(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
12 December 2024 (12.12.2024)

WIPO | PCT

(10) International Publication Number
WO 2024/251800 A1

(51) International Patent Classification:
A61M 5/20 (2006.01) *A61M 5/32* (2006.01)

(21) International Application Number:
PCT/EP2024/065444

(22) International Filing Date:
05 June 2024 (05.06.2024)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
23315235.4 05 June 2023 (05.06.2023) EP

(71) Applicant: **SANOFI** [FR/FR]; 46 avenue de la Grande Armée, 75017 Paris (FR).

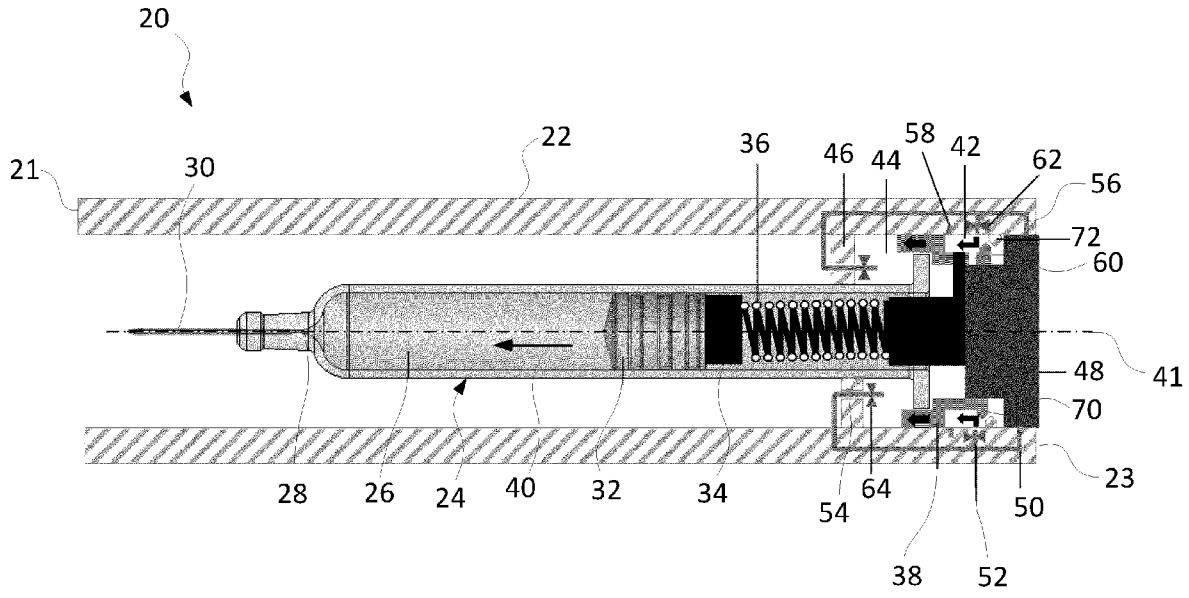
(72) Inventors: **GEIGER, Claus**; c/o Sanofi-Aventis Deutschland GmbH, 65926 Frankfurt am Main (DE). **KEIM, Moritz**; c/o Sanofi-Aventis Deutschland GmbH, 65926 Frankfurt am Main (DE). **KÜHN, Bernd**; c/o Sanofi-Aventis Deutschland GmbH, 65926 Frankfurt am Main (DE). **SCHABBACH, Michael**; c/o Sanofi-Aventis Deutschland GmbH, 65926 Frankfurt am Main (DE). **WERNER, Meinolf**; c/o GPE GmbH, 67551 Worms (DE).

(74) Agent: **SCHMIDT, Christian**; Zwicker Schnappauf & Partner Patentanwälte PartG mbB, Hansastr. 32, 80686 München (DE).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, MG, MK, MN, MU, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH,

(54) Title: DRUG DELIVERY DEVICE

FIG. 1



(57) Abstract: A drug delivery device (20) is provided. The drug delivery device (20) comprises: a housing (22) for accommodating a drug container (24); a separating wall (38), being in an initial position in an initial state of the drug delivery device (20), being movable relative to the housing (22) for the dispensing operation, and sealingly separating a first chamber (42) within the housing (22) from a second chamber (44) within the housing (22); a pressure source for providing a predetermined gas pressure, the pressure source being configured for communicating with the first chamber (42) for driving the separating wall (38) to an operating position of the separating wall (38) for the dispensing operation, and for communicating with the second chamber (44) for driving the separating wall (38) from the operating position to a final position of the separating wall (38) after the dispensing operation is finished.

WO 2024/251800 A1

[Continued on next page]

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, CV, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SC, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, ME, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *of inventorship (Rule 4.17(iv))*

Published:

— *with international search report (Art. 21(3))*

Title

Drug delivery device

Background

The present disclosure relates to a drug delivery device.

In drug delivery devices, drug is often delivered to a user via a needle which pierces the skin of the user (e.g. a patient). The drug may be accommodated within a drug container of the drug delivery device, e.g. within a syringe arranged or to be arranged within the drug delivery device. Conventional drug delivery devices comprising syringes and an associated drive mechanism have a shape basically corresponding to the shape of the syringe. In particular, conventional drug delivery devices comprising syringes have an elongated cylindrical shape, wherein an axis of the drug delivery device may correspond to an axis of the needle. Such a drug delivery device may often be referred to as pen-type device. A needle of the syringe may be protected by a needle sleeve, a needle shield, and/or a cap of the drug delivery device.

In many conventional drug delivery devices, the force needed for the dispensing operation is introduced mechanically. However, when a relative high amount of drug shall be injected by the drug delivery device, a corresponding high force has to be applied in order to dispense the drug and mechanical approaches are limited in this context. Alternative drive concepts may be advantageous to deliver a larger amount of medication. Further, with mechanical solutions, the required installation space within the drug delivery devices often is comparatively large. Furthermore, with increasing digitalization, there may be a need for new forms of controllable drives for drug delivery devices.

Summary

It is an object of the present disclosure to facilitate improvements associated with drug delivery devices, particularly with respect to size and operability.

This object is achieved by the disclosed subject-matter, for example by the subject-matter defined in the appended independent claim. Advantageous refinements and developments are subject to dependent claims and/or set forth in the description below.

One aspect of the present disclosure relates to a drug delivery device, comprising: a housing for accommodating a drug container; a separating wall, the separating wall being in an initial position in an initial state of the drug delivery device, the separating wall being movable relative to the housing, e.g. towards a distal end of the housing or away from a proximal end of the housing, for a dispensing operation, and the separating wall sealingly separating a first chamber within the housing from a second chamber within the housing; a pressure source for providing a predetermined gas pressure, the pressure source being configured for communicating with the first chamber for driving the separating wall to an operating position of the separating wall for the dispensing operation, and for communicating with the second chamber for driving the separating wall from the operating position to a final position of the separating wall after the dispensing operation is finished. The separating wall may be configured to sealingly separate the first chamber within the housing from the second chamber within the housing in the initial and/or operating position of the separating wall. The separating wall may also be configured to sealingly separate the first chamber within the housing from the second chamber within the housing in the initial, final and/or operating position of the separating wall.

The housing may have a distal end for facing an injection site during the dispensing operation and may have a proximal end facing away from the distal end, e.g. if the drug delivery device is a pen-type drug delivery device. The separating wall may be movable towards the distal end of the housing or away from the proximal end for the dispensing operation. The housing may have an elongate shape. The first chamber may be arranged between the separating wall and the proximal end of the housing and the second chamber may be arranged between the separating wall and the distal end of the housing. The pressure source may be configured for communicating with the first chamber for driving the separating wall towards the distal end of the housing or away from the proximal end of the housing to the operating position of the separating wall for the dispensing operation, and for communicating with the second chamber for driving the separating wall from the operating position towards the proximal end of the housing or away from the distal end of the housing to the final position of the separating wall after the dispensing operation is finished. The drug container may be arranged within the housing. If the drug container is arranged within the housing, a distal end of the drug container may face the distal end of the housing and/or a proximal end of the drug container may the proximal end of the housing. The drug container may contain a drug. The drug may be a medicament.

The drug delivery device may be referred to as automatically operated syringe and/or auto-injector. The drug delivery device may be a fully functional drug delivery device. The described drug delivery device may be driven by gas. In an autoinjector the energy for the drug delivery operation may be prestored in an energy storage member. That is to say, the user does not

have to provide the energy for the drug delivery operation, e.g. when preparing the drug delivery device for use. Rather, this energy may be preloaded into the system by the manufacturer. For example, a gas cartridge comprising gas, e.g. propellant gas, under high pressure or a battery for driving a pump for generating the gas pressure may be used as the energy storage member to provide the energy for the drug delivery operation.

The drug delivery device enables to firstly bring an injection member of the drug delivery device in contact with an injection site by the separating wall being moved from its initial position to its operating position. For example, in case of a needle as injection member, the needle may pierce the skin of a user, when the separating wall is moved from its initial position to its operating position. In other embodiments, in case of a nozzle as injection member, the nozzle may come in contact with the injection site, when the drug container is moved from its initial position to its operating position. Then, a drug within a drug chamber of the drug container may be injected into the injection site via the injection member and by the gas pressure within the first chamber (e.g. only due to the energy transferred with the drug onto the skin; in other words, the drug delivery device may be a needleless jet injector).

The separating wall and/or the pressure source may be configured for injecting the drug into the injection site, while the separating wall is in its operating position. Further, the drug delivery device may enable to protect or retract the injection member after the injection of the drug so that there is no risk of injury for the user by retracting the separating wall from its operating position to its final position. A motion sequence of the separating wall, which may lead to a movement of the injection member to the injection site firstly, to an injection of the drug secondly, and finally to a retraction of the separating wall into its final position, may be achieved with gas, e.g. compressed air, only. Each of the positions of the separating wall may be reached only after the separating wall has assumed the previous position.

In one embodiment, the separating wall may be formed by or be a separating member. Hence, features described in connection with the separating wall do also apply to the separating member and vice versa.

In one embodiment, the separating wall is configured to hold the drug container such that the drug container is moved together with the separating wall, e.g. when the separating wall is moved from its initial position to its operating position and/or when the separating wall is moved from its operating position to its final position. If the drug container is arranged within the housing, the separating wall may be coupled to the drug container in order to hold and move the drug container relative to the housing. Thus, the drug container may be moved together with the separating wall relative to the housing. When the separating wall is in its initial position, the drug

container also may be in its initial position. When the separating wall is in its operating position, the drug container may be in its operating position also. When the separating wall is in its final position, the drug container may be in its final position also.

In one embodiment, the drug delivery device comprises a fluid channel within the housing. The fluid channel may communicate with the pressure source. The fluid channel may be configured for enabling a communication between the pressure source and/or the first chamber. The fluid channel may be configured for preventing a (fluid) communication between the pressure source and the second chamber in the initial state. The fluid channel may be configured for preventing the (fluid) communication between the first chamber and the pressure source and/or for enabling the communication of the second chamber with the pressure source after the dispensing operation is finished. The fluid channel may enable to distribute the gas and thereby the gas pressure to that area of the drug delivery device where the gas and the gas pressure are currently needed. The fluid channel may extend from the pressure source to the first chamber and to the second chamber. For example, the fluid channel may have three branches. A first branch of the fluid channel may extend to the first chamber, a second branch of the fluid channel may extend to the second chamber, and a third branch of the fluid channel extend to the pressure source. Which branch of the fluid channel currently is in (fluid) communication with the pressure source may depend on the position of the separating wall.

