext: TNG) is a biotechnology company focused on designing and developing targeted immunotherapies for the treatment of cancer. Transgene's programs utilize viral vector technology with the goal of indirectly or directly killing cancer cells.
The Company's clinical-stage programs consist of a portfolio of therapeutic vaccines and oncolytic viruses: TG4050, the first individualized therapeutic vaccine based on the *myvac*® platform, TG4001 for the treatment of HPV-positive cancers, as well as TG6002, BT-001 and TG6050, three oncolytic viruses based on the Invir.IO® viral backbone. With Transgene's *myvac*® platform, therapeutic vaccination enters the field of precision medicine with a novel immunotherapy that is fully tailored to each individual. The *myvac*® approach allows the generation of a virus-based immunotherapy that encodes patient-specific mutations identified and selected by Artificial Intelligence capabilities provided by its partner NEC.
With its proprietary platform Invir.IO®, Transgene is building on its viral vector engineering expertise to design a new generation of multifunctional oncolytic viruses. Transgene has an ongoing Invir.IO® collaboration with AstraZeneca.
Additional information about Transgene is available at: www.transgene.fr
Follow us on Twitter: @TransgeneSA

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Appendix A: Financial statements 2022

CONSOLIDATED BALANCE SHEET, IFRS

(in € thousands)

Assets	December 31,2022	December 31,2021
CURRENT ASSETS		
Cash and cash equivalents	4,403	5,911
Other current financial assets	22,423	43,658
Cash, cash equivalents and other current financial assets	**26,826**	**49,569**
Trade receivables	2,789	10,133
Other current assets	2,546	2,543
Assets available for sale	14,345	-
Total current assets	**46,506**	**62,245**
NON-CURRENT ASSETS		
Property, plant and equipment	11,177	11,295
Intangible assets	77	92
Non-current financial assets	1,673	20,772
Other non-current assets	7,003	7,434
Total non-current assets	**19,930**	**39,593**
TOTAL ASSETS	**66,436**	**101,838**

Liabilities and equity	December 31,2022	December 31,2021
CURRENT LIABILITIES		
Trade payables	6,965	7,692
Current financial liabilities	1,192	1,395
Provisions for risks and expenses	23	48
Other current liabilities	4,602	5,454
Total current liabilities	**12,782**	**14,589**
NON-CURRENT LIABILITIES		
Non-current financial liabilities	12,327	15,241
Employee benefits	3,282	3,958
Other non-current liabilities	204	841
Total non-current liabilities	**15,813**	**20,040**
Total liabilities	**28,595**	**34,629**
EQUITY		
Share capital	50,102	48,886
Share premiums and reserves	71,621	70,374
Retained earnings	(50,628)	(31,092)
Profit/(loss) for the period	(32,804)	(19,536)
Other comprehensive income/(loss)	(450)	(1,423)
Total equity attributable to the Company's shareholders	**37,841**	**67,209**
TOTAL LIABILITIES AND EQUITY	**66,436**	**101,838**

Consolidated income statement, IFRS

(in € thousands, except for per-share data)

	December 31,2022	December 31,2021
Revenue from collaborative and licensing agreements	3,126	9,993
Government financing for research expenditure	6,876	7,021
Other income	342	399
Operating income	**10,344**	**17,413**
Research and development expenses	(32,168)	(32,883)
General and administrative expenses	(7,912)	(7,369)
Other expenses	(168)	(686)
Operating expenses	**(40,248)**	**(40,938)**
Operating income/(loss)	**(29,904)**	**(23,525)**
Financial income/(loss)	(2,900)	3,989
Income/(loss) before tax	**(32,804)**	**(19,536)**
Income tax expense	-	-
NET INCOME/(LOSS)	**(32,804)**	**(19,536)**
Basic earnings per share (€)	(0.33)	(0.21)
Diluted earnings per share (€)	(0.33)	(0.21)

Cash Flow statement, IFRS

(in € thousands)

	December 31,2022	December 31,2021
Cash flow from operating activities		
Net income/(loss)	(32,804)	(19,536)
Cancellation of financial income/(loss)	2,900	(3,989)
Elimination of non-cash items		
Provisions	191	(1,031)
Depreciation and amortization	1,686	2,521
Share-based payments	2,675	3,002
Others	(41)	(112)
Net cash generated from/(used in) operating activities before change in working capital and other operating cash flow	**(25,393)**	**(19,145)**
Change in operating working capital requirements		
Current receivables and prepaid expenses	7,301	(7,745)
Research tax credit (RTC)	(198)	(993)
Other current assets	226	(242)
Trade payables	(750)	2,657
Prepaid income	(804)	(1,124)
Other current liabilities	(685)	683
Net cash used in operating activities	**(20,303)**	**(25,909)**
Cash flows from investing activities		
(Acquisitions)/disposals of property, plant and equipment	(1,497)	(671)
(Acquisitions)/disposals of intangible assets	(38)	(15)
(Acquisitions)/disposals of non-consolidated equity securities	-	17,193
(Acquisitions) of other financial assets	-	(40,000)
Disposals of other financial assets	21,500	17,418
Other (acquisitions)/disposals	307	286
Net cash used in investing activities	**20,272**	**(5,789)**
Cash flow from financing activities		
Net financial income/(loss) proceeds	(646)	(167)
Gross proceeds from the issuance of shares	-	34,129
Share issue costs	-	(787)
Conditional subsidies	455	603
Net amounts received for financing of tax credits	(5)	16
Bank borrowing	-	(197)
Financial leases and change in lease obligations	(1,281)	(1,277)
Net cash generated from/(used in) financing activities	**(1,477)**	**32,320**
Exchange rate differences on cash and cash equivalents	-	12
Net increase/(decrease) in cash and cash equivalents	**(1,508)**	**634**
Cash and cash equivalents at beginning of period	5,911	5,277
Cash and cash equivalents at end of period	**4,403**	**5,911**
Investments in other current financial assets	22,423	43,658
Cash, cash equivalent and other current financial assets	**26,826**	**49,569**

