RA DDR. RENATE HOLZEISEN
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EUROPEAN COURT

ACTION FOR ANNULMENT pursuant to Art. 263 TFEU

Plaintiff:

RA DDr. Renate Holzeisen in her institutional capacity as a member of the South Tyrolean Provincial Council and thus as a representative of the population of the Autonomous Province of Bolzano pursuant to Art. 48/bis of Decree of the President of the Italian Republic No. 670 of 31.08.1972 (Statute of Autonomy of the Autonomous Province of Bolzano) and in her personal capacity as a citizen of the Italian Republic

Defendant:

European Commission Subject:

(1) **Commission Implementing Decision of February 12, 2025, on the granting of a marketing authorization for the medicinal product for human use "KOSTAIVE – Zapomeran" in accordance with Regulation (EC) No. 726/2004 of the European Parliament and of the Council**

1. Ms. Renate Holzeisen, born in Bolzano on September 10, 1966, in her capacity as a member of the South Tyrolean Provincial Council (Doc**. A.1**.), residing in 39100 Bolzano. Silvius-Magnago-Platz No. 6, in her capacity as a member of the South Tyrolean Provincial Council and thus, pursuant to Art. 48/bis of Decree of the President of the Italian Republic No. 670 of August 31, 1972 (Statute of Autonomy of the Autonomous Province of Bolzano) representative of the population of the Autonomous Province of Bolzano (approx. 540,000 citizens) – **Doc. A.2,** and in her capacity as a citizen of the EU Member State Italy, represented and defended by herself as a lawyer admitted to the highest courts in Italy, registered with the Bolzano Bar Association and with offices at I-39100 Bolzano, Bahnhofallee No. 7,

PRECISELY BECAUSE

2. **By Commission Implementing Decision of February 12, 2025** – Doc. **A.3. (**published in the Official Journal of the European Union on March 31, 2025 – Doc. A**.4.**) **on the granting of a marketing authorization for the medicinal product for human use "Kostaive-Zapomeran" in accordance with Regulation (EC) No. 726/2004 of the European Parliament and of the Council,**
Having regard to Regulation (EC) No. 726/2004 of the European Parliament and of the Council of March 31, 2004, laying down Union procedures for the authorization and supervision of medicinal products for human use and establishing a European Medicines Agency, and in particular Article 10(2) thereof, Having regard to the application submitted by Arcturus Therapeutics Europe B.V. on August 17, 2023
Having regard to the opinion of the European Medicines Agency, delivered by the Committee for Medicinal Products for Human Use on December 12, 2024,
Whereas:

(1) The medicinal product "Kostaive – Zapomeran" complies with the requirements of Directive 2001/83/EC of the European Parliament and of the Council of November 6, 2001, on the Community code relating to medicinal products for human use.
(2) Consequently, its marketing authorization should be granted.
(3) The Committee for Medicinal Products for Human Use considered that Zapomeran was a new active substance.
(4) The measures provided for in this decision are in accordance with the opinion of the Standing Committee on Medicinal Products for Human Use

: Article 1

The medicinal product "Kostaive – Zapomeran," the characteristics of which are summarized in Annex I to this decision, is authorized **in accordance with Article 3 of Regulation (EC) No. 726/2004**. "Kostaive-Zapomeran" shall be entered in the Union Register of Medicinal Products under the following number: EU/1/24/1873.

Article 2

The placing on the market of the medicinal product referred to in Article 1 shall be subject to compliance with the conditions set out in Annex II, in particular as regards manufacturing, importation, and supply.

Article 3

The labeling and package leaflet of the medicinal product referred to in Article 1 shall comply with the conditions set out in Annex III.

Article 4

The authorization shall be valid for five years from the date of notification of this decision.

Article 5

This decision is addressed to Arcturus Therapeutics Europe B.V., Claude Debussylaan 10, 1082 MD Amsterdam, Netherlands.

3. Three (III) annexes are attached to the above-mentioned Commission Implementing Decision: Annex I (summary of product characteristics), Annex II (A. Manufacturers of the active substance of biological origin and manufacturers responsible for batch release, B. Conditions or restrictions on supply and use, C. Other conditions and restrictions of the marketing authorization, D. Conditions or restrictions for the safe and effective use of the medicinal product) Annex III (Labeling and package leaflet) (Doc. A**.5)**.

4. **Annex I to the contested** Commission **Implementing Decision** shows that **KOSTAIVE** has been **authorized as a COVID-19 sa-mRNA vaccine**. And that KOSTAIVE **is** a **single-stranded sa-mRNA replicon with a 5' cap structure, produced by cell-free in vitro transcription from the corresponding DNA templates encoding a replicase and the spike glycoprotein of the original SARS-CoV-2 strain with the D614G mutation.** KOSTAIVE is used in individuals 18 years of age and older for active immunization to prevent COVID-19. KOSTAIVE consists of a self-amplifying mRNA that encodes the spike protein of SARS-CoV-2 and is encapsulated in lipid nanoparticles. The self-amplifying mRNA is designed so that, after intramuscular injection, additional copies of mRNA are produced in the host cells to achieve enhanced expression of the spike protein antigen. According to the information in Annex I, mRNA self-amplification is temporary and does not produce infectious particles.

5. **However, experts with institutional responsibility, such as Dott. Maurizio Federico, head of the National Institute for Global Health at the Istituto Superiore di Sanità (Italian National Institute of Health) in Rome, see a very real danger of long-lasting mRNA self-amplification and the transmission of sa-mRNA to other humans, as well as to animals, plants, and the environment in general.** See **Doc. A.6.** for the publication in ***the International Journal of Molecular Sciences*** **of the scientific article *The Potential of Extracellular Vesicle-Mediated Spread of Self-Amplifying RNA and a Way to Mitigate it*** by **Dott. Maurizio Federico, National Center for Global Health, Istituto Superiore di Sanità Rome.**

6. **In his scientific paper funded by the Italian Ministry of Health, Dr. M. Federico explains that excessive intracellular accumulation of sa-RNA is a significant disadvantage because, as**

already described in alphavirus-infected cells, the recipient cell can respond by incorporating excess RNA molecules into extracellular vesicles (EVs). These EVs can detach and invade neighboring or distant cells, where the EV-associated sa-RNA can start a new replication cycle. This mechanism leads to unwanted and unnecessary spread of sa-RNA throughout the body, raising relevant safety concerns. In his scientific work, Dott. Federico di outlines the molecular mechanisms by which sa-RNAs are transferred between different cells/tissues. Dott. M. Federico concludes that, based on current knowledge, improving the safety of sa-RNA-based vaccines for use in healthy humans is essential!

7. Dr. Federico writes: *"On December 12, 2024, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) recommended the approval of the drug KOSTAIVE. On February 12, 2025, the European Commission granted marketing authorization in accordance with the EMA's recommendation. KOSTAIVE is the trade name of the ARCT-154 vaccine, which, like mRNA-based vaccines, should be defined as a prodrug. It is a pharmaceutical product based on lipid vesicles containing self-replicating RNA molecules that encode the stabilized spike protein of SARS-CoV-2 and are intended to protect against COVID-19 disease...*

Based on this consistent experimental evidence, similar processes can be expected to occur in cells invaded by saRNAs. EVs released from these cells can invade both neighboring and distant cells and tissues, and the spread of saRNA-loaded EVs can lead to virus-like expansion. The EV-mediated spread of saRNA may also be facilitated by LNP-saRNA molecules that escape endosomal degradation being directly loaded into exosomes.... *While these mechanisms may be beneficial in terms of desired immunogenicity, they should be considered "**off-target" processes**. **Unlike most viruses, EVs can enter cells in any tissue/organ because they enter cells via multiple mechanisms.***
In this scenario, the only obstacle to the spread of saRNA EVs would be the adaptive immune response triggered against the antigens expressed by the saRNA.
However, both humoral and cellular immune responses take days to develop efficiently, while the saRNA replication cycle is likely to be completed within

hours and EVs can spread within minutes.
Further results from biodistribution studies support the idea that saRNA may have replicative potential in vivo.
The rabies glycoprotein led to the distribution of the vaccine in the lungs, liver, and spleen of rats within two days. Significantly, the saRNA load detected in the lungs increased more than a hundredfold on the fifteenth day after injection. A sharp increase in saRNA concentrations was also documented in the liver and spleen eight days after injection....