In one embodiment, the drug delivery device comprises a first valve which is configured for coupling the pressure source to the first chamber via the fluid channel in the initial state of the drug delivery device and/or for decoupling the first chamber from the pressure source after the dispensing operation is finished. The drug delivery device may further comprise a second valve which is configured for decoupling the second chamber from the pressure source in the initial state and/or for coupling the second chamber with the pressure source after the dispensing operation is finished. For example, the first valve may be arranged at the first branch of the fluid channel and/or the second valve may be arranged at the second branch of the fluid channel. The first and second valve enable an easy way to couple the pressure source to the first chamber via the fluid channel in the initial state of the drug delivery device and to decouple the first chamber from the pressure source after the dispensing operation is finished and, respectively, to decouple the second chamber from the pressure source in the initial state and to couple the second chamber with the pressure source after the dispensing operation is finished.

In one embodiment, the first valve is configured for coupling the pressure source to the first chamber via the fluid channel, e.g. when the gas pressure within the first chamber is below a predetermined first pressure threshold, and/or for decoupling the first chamber from the

pressure source, e.g. when the gas pressure within the first chamber corresponds to or exceeds the predetermined first pressure threshold. In other embodiments, e.g. alternatively or additionally, the second valve may be configured for decoupling the second chamber from the pressure source, e.g. when the gas pressure in the fluid channel is below a predetermined second pressure threshold, and/or for coupling the second chamber with the pressure source, e.g. when the gas pressure within the fluid channel corresponds to or exceeds the predetermined second pressure threshold. The first pressure threshold may be smaller than the second pressure threshold. In other embodiments, the first pressure threshold may correspond to the second pressure threshold, e.g. the thresholds may be equal.

In one embodiment, the drug delivery device comprises a flexible gas tube. The flexible gas tube may be coupled or couplable to the drug container and which is configured for squeezing a drug out of the drug container upon being pressurized such that the drug is dispensed from the drug delivery device. The gas tube may be pressurized by filling gas into the gas tube. When the gas tube is filled by gas, the gas tube is inflated, and the volume occupied by the gas tube and thereby a length of the gas tube may be increased, e.g. compared to the "empty", e.g. non-pressurized, gas tube.

The drug container may comprise a reservoir for accommodating the drug. The gas tube may act on the drug container such that the drug may be squeezed out of the reservoir by the gas tube. For example, the gas tube may act on a pressure member such that the pressure member may squeeze the drug out of the reservoir. For example, the gas tube may push the pressure member in a dispensing direction (e.g. towards the distal end of the housing or away from the proximal end) upon being pressurized because of the increased length of the pressurized gas tube. The pressure member may be a stopper, which may be movably arranged within the drug container and/or which may sealingly close the reservoir, e.g. if the drug container is a syringe or cartridge. In other embodiments, the pressure member may be a plunger for moving the stopper in the dispensing direction. The stopper may sealingly close the reservoir of the drug container proximally. The drug may be enclosed by inner walls of the drug container and by the stopper. In other embodiments, e.g. if the drug container is a pouch, the pressure member may be the plunger and may be pressed against the outside of a flexible wall of the pouch for squeezing the pouch and the drug out of the pouch. The gas tube may communicate with the first chamber, e.g. at a proximal end of the gas tube. The gas tube, e.g. the pressurized and/or non-pressurized gas tube, may have the form of a helix. The plunger may be arranged between the gas tube and the stopper. Thus, the plunger may be coupled or couplable to the stopper and/or the gas tube. The plunger may be configured for being pushed by the gas tube and for pushing the stopper in the dispensing direction. Thus, the plunger may act as a pressure transferring element and/or may be regarded as the pressure member.

In one embodiment, the gas tube is configured for communicating with the first chamber, e.g. when the separating wall is in its operating position, and/or for being decoupled from the first chamber, e.g. when the separating wall is in its initial and/or final position.

In one embodiment, the separating wall comprises a gas conduit. The gas conduit may be provided to communicatively couple the first chamber and the gas tube, e.g. when the separating wall is in its operating position. When the separating wall is not in its operating position, the gas conduit may be closed and/or not in communication with the pressure source. Thus, the gas tube may not be pressurized while the separating wall (and thereby the drug container) is not in the operating position.

In one embodiment, the gas tube comprises an opening for receiving the gas, e.g. when the separating wall is in its operating position. The opening may be closed when the separating wall is not in its operating position. For example, the opening may be closed when the separating wall (and thereby the drug container) is in the initial position. The opening for receiving the gas may be formed at a proximal end of the gas tube, the proximal end of the gas tube facing the proximal end of the housing.

In one embodiment, the gas conduit and the opening of the gas tube may be formed and arranged such that the gas conduit and/or the opening are closed, when the separating wall is in its initial and/or final position. In other embodiments, e.g. alternatively or additionally, the gas conduit and the opening of the gas tube may be formed and arranged such that the gas conduit and/or the opening are opened, such that an interior of the gas tube may communicate with the first chamber via the opening and the gas conduit, for example when the separating wall is in its operating position.

In one embodiment, the drug delivery device comprises a closing body, e.g. for closing the gas conduit of the separating wall and the opening of the gas tube. The closing body may be arranged at the housing. The closing body may be arranged to cover the gas conduit of the separating wall and/or the opening of the gas tube, e.g. when the separating wall is in its initial and/or final position, and/or arranged to expose the gas conduit and/or the opening, e.g. when the separating wall is in its operating position.

In one embodiment, the pressure source comprises or forms the closing body. This may contribute to a simple design of the drug delivery device, because no separate closing body has to be arranged. This may contribute to an easy, quick, and/or cost-efficient drug delivery device.

In one embodiment, the drug delivery device comprises at least one first engaging element. The at least one first engaging element may be arranged at the separating wall. In other embodiments, e.g. alternatively or additionally, the drug delivery device comprises at least one second engaging element. The at least one second engaging element may be arranged at the housing. The first and second engaging elements may be configured for being engaged to each other, e.g. when the separating wall (and, optionally, thereby the drug container) reaches its final position. This may prevent the drug container from being moved proximally and/or distally, after the dispensing operation of the device has been finished and/or after the injection member has been retracted from the injection site.

In one embodiment, the drug delivery device comprises an end stop being coupled, e.g. fixed, to the housing and being configured for preventing the separating wall from being moved further, e.g. when the separating wall reaches its operating position. The end stop may define the operating position of the separating wall. The end stop may be arranged at a distal side of the separating wall, wherein the distal side may face the distal end of the housing and/or face away from the proximal end of the housing. The end stop may block the separating wall from further moving in the distal or dispensing direction. The end stop may be configured for preventing the separating wall from being moved further towards the distal end of the housing or further away from the proximal end of the housing, e.g. when the separating wall reaches or is in its operating position.

The drug delivery device may comprise a needle as injection member for injecting the drug into an injection site, wherein the needle may be communicatively coupled to the drug container at an outlet of the drug container. The needle may be configured for piercing the skin of the user. The needle may extend in a direction parallel to an axis of the drug delivery device and/or parallel to the dispensing direction, e.g. along an axis extending from the proximal to the distal end (of the housing). A tip of the needle arranged to pierce the users skin may be furthest away from the proximal end of the housing and/or define the distal end (of the needle). The needle may be in or may be brought into fluid communication with an interior of the drug container, in particular with the reservoir. The needle may be integrated into the drug container. The drug, e.g. a liquid medicament, may be expediently arranged in the interior of the drug container. The drug container may be a syringe, e.g. a syringe with a preinstalled needle, such as a staked needle. Alternatively, the drug container may be a cartridge, which may have to be brought into fluid communication with the needle, e.g. by piercing a cartridge septum with the needle. Optionally, the drug delivery device may comprise a second needle. The second needle may be used to pierce the container, e.g. a cartridge septum. A first needle (e.g. the needle for piercing the skin and/or for injecting the drug into the injection site) may communicate with the second

needle, e.g. by a (flexible) drug conduit, for guiding the drug from the drug container through the second needle towards the first needle.

In one embodiment, the drug container is a syringe. Alternatively, the drug container may be a cartridge. The drug container may comprise the needle, e.g. the first or second needle, or may be coupled with the needle, e.g. the first or second needle, manually before using the drug delivery device or automatically when using the drug delivery device.

In one embodiment, the drug delivery device comprises the drug container, wherein the drug container comprises the reservoir in which the drug is accommodated.

We note that features described above and below in conjunction with different embodiments or aspects can be combined with one another, even if such a combination is not explicitly disclosed herein above or below. Further features, advantages and expediencies of the disclosure and, particularly, of the proposed concepts will become apparent from the following description of the exemplary embodiments in conjunction with the drawings.

Brief description of the drawings

Figure 1 illustrates a cross-sectional side view of an exemplary embodiment of a drug delivery device in an initial state of the drug delivery device.

Figure 2 illustrates a cross-sectional side view of the drug delivery device of figure 1 in an operating state of the drug delivery device.

Figure 3 illustrates an expanded structural formula, molecular formula, and molecular weight of fitusiran.

Description of the exemplary embodiments

Identical elements, elements of the same kind and identically or similarly acting elements may be provided with the same reference numerals in the drawings.

Figure 1 illustrates a cross-sectional side view of an exemplary embodiment of a drug delivery device in an initial state of the drug delivery device 20. The drug delivery device 20 may be referred to as automatically operated syringe and/or auto-injector. The drug delivery device 20 may be a fully functional drug delivery device 20. The drug delivery device 20 may be a single shot device, i.e. it may be provided to dispense only one dose. The drug delivery device 20 may

be a disposable drug delivery device 20, that is to say a drug delivery device 20 which is disposed of after its use. The drug delivery device 20 may be driven by gas. In other embodiments, the drug delivery device 20 may be reusable and/or refillable.

The drug delivery device 20 comprises a housing 22, a pressure arrangement and a plunger arrangement. The housing 22 comprises a distal end 21 and a proximal end 23 facing away from the distal end 21. The distal end 21 may be configured for facing an injection site, during usage of the drug delivery device 20. For example, during a dispensing operation of the drug delivery device 20, the distal end 21 of the housing 22 may be arranged on the skin of a user. In this context, the distal end 21 of the housing 22 may be referred to as bearing surface. The housing 22 may be provided to retain and/or retains a drug container 24 in its interior. If the drug container 24 is arranged within the housing 22, a distal end of the drug container 24 may face the distal end 21 of the housing 22 and a proximal end of the drug container 24 may face the proximal end 23 of the housing 22.

The drug container 24 comprises an outlet 28 at or close to a dispensing end, i.e. a distal end, of the drug container 24. A needle 30 may be arranged at the distal end of the drug container 24. The needle 30 may open out into the outlet 28 and/or may communicate with the outlet 28. The drug container 24 may comprise a reservoir 26. A drug, i.e. a medicament, e.g. liquid medicament, may be arranged within the reservoir 26. The reservoir 26 may be fluid-tightly closed by a stopper 32. So, the drug may be enclosed by inner walls of the drug container 24 and by the stopper 32. The stopper 32 may be movably retained in the drug container 24 and may seal the drug container 24 proximally. The stopper 32 may be displaced towards the outlet 28 of the drug container 24 by a pressure member of the pressure arrangement to dispense the drug retained within the reservoir 26 through the outlet 28 and the needle 30. In particular, the stopper 32 may be movable in a dispensing direction 40 towards the outlet 28. When the stopper 32 is moved in the dispensing direction 40 by the pressure member, the drug is dispensed through the outlet 28 and the needle 30. The dispensing direction 40 may be parallel to an axis 41 of the drug delivery device 20. In other embodiments, the drug container 24 may be a pouch. In the latter case, the pressure member may be pressed against the outside of a flexible wall of the pouch for squeezing the pouch and thereby the drug out of the pouch.