Appendix B: Management Discussion of 2022 Financials

Operating income

Income from collaboration and licensing agreements represented €3.1 million in 2022 versus €10.0 million in 2021. The income consisted primarily of research and development services recognized from the collaboration with AstraZeneca over the period amounting to €3.1 million in 2022 (versus €9.9 million in 2021). This difference is mainly due to the first license option exercised by AstraZeneca in 2021 for €7.1 million, for an oncolytic virus developed by Transgene.

Public funding for research expenses accounted for €6.9 million in 2022 (versus €7.0 million in 2021), mainly due to research tax credit.

Other income

Other income amounted to €0.3 million in 2022 versus €0.4 million in 2021. This consisted for €0.2 million of the NEOVIVA repayable advances at a preferred rate in 2022, as in 2021.

Operating expenses

Research and development (R&D) expenses

R&D expenses amounted to €32.2 million in 2022 versus €32.9 million in 2021.

The following table details R&D expenses by type:

(in € millions)	**Dec. 31, 2022**	**Dec. 31, 2021**
Payroll costs	12.2	12.4
Share-based payments	1.4	1.7
Intellectual property expenses and licensing costs	1.1	1.1
External expenses for clinical projects	6.2	6.3
External expenses for other projects	4.3	4.5
Operating expenses	5.4	5.1
Depreciation, amortization and provisions	1.6	1.8
RESEARCH AND DEVELOPMENT EXPENSES	**32.2**	**32.9**

Payroll costs allocated to R&D (salaries, employer contributions and related expenses) amounted to €12.2 million in 2022 compared to €12.4 million in 2021.

Share-based payments amounted to €1.4 million in 2022, versus €1.7 million in 2021.

External expenses for clinical projects amounted to €6.2 million in 2022, compared to €6.3 million in 2021.

Other external expenses, including expenses for research and industrial activities, were €4.3 million in 2022, versus €4.5 million in 2021.

Operating expenses, including the cost of operating research and manufacturing laboratories, amounted to €5.4 million in 2022, compared to €5.1 million in 2021. This increase is mainly due to internal manufacturing activities, especially for the individualized vaccine TG4050.

General and administrative (G&A) expenses

General and administrative (G&A) expenses amounted to €7.9 million in 2022 versus €7.4 million in 2021.

The following table details G&A expenses by type:

(in € millions)	**Dec. 31, 2022**	**Dec. 31, 2021**
Payroll costs	3.3	3.4
Share-based payments	1.3	1.3
Fees and administrative expenses	2.3	1.9
Other general and administrative expenses	0.9	0.7
Depreciation, amortization and provisions	0.1	0.1
GENERAL AND ADMINISTRATIVE EXPENSES	**7.9**	**7.4**

Payroll costs allocated to G&A stood at €3.3 million in 2022, compared to €3.4 million in 2021.

Share-based payments amounted €1.3 million in 2022 as in 2021.

Fees and administrative expenses were at €2.3 million in 2022, versus €1.9 million in 2021.

Financial income

Net financial income resulted in a net loss of €2.9 million in 2022 versus a net income of €4.0 million in 2021.

As of December 31, 2022, the Company reevaluated its shareholding in Tasly BioPharmaceuticals shares with a value of €14.3 million, reflected its estimate of the fair value of these shares, based on third-party's proposal.

The valuation of ADNA conditional advances as of December 31, 2022, generated a financial income of €2.2 million, compared to a financial income of €0.7 million in 2021.

Net income (loss)

The net loss was €32.8 million in 2022, compared with a net loss of €19.5 million in 2021.

The net loss was €0.33 per share in 2022, compared with a net loss per share of €0.21 in 2021.

Investments

Investments in tangible and intangible assets amounted €2.2 million in 2022 (€1.1 million in 2021).

Repayable advances and loans

Transgene has been leading a research program, NEOVIVA, supported by Bpifrance. The Company received €0.5 million in repayable advances from this program in 2022. The Company could receive up to €2.6 million (€0.2 million in grants and €2.4 million in repayable advances) over a five-year period.

Liquidity and capital resources

As of December 31, 2022, the Company had €26.8 million in cash available, compared with €49.6 million as of December 31, 2021. In addition, Transgene still holds Tasly BioPharmaceuticals shares valued at €14.3 million at the end of December 2022. The Company is expecting to sell its shareholding in Tasly BioPharmaceuticals in mid-2023.

Cash burn

The Company's net cash burn amounted to €22.8 million in 2022, versus €10.0 million in 2021, excluding capital increase.

Post-closing events

N/**A**