8. *The expected consequences of saRNA spread depend largely on the biological activity of the expressed gene of interest.* ***In the case of the stabilized full-length SARS-CoV-2 protein, some special considerations are necessary.*** *First****, the long-lasting presence of spike, which is mainly a consequence of the persistence of the vaccine mRNA,*** *has been* ***documented in vaccinees,*** *suggesting that the* ***immune response cannot rapidly eliminate cells expressing the SARS-CoV-2 spike protein.*** *Second, the* ***SARS-CoV-2 spike protein*** *is known* ***to associate with exosomes.*** *Therefore****, it should be investigated whether spike-expressing exosomes can more easily penetrate ACE2-expressing cells and release saRNA molecules, and what the consequences of this are. Finally, and probably most importantly, the effect of SARS-CoV-2 spike protein expression diffusing through the body should be evaluated in terms of its overall toxicity resulting from binding to ACE2 as well as additional molecular targets, leading to adverse effects such as inflammatory responses, immune dysregulation, and autoimmunity.***
In any case, a distinctive feature of saRNAs is their potential ability to spread throughout the body. Therefore, the search for a method to mitigate/prevent their uncontrolled spread appears to be very necessary... Apart from the not-so-obvious advantages of this new generation of COVID-19 vaccines, the use of saRNA in healthy individuals raises unprecedented safety questions that have only been partially investigated to date...
9. *However, nothing is known about the possible spread of saRNA molecules. Here****, a realistic mechanism of intercellular saRNA transmission can be assumed, based on previous experimental findings****. A special feature of saRNA molecules is their efficiency in self-replication, just like viral genomes. In contrast to the replication cycle of true viruses, however, full-length saRNA molecules are expected to accumulate intracellularly because they cannot leave the cell after association with viral structural proteins.*** *Unlike many other virus types, the genome of alphaviruses is efficiently incorporated into the emerging*

virus particles and, as has been shown for the chikungunya virus, also in EVs.

10. *For these reasons, it seems reasonable to investigate whether the intracellular accumulation of full-length saRNA is associated with the formation of saRNA-incorporating EVs. The association of viral RNA with EVs is not new in virology. For example, lentiviruses utilize the intercellular transport of exosomes both for the biogenesis of viral particles and as a route of infection. Similarly, transmission via EVs has been described for HBV, HCV, HSV, and dengue virus.*
11. ***A thorough investigation of the possible association of saRNA with EVs is also urgently needed in light of the recently launched vaccine for the expression of SARS-CoV-2 spike, i.e., a biologically active protein that can bind and activate the widely distributed ACE2 cell receptor. Excessive redistribution of spike-expressing saRNA may exacerbate the adverse effects already described for mRNA-based vaccines and increase the number of cells that can be attacked and killed by the induced anti-spike immune response.*** *It has been reported that expression of the viral envelope protein (i.e., spike) is not necessary for replication of the alphavirus genome incorporated into EVs. However, it is expected that the association of SARS-CoV-2 spike with these EVs facilitates their transport into ACE2-expressing cells, further complicating the overall scenario.*

    Several other facts make urgent investigation of the possible saRNA-EV association necessary. First, many authors have shown that ***circulating EVs can easily migrate into lung tissue****. In this context, it has been found that* ***EVs associated with the capsid-deficient SFV genome replicate quite efficiently in the lungs, even better than the wild-type virus****. Second, easily detectable amounts of EVs have been found in connection with exhalation from the lungs.* ***Therefore, not only body fluids but also exhalation from the lungs could be a way to transmit saRNA-incorporating EVs, opening up the theoretical possibility of environmental exposure.*** *Third,* ***EVs do not recognize effective species barriers.***
12. **<u>Experts in important institutional roles, such as Dott. M. Federico, therefore warn urgently against the spreading of substances such as KOSTAIVE, i.e., against transmission to humans, animals, and plants, i.e., to the environment as a whole.</u>**

<u>Legal standing according to Art. 263 TFEU</u>

13. **Due to the concrete risk of KOSTAIVE spreading (see Doc. A.6), everyone in the EU living here is citizen directly and directly by**

contested decision of the EU Commission and thus have standing to sue.

14. The implementing decision **approved** the **demonstrably experimental genetically engineered substance "KOSTAIVE – Zapomeran"** (hereinafter "KOSTAIVE") **as a "vaccine" for adults** for a period of five years without conditions. This is **despite the fact that KOSTAIVE corresponds in composition and function to a medicinal product for advanced therapies (gene therapy)** and its **efficacy and safety** have **never** been **proven**.

15. **On the plaintiff's interest in legal protection with regard to the implementing decision**

    In order to assess whether the plaintiff and the South Tyrolean population it represents institutionally can challenge the implementing decision by means of an action for annulment, it must be examined whether this decision has binding legal effects on the plaintiff and the South Tyrolean population it represents institutionally. **In doing so, reference must be made to its subject matter, its content, its substance, its scope, its effects, and also to the factual and legal context in which the decision is made, and not to its nature, its form, its designation, or its medium of transmission**

    (see judgments of the Court of 8 March 2012, Octopharma Pharmazeutica Produktionsgesellschaft mbH v Commission, T-573/10, paragraph 30, and of 10 July 2019, Pilatus Bank plc v European Central Bank (ECB), T-687/18, paragraph 16).

16. **The objective of protecting health is given priority in EU medicinal products authorization law**. Recital 13 of Regulation (EC) No. 726/2004 states: *"In the interests of public health, decisions on authorization under the centralized procedure should be based on objective scientific criteria relating to the quality, **safety**, and efficacy of the medicinal product concerned, to the exclusion of economic or other considerations."*

17. **The key point of implementation is a reservation of approval for the marketing of medicinal products. Such a reservation of approval is standardized for the centralized procedure in Article 3(1) of Regulation 726/2004.**

18. **The contested implementing decision is a legal act with the character of a regulation.**

19. As is well known, the Treaty of Lisbon included the category of decisions in the category of binding legal acts (Art. 288 TFEU). **Decisions can also have abstract general effects, regardless of whether they are addressed to a specific recipient or not**.

20. **Although the implementing decision is formally addressed to Arcturus Therapeutics Europe B.V., it has general applicability, which directly affects the interests of the plaintiff and the population of the Autonomous Province of Bolzano (Italy) that it represents institutionally, as it does not require mediation in the form of a discretionary implementing act.**
21. **The implementing decision consists, among other things, of extensive annexes, which are essentially of general application and in some cases are even addressed directly to healthcare professionals, users in general, and potential vaccine recipients.**
22. The following emerges from the analysis of the EPRS "Medicinal products in the European Union – The legal framework for medicinal products for human use" (April 2015 – **Doc. A. 7**):

    "The fundamental objective of the EU's pharmaceutical legislation is to protect public health ... is the common thread running through the entire legal framework for medicinal products....

    *EU pharmaceutical legislation covers the entire life cycle of a medicinal product, from manufacture to clinical trials, **marketing authorization**, **pharmacovigilance**, and **patient information**. ...*

    *The legal basis for medicinal products for human use is Article 168 TFEU: "In defining and implementing all Union policies and activities, a **high level of human health protection** shall be ensured."*

    *The European Parliament and the Council contribute to the achievement of this objective by adopting "measures to define high **standards of quality and safety for medicinal products** and medical devices" ....*

    ***The EU regulatory system for medicinal products – Medicinal products may only be placed on the market in the EU after a marketing authorization has been granted, and in order to obtain this authorization, they must first** undergo **rigorous testing and evaluation of their quality, safety, and efficacy**...*

    *The relevant provisions are mainly contained in Directive 2001/83/EC and Regulation (EC) No. 726/2004 ... **the granting of the authorization ... is proof that the medicinal product meets the required standards**.*
23. The EPRS states the following about the **centralized marketing authorization procedure regulated by Regulation (EC) No. 726/2004 (Doc. A. 7):**

    *"The Regulation introduces a single scientific evaluation procedure of the highest standard for all medicinal products falling within its scope, **with the aim of 'maintaining the confidence of patients and healthcare professionals in this** assessment', **particularly in the context of the emergence of new therapies** ...*

The centralized procedure leads to a single approval for marketing authorization that is valid in all Member States ...

Under the centralized procedure, a company submits its application directly to the EMA ...

***After considering the opinion, the Commission may grant an EU-wide legally binding marketing authorization**.*

Once this has been granted, the marketing authorization holder can start marketing the medicinal product in the EU. ...

3.4. ***Advanced therapy medicinal products. Advanced therapy medicinal products (ATMPs) are regulated by Regulation (EC) No. 1394/2007 (the ATMP Regulation). ATMPs are novel biotechnological medicinal products based on cells and tissues. They include: - Gene therapy medicinal** products…. In 2012, the Commission conducted a public consultation on the application and impact of the ATMP Regulation. The results were published in a report (**Doc. A.8)** in April 2014.*

This report concludes that, despite the great potential benefits of these therapies for patients, there are still many unknown elements and that appropriate controls are therefore necessary to prevent negative consequences for public health. ...