The needle 30 may be an integral part of the drug container 24, e.g. (permanently or releasably) connected to a drug container body of the drug container 24 or separate from the drug container 24. In the first case, the drug container 24 may be a syringe. In the second case, the drug container 24 may be a cartridge. In case a cartridge is used as drug container 24, initially, the drug container 24 and the needle 30 may be fluidly disconnected, and a fluid communication between the reservoir 26 and the needle 30 may be only established during operation of the

drug delivery device 20, e.g. by the needle 30 piercing a septum of the cartridge. Further, instead of only one single needle, two separate needles may be arranged. In this context, the needle 30 for piercing the skin of the user may be referred to as first needle 30 and a second needle (not shown) may be used for piercing the septum of the cartridge, wherein the first needle 30 and the second needle may communicate with each other via a drug conduit (not shown).

The pressure arrangement may comprise a first chamber 42, a second chamber 44, a separating wall 38 sealingly separating the first chamber 42 from the second chamber 44, and a pressure source for providing a predetermined gas pressure. Further, the pressure arrangement may comprise an end stop 46, a closing body 48 and a fluid channel 50.

The separating wall 38 may be in its initial position in the initial state of the drug delivery device 20, as shown in figure 1. The separating wall 38 may be movable towards the distal end 21 of the housing 22 for the dispensing operation. The separating wall 38 sealingly separates the first chamber 42 from the second chamber 44. The first and second chamber 42, 44 are arranged within the housing 22. The first chamber 42 may be arranged between the separating wall 38 and the proximal end 23 of the housing 22. The second chamber 44 may be arranged between the separating wall 38 and the distal end 21 of the housing 22. The separating wall 38 may be configured to hold the drug container 24 such that the drug container 24 may be moved together with the separating wall 38, when the separating wall 38 is moved from its initial position to its operating position and when the separating wall 38 is moved from its operating position to its final position. The separating wall 38 may be coupled to the drug container 24 in order to hold and move the drug container 24 relative to the housing 22. When the separating wall 38 is in its initial position, the drug container 24 also may be in its initial position. When the separating wall 38 is in its operating position, the drug container 24 may be in its operating position also. When the separating wall 38 is in its final position, the drug container 24 may be in its final position also.

The pressure source may comprise a gas cartridge. The gas cartridge may be pre-filled with gas, e.g. propellant gas, under high pressure, e.g. by a manufacturer of the drug delivery device. In other embodiments, the drug delivery device 20 may comprise an electrical pump and a battery for driving the pump for generating the gas pressure within the gas cartridge. The electrical pump may be controlled by a controller (not shown) of the drug delivery device 20. The pressure source may comprise or may form the closing body 48. In other words, the pressure source may act and/or may be used as the closing body 48 and/or the pressure source and the closing body 48 may be embodied by the same entity. In other embodiments, the pressure source may be arranged separate from the closing body 48. The pressure source

may be configured for communicating with the first chamber 42 for driving the separating wall 38 towards the distal end 21 of the housing 22 to an operating position of the separating wall 38 for the dispensing operation (see figure 2). The pressure source may be configured for communicating with the second chamber 44 for driving the separating wall 38 from the operating position (see figure 2) towards the proximal end 23 of the housing 22 to a final position of the separating wall 38 after the dispensing operation is finished (not shown). The separating wall 38 is configured to sealingly separate the first chamber 42 within the housing 22 from the second chamber 44 within the housing 22 in the initial, final and/or operating position of the separating wall (38).

The fluid channel 50 may be formed within and/or by the housing 22, e.g. by a recess within the housing 22. The fluid channel 50 may communicate with the pressure source. The fluid channel 50 may be configured for enabling a communication between the pressure source and the first chamber 42 and for preventing a communication between the pressure source and the second chamber 44 in the initial state of the drug delivery device 20. The fluid channel 50 may be configured for preventing the communication between the first chamber 42 and the pressure source and for enabling the communication of the second chamber 44 with the pressure source after the dispensing operation is finished. The fluid channel 50 may be configured to distribute the gas and thereby the gas pressure from the pressure source to that area of the drug delivery device 20 where the gas and the gas pressure are currently needed, e.g. the first chamber 42, the second chamber 44 and/or the gas tube 36. The fluid channel 50 may extend from the pressure source to the first chamber 42 and to the second chamber 44. For example, the fluid channel 50 may have three branches. A first branch 52 of the fluid channel 50 may extend to the first chamber 42, a second branch 54 of the fluid channel 50 may extend to the second chamber 44, and a third branch 56 of the fluid channel 60 may extend to the pressure source, e.g. the closing body 48.

The pressure arrangement may further comprise a first valve 62. The first valve 62 may be arranged at an inlet to the first chamber 42. For example, the first valve 62 may be arranged at the first branch 52 of the fluid channel 50. The first valve 62 may be configured for coupling the pressure source to the first chamber 42 via the fluid channel 50, in particular via the first branch 52 of the fluid channel 50, in the initial state of the drug delivery device 20. In particular, the first valve 62 may be configured for coupling the pressure source to the first chamber 42 via the fluid channel 50, when the gas pressure within the first chamber 42 is below a predetermined first pressure threshold. The first valve 62 may be a pressure relief valve which closes as soon as the overpressure within the first chamber 42 reaches the first pressure threshold. At the same time, the first valve 62 may allow the overpressure in the first chamber 42 to escape to the atmosphere through a vent opening 58 within the housing 22. The first valve 62 may be further

configured for decoupling the first chamber 42 from the pressure source after the dispensing operation is finished. So, the first valve 62 may be configured for decoupling the first chamber 42 from the pressure source, when the gas pressure within the first chamber 42 corresponds to or exceeds the first pressure threshold.

The pressure arrangement may further comprise a second valve 64. The second valve 64 may be arranged at the second branch 54 of the fluid channel 50. The second valve 64 may be configured for decoupling the second chamber 44 from the pressure source in the initial state of the drug delivery device 20. In particular, the second valve 64 may be configured for decoupling the second chamber 44 from the pressure source, when the pressure in the fluid channel 50 is below a second predetermined pressure threshold. In addition, the second valve 64 may be configured for coupling the second chamber 44 with the pressure source, when the gas pressure within the fluid channel 50 corresponds to or exceeds the second pressure threshold. The second valve 64 further may be configured for coupling the second chamber 44 with the pressure source after the dispensing operation is finished. The first predetermined pressure threshold may be smaller than or may be the same as the second predetermined pressure threshold.

The plunger arrangement may comprise a plunger 34 and a gas tube 36, in particular a flexible and/or inflatable gas tube. The plunger 34 may be referred to as pressure member. The plunger 34 may be arranged between the gas tube 36 of the plunger arrangement and the stopper 32. The plunger 34 may be coupled or couplable to the stopper 32 and/or the gas tube 36. The plunger 34 may be configured for being pushed by the gas tube 36 and for pushing the stopper 32 towards the distal end 21 of the housing 22. So, the plunger 34 may act as a pressure transferring element.

The flexible gas tube 36 may be inflatable. The gas tube 36 may be coupled or couplable to the drug container 24. The flexible gas tube 36 may be configured for squeezing the drug out of the drug container 24 upon being pressurized such that the drug is dispensed from the drug delivery device 20. The gas tube 36 may be pressurized by filling gas, e.g. air, into the gas tube 36, e.g. by the pressure source. When the gas tube 36 is filled with gas, the gas tube 36 is inflated, and the volume occupied by the gas tube 36 and a length of the gas tube 36 are increased. The pressurized gas tube 36 may have the form of a helix. The gas tube 36 may comprise an opening 78 (see figure 2) for receiving the gas at a proximal end 74 of the drug container 24. The opening 78 may be closed when the separating wall 38 is not in its operating position, e.g. when the separating wall 38 is in its initial position as shown in figure 1.

The gas tube 36 may be configured for communicating with the first chamber 42, when the separating wall 38 is in its operating position, and for being decoupled from the first chamber 42, when the separating wall 38 is in its initial or final position. For example, the separating wall 38 may comprise a gas conduit 60 communicatively coupling the first chamber 42 and the gas tube 36, when the separating wall 38 is in its operating position (see figure 2). When the separating wall 38 is not in its operating position, the gas conduit 60 may be closed. So, the gas tube 36 may not be pressurized while the separating wall 38 and thereby the drug container 24 are not in their operating positions. In particular, the gas conduit 60 and the opening 78 of the gas tube 36 may be formed and arranged such that the gas conduit 60 and/or the opening 78 are closed, when the separating wall 38 is in its initial and/or final position, and that the gas conduit 60 and the opening 78 are opened such that an interior of the gas tube 36 may communicate with the first chamber 42 via the opening 78 and the gas conduit 60, when the separating wall 38 is in its operating position. For example, the closing body 48 may be configured for closing the gas conduit 60 of the separating wall 38 and the opening 78 of the gas tube 36 when the separating wall 38 and the drug container 24 are in their initial and/or final positions. The closing body 48 may be arranged at the housing 22. The closing body 48 may cover the gas conduit 60 of the separating wall 38 and the opening 78 of the gas tube 36, when the separating wall 38 is in its initial and/or final position, and may expose the gas conduit 60 and the opening 78, when the separating wall 38 is in its operating position.

The gas tube 36 may act on the drug container 24 such that the drug may be squeezed out of the drug container 24 by the gas tube. For example, the gas tube 36 may act on the pressure member such that the pressure member may squeeze the drug out of the reservoir 26. For example, the gas tube 36 may push the pressure member in the dispensing direction 40 towards the distal end 21 of the housing 22 upon being pressurized. The pressure member may be the 32 stopper or the plunger 34, or may comprise the stopper 32 and/or the plunger 34.

The drug delivery device 20 may comprise first engaging elements 70 being arranged at the separating wall 38 and second engaging elements 72 being arranged at the housing 22. The first and second engaging elements 70, 72 are configured for being engaged to each other, if the separating wall 38 and thereby the drug container 24 reach their final position (not shown).

The drug delivery device 20 may comprise an end stop 46 being coupled to the housing 22. The end stop 46 may be arranged at a distal side of the separating wall 38. The end stop 46 may be configured for preventing the separating wall 38 from being moved further towards the distal end 21 of the housing 22, when the separating wall 38 reaches its operating position. So, the end stop 46 may define the operating position of the separating wall 38.

The drug delivery device 20 may comprise a cap (not shown). The cap may be arranged at a dispensing end of the needle 30. The cap may be detachably connected to the remainder of the drug delivery device 20, e.g. to the housing 22. The cap may cover a tip of the needle 30.

Figure 1 shows the initial state of the drug delivery device 20 before inserting the needle 30 into the injection site and before injecting the drug into the injection site. When the drug delivery device 20 is activated, compressed gas, e.g. air, flows through the fluid path 50 and fills the first chamber 42. Due to the corresponding overpressure in the first chamber 42, the separating wall 38 may be moved in the dispensing direction 40 and thus moves the drug container 24 into its operating position (see figure 2). When the separating wall 38 and the drug container 24 are moved from their initial positions to their operating positions, the injection member is brought into contact with the injection site. For example, in case of the needle 30 being the injection member, the needle 30 may pierce the skin of the user, when the separating wall 38 and the drug container 24 are moved from their initial positions to their operating positions.