4.4 Information for patients - Patients must be properly informed about medicinal products . .** ... 4.4.1. **Legislative approach The legal basis for patient information is Directive 2001/83/EC. Medicinal products must be accompanied by information in the form of labeling and a package insert.

***This information must be legible and clearly understandable. The information must be drafted in consultation with patient groups**. ...*

Regulation (EC) No 726/2004 introduced further criteria relating to patient information. These include: - the requirement to publish a European Public Assessment Report (EPAR), including a user-friendly summary of product characteristics; - the basis for access to information on pharmacovigilance and clinical trials; - the creation of a database on medicinal products that is accessible to the general public (EudraPharm).

24. The following is evident from the **Commission's report to the EU Parliament and the Council of March 22, 2017, pursuant to Art. 59 (4) Directive 2001/83/EC (Doc. A. 9)**:

2. ***Legal framework -** The summary of product characteristics, the content of which is described in Article 11 of Directive 2001/83/EC, and the **package leaflet**, the content of which is described in Article 59 of Directive 2001/83/EC, **form an integral part** of the **marketing authorization (approval) of medicinal products** in the*

Union in accordance with Article 6 of Directive 2001/83/EC and Article 3 of Regulation (EC) No. 726/2004.
According to Article 8(3)(j) of Directive 2001/83/EC and Article 6(1) of Regulation (EC) No. 726/2004, in order for the authorization to be granted, the application for authorization must be accompanied by a summary of product characteristics and a package leaflet...
When the competent authorities in the Member States grant a marketing authorization, they shall communicate the summary of product characteristics they have approved to the marketing authorization holder (Article 21(2) of Directive 2001/83/EC). and the relevant competent national authority shall make the authorization, together with the package leaflet and the summary of product characteristics, available to the public without delay for each medicinal product it authorizes (Article 21(3) of Directive 2001/83/EC).
In the case of decisions on centralized marketing authorizations pursuant to Article 10 of Regulation (EC) No. 726/2004, the final decision of the Commission shall be communicated to the marketing authorization holder together with the summary of product characteristics and the package leaflet **(and made available to the public** ... see *https://ec.europa.eu/health/documents/community-register/html/*) ...
Once a marketing authorization has been granted, the content of the summary of product characteristics may not be changed unless the competent authority that granted the marketing authorization approves the change*. The* ***summary of product characteristics is the basis of information for healthcare professionals for the safe***
and effective use of the medicinal product*.*
Specific aspects of treatment related to the use of the medicinal product or its effects should be mentioned in the summary of product characteristics*. Likewise, any warnings applicable to the medicinal product in question should be included.*
The ***package leaflet provides comprehensive information for the safe and proper use of the medicinal product****.* ***The package leaflet is primarily intended for the patient/user****. A carefully designed and clearly worded package leaflet ensures that the information can be used by as many people as possible.*

25. **The content of the implementing decision is therefore also specifically aimed at healthcare professionals, public health authorities, and vaccine recipients.**
26. **Since the content of the package insert and the summary of product characteristics is determined exclusively by a decision of the Commission, and since the content of the package insert and the summary of product characteristics is an essential and integral part of the implementing decision, addresses the the implementing decision is also addressed *de facto* to all those groups of persons who, according to the Directive**

2001/83 EC, a right to package inserts and professional information that comply with EU law
and professional information.

27. According to Art. 11 of Directive 2001/83 EC, last paragraph, the following applies:
"All medicinal products shall include a standard text expressly requesting healthcare professionals to report suspected adverse reactions in accordance with the national spontaneous reporting system referred to in Article 107a(1)."
28. **The pharmacovigilance requirements for vaccines are far less stringent than for advanced therapy medicinal products (gene therapy).**
29. **It is the case law of the EU** (see above para. 15) **that it is not the nature, form, or designation of an act or decision of an EU institution that is decisive for assessing the legal effects of the act or decision of the EU institution, but rather its subject matter, content, substance, scope, effects, and also the factual and legal context.**
30. **It is indisputable that the substance marketed as KOSTAIVE could never be used in vaccination programs in EU member states if it had been approved as a "vaccine" rather than as a medicinal product for advanced therapies (gene therapy).**
The point is **that a pharmaceutical-therapeutic classification of the substance KOSTAIVE as a "vaccine" instead of a "medicinal product for advanced therapies (gene therapy)" that completely disregards its actual nature and mode of action leads to KOSTAIVE being used on a massive scale as a "vaccine," demonstrably endangering the health and lives of EU citizens, and also being transmitted to non-vaccinated individuals and the environment in general due to the concrete risk of spreading.**
31. **If KOSTAIVE had not been approved as a "vaccine" by the Commission, EU member states, including Italy, would never have been able to include this substance in a**
"vaccination program."
32. Therefore, **the annulment changes the legal status of the plaintiff and the population of the Autonomous Province of Bolzano, which it represents institutionally, in a significant way.**

33. **If KOSTAIVE is withdrawn from the market, this substance can no longer be used in vaccination programs**.
34. The above also shows that **the plaintiff and the South Tyrolean population it represents are directly affected**.
35. Nevertheless**, proof of individual concern** is **not necessary, as the contested decision of the Commission is a legal act of a regulatory nature that** has **a general abstract effect**.

The characteristics of the medicinal product stated in the marketing authorization are generally applicable, as they apply not only to the pharmaceutical company submitting the application, but also to the Member States, all authorities, healthcare professionals, and vaccine recipients.

36. Article 59 of Directive 2001/83/EC stipulates that the package leaflet must be drawn up in accordance with the summary of product characteristics. Among other things, it must contain **the pharmaceutical-therapeutic class or mode of action in a form that is easily understandable for the patient in order to identify the medicinal product**.
37. **Contrary to its actual mode of action and composition, KOSTAIVE is described in the package insert as a** Covid-19 sa-mRNA **vaccine.**
38. **Both the summary of product characteristics and the package insert are completely misleading in the case of KOSTAIVE**!
39. **General abstract and immediate effect of the classification and approval procedure treatment as a (conventional) "vaccine" of an experimental substance analogous to gene therapies in terms of mode of action and composition**.
40. Both in the contested implementation decision (Doc. **A.3**) and in the accompanying annexes (Doc. **A.5**), which form an essential and integral part of the decision, **KOSTAIVE** is **declared to be a "vaccine**."
    This has an **abstract, general, and immediate effect that does not require any further implementing acts.**
41. **This is because, based on this completely misleading and EU-illegal classification of the substance KOSTAIVE under pharmaceutical law, the provisions applied for market authorization, the extremely reduced and completely inadequate risk management (RMP) and the absolutely inadequate pharmacovigilance to be exercised by the authorities and health professionals have been based solely on the guidelines issued by the WHO for conventional vaccines in 2005!**
42. **The implementing decision has a generally abstract effect, as it allows a dangerous experimental substance based on genetic engineering, which corresponds in its mode of action to a gene therapy product, to be marketed as a "vaccine" for use on the entire adult population with the label "safe**."
43. **No genotoxicity studies, carcinogenicity studies, or mutagenicity studies (i.e., studies on the risk of DNA modification) were conducted.**
44. This has an **abstract, general effect on the entire EU population, as a highly dangerous experimental substance based on genetic engineering**

has been **launched on the market for mass use through "vaccination campaigns" across the EU**.

45. The following section explains that **the main difference between the approval process for a genetically engineered drug and that for conventional vaccines is that, in the case of genetically engineered products, the risk factors to be considered include the degree of integration of nucleic acid sequences or genes into the human genome, long-term functionality, and oncogenicity risk.**
46. Annex I to the contested implementing decision (Doc. **A.5**.) states under point 5.2 that no pharmacokinetic studies were submitted for the authorization and under point 5.3 that neither genotoxicity nor carcinogenicity studies were conducted.
    5.2. that **no pharmacokinetic studies** were submitted for approval, and point 5.3. explicitly states that **neither genotoxicity nor carcinogenicity studies** were **conducted**.
47. The **protection of the human genome is enshrined at the supranational and international level due to its fundamental importance**. See the 1997 Council of Europe Convention on Human Rights and Biomedicine and the Universal Declaration on the Human Genome and Human Rights of the 29th UNESCO General Conference in November 1997.