Figure 2 illustrates a cross-sectional side view of the drug delivery device of figure 1 in the operating state of the drug delivery device 20. In the operating state the needle 30 is inserted into the injection site and the drug is injected into the injection site.

When the separating wall 38 and the drug container 24 are moved from their initial positions (see figure 1) to their operating positions shown in figure 2, the gas conduit 60 and the opening 78 may be opened so that the first chamber 42 and the gas tube 36 may be connected and may communicate with each other. Then, the gas tube 36 may be filled with compressed air and thereby pressurized and inflated. The gas tube 36 may expand in the dispensing direction 40 and may press the plunger 34 against the stopper 32. In particular, an accordion-like expansion of the gas tube 36 may push the plunger 34 towards its distal position. The stopper 32 may be moved by the plunger 34 in the dispensing direction 40 and the drug may be dispensed through the outlet 28 and/or the needle 30. As soon as the plunger 34 has reached its distal position, which may be its end position, the overpressure in the first chamber 42 continues to build up. When the overpressure within the first chamber 42 reaches the predetermined first pressure threshold, the first valve 62 closes the first branch 52. The closing of the first valve 62 and the first branch 52 may cause an overpressure to build up in the fluid channel 50 upstream of the second valve 64. When the overpressure in the fluid channel 50 reaches a second predetermined pressure threshold, the second valve 64 may open so that the second chamber 44 may be filled with the gas. If there is only atmospheric pressure in the first chamber 42 and if the vent opening 58 is permanently open, the gas pressure in the second chamber 44 may be sufficient to press the separating wall 38 together with the drug container 24 in a direction opposite to the dispensing direction 40 into their final positions, which may be beyond their

initial positions (in other words: the final position may be proximally offset from the initial position). During this movement, the needle 30 may be withdrawn from the skin. In the final position, the separating wall 38 may be locked by the engaging elements 70, 72 being engaged to each other. For example, the first engaging elements 70 may snap in behind the second engaging elements 72, when the separating wall 38 reaches its final position. The separating wall 38 and the drug container 24 may be locked (e.g. against distal and/or proximal movement) and thereby secured in their final positions to permanently protect the needle 30 after its use.

The proposed autoinjector may be gas-driven with automatic needle insertion and/or automatic needle retraction. However, it should be noted that the proposed movability of the separating wall also offers the other options and is not limited to autoinjectors with needle injection and/or needle withdrawal. Rather, the separating wall can be used to selectively couple a needle shroud to the pressure source to deploy the needle shroud to cover a needle in its final position.

The terms “drug” or “medicament” are used synonymously herein and describe a pharmaceutical formulation containing one or more active pharmaceutical ingredients or pharmaceutically acceptable salts or solvates thereof, and optionally a pharmaceutically acceptable carrier. An active pharmaceutical ingredient (“API”), in the broadest terms, is a chemical structure that has a biological effect on humans or animals. In pharmacology, a drug or medicament is used in the treatment, cure, prevention, or diagnosis of disease or used to otherwise enhance physical or mental well-being. A drug or medicament may be used for a limited duration, or on a regular basis for chronic disorders.

As described below, a drug or medicament can include at least one API, or combinations thereof, in various types of pharmaceutical formulations, for the treatment of one or more diseases. Examples of API may include small molecules having a molecular weight of 500 Da or less; polypeptides, peptides and proteins (e.g., hormones, growth factors, antibodies, antibody fragments, and enzymes); carbohydrates and polysaccharides; and nucleic acids, double or single stranded DNA (including naked and cDNA), RNA, antisense nucleic acids such as antisense DNA and RNA, small interfering RNA (siRNA), ribozymes, genes, and oligonucleotides. Nucleic acids may be incorporated into molecular delivery systems such as vectors, plasmids, or liposomes. Mixtures of one or more drugs are also contemplated.

The drug or medicament may be contained in a primary package or “drug reservoir” adapted for use with a drug delivery device. The drug reservoir 101a may be, e.g., a cartridge, syringe, reservoir, or other solid or flexible vessel (bag) configured to provide a suitable chamber for storage (e.g., short- or long-term storage) of one or more drugs. For example, in some instances, the chamber may be designed to store a drug for at least one day (e.g., 1 to at least

30 days). In some instances, the chamber may be designed to store a drug for about 1 month to about 2 years. Storage may occur at room temperature (e.g., about 20°C), or refrigerated temperatures (e.g., from about - 4°C to about 4°C). In some instances, the drug reservoir may be or may include a dual-chamber cartridge configured to store two or more components of the pharmaceutical formulation to-be-administered (e.g., an API and a diluent, or two different drugs) separately, one in each chamber. In such instances, the two chambers of the dual-chamber cartridge may be configured to allow mixing between the two or more components prior to and/or during dispensing into the human or animal body. For example, the two chambers may be configured such that they are in fluid communication with each other (e.g., by way of a conduit between the two chambers) and allow mixing of the two components when desired by a user prior to dispensing. Alternatively or in addition, the two chambers may be configured to allow mixing as the components are being dispensed into the human or animal body.

The drugs or medicaments contained in the drug delivery devices as described herein can be used for the treatment and/or prophylaxis of many different types of medical disorders. Examples of disorders include, e.g., diabetes mellitus or complications associated with diabetes mellitus such as diabetic retinopathy, thromboembolism disorders such as deep vein or pulmonary thromboembolism. Further examples of disorders are acute coronary syndrome (ACS), angina, myocardial infarction, cancer, macular degeneration, inflammation, hay fever, atherosclerosis and/or rheumatoid arthritis. Examples of APIs and drugs are those as described in handbooks such as Rote Liste 2014, for example, without limitation, main groups 12 (anti-diabetic drugs) or 86 (oncology drugs), and Merck Index, 15th edition.

Examples of APIs for the treatment and/or prophylaxis of type 1 or type 2 diabetes mellitus or complications associated with type 1 or type 2 diabetes mellitus include an insulin, e.g., human insulin, or a human insulin analogue or derivative, a glucagon-like peptide (GLP-1), GLP-1 analogues or GLP-1 receptor agonists, or an analogue or derivative thereof, a dipeptidyl peptidase-4 (DPP4) inhibitor, or a pharmaceutically acceptable salt or solvate thereof, or any mixture thereof. As used herein, the terms “analogue” and “derivative” refers to a polypeptide which has a molecular structure which formally can be derived from the structure of a naturally occurring peptide, for example that of human insulin, by deleting and/or exchanging at least one amino acid residue occurring in the naturally occurring peptide and/or by adding at least one amino acid residue. The added and/or exchanged amino acid residue can either be codable amino acid residues or other naturally occurring residues or purely synthetic amino acid residues. Insulin analogues are also referred to as "insulin receptor ligands". In particular, the term „derivative” refers to a polypeptide which has a molecular structure which formally can be derived from the structure of a naturally occurring peptide, for example that of human insulin, in

which one or more organic substituent (e.g. a fatty acid) is bound to one or more of the amino acids. Optionally, one or more amino acids occurring in the naturally occurring peptide may have been deleted and/or replaced by other amino acids, including non-codeable amino acids, or amino acids, including non-codeable, have been added to the naturally occurring peptide.

Examples of insulin analogues are Gly(A21), Arg(B31), Arg(B32) human insulin (insulin glargine); Lys(B3), Glu(B29) human insulin (insulin glulisine); Lys(B28), Pro(B29) human insulin (insulin lispro); Asp(B28) human insulin (insulin aspart); human insulin, wherein proline in position B28 is replaced by Asp, Lys, Leu, Val or Ala and wherein in position B29 Lys may be replaced by Pro; Ala(B26) human insulin; Des(B28-B30) human insulin; Des(B27) human insulin and Des(B30) human insulin.

Examples of insulin derivatives are, for example, B29-N-myristoyl-des(B30) human insulin, Lys(B29) (N- tetradecanoyl)-des(B30) human insulin (insulin detemir, Levemir®); B29-N-palmitoyl-des(B30) human insulin; B29-N-myristoyl human insulin; B29-N-palmitoyl human insulin; B28-N-myristoyl LysB28ProB29 human insulin; B28-N-palmitoyl-LysB28ProB29 human insulin; B30-N-myristoyl-ThrB29LysB30 human insulin; B30-N-palmitoyl- ThrB29LysB30 human insulin; B29-N-(N-palmitoyl-gamma-glutamyl)-des(B30) human insulin, B29-N-omega-carboxypentadecanoyl-gamma-L-glutamyl-des(B30) human insulin (insulin degludec, Tresiba®); B29-N-(N-lithocholyl-gamma-glutamyl)-des(B30) human insulin; B29-N-(ω-carboxyheptadecanoyl)-des(B30) human insulin and B29-N-(ω-carboxyheptadecanoyl) human insulin.

Examples of GLP-1, GLP-1 analogues and GLP-1 receptor agonists are, for example, Lixisenatide (Lyxumia®), Exenatide (Exendin-4, Byetta®, Bydureon®, a 39 amino acid peptide which is produced by the salivary glands of the Gila monster), Liraglutide (Victoza®), Semaglutide, Taspoglutide, Albiglutide (Syncria®), Dulaglutide (Trulicity®), rExendin-4, CJC-1134-PC, PB-1023, TTP-054, Langlenatide / HM-11260C (Efpeglenatide), HM-15211, CM-3, GLP-1 Eligen, ORMD-0901, NN-9423, NN-9709, NN-9924, NN-9926, NN-9927, Nodexen, Viador-GLP-1, CVX-096, ZYOG-1, ZYD-1, GSK-2374697, DA-3091, MAR-701, MAR709, ZP-2929, ZP-3022, ZP-DI-70, TT-401 (Pegapamodtide), BHM-034. MOD-6030, CAM-2036, DA-15864, ARI-2651, ARI-2255, Tirzepatide (LY3298176), Bamadutide (SAR425899), Exenatide-XTEN and Glucagon-Xten.

An example of an oligonucleotide is, for example: mipomersen sodium (Kynamro®), a cholesterol-reducing antisense therapeutic for the treatment of familial hypercholesterolemia or RG012 for the treatment of Alport syndrom.

Examples of DPP4 inhibitors are Linagliptin, Vildagliptin, Sitagliptin, Denagliptin, Saxagliptin, Berberine.

Examples of hormones include hypophysis hormones or hypothalamus hormones or regulatory active peptides and their antagonists, such as Gonadotropine (Follitropin, Lutropin, Choriongonadotropin, Menotropin), Somatropine (Somatropin), Desmopressin, Terlipressin, Gonadorelin, Triptorelin, Leuprorelin, Buserelin, Nafarelin, and Goserelin.

Examples of polysaccharides include a glucosaminoglycane, a hyaluronic acid, a heparin, a low molecular weight heparin or an ultra-low molecular weight heparin or a derivative thereof, or a sulphated polysaccharide, e.g. a poly-sulphated form of the above-mentioned polysaccharides, and/or a pharmaceutically acceptable salt thereof. An example of a pharmaceutically acceptable salt of a poly-sulphated low molecular weight heparin is enoxaparin sodium. An example of a hyaluronic acid derivative is Hylan G-F 20 (Synvisc®), a sodium hyaluronate.

The term “antibody”, as used herein, refers to an immunoglobulin molecule or an antigen-binding portion thereof. Examples of antigen-binding portions of immunoglobulin molecules include F(ab) and F(ab')2 fragments, which retain the ability to bind antigen. The antibody can be polyclonal, monoclonal, recombinant, chimeric, de-immunized or humanized, fully human, non-human, (e.g., murine), or single chain antibody. In some embodiments, the antibody has effector function and can fix complement. In some embodiments, the antibody has reduced or no ability to bind an Fc receptor. For example, the antibody can be an isotype or subtype, an antibody fragment or mutant, which does not support binding to an Fc receptor, e.g., it has a mutagenized or deleted Fc receptor binding region. The term antibody also includes an antigen-binding molecule based on tetravalent bispecific tandem immunoglobulins (TBTI) and/or a dual variable region antibody-like binding protein having cross-over binding region orientation (CODV).

The terms “fragment” or “antibody fragment” refer to a polypeptide derived from an antibody polypeptide molecule (e.g., an antibody heavy and/or light chain polypeptide) that does not comprise a full-length antibody polypeptide, but that still comprises at least a portion of a full-length antibody polypeptide that is capable of binding to an antigen. Antibody fragments can comprise a cleaved portion of a full length antibody polypeptide, although the term is not limited to such cleaved fragments. Antibody fragments that are useful in the present invention include, for example, Fab fragments, F(ab')2 fragments, scFv (single-chain Fv) fragments, linear antibodies, monospecific or multispecific antibody fragments such as bispecific, trispecific, tetraspecific and multispecific antibodies (e.g., diabodies, triabodies, tetrabodies), monovalent or multivalent antibody fragments such as bivalent, trivalent, tetravalent and multivalent

antibodies, minibodies, chelating recombinant antibodies, tribodies or bibodies, intrabodies, nanobodies, small modular immunopharmaceuticals (SMIP), binding-domain immunoglobulin fusion proteins, camelized antibodies, and VHH containing antibodies. Additional examples of antigen-binding antibody fragments are known in the art.

The terms "Complementarity-determining region" or "CDR" refer to short polypeptide sequences within the variable region of both heavy and light chain polypeptides that are primarily responsible for mediating specific antigen recognition. The term "framework region" refers to amino acid sequences within the variable region of both heavy and light chain polypeptides that are not CDR sequences, and are primarily responsible for maintaining correct positioning of the CDR sequences to permit antigen binding. Although the framework regions themselves typically do not directly participate in antigen binding, as is known in the art, certain residues within the framework regions of certain antibodies can directly participate in antigen binding or can affect the ability of one or more amino acids in CDRs to interact with antigen.

Examples of antibodies are anti PCSK-9 mAb (e.g., Alirocumab), anti IL-6 mAb (e.g., Sarilumab), and anti IL-4 mAb (e.g., Dupilumab).

Further examples of APIs for the prophylaxis of hemophilia A or B, with or without inhibitors, include an siRNA targeting antithrombin. An example of an siRNA targeting antithrombin is fitusiran. The term "prophylaxis" and "prophylactic treatment" are used interchangeably herein

Pharmaceutically acceptable salts of any API described herein are also contemplated for use in a drug or medicament in a drug delivery device. Pharmaceutically acceptable salts are for example acid addition salts and basic salts.

Those of skill in the art will understand that modifications (additions and/or removals) of various components of the APIs, pharmaceutical formulations, apparatuses, methods, systems and embodiments described herein may be made without departing from the full scope and spirit of the present invention, which encompass such modifications and any and all equivalents thereof.

An example drug delivery device may involve a needle-based injection system as described in Table 1 of section 5.2 of ISO 11608-1:2014(E). As described in ISO 11608-1:2014(E), needle-based injection systems may be broadly distinguished into multi-dose container systems and single-dose (with partial or full evacuation) container systems. The container may be a replaceable container or an integrated non-replaceable container.

As further described in ISO 11608-1:2014(E), a multi-dose container system may involve a needle-based injection device with a replaceable container. In such a system, each container holds multiple doses, the size of which may be fixed or variable (pre-set by the user). Another multi-dose container system may involve a needle-based injection device with an integrated non-replaceable container. In such a system, each container holds multiple doses, the size of which may be fixed or variable (pre-set by the user).

As further described in ISO 11608-1:2014(E), a single-dose container system may involve a needle-based injection device with a replaceable container. In one example for such a system, each container holds a single dose, whereby the entire deliverable volume is expelled (full evacuation). In a further example, each container holds a single dose, whereby a portion of the deliverable volume is expelled (partial evacuation). As also described in ISO 11608-1:2014(E), a single-dose container system may involve a needle-based injection device with an integrated non-replaceable container. In one example for such a system, each container holds a single dose, whereby the entire deliverable volume is expelled (full evacuation). In a further example, each container holds a single dose, whereby a portion of the deliverable volume is expelled (partial evacuation).

Fitusiran as the API for the medicament in the device

Fitusiran is a synthetic, chemically modified double-stranded small interfering RNA (siRNA) oligonucleotide covalently linked to a tri-antennary N-acetyl-galactosamine (GalNAc) ligand targeting AT3 mRNA in the liver, thereby suppressing the synthesis of antithrombin. *See, e.g.*, Pasi et al., *N Engl J Med.* (2017) 377(9):819-28. The nucleosides in each strand of fitusiran are connected through either 3'-5' phosphodiester or phosphorothioate linkages, thus forming the sugar-phosphate backbone of the oligonucleotide.

The sense strand and the antisense strand contain 21 and 23 nucleotides, respectively. The 3' end of the sense strand is conjugated to the GalNAc containing moiety (referred to herein as L96) through a phosphodiester linkage. The sense strand contains two consecutive phosphorothioate linkages at its 5' end. The antisense strand contains four phosphorothioate linkages, two at the 3' end and two at the 5' end. The 21 nucleotides of the sense strand hybridize with the complementary 21 nucleotides of the antisense strand, thus forming 21 nucleotide base pairs and a two-base overhang at the 3'-end of the antisense strand. See also U.S. Pat. 9,127,274, U.S. Pat. 11,091,759, US2020/0163987A1, and WO 2019/014187, the entire contents each of which are expressly incorporated herein by reference.

The two nucleotide strands of fitusiran are shown below:

sense strand: 5'Gf-ps-Gm-ps-Uf-Um-Af-Am-Cf-Am-Cf-Cf-Af-Um-Uf-Um-Af-Cm-Uf-Um-Cf-Am-Af-L96 3' (SEQ ID NO:1), and

antisense strand: 5' Um-ps-Uf-ps-Gm-Af-Am-Gf-Um-Af-Am-Af-Um-Gm-Gm-Uf-Gm-Uf-Um-Af-Am-Cf-Cm-ps-Am-ps-Gm 3' (SEQ ID NO:2),

wherein

Af = 2' -deoxy- 2'-fluoroadenosine

Cf = 2' -deoxy- 2'-fluorocytidine

Gf = 2' -deoxy- 2'-fluoroguanosine

Uf = 2' -deoxy- 2'-fluorouridine

Am = 2'-O-methyladenosine

Cm = 2'-O-methylcytidine

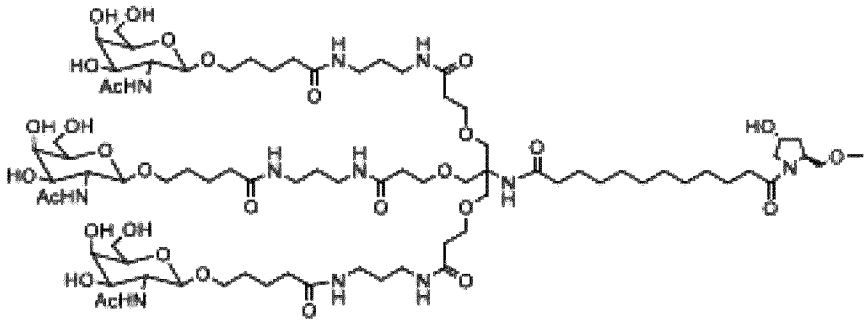
Gm = 2'-O-methylguanosine

Um = 2'-O-methyluridine

"-" (hyphen) = 3'-5' phosphodiester linkage sodium salt

"-ps-" = 3'-5' phosphorothioate linkage sodium salt

and wherein L96 has the following formula:



(I).

As used herein, the terms 2' -deoxy- 2'-fluoroadenosine and 2'-fluoroadenosine may be used interchangeably.

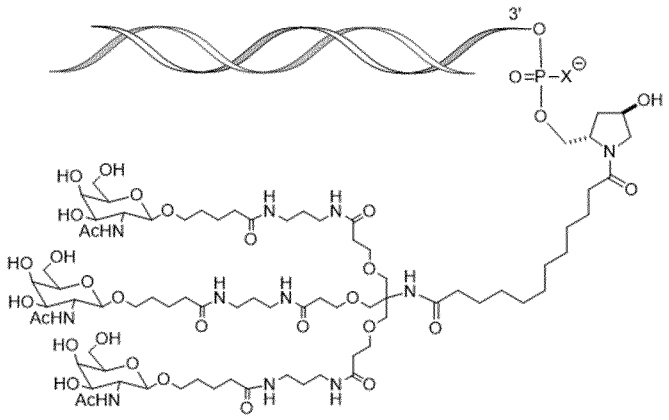
As used herein, the terms 2' -deoxy- 2'-fluorocytidine and 2'-fluorocytidine may be used interchangeably.

As used herein, the terms 2' -deoxy- 2'-fluoroguanosine and 2'-fluoroguanosine may be used interchangeably.

As used herein, the terms 2' -deoxy- 2'-fluorouridine and 2'-fluorouridine may be used interchangeably.

The expanded structural formula, molecular formula, and molecular weight of fitusiran are shown in Figure 3.

The structure of fitusiran can also be described using the following diagram, wherein the X is O:



Fitusiran is shown in Figure 3 in sodium salt form.

In some embodiments, the device delivers fitusiran in an aqueous solution, wherein fitusiran is at a concentration of about 40 to about 200 mg/mL (e.g., about 50 to about 150 mg/mL, about 80 to about 110 mg/mL, or about 90 to about 110 mg/mL). As used herein, values intermediate to recited ranges and values are also intended to be part of this disclosure. In addition, ranges of values using a combination of any of recited values as upper and/or lower limits are intended to be included. In further embodiments, the pharmaceutical formulation comprises fitusiran in an aqueous solution at a concentration of about 40, about 50, about 75, about 100, about 125, about 150, or about 200 mg/mL. In certain embodiments, fitusiran is provided in an aqueous solution at a concentration of about 100 mg/mL.

The term “deliver,” “delivers,” or “delivering” is intended to mean “administer,” “administers,” or “administering.”

Unless specifically stated or otherwise evident from the context, as used herein, the term “approximately” or "about" refers to a value that is within an acceptable error range for a particular value determined by a person of ordinary skill, a portion of which will depend on how the measurement or determination is made. For example, “approximately” or "about" may mean a range of up to 10% (ie, ±10%). Therefore, “approximately” or "about" can be understood as greater than or less than 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, 0.5%, 0.1 %, 0.05%, 0.01%, or 0.001%. When a specific value is provided in this disclosure, unless otherwise stated, the meaning of “approximately” or "about" should be assumed to be within an acceptable error range for that specific value.