48. **Generally abstract and immediate effect due to gross criminal deception and the fundamental prevention of informed and therefore free consent to the injection of the substance, and due to the contamination of the environment, including people not directly treated with it.**
49. **At the community and international level, the fundamental right of humans is enshrined that no pharmacological experiments may be carried out on them without their free and informed consent (Regulation (EU) No. 536/2014, Nuremberg Code).**
50. By **categorizing KOSTAIVE as a "vaccine," which does not correspond to its actual mode of action, the EU population is being grossly misled and therefore cannot give free consent to the injection of this substance!** In addition, even people who decide against "vaccination" with KOSTAIVE are exposed to the **concrete risk of spreading, i.e., transmission of the substance by "vaccinated" individuals**! There is a concrete risk of **contamination of the entire environment by EVs that do not recognize species barriers** (see Doc. A**.6)**.
51. **The grossly deceived population of the EU is *de facto* exposed to a criminal pharmacological mass experiment by the implementing decision.**
    This generally abstract effect does not require an implementing act, but results directly and immediately from the implementing decision.
52. As has been observed continuously for four years now with the mRNA Covid-19 "vaccines," **the spike protein causes massive inflammation in the body**

and cell death in the body. Point 4.4 of Annex I to the contested decision therefore refers to the high risk of myocarditis and pericarditis. Due to the specific risk of KOSTAIVE spreading to the environment (including people not directly treated with it), the approval of this substance is a clear violation of the principle of consent for "medical" treatment.

53. The implementing decision radically violates **Regulation (EU) No. 536/2014 on clinical trials on medicinal products for human use, as well as the Nuremberg Code**.

54. **The misrepresentation of facts in the contested implementing decision automatically leads to mass involuntary treatment with an experimental substance.**

55. ***De facto*, the contested implementing decision has degraded EU citizens from their position as human beings with a fundamental right to life and health and guaranteed human dignity to that of laboratory animals.**

GROUNDS FOR THE ACTION

GROUND I

56. **Gross violation of Articles 168 and 169 TFEU, Articles 1, 3, 35, and 38 EU Charter, of Directive 2001/83/EC, Articles 8, 11, 26, 54, 58, 59, 86 et seq. 101 et seq., Annex I, Part I, Part III, Part IV, and Regulation (EC) No. 726/2004, Articles 3 to 7, 10a, 12, 14-a, and the UN Declaration on the Human Genome and Human Rights**

by circumventing the high testing standards required for gene-based medicinal products

(1) on the basis of an unfounded and factually illogical exclusion of the application of the marketing authorization provisions intended for advanced therapy medicinal products to substances that are declared purely formally as vaccines against infectious diseases but in fact correspond to gene therapy medicinal products

(2) in any case, due to the failure to involve the specific EMA committee for advanced therapies, which is necessary regardless of the classification as a gene therapy, solely on the basis of the genetic structure and mode of action of the substance

(3) in any case due to violation of the for on requirements vaccines

Necessary incidental review of conformity with Article 277 TFEU of Commission Directive 2009/120/EC of September 14, 2009

(1)

57. **Under the then President of the European Commission, José Manuel Barroso— who now, significantly, holds the position of CEO of the GAVI Vaccine Alliance** (Doc. **A.12**) **amended EU Directive 2001/83/EC of the Parliament and of the Council to the effect that substances declared as vaccines against infectious diseases are not considered gene therapy products.**

The following is a literal quote from COMMISSION DIRECTIVE 2009/120/EC of September 14, 2009, amending Directive 2001/83/EC of the European Parliament and of the Council on the Community code relating to medicinal products for human use, as regards advanced therapy medicinal products, ANNEX
*"PART IV **ADVANCED THERAPEUTIC MEDICINAL PRODUCTS**," the following:*
2.1. Gene therapy medicinal product
*A **gene therapy** medicinal product is defined as a biological medicinal product that has the following characteristics:*

*a) **It contains an active substance that contains or consists of a recombinant nucleic acid that is used in or administered to humans** to regulate, repair, replace, **add**, or remove **a nucleic acid sequence**.*

*b) **Its** therapeutic, **prophylactic**, or diagnostic **effect is directly related to the recombinant nucleic acid sequence it contains or to the product resulting from the expression of this sequence. Vaccines against infectious diseases are not gene therapies**.*

58. **This one absolutely formulated sentence, *"Vaccines against infectious diseases are not gene therapy products,"* means that, regardless of their composition and mode of action, substances are defined as "vaccines against infectious diseases," are simply excluded from the much stricter and more demanding regulatory requirements for approval that the legislator has necessarily imposed on gene therapies and, more generally, on advanced therapy medicinal products.**

59. This leads to the absurd situation that substances, although structured and acting like gene therapies, are exempt from the strict EU approval regulations for advanced therapy medicinal products necessary to protect the health of the entire EU population simply because they are defined as "vaccines against infectious diseases"

, are exempt from the strict EU approval regulations for advanced therapy medicinal products necessary to protect the health of the entire EU population and are treated like conventional vaccines, with which they have nothing in common!

60. **A conventional "vaccine" contains an antigen.**
KOSTAIVE does not contain any antigens, but rather the blueprint for the stabilized spike protein of the SARS-CoV-2 virus, which is a dangerous toxin and thus a foreign substance that the body is supposed to produce itself. KOSTAIVE is therefore a so-called *pro-drug*.
Therefore, the injection immediately causes the body to produce a harmful substance and not, as with conventional vaccines, a specific defense or protective substance. The formation of antibodies and thus protective substances only occurs in the second step.

61. It is absolutely incomprehensible why substances that contain or consist of nucleic acid, which are injected into humans to add a nucleic acid sequence (in this specific case, the sa-mRNA, which is then supposed to lead to the production of the SARS-Cov-2 spike protein), are excluded from the definition of
"gene therapy" and thus from the necessarily very strict approval regulations for "medicinal products for advanced therapies."

62. Unless, in 2009, in deliberate violation of the most fundamental principles of pharmaceutical law – and thus of the precautionary principle and the fundamental right **to life and health** enshrined in EU law – the conditions were created for substances that *de facto* act as gene therapies to be approved without having to comply with the necessarily strict approval requirements for gene therapies. This appears to be precisely the case.

63. "The approval of gene therapies as conventional vaccines was based on scientifically and medically invalid grounds. This has unforeseeable consequences for the health of the population.

64. Gene-based drugs intended for a small number of patients with very specific clinical pictures are subject to high testing standards – but, absurdly, this does not apply to gene-based drugs that are declared purely "formally" as "vaccines for infectious diseases" (such as KOSTAIVE) and are injected into healthy (!) people.

65. This was due to the influence of powerful lobbies: As explained above, Directive No. 2009/120/EC, adopted by the European Commission in 2009 without the involvement of the European Parliament, excluded "vaccines against infectious diseases" from the group of specially regulated gene therapies by redefining them in legal terms: "*Vaccines against infectious diseases are not gene therapy products*." This definition was only amended after a statement from the pharmaceutical industry

(Doc. **A.10**). **The original draft directive** (Doc. **A.11**) **had provided for a broad definition of gene therapy in favor of protecting public health, which would also have covered gene-based COVID-19 injections.**

66. Among other things, the pharmaceutical companies argued that the strict safety requirements provided for in the draft directive would make the production of mRNA gene therapies significantly more expensive. The **EU Commission, under the chairmanship of the current CEO of the GAVI vaccine alliance**, **José Manuel Barroso** (Doc. **A.**10), subsequently amended the text of the directive.

67. **The exclusion of gene-based vaccines against infectious diseases from the group of gene therapies saves manufacturers numerous time-consuming and costly preclinical studies. However, these are essential for assessing the safety of the drug and the people participating in clinical trials.**

68. Clinical trials may not be initiated without the results of preclinical studies. These studies typically examine, among other things, the distribution of drugs in the body, their biochemical conversion and degradation, and their excretion in the context of pharmacokinetics—in the case of gene therapies, this includes the risk of gene transfer to the germ line—possible changes in the genetic material of cells (genotoxicity), cancer risks, the influence of the drug on important parameters for basic functions of the human body (safety pharmacology), and interactions with other drugs.

69. **The consequence of the redefinition: no genotoxicity, carcinogenicity, or mutagenicity studies were conducted for KOSTAIVE.**

70. KOSTAIVE is an **experimental mRNA-based substance** that has **absolutely nothing to do with conventional vaccines in terms of its mode of action and manufacture**.

In the European Commission's implementing decision contested here (Doc. **A. 3**) approving KOSTAIVE as a vaccine, it states verbatim

*"(4) The Committee for Medicinal Products for Human Use considered that Zapomeran is a **new active substance**."*

71. In Annex I, point 5 (Pharmacological properties) to the contested implementing decision of October 10, 2022 (Doc. **A**.**5**), the mechanism of action is described as follows:

KOSTAIVE consists of self-amplifying mRNA that codes for the SARS-CoV-2 spike protein and is encapsulated in lipid nanoparticles. The self-amplifying mRNA is designed so that, after intramuscular injection, additional copies of mRNA are produced in the host cells to achieve enhanced expression of the spike protein antigen..."

72. RNA is a nucleic acid and is essential for protein synthesis. The blueprint for proteins in the human body is stored in the human genome, in the DNA in the cell nucleus, where it is transcribed into mRNA. Once the mRNA with the blueprint for the protein is formed, the mRNA leaves the cell nucleus. Outside the cell nucleus, ribosomes read this blueprint and form the corresponding protein. There are more than a hundred thousand mRNA molecules in a human cell at any given time. The ribosomes can only read the information within a short period of time, as mRNA usually decays rapidly.

73. In the case of the "mRNA vaccine," however, the mRNA is synthetically produced in the laboratory. According to observations made over the past four years and now confirmed in countless peer-reviewed studies — which stands in stark contrast to the official claim made to the population that this synthetic mRNA remains in the upper arm muscle (where the injection takes place) — this substance enters the entire body and can even cross the blood-brain barrier (*Nature Neuroscience, The S1 protein of SARS-CoV-2 crosses the blood-brain barrier in mice, Elizabeth M. Rhea et al)* and has been found in the bodies of people treated with this substance even months after injection. **Once a few particles are absorbed and the spike protein is produced by them, this spike protein can facilitate the passage of further "vaccine" particles into the brain (**A *Case Report: Multifocal Necrotizing Encephalitis and Myocardities after BNT162b2 mRNA Vaccination against Covid-19)*.

74. **There is not only great concern, but clear evidence that synthetic mRNA injected into the body can reverse transcribe into DNA, and that these DNA copies can insert themselves into the DNA of human cells, i.e., into the human genome**. **Therefore, the genetic information of the RNA can contaminate and alter the human genome (***Intercellular Reverse Transcription of Pfizer BioNTech COVID-19 mRNA Vaccine BNT162b in vitro in human liver cell line, Markus Alden et al; Potential mechanisms for human genome integration of Genetic Code from SARS-CoV-2-mRNA vaccination: implication for disease – Kyriakopoulos et. al)*.

75. The scientific report *"The immunological and biochemical principles of mRNA vaccine toxicity"* by two microbiologists and a pulmonologist (Dr. Michael Palmer, Prof. Sucharit Bhakdi, Dr. Wolfgang Wodarg – Doc. **A. 13**) shows that **reverse transcription of RNA into DNA** is **a mechanism that has been known for many decades (since the 1970s)**! Therefore, it is nothing new, and above all, nothing that can simply be ruled out. Quite the contrary! The risk of reverse transcription increases, of course, with each additional injection.

76. The experts write: "***Apparently, EMA's experts were assuming that RNA in general will not affect the integrity of the host cell genome. The first***

exception to this rule has been known since 1970 ... it could hardly be considered a novelty in 2020."

77. The mRNA-based substance KOSTAIVE has been formally categorized as a "vaccine," even though, as the facts show, it does not function as a vaccine in any way. It is clear that the mRNA substance KOSTAIVE is a substance that has been categorized as a "vaccine" due to "convenience labeling," even though it does not function as a conventional vaccine, but is a **pro-drug** that **is structured and acts like a gene therapy** and should therefore be classified as **an advanced therapy medicinal product**.

78. Although KOSTAIVE has been formally defined by the EMA as a vaccine against an infectious disease, and therefore, according to Commission Directive 2009/120/EC of September 14, 2009, and Directive 2001/83/EC Annex IV Point 2.1. last sentence, the effective nature and mode of action of KOSTAIVE is that of a gene therapy product. It is therefore necessary to apply the provisions laid down by the European legislator for this particular product category.

79. **The main difference between the authorization procedure for advanced therapy medicinal products (including gene therapy medicinal products) and that for conventional vaccines can be summarized as follows.**

80. For gene therapy products, Annex I, Part IV of Directive 2001/83 stipulates, among other things, the following:

1. Introduction: ... **Risk factors to be taken into account may include: ... the degree of integration of nucleic acid sequences or genes into the genome, long-term functionality, oncogenicity risk, and the method of administration or application ...**

3 Special requirements for Module 3

3.2.2. Special requirements

In addition to the requirements of Part I, Sections 3.2.1. and 3.3.3. of this Annex, the following requirements apply:

a) Information shall be provided on all starting materials used in the manufacture of the active substance, including the products required for the genetic modification of human cells ...

"4.2. **Special requirements for gene therapy products**

4.2.1. **Pharmacology**

a) In vitro and in vivo studies on effects related to the proposed therapeutic purpose (i.e., **pharmacodynamic studies to demonstrate the principle of action (*"proof of* concept")) using specifically designed models and relevant animal species to demonstrate that the nucleic acid sequence reaches the intended target (target organ or cells) and performs its intended function (degree of expression and**

functional activity). <u>The functional duration of the nucleic acid sequence and the proposed dosage regimen in clinical trials must be specified</u>.

b) **Target selectivity: If a gene therapy product is intended to perform a selective function or a function limited to the target, studies confirming the specificity and duration of function and activity in the target cells and tissues must be submitted**.

<u>Note:</u> Contrary to the claim made to the public that mRNA COVID-19 "vaccines" remain in the affected upper arm muscle and that the formation of the spike protein is concentrated there, both the nanolipids and the spike protein have been detected throughout the human body! Palmer et al. state the following in their expert opinion on mRNA vaccines in general (Doc. A**.13)**: *"2.1. **mRNA vaccines are distributed throughout the body and prominently affect the blood vessels." The assertion that the mRNA/lipid nanoparticles remain at the site of injection is now widely known to be a blatant untruth. The "vaccines" rapidly spread from the site of injection to regional lymph nodes and to the blood circulation** ... Moreover, in contrast to most viruses, **mRNA vaccine nanoparticles can be taken up by any cell type, including the endothelium, which forms the innermost cell layer of the blood vessels.... 2.2. The expression of spike protein in the body is widespread and long-lasting. Studies on a model mRNA vaccine have shown that the lipid nanoparticles, after intramuscular injection, rapidly enter the bloodstream. They subsequently accumulate preferentially in certain organs including the liver, the spleen, and the ovaries. ... at least the blood vessels themselves are exposed to the vaccine in every organ and every tissue, from which we have to expect widespread expression of the foreign** antigen... **Another important consideration is how soon the antigen is expressed, and how long this expression lasts....A fairly long-lasting expression of spike after mRNA vaccination was also reported by Röltgen et al., who still detected the spike protein in lymph nodes 60 days after the second injection, and at this same time point also showed the continued presence of mRNA encoding the spike**. Similarly, Magen et al. detected strong spike protein expression and continued presence of the RNA one month after vaccination...."*

<u>See also the scientific article by Dott</u>. Maurizio Federico, Director of the National Center for Global Health at the Istituto Superiore di Sanità (Rome) – **Doc. A.14.**

The Immunologic Downsides Associated with the Powerful Translation of Current COVID-19 Vaccine mRNA Can Be Overcome by Mucosal Vaccines, funded by the Italian Ministry of Health and published in the scientific journal Vaccines In this scientific article, the

Director of the National Center for Global Health at the Italian National Institute of Health (ISS) explains, among other things: "*Powerful mRNA translation coupled with Spike overproduction can lead to the dysregulation of ACE-2 signaling and cytokine production, antibody cross-reaction against unspecific molecular targets, the emergence of both auto- and anti-idiotype antibodies, and immune responses of uncertain significance against unknown products. In addition, the cytokines produced after Spike/ACE-2 binding can unfavorably influence the fate of still 'dormant' tumors and pre-existent autoimmune pathologies as well as chronic inflammation."*

4.2.2. **Pharmacokinetics**

a) Biodistribution **studies** must include investigations of persistence, clearance, and mobilization. **Biodistribution studies must** also **address the risk of gene transfer to the germ line.**

Note: Palmer et al. in their expert opinion on mRNA vaccines in general (Doc. **A.13**): ***"4.2 Pharmacokinetics of mRNA vaccines****. The properties of the lipid nanoparticles ... exert a strong influence on their transport and their fate within the human body. 4.2.1 Organ distribution of model mRNA vaccines. ... the transport of vaccine lipid nanoparticles may resemble that of lipoproteins ... the amount of lipoprotein particles taken up and turned over varies greatly between the cells of different organs. The following organs take up particularly large amounts:*