While the fitusiran dosage weight described herein refers to the weight of fitusiran free acid (active moiety), administration of fitusiran to patients herein refers to administration of fitusiran sodium (drug substance) provided in a pharmaceutically suitable aqueous solution (e.g., a phosphate-buffered saline at a physiological pH). For example, about 100 mg/mL fitusiran means about 100 mg of fitusiran free acid (equivalent to about 106 mg fitusiran sodium, the drug substance) per mL. Unless otherwise indicated, a fitusiran weight recited in the present disclosure is the weight of fitusiran free acid (the active moiety).

In some embodiments, a pharmaceutical formulation in the device comprises fitusiran in a phosphate-buffered saline. The phosphate concentration in the solution may be about 1 to about 10 mM (e.g., about 2, about 3, about 4, about 5, about 6, about 7, about 8, or about 9 mM), with a pH of about 6.0-8.0. The pharmaceutical formulations herein may include a stabilizing agent such as EDTA. The pharmaceutical formulations may be preservative-free. In some embodiments, the fitusiran pharmaceutical formulation in the device is preservative-free and comprises, consists of, or consists essentially of about 100 mg of fitusiran per mL of an approximately 5 mM phosphate buffered saline (PBS) solution. In some embodiments, the fitusiran pharmaceutical formulation in the device is preservative-free and comprises, consists of, or consists essentially of fitusiran in an approximately 5 mM phosphate buffered saline (PBS) solution. The PBS solution is composed of sodium chloride, dibasic sodium phosphate (heptahydrate), and monobasic sodium phosphate (monohydrate). Sodium hydroxide solution and diluted phosphoric acid may be used to adjust the pH of the pharmaceutical formulation to about 7.0 or about 7.1.

In some embodiments, the fitusiran pharmaceutical formulation in the device for subcutaneous delivery contains fitusiran in a 5 mM phosphate buffered saline having 0.64 mM NaH_2PO_4, 4.36 mM Na_2HPO_4, and 84 mM NaCl at pH 7.0. In certain embodiments, the pharmaceutical formulation of fitusiran solution for subcutaneous delivery is shown in **Table 1** below:

Table 1. Exemplary Fitusiran Pharmaceutical Formulation

Components	**Pharmaceutical Formulation**	
	Percentage [%]	Per ml [mg]
Fitusiran (active moiety) [equivalent to fitusiran sodium]	10	100 [106]
Sodium chloride	0.49	4.909
Dibasic sodium phosphate (heptahydrate)	0.12	1.169
Monobasic sodium phosphate	<0.01	0.0885

(monohydrate)		
Phosphoric acid, concentrated	-	q.s. pH 7.0
Sodium hydroxide	-	q.s. pH 7.0
Water for subcutaneous delivery	q.s. 100	q.s. 1 mL

*q.s.: quantum satis

In some embodiments, the pharmaceutical formulation of fitusiran solution for subcutaneous delivery with the device can be described as shown in **Table 2** below.

Table 2. Exemplary Fitusiran Pharmaceutical Formulation

Components	**Pharmaceutical Formulation (mg)**
Fitusiran (active moiety) [equivalent to fitusiran sodium]	100 [106]
$NaH_2PO_4*H_2O$	0.0885
$Na_2HPO_4*7H_2O$	1.169
NaCl	4.909
0.1 N NaOH	q.s.
0.1 M H_3PO_4	q.s.
Purified water	*Ad* 1 mL

In some embodiments, the device may be used to deliver a single dose of fitusiran wherein the single dose comprises about 20 to about 80 mg of fitusiran (e.g., about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, or about 80 mg). In some embodiments, the device may be used to deliver single dose of fitusiran, wherein the single dose comprises about 1 to about 30 mg of fitusiran (e.g., about 1.25 mg, about 2.5 mg, about 5 mg, about 10 mg, about 20 mg, or about 30 mg).

In one embodiment, the device may be used to deliver a single dose of about 80 mg of fitusiran. In one embodiment, the device may be used to deliver a single dose of about 50 mg of fitusiran. In one embodiment, the device may be used to deliver a single dose of about 20 mg of fitusiran. In one embodiment, the device may be used to deliver a single dose of about 30 mg of fitusiran. In one embodiment, the device may be used to deliver a single dose of about 10 mg of fitusiran. In one embodiment, the device may be used to deliver a single dose of about 5 mg of fitusiran. In one embodiment, the device may be used to deliver a single dose of about 2.5 mg of fitusiran. In one embodiment, the device may be used to deliver a single dose of about 1.25 mg of fitusiran.

In some embodiments, the single dose of fitusiran may be delivered in about 0.5 mL to about 1 mL delivery volumes (e.g., about 0.5 mL, about 0.6 mL, about 0.7 mL, about 0.8 mL, about 0.9 mL, or about 1 mL). Other delivery volumes described herein may also be used.

In one embodiment, the device may be used to deliver a single dose of about 80 mg of fitusiran in about 0.8 mL (about 100 mg fitusiran/mL). In one embodiment, the device may be used to deliver a single dose of about 50 mg of fitusiran in about 0.5 mL (about 100 mg fitusiran/mL). In one embodiment, the device may be used to deliver a single dose of about 20 mg of fitusiran in about 0.5 mL (about 40 mg fitusiran/mL). In one embodiment, the device may be used to deliver a single dose of about 30 mg of fitusiran in about 0.5 mL (about 60 mg fitusiran/mL). In one embodiment, the device may be used to deliver a single dose of about 10 mg of fitusiran in about 0.5 mL (about 20 mg fitusiran/mL). In one embodiment, the device may be used to deliver a single dose of about 5 mg of fitusiran in about 0.5 mL (about 10 mg fitusiran/mL). In one embodiment, the device may be used to deliver a single dose of about 2.5 mg of fitusiran in about 0.5 mL (about 5 mg fitusiran/mL). In one embodiment, the device may be used to deliver a single dose of about 1.25 mg of fitusiran in about 0.5 mL (about 2.5 mg fitusiran/mL).

In one embodiment, the device delivers fitusiran at a prophylactically effective amount to prophylactically treat hemophilia (e.g., hemophilia A or B, in a patient with or without inhibitors) in a patient in need thereof (e.g., a hemophilia A or B patient, with or without inhibitors). "Prophylactically effective amount" refers to the amount of fitusiran that helps the patient with hemophilia A or B, with or without inhibitors to achieve a desired clinical endpoint such as reducing the Annualized Bleeding Rate (ABR), Annualized Joint Bleeding Rate (AjBR), Annualized Spontaneous Bleeding Rate (AsBR), or the frequency of bleeding episodes. As used herein in the context of fitusiran, the term "treat" "treating," or "treatment" includes prophylactic treatment of the disease and refers to achievement of a desired clinical endpoint.

A hemophilia A or B patient with inhibitors refers to a patient who has developed alloantibodies to the factor he/she has previously received (e.g., factor VIII for hemophilia A patients or factor IX for hemophilia B patients). A hemophilia A or B patient with inhibitors may become refractory to replacement coagulation factor therapies. A patient without inhibitors refers to a patient who does not have such alloantibodies. The present treatment methods may be beneficial for hemophilia A patients with inhibitors, as well as for hemophilia B patients with inhibitors.

As used herein, a patient with "hemophilia A or B, with or without inhibitors," or refers to 1) a hemophilia A patient with inhibitors, or 2) a hemophilia B patient with inhibitors, 3) a hemophilia A patient without inhibitors, or 4) a hemophilia B patient without inhibitors. As used herein, a patient refers to a human patient. A patient can also refer to a human subject.

In some embodiments, the device may be used to prophylactically treat a patient with hemophilia A or B, with or without inhibitors, with a subcutaneous dose of about 50 mg of fitusiran once every two months (or every eight weeks). In other embodiments, the device may be used to prophylactically treat a patient with hemophilia A or B, with or without inhibitors, with a subcutaneous dose of about 50 mg of fitusiran every month (or every four weeks). In yet other embodiments, the device may be used to prophylactically treat a patient with hemophilia A or B, with or without inhibitors, with a subcutaneous dose of about 80 mg of fitusiran every two months (or every eight weeks). In yet other embodiments, the device may be used to prophylactically treat a patient with hemophilia A or B, with or without inhibitors, with a subcutaneous dose of about 80 mg of fitusiran every month (or every four weeks). In yet other embodiments, the device may be used to prophylactically treat a patient with hemophilia A or B, with or without inhibitors, with a subcutaneous dose of about 20 mg of fitusiran every two months (or every eight weeks). In yet other embodiments, the device may be used to prophylactically treat a patient with hemophilia A or B, with or without inhibitors, with a subcutaneous dose of about 20 mg of fitusiran every month (or every four weeks). In yet other embodiments, the device may be used to prophylactically treat a patient with hemophilia A or B, with or without inhibitors, with a subcutaneous dose of about 10 mg of fitusiran every month (or every four weeks). In yet other embodiments, the device may be used to prophylactically treat a patient with hemophilia A or B, with or without inhibitors, with a subcutaneous dose of fitusiran at about 30 mg every month (or every four weeks). In yet other embodiments, the device may be used to prophylactically treat a patient with hemophilia A or B, with or without inhibitors, with a subcutaneous dose of fitusiran at about 5 mg every month (or every four weeks). In yet other embodiments, the device may be used to prophylactically treat a patient with hemophilia A or B, with or without inhibitors, with a subcutaneous dose of fitusiran at about 2.5 mg every month (or every four weeks). In yet other embodiments, the device may be used to prophylactically treat a patient with hemophilia A or B, with or without inhibitors, with a subcutaneous dose of fitusiran at about 1.25 mg every month (or every four weeks).

Accordingly, provided herein is a method of prophylactic treatment of a patient with hemophilia A or hemophilia B, with or without inhibitors, comprising subcutaneously delivering with the device a prophylactically effective amount of fitusiran to the patient in need thereof. The prophylactically effective amount of fitusiran may be any dose provided herein, such as about 1 to about 80 mg, about 1 to about 30 mg, or about 20 to about 80 mg. The prophylactically effective amount of fitusiran may be, for example, about 1.25 mg, about 2.5 mg, about 5 mg, about 25 mg, about 30 mg, about 50 mg, or about 80 mg. The prophylactically effective amount of fitusiran may be delivered every month (or every four weeks) or once every two months (or

every eight weeks). Fitusiran may be delivered in about 0.5 mL to about 1 mL delivery volumes (e.g., about 0.5 mL, about 0.6 mL, about 0.7 mL, about 0.8 mL, about 0.9 mL, or about 1 mL).

As an example, a method of prophylactic treatment of a patient with hemophilia A or hemophilia B, with or without inhibitors, may comprise subcutaneously delivering with the device about 50 mg of fitusiran to the patient in need thereof every month (or every four weeks) or once every two months (or every eight weeks). The about 50 mg of fitusiran may be delivered in about 0.5 mL PBS (at a concentration of about 100 mg fitusiran/mL).

Further provided herein is a method of reducing the frequency of bleeding episodes in a patient with hemophilia A or B, with or without inhibitors, comprising subcutaneously delivering with the device a prophylactically effective amount of fitusiran to the patient in need thereof. The prophylactically effective amount of fitusiran may be any dose provided herein, such as about 1 to about 80 mg, about 1 to about 30 mg, or about 20 to about 80 mg. The prophylactically effective amount of fitusiran may be, for example, about 1.25 mg, about 2.5 mg, about 5 mg, about 25 mg, about 30 mg, about 50 mg, or about 80 mg. The prophylactically effective amount of fitusiran may be delivered every month (or every four weeks) or once every two months (or every eight weeks). Fitusiran may be delivered in about 0.5 mL to about 1 mL delivery volumes (e.g., about 0.5 mL, about 0.6 mL, about 0.7 mL, about 0.8 mL, about 0.9 mL, or about 1 mL).