1. *The liver has a central place in lipoprotein metabolism...*
2. *Endocrine glands which produce steroid hormones ... These include the testes, the ovaries, and the adrenal glands.*
3. *The placenta requires lipoprotein both for supplying the fetus and for its own production of progestin hormones, which are necessary to sustain pregnancy.*
4. *The lactating breast glands acquire fat and cholesterol from lipoproteins and repackage them for release into breast milk.*

With this in mind, we can understand some of the observations on the distribution of mRNA vaccines within the body …Moderna, according to EMA's report on this vaccine, … submitted some animal data on a model vaccine … In this study, the levels of mRNA rather than of the lipids were measured. The results of Moderna's study are incompletely described in the report, but on page 47 we read:
Increased mRNA concentrations (compared to plasma levels) were found in the spleen and eye. … Low levels of mRNA could be detected in all examined tissues except the kidney. This included heart, lung, testis, and also brain tissues … liver distribution of mRNA-1647 is also evident in this study, consistent with the literature reports that liver is a common target organ of LNPs." …
regardless of the tissue in any specific organ, at least the blood vessels and their endothelium will be exposed to the vaccine particles in each and every organ. Accordingly, vasculitis and thromboembolic events are somewhat

likely to occur in all organs. Additional tissue-specific pathology might be expected to focus on organs with high levels of accumulation*. However, as we will see presently, the findings of these animal studies likely do not give a complete picture of mRNA vaccine distribution in practice. 4.2.2. Correlation of model vaccine organ distribution with histopathological findings … **we have seen evidence of inflammation and of vaccine-induced spike protein expression in heart muscle** .. and the brain …, even though these organs accumulated only comparatively low or moderate levels of the model vaccine in Pfizer's and Moderna's animal experiments. **The observed inflammation is particularly remarkable with respect to the brain, which is supposed to be protected by the blood-brain barrier. In this context, we must note two important caveats:***

1. The blood-brain barrier breaks down when the brain tissue is afflicted by inflammation. Accordingly, vasculitis within the brain that was induced by the first injection of an mRNA vaccine might soften up the blood-brain barrier and facilitate the entry of vaccine particles delivered with a subsequent booster injection. It would therefore have been important to examine the organ distribution of the vaccine not only after the first injection, but also after one or more repeat injections. However, this was not done in Pfizer's and Moderna's animal studies.

2. ***The SARS-CoV-2 spike protein has been shown in several studies to compromise the integrity of the blood-brain barrier ... Spike protein which may be expressed elsewhere but reaches the brain through the bloodstream may facilitate penetration of vaccine particles into the brain ... These considerations, in combination with histopathological findings, strongly suggest that mRNA vaccines distribute more widely and effectively than Pfizer's and Moderna's very limited animal studies on model vaccines would indicate ...***

4.2.3. Time course of elimination and duration of activity*. We had seen in Section 4.1.4. that the **mRNA can become separated from the lipids after the cellular uptake of the vaccine nanoparticles. The elimination of both ingredients must therefore be considered separately**.*

4.2.3.1. Time course of mRNA elimination*. ... it must be stressed that none of these studies used the mRNA deployed in the COVID-19 vaccines, and furthermore that all studies were carried out in rodents. These results can therefore not be directly applied to the current crop of mRNA vaccines and their use in human patients. ... **Covid-19 vaccine mRNA has been detected 60 days after injection in lymph nodes ... and 30 days after injection in muscle tissue of a limb other than the one that had been injected ... Long-lasting persistence of the vaccine mRNA in blood plasma samples of injected patients was recently reported by Fertig et al. ... these studies on humans show that the vaccine***

mRNAs may persist much longer than Pfizer's and Moderna's animal studies would suggest.

4.2.3.2. Time course of lipid elimination. *…According to EMA report ..* ***Moderna submitted no data on the elimination of the two synthetic lipids contained in their Covid-19 mRNA vaccine****. … While EMA reassures us that accumulation of the lipids within the body is unlikely, we must note that firstly the information provided is entirely insufficient by the usual standards of drug development and approval, and secondly that absence of lipid accumulation does not imply absence of cumulative toxicity."*

b) As part of the environmental impact assessments, **studies on excretion and the risk of transfer to third parties** must **be submitted**; otherwise, this must be sufficiently justified in the application due to the nature of the drug in question. As Dott. Federico demonstrates in his scientific article (Doc. A**.6)**, **there is a concrete risk of excretion into the environment and transfer to third parties with KOSTAIVE, even without a species barrier.**

4.2.3. Toxicology

a) **The toxicity of the finished gene therapy product must be assessed**. In addition, depending on the type of medicinal product, **active substances and excipients must be tested separately**, and the in vivo effect of products not intended for physiological function but encoded by the nucleic acid sequence must be assessed.

Note: Palmer et al in their expert opinion on mRNA vaccines in general (Doc. **A.13**): *4.3. Lipid nanoparticle toxicity. ... two synthetic lipid species. The PEG-conjugated lipids are the less abundant of the two, and the only mechanism of harm on record consists in allergic reactions to these lipids. In contrast,* ***the cationic lipids account for almost half of the total lipid in the vaccine LNPs, and they can exert toxicity outright, without any "assistance" from the adaptive immune system.*** *...*

4.3.2. ***Inflammatory signaling by cationic lipids. Several experimental studies have shown that cationic lipids similar to those used in the Pfizer and Moderna COVID-19 vaccines induce strong inflammatory reactions. … This agrees with the frequent observation of local and also systemic inflammatory reactions among COVID-19 vaccine*** *recipients…."*

5. Genotoxicity of mRNA vaccines … 5.2.1.4. Summary. Even though this had not yet been experimentally demonstrated when the COVID-19 mRNA vaccines were given emergency approval, ***there was ample precedent to suggest the strong possibility that DNA copies of the vaccine mRNA would arise and be inserted into the cellular genome. Rather than dismissing this risk as they did, the EMA and other regulators should have required Pfizer and Moderna to carry out***

***The necessary studies to exclude this risk before giving the green light for authorization**... **The results reported by Aldén et al**., even though preliminary in some respects, raise some very serious questions that **can no longer be ignored by the regulatory authorities**... **Gene inactivation. Insertion may occur within a gene and disrupt it. This can lead to the loss of important cellular gene products (i.e., proteins) and thus, potentially, to the development of disease, including cancer**. ... **Gene regulation. Transcriptional and epigenetic regulation mechanisms may be affected, thus modulating protein expression levels upward and downward with unpredictable and undesirable results.** Indirect regulatory effects may affect even distant genes located on other chromosomes." ... **Activation of** oncogenes... **the occurrence of malignancies through DNA integration and activation of cancer-promoting genes (oncogenes) has been demonstrated in clinical trials** ... for the genetic treatment of children .... **These malignancies will typically become manifest only several years after the completion of treatment.** Therefore, thorough **long-term investigations concerning possible genotoxic effects of chromosomal integration are absolutely necessary, in both the pre-clinical and clinical trial stages, for a valid benefit-risk** analysis…. **The risk of insertion into the chromosomal DNA must be taken seriously**…. **Autoimmune-like disease. Integration of the spike protein gene into the host cell could lead to permanent expression of this antigen and thus induce chronic autoimmune-like** disease… **Germline integration.** … Pfizer's own experiments indicate a high level of vaccine accumulation in the ovaries … Furthermore, LINE-1 and other retrotransposons are active and cause genomic insertion events in human oocytes.*

*... Taken together, these **findings indicate that the mRNA gene sequences may be integrated into the DNA of oocytes, and hence into the human germline. Insertion into male germline cells cannot be ruled out** either, even though in the cited animal study the tissue levels of the model mRNA vaccine in the testes were significantly lower than in the ovaries. Should this indeed come to **pass—should the germline cells of vaccinated individuals be rendered transgenic—then the risk of spawning or conceiving transgenic children will not be limited to these individuals only, but it will necessarily be shared by their current or future spouses. In effect, an entire generation of future parents will be exposed to this risk.** ... Summary. **Integration of the mRNA sequences into somatic cells is likely and implies a risk of cancer and of autoimmune disease. Moreover, the risk of germline integration, resulting in transgenic offspring, cannot be denied. These risks must urgently be addressed through in-depth animal studies. Meanwhile, the authorizations of any and all mRNA vaccines in current use must urgently be revoked.***

b) Studies on toxicity after a single administration can be combined with studies on pharmacological and pharmacokinetic safety, for example on persistence.