As an example, a method of reducing the frequency of bleeding episodes in a patient with hemophilia A or B, with or without inhibitors, may comprise subcutaneously delivering with the device about 50 mg of fitusiran to the patient in need thereof every month (or every four weeks) or once every two months (or every eight weeks). The about 50 mg of fitusiran may be delivered in about 0.5 mL PBS (at a concentration of about 100 mg fitusiran/mL).

Also, provided herein is a method of reducing the ABR in a patient with hemophilia A or B, with or without inhibitors, comprising subcutaneously delivering with the device a prophylactically effective amount of fitusiran to the patient in need thereof. The prophylactically effective amount of fitusiran may be any dose provided herein, such as about 1 to about 80 mg, about 1 to about 30 mg, or about 20 to about 80 mg. The prophylactically effective amount of fitusiran may be, for example, about 1.25 mg, about 2.5 mg, about 5 mg, about 25 mg, about 30 mg, about 50 mg, or about 80 mg. The prophylactically effective amount of fitusiran may be delivered every month (or every four weeks) or once every two months (or every eight weeks). Fitusiran may be delivered in about 0.5 mL to about 1 mL delivery volumes (e.g., about 0.5 mL, about 0.6 mL, about 0.7 mL, about 0.8 mL, about 0.9 mL, or about 1 mL).

As an example, a method of reducing the ABR in a patient with hemophilia A or B, with or without inhibitors, may comprise subcutaneously delivering with the device about 50 mg of fitusiran to the patient in need thereof every month (or every four weeks) or once every two months (or every eight weeks). The about 50 mg of fitusiran may be delivered in about 0.5 mL PBS (at a concentration of about 100 mg fitusiran/mL).

Also, provided herein is a method of reducing the AjBR in a patient with hemophilia A or B, with or without inhibitors, comprising subcutaneously delivering with the device a prophylactically effective amount of fitusiran to the patient in need thereof. The prophylactically effective amount of fitusiran may be any dose provided herein, such as about 1 to about 80 mg, about 1 to about 30 mg, or about 20 to about 80 mg. The prophylactically effective amount of fitusiran may be, for example, about 1.25 mg, about 2.5 mg, about 5 mg, about 25 mg, about 30 mg, about 50 mg, or about 80 mg. The prophylactically effective amount of fitusiran may be delivered every month (or every four weeks) or once every two months (or every eight weeks). The fitusiran may be delivered in about 0.5 mL to about 1 mL delivery volumes (e.g., about 0.5 mL, about 0.6 mL, about 0.7 mL, about 0.8 mL, about 0.9 mL, or about 1 mL).

As an example, a method of reducing the AjBR in a patient with hemophilia A or B, with or without inhibitors, may comprise subcutaneously delivering with the device about 50 mg of fitusiran to the patient in need thereof every month (or every four weeks) or once every two months (or every eight weeks). The about 50 mg of fitusiran may be delivered in about 0.5 mL PBS (at a concentration of about 100 mg fitusiran/mL).

Also, provided herein is a method of reducing the AsBR in a patient with hemophilia A or B, with or without inhibitors, comprising subcutaneously delivering with the device a prophylactically effective amount of fitusiran to the patient in need thereof. The prophylactically effective amount of fitusiran may be any dose provided herein, such as about 1 to about 80 mg, about 1 to about 30 mg, or about 20 to about 80 mg. The prophylactically effective amount of fitusiran may be, for example, about 1.25 mg, about 2.5 mg, about 5 mg, about 25 mg, about 30 mg, about 50 mg, or about 80 mg. The prophylactically effective amount of fitusiran may be delivered every month (or every four weeks) or once every two months (or every eight weeks). Fitusiran may be delivered in about 0.5 mL to about 1 mL delivery volumes (e.g., about 0.5 mL, about 0.6 mL, about 0.7 mL, about 0.8 mL, about 0.9 mL, or about 1 mL).

As an example, a method of reducing the AsBR in a patient with hemophilia A or B, with or without inhibitors, may comprise subcutaneously delivering with the device about 50 mg of fitusiran to the patient in need thereof every month (or every four weeks) or once every two

months (or every eight weeks). The about 50 mg of fitusiran may be delivered in about 0.5 mL PBS (at a concentration of about 100 mg fitusiran/mL).

Any invention described herein is not limited by the description in conjunction with the exemplary embodiments. Rather, the invention and the associated disclosure comprise any new feature as well as any combination of features, particularly including any combination of features in the patent claims, even if said feature or said combination per se is not explicitly stated in the patent claims or exemplary embodiments.

Reference numerals

20	drug delivery device
21	distal end of housing
22	housing
23	proximal end of housing
24	drug container
26	reservoir
28	outlet
30	needle
32	stopper
34	plunger
36	gas tube
38	separating wall
40	dispensing direction
41	axis
42	first chamber
44	second chamber
46	end stop
48	closing body
50	fluid channel
52	first branch
54	second branch
56	third branch
58	vent opening
60	gas conduit
62	first valve
64	second valve
70	first engaging elements
72	second engaging elements
74	proximal end of drug container
76	distal end of drug container
78	opening

Claims

1. A drug delivery device (20), comprising:

a housing (22) for accommodating a drug container (24);

a separating wall (38), the separating wall (38) being in an initial position in an initial state of the drug delivery device (20), the separating wall (38) being movable relative to the housing (22) for a dispensing operation, and the separating wall (38) sealingly separating a first chamber (42) within the housing (22) from a second chamber (44) within the housing (22); and

a pressure source for providing a predetermined gas pressure, the pressure source being configured for communicating with the first chamber (42) for driving the separating wall (38) to an operating position of the separating wall (38) for the dispensing operation, and for communicating with the second chamber (44) for driving the separating wall (38) from the operating position to a final position of the separating wall (38) after the dispensing operation is finished.

2. The drug delivery device in accordance with claim 1, wherein

the separating wall (38) is configured to hold the drug container (24) such that the drug container (24) is moved together with the separating wall (38), when the separating wall (38) is moved from its initial position to its operating position and when the separating wall (38) is moved from its operating position to its final position.

3. The drug delivery device (20) of any one of claims 1 or 2, comprising a fluid channel (50) within the housing (22), the fluid channel (50) communicating with the pressure source and being configured for

enabling a communication between the pressure source and the first chamber (42) and for preventing a communication between the pressure source and the second chamber (44) in the initial state; and

preventing the communication between the first chamber (42) and the pressure source and for enabling the communication of the second chamber (44) with the pressure source after the dispensing operation is finished.

4. The drug delivery device (20) of claim 3, comprising:

a first valve (62) which is configured for coupling the pressure source to the first chamber (42) via the fluid channel (50) in the initial state of the drug delivery device (20) and for decoupling the first chamber (42) from the pressure source after the dispensing operation is finished; and

a second valve (64) which is configured for decoupling the second chamber (44) from the pressure source in the initial state and for coupling the second chamber (44) with the pressure source after the dispensing operation is finished.

5. The drug delivery device (20) of claim 4, wherein

the first valve (62) is configured for coupling the pressure source to the first chamber (42) via the fluid channel (50), when the gas pressure within the first chamber (42) is below a predetermined first pressure threshold, and for decoupling the first chamber (42) from the pressure source, when the gas pressure within the first chamber (42) corresponds to or exceeds the first pressure threshold; and/or

the second valve (64) is configured for decoupling the second chamber (44) from the pressure source, when the pressure in the fluid channel (50) is below a predetermined second pressure threshold, and for coupling the second chamber (44) with the pressure source, when the gas pressure within the fluid channel (50) corresponds to or exceeds the second pressure threshold.

6. The drug delivery device (20) of any one of the preceding claims, comprising

a flexible gas tube (36), which is coupled or couplable to the drug container (24) and which is configured for squeezing a drug out of the drug container (24) upon being pressurized such that the drug is dispensed from the drug delivery device (20).

7. The drug delivery device (20) of claim 6, wherein

the gas tube (36) is configured for communicating with the first chamber (42), when the separating wall (38) is in its operating position, and for being decoupled from the first chamber (42), when the separating wall (38) is in its initial and/or final position.

8. The drug delivery device (20) of claim 7, wherein

the separating wall (38) comprises a gas conduit (60) communicatively coupling the first chamber (42) and the gas tube (36), when the separating wall (38) is in its operating position.

9. The drug delivery device (20) of any of claims 7 or 8, wherein

the gas tube (36) comprises an opening (78) for receiving the gas, when the separating wall (38) is in its operating position.

10. The drug delivery device (20) of claims 8 and 9, wherein

the gas conduit (60) and the opening (78) of the gas tube (36) may be formed and arranged such that the gas conduit (60) and/or the opening (78) are closed, when the separating wall (38) is in its initial and/or final position, and that the gas conduit (60) and the

opening (78) are opened such that an interior of the gas tube (36) may communicate with the first chamber (42) via the opening (78) and the gas conduit (60), when the separating wall (38) is in its operating position.

11. The drug delivery device (20) of claim 10, comprising a closing body (48) for closing the gas conduit (60) of the separating wall (38) and the opening (78) of the gas tube (36), the closing body (48) being arranged at the housing (22) covering the gas conduit (60) of the separating wall (38) and the opening (78) of the gas tube (36), when the separating wall (38) is in its initial and/or final position, and exposing the gas conduit (60) and the opening (78), when the separating wall (38) is in its operating position.

12. The drug delivery device (20) of claim 11, wherein the pressure source comprises or forms the closing body (48).

13. The drug delivery device (20) of any one of the preceding claims, comprising:

at least one first engaging element (70) being arranged at the separating wall (38); and

at least one second engaging element (72) being arranged at the housing (22),

wherein the first and second engaging elements (70, 72) are configured for being engaged to each other, when the separating wall (38) and thereby the drug container (24) reach their final position.

14. The drug delivery device (20) of any one of the preceding claims, comprising an end stop (46) being coupled to the housing (22) and being configured for preventing the separating wall (38) from being moved further, when the separating wall (38) reaches its operating position.

15. The drug delivery device (20) of any one of the preceding claims, comprising the drug container (24), wherein the drug container (24) comprises a reservoir (26) in which a drug is accommodated.

16. The drug delivery device (20) of any one of the preceding claims, wherein the first chamber (42) is arranged between the separating wall (38) and the proximal end of the housing (22) and the second chamber (44) is arranged between the separating wall (38) and the distal end of the housing (22).

17. The drug delivery device (20) of any one of the preceding claims, wherein the separating wall (38) is configured to sealingly separate the first chamber (42) within the housing (22) from the second chamber (44) within the housing (22) in the initial, final and operating position of the separating wall (38).