c) **Studies on toxicity following repeated administration must be submitted if multiple administration to humans is intended**. The method of administration and the administration schedule must be closely aligned with the planned clinical dosage. **In cases where a single dose may result in persistent function of the nucleic acid sequence in humans, studies on toxicity following repeated administration should be considered. <u>These studies may be longer than standard toxicity studies, depending on how long the gene therapy product persists and what potential risks are anticipated.</u>** The duration must be justified.

d) **Genotoxicity should be investigated**.

e) **Carcinogenicity must be investigated** ... depending on the type of drug, ... the tumorigenic potential must be evaluated in relevant in vivo/in vitro models.
In his scientific paper *The Immunologic Downsides Associated with the Powerful Translation of Current Covid-19 Vaccines mRNA*, published in *Vaccines* (Doc. **A.14**), Dr. M. Federico points out that mRNA substances promote the development of tumors! However, according to point 5.3 of Annex I to the EU Commission's implementing decision contested here, neither genotoxicity nor carcinogenicity studies were conducted, with the succinct justification that "the components of the vaccine (lipids and mRNA) are not expected to have genotoxic potential." **This is pure criminality with immeasurable consequences and must be stopped immediately!**

f) **Reproductive and developmental toxicity: Studies on the effects on fertility and general reproductive function must be submitted. Studies on embryonic, fetal, and perinatal toxicity and studies on germline transmission must also be submitted**; ...

g) **Additional toxicity studies**

- **Integration studies: Integration studies must be submitted for each gene therapy product**, unless their absence is scientifically justified, e.g., because the nucleic acid sequences do not penetrate the cell nucleus. **For gene therapy products that are not expected to be capable of integration, integration studies must nevertheless be conducted if the biodistribution data indicate a risk of germline transmission.**

- **Immunogenicity and immunotoxicity: Potential immunogenic and immunotoxic effects must be investigated. ...**

5. Special requirements for Module 5

5.1. Special requirements for all advanced therapy medicinal products

5.1.1. The specific requirements in this section of Part IV apply in addition to the requirements set out in Part 1, Module 5 of this Annex....

5.1.6. **Efficacy must be demonstrated for the intended use by relevant results from clinical studies in which clinically meaningful endpoints for the intended use were used**. Under certain clinical conditions, proof of long-term efficacy may be required. The strategy for assessing long-term efficacy must be described.

5.1.7. The risk management plan shall include a strategy for long-term monitoring of safety and efficacy....

5.2. Special requirements for gene therapy products

5.2.1. **Human pharmacokinetic studies**

Studies on pharmacokinetics in humans must include the following:

a) Studies on the excretion of the gene therapy product;
b) Studies on biodistribution;
c) Pharmacokinetic studies on the drug and the active components produced by gene expression (e.g., expressed proteins or genomic signatures).

5.2.2. Human pharmacodynamic studies

In pharmacodynamic studies in humans, the expression and function of the nucleic acid sequence must be investigated after administration of the gene therapy product.

5.2.3. Safety studies

The following must be investigated in safety studies: ...

c) Replacement of existing genome sequences ("resortment");
d) Neoplastic proliferation due to insertion mutagenesis.

81. **With regard to "vaccines," the European Community Code for Medicinal Products for Human Use (Directive 2001/83/EC) only provides for the following very meager regulations, all of which refer exclusively to conventional vaccines based on antigens and have nothing in common with sa-mRNA injections such as KOSTAIVE.**

82. **Vaccines are listed in Part III of Annex I to Directive 2011/83/EC on biological medicinal products.**

83. In **point 1.**2, the European Medicines Code defines the requirements for the authorization of vaccines in **Part III** of its Annex, but refers exclusively to substances based on an antigen.

84. There is absolutely no mention of the additional (apart from the general) requirements for advanced therapy medicinal products in relation to vaccines!

85. **The legal finding that, regardless of their actual composition and mode of action, "vaccines against infectious diseases" are not gene therapy products is factually and scientifically unfounded, and the relevant passages of Directive 2001/83/EC of the European Parliament and of the Council (i.e., Annex I, Part IV, point 2.1, last sentence) and Commission Directive 2009/120/EC (i.e., Annex, Part IV, Point 2.1, last paragraph) must be recognized as grossly contrary to EU law within the framework of incidental review of norms pursuant to Art. 277 TFEU, with the necessary consequences.**

86. Furthermore, based on the above, **the gross violation of EU law by the approval procedure and the marketing authorization of KOSTAIVE must be determined and declared, and as a result, the EU Commission's implementing decision challenged here must be declared null and void.**

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GROUND OF ACTION II

87. **Violation of Regulation (EU) No. 536/2014 of the European Parliament and of the Council of April 16, 2014, on clinical trials on medicinal products for human use**

EU citizens, including the youngest (and the unborn), are being abused as guinea pigs for an illegally administered and transmissible experimental substance. An illegal pharmacological-genetic and criminally relevant experiment is being carried out on the entire EU population.

88. According to Recital (27) of Regulation (EU) No. 536/2014, "**Human dignity and the right to the integrity of the human body are recognized in the Charter of Fundamental Rights of the European Union** (hereinafter referred to as "the Charter"). In particular, the Charter states that **any medical or biological intervention may only be carried out with the free and informed consent of the person concerned.** Directive 2001/20/EC contains detailed provisions on the protection of trial participants. These provisions should be maintained.

89. According to recital (30) of the Regulation: "In accordance with international guidelines, informed consent should be given in writing by a trial participant. ... Before informed consent is obtained, the potential trial participant should be provided with information in a conversation conducted in a language that he or she easily understands. The trial participant should have the opportunity to ask questions at any time. ..."

90. According to Article 3 of the Regulation: "**A clinical trial may only be conducted if**
    a) **The rights, safety, dignity, and well-being of the trial participants are protected and take precedence over all other interests**, and
    ...

According to Article 4 of the Regulation, a clinical trial must undergo scientific and ethical review and be approved in accordance with the Regulation.
Particularly strict rules apply to minors and other vulnerable populations (Article 10 of the Regulation).
Chapter V (Protection of trial participants and informed consent) of Article 28 (General provisions) of the Regulation stipulates that a clinical trial may only be conducted under the following conditions: ...

b) the trial participants ... have been informed in accordance with Article 29(2) to (6);
c) the trial participants ... have given their informed consent in accordance with Article 29(1), (7), and (8);
d) the right of examination participants to physical and mental integrity ... shall be preserved.

In Article 29 (informed consent), the EU legislator has stipulated the following:

(1) Informed consent shall be given in writing, dated, and signed after appropriate information has been provided.
(2) The information provided to the trial participant ... in order to obtain informed consent must
    a) enable the trial participant or their legal representative to understand
        i) the nature, objectives, benefits, consequences, risks, and disadvantages of the clinical trial;...
    b) be comprehensive, concise, clear, relevant, and understandable to laypersons;
    c) be communicated during a prior discussion conducted by a member of the trial team who is ... appropriately qualified;
    d) Contain information on the applicable procedure for compensation for damages referred to in Article 76(1) and
    e) the EU trial number and information on the availability of the results of the clinical trial referred to in paragraph 6.
(3) The information referred to in paragraph 2 shall be recorded in writing and made available to the trial participant. ...

91. For clinical trials involving minors, the stricter rules provided for in Article 32 of the Regulation shall also apply.

92. **The EU population, such as the plaintiff and the population of the Autonomous Province of Bolzano represented institutionally by the plaintiff, are being subjected to a mass experiment by the EU Commission and the EMA as guinea pigs for experimental substances based on genetic engineering.**

93. The EU population is not being told that
    (i) the mRNA-based so-called Covid-19 "vaccines," such as KOSTAIVE, are substances that, due to their composition and mode of action, correspond to gene therapies and thus to advanced therapy medicinal products,
    (ii) not even the studies required for genetically engineered "vaccines" have been carried out,
    (iii) there is no pharmacovigilance appropriate to the properties and mode of action of this substance, and therefore the data collected on side effects (especially the most serious ones, such as deaths) are dramatically underreported,
    (iv) there is a concrete risk of spreading and thus of transmission to other humans and the environment in general – without species barriers.

94. **The mass direct and indirect (due to spreading) use of this experimental substance, including on children, under false pretenses, is a gross violation of the Nuremberg Code, because only those who are correctly and fully informed can make a "free" decision. And due to the concrete risk of transmission into the environment, any free decision is ruled out from the outset!**
    The deliberately misled population cannot make a "free" decision, and all from the vaccine recipients signed "Declarations of consent" are null and void.

95. In the present case, the approval and thus the use in humans is not based on the legally required comprehensive study results, as detailed in Annex I "analytical, toxicological-pharmacological and medical or clinical requirements and evidence relating to trials with medicinal products" of Directive 2001/83/EC.

96. **As explained in Grounds of Appeal I, essential study data that would have been required unconditionally in the case of regular drug approval is missing**. This is compounded by serious scientific misconduct and undeclared safety concerns, so **that**, taken as a whole, the **limit for human trials by approval as "vaccine" despite insufficient study results and the concrete risk of spreading into the environment**.

97. The principles governing the **requirements for consent in medical studies set out in the Declaration of Helsinki** date back to the **Nuremberg Code**, which has also been incorporated into the **criminal offenses defined in the Rome Statute of the International Criminal Court**.

98. **International law is not only an "integral part" of the Union's legal order. Legal acts of the Commission that systematically and comprehensively violate *jus cogens* are *ipso jure* null and void in accordance with Article 53 of the Vienna Convention on the Law of Treaties,** which **is recognized under customary international law (**see further references in the literature: *Schmalenbach,* in: Calliess/Ruffert, EUV/AEUV (fn. 1), Art. 216, para. 50; *Tomuschat,* in: von der Groeben/Schwarze, EUV/EGV (fn. 10), Art. 281, para. 43; for details, see *Schmalenbach,* in: Europarecht als Mehrebenensystem (fn. 4), 67 (75 ff.).

99. Apart from that, the agreement under international treaty law between the International Criminal Court and the European Union on cooperation and assistance of 10 April 2006, OJ 2006 L 115, p. 50) stipulates in Art. 4 that the EU must observe the relevant provisions of the Statute.

100. **The conduct of medical or scientific experiments on humans in peacetime that violate the principles of medical ethics constitutes a violation of the Rome Statute of the International Criminal Court, as these are the result of the actions of the Commission or Union policy. Under the alternative offense of Article 7(1)(k) of the Rome Statute of the International Criminal Court, with reference to the prohibition in wartime of "inhuman treatment, including biological experiments" and "wilfully causing great suffering or serious injury to body or health" under Article 8(2)(a) of the Rome Statute for the deliberate commission of "other inhumane acts of a similar character" can be punished as "crimes against humanity" if they cause great suffering or serious impairment to physical integrity as a result of state action or the actions of EU institutions.** For this reason, too, the EU Commission's implementing decision challenged here must be declared null and void.

PLAINTIFF'S THIRD GROUND

101. **Nullity of the contested implementing decision due to gross violation of Articles 168 and 169 TFEU and Articles 1, 3, 35, and 38 of the EU Charter**

102. Based on the facts and circumstances set out above and documented in this statement of claim, it is clear that the contested implementing decision of the EU Commission (Doc. **A.3**), which is based on Article 168 TFEU (public health) of

EU legislators have grossly violated established principles. **The EU legislator has guaranteed EU citizens that a high level of health protection must be ensured in the definition and implementation of all Union policies and activities.** The Union's action should be aimed **at** improving the health of the population, preventing human illness and **obviating sources of danger to physical and mental health**.

103. **The EU must take measures to establish high standards of quality and safety for medicinal products and medical devices**.

104. All these obligations under Article 168 TFEU have been grossly violated by the European Commission with the implementing decision contested here and with Directive 2009/120/EC (Annex concerning Part IV, point 2.1, last sentence), as well as by the European Parliament and the Council with Directive 2001/83/EC – Annex I, Part IV, point 2.1, last sentence, thereby placing the plaintiff and the population of the Autonomous Province of Bolzano (and the entire EU population) represented by it in a situation that seriously endangers their health and lives.

105. In **Article 1 of the EU Charter (Human dignity)**, the EU legislator declares:
Human dignity is inviolable!
The decision contested here, as well as the sections of the directives outlined above, which are to be subjected to incidental judicial review, grossly violate human dignity!

106. **Article 3 of the EU Charter (Right to integrity)** guarantees the following to every person in the EU: (1) **Everyone has the right to physical and mental integrity. (2) In the field of medicine and biology, the following must be observed in particular: the free consent of the person concerned after prior information in accordance with the procedures laid down by law,** ..., **the prohibition of using the human body and its parts as such for profit,** ....

107. **Article 35 of the EU Charter (health protection)** guarantees every person within the EU that **a high level of human health protection shall be ensured in the definition and implementation of all Union policies and activities**.

108. **Article 169 TFEU (consumer protection**) guarantees consumers that the EU shall contribute to **protecting the health** and safety of consumers and promoting their **right to information** in order to ensure a high level of consumer protection.

109. And according to Article 38 of the EU Charter (consumer protection), the Union's policies should represent a high level of consumer protection.

110. In view of the above, it is clear that, with the implementing decision contested here, the EU Commission has also grossly violated the plaintiff's fundamental right to consumer protection and the obligations applicable to the Commission in particular under Article 169 TFEU

, which apply in particular to the Commission.

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111. The plaintiff therefore requests that this court, on the basis of the multiple serious violations of applicable EU law cited, by means of a legal act of a regulatory nature which directly and personally affects the plaintiff and the population of the Autonomous Province of Bolzano that it represents institutionally, declare the Commission's implementing decision contested here to be null and void on the grounds of gross illegality under EU law. The plaintiff also requests that the parts of Directive 2001/83/EC of the European Parliament and of the Council and Directive 2009/120/EC of the Commission (Annex I and Annex - Part IV, point 2.1, last sentence) be recognized and declared to be contrary to EU law within the framework of the incidental review of norms to be carried out pursuant to Article 277 TFEU due to violation of overriding EU legal principles on medicinal products and the obligation to protect human rights also enshrined in EU law, together with the necessary legal consequences.

Bolzano/Italy June 9, 2025

RA DDr. Renate Holzeisen

The following documents are filed:

The following documents are filed:

A.1 Proof of institutional function as a member of the South Tyrolean Provincial Council by RA DDr. Renate Holzeisen; pp. 1 to 2 of the annexes; para. 1

A.2 Art. 48/bis Decree of the Italian President of the Republic of Italy No. 670 of August 31, 1972; pp. 3 to 148 of the annexes; (color print), para. 1

A.3 EU Commission**,** Implementing Decision of February 12, 2025; pp. 149 to 152 of the annexes; paras. 1, 40, 102

A.4 Proof Date Publication in the Official Journal of the EU on March 31, 2025; pp. 153 to 166 of the annexes; para. 2

A.5 Annexes to the EU Commission Implementing Decision of February 12, 2025; pp. 167 to 200 of the annexes; paras. 3, 40, 46, 71

A.6 The Potential of Extracellular Vesicle-Mediated Spread of Self-Amplifying RNA and aWay to Mitigate It, Maurizio Federico; pp. 201 to 213 of the annexes; (color print), paras. 5, 13, 50, 80

A.7 European Parliament – Medicinal Products in the European Union – The Regulatory Framework for Medicinal Products for Human Use, Scientific Service for Members, April 2015; pp. 214 to 246 of the annexes; (color print), para. 21

A.8 EU Commission Report on Advanced Therapy Medicinal Products 28.3.14; pp. 247 to 262 of the annexes; (color print), paras. 22, 23

A.9 EU Commission Report COM(2017) 135 final I 22.3.2017; pp. 263 to 273 of the annexes; para. 24

A.10 European Commission, Enterprise and Industry Directorate-General, Implementation of the Advanced Therapies' Regulation, Amendments to Annex I to Directive 2001/83/EC as regards advanced therapy medicinal products, July 9, 2008; pp. 274 to 279 of the annexes; (color print), 65, 66

A.11. European Commission, Implementation of the Advanced Therapies' Regulation – Public Consultation Paper – Proposals to amend Annex I to Directive 2001/83/EC as regards Advanced Therapy Medicinal Products, April 8, 2008; pp. 280 to 295 of the annexes; para. 65

A.12 Excerpt from GAVI website – board – CEO José Manuel Barroso; pp. 296 to 298 of the appendices; (color print), para. 57

A.13 Michael Palmer MD, Sucharit Bhakdi MD, Wolfgang Wodarg MD, The immunological and biochemical principles of mRNA vaccine toxicity; pp. 299 to 389 of the appendices; (color print), paras. 75, 80

A.14 The Immunologic Downsides Associated with the Powerful Translation of Current COVID-19 Vaccine mRNA Can Be Overcome by Mucosal Vaccines, Maurizio Federico; pp. 390 to 399 of the appendices; (color print), para. 80