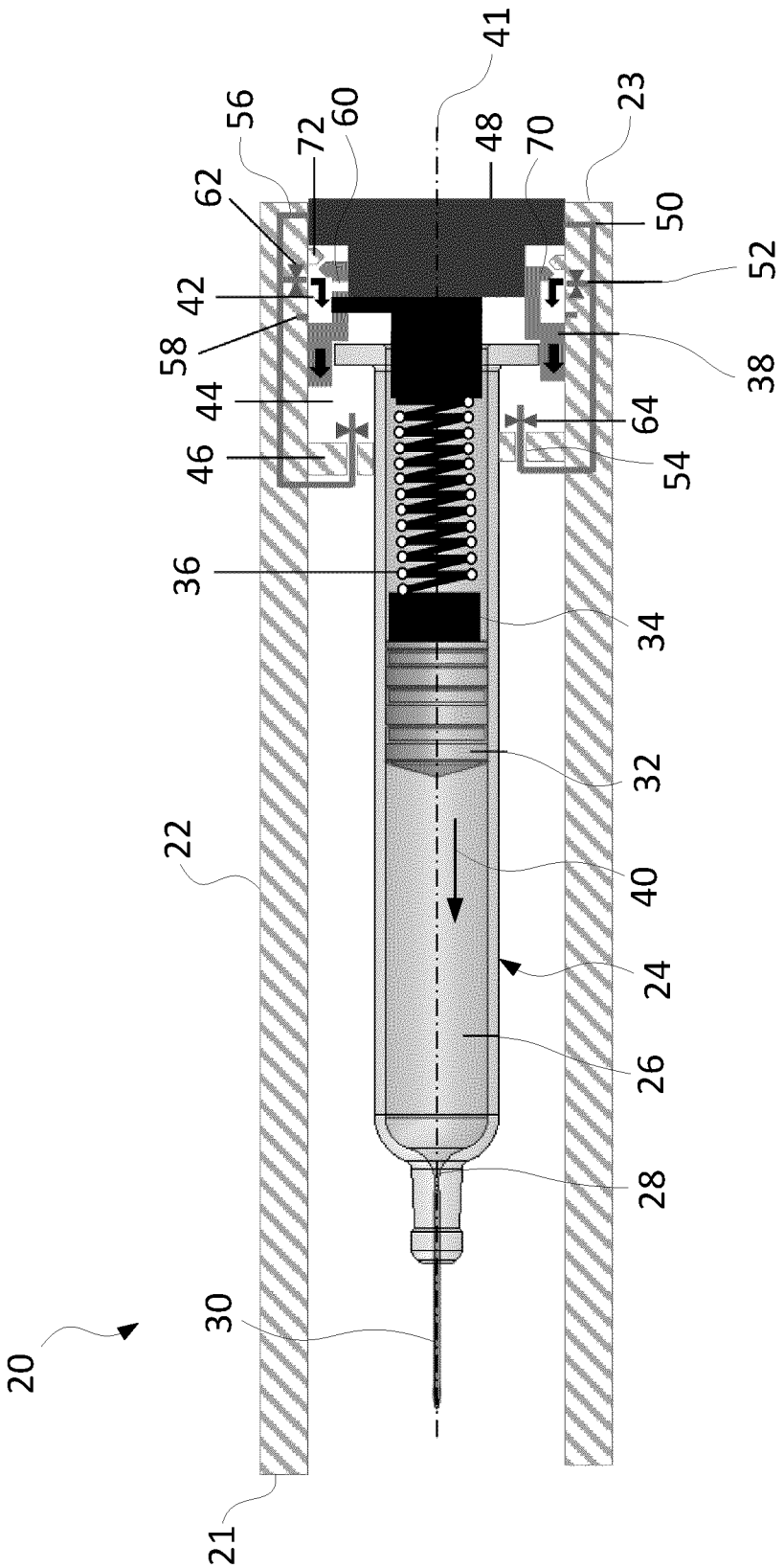

41
56
72
60
48
70
23
62
50
52
42
58
38
44
64
46
54
36
34
32
22
40
24
26
28
20
30
21

FIG. 1

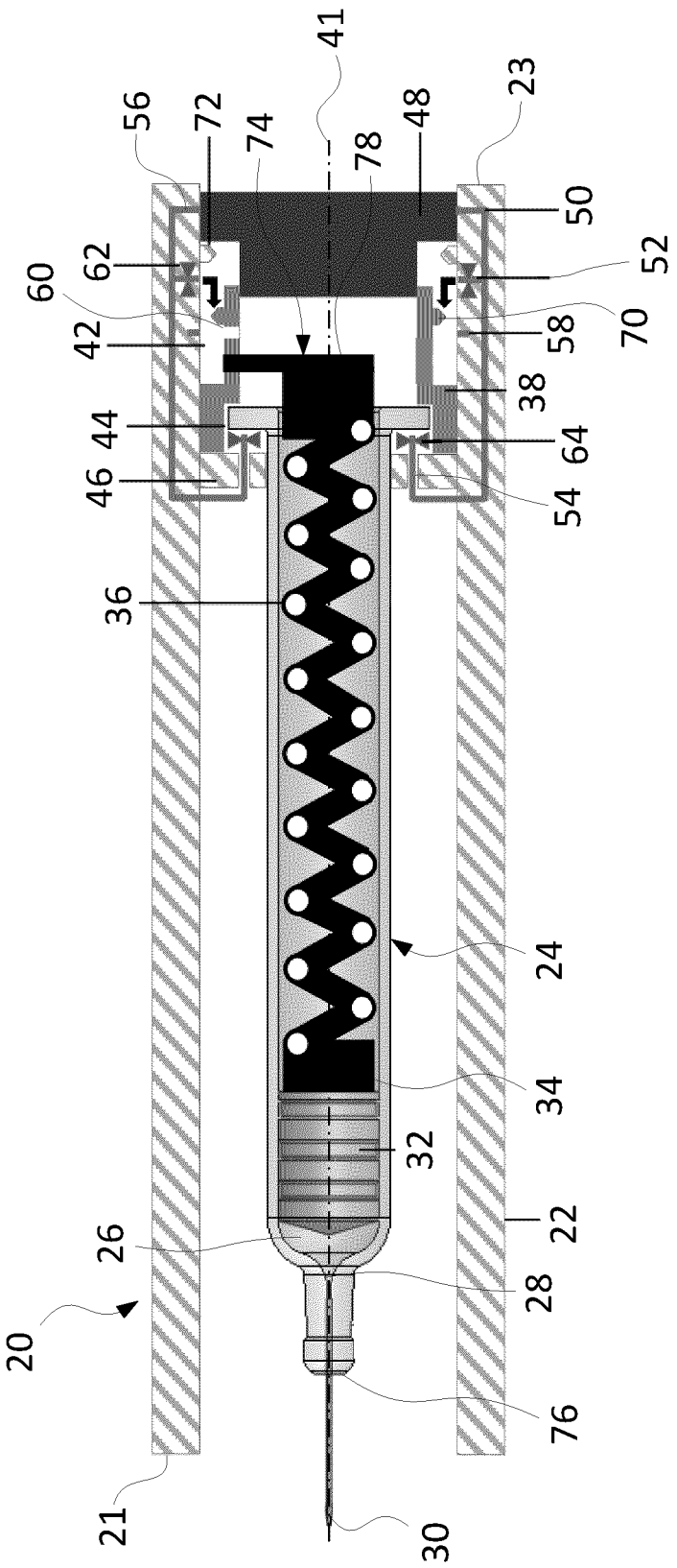
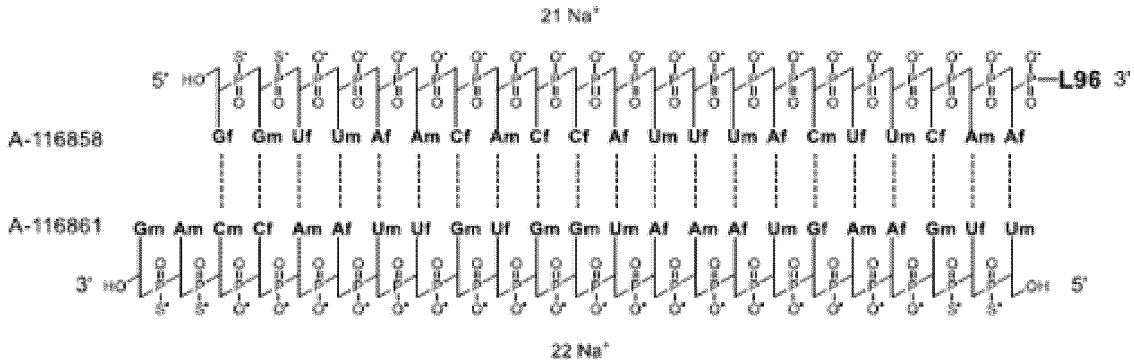
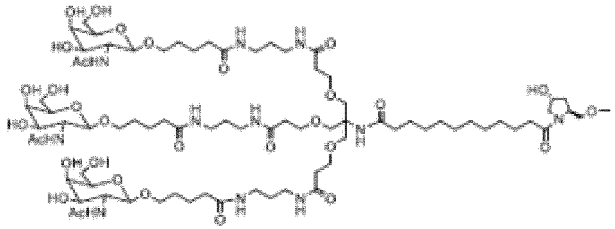

41
23
56
72
74
78
48
50
52
62
60
70
58
42
38
44
64
46
54
36
24
34
32
22
26
28
20
76
21
30

FIG. 2



Af, Cf, Gf, Uf = 2'-F ribonucleosides
Am, Cm, Gm, Um = 2'-OMe ribonucleosides

L96 =



Molecular formula and molecular mass

	Fitusiran (Duplex)	A-116858 (Sense strand)	A-116861 (Antisense strand)
Molecular formula sodium salt	$C_{520}H_{636}F_{21}N_{175}Na_{43}O_{309}P_{43}S_6$	$C_{285}H_{369}F_{12}N_{85}Na_{21}O_{164}P_{21}S_2$	$C_{235}H_{267}F_9N_{90}Na_{22}O_{145}P_{22}S_4$
Molecular formula free acid	$C_{520}H_{679}F_{21}N_{179}O_{309}P_{43}S_6$	$C_{285}H_{390}F_{12}N_{85}O_{164}P_{21}S_2$	$C_{235}H_{289}F_9N_{90}O_{145}P_{22}S_4$
Molecular weight sodium salt	17,193 Da	9,035 Da	8,159 Da
Molecular weight free acid	16,248 Da	8,573 Da	7,675 Da

Fig. 3

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2024/065444

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M5/20 A61M5/32
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	US 2020/197611 A1 (O'CONNOR JOSEPH PATRICK [US]) 25 June 2020 (2020-06-25) figures 12, 13, 14, 15, 16, 17, 18, 1-11, 19-27 paragraphs [0097] - [0111], [0057] - [0096], [0112] - [0127] -----	1,2, 13-17 3-12

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance;; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance;; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
5 September 2024	23/09/2024

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Benes, Václav

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2024/065444

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:

   a. [ ] forming part of the international application as filed.

   b. [X] furnished subsequent to the international filing date for the purposes of international search (Rule 13*ter*.1(a)).

      [X] accompanied by a statement to the effect that the sequence listing does not go beyond the disclosure in the international application as filed.

2. [ ] With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this report has been established to the extent that a meaningful search could be carried out without a WIPO Standard ST.26 compliant sequence listing.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2024/065444

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2020197611 A1	25-06-2020	AU 2018307470 A1	16-01-2020
		CA 3071249 A1	31-01-2019
		CN 110913931 A	24-03-2020
		EP 3658208 A1	03-06-2020
		JP 6938691 B2	22-09-2021
		JP 2020525171 A	27-08-2020
		US 2020197611 A1	25-06-2020
		WO 2019023053 A1	31-01-2019