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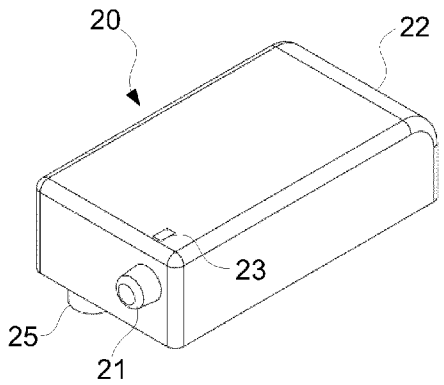

Fig. 1

(57) Abstract: A drug delivery device (20) is provided. The drug delivery device (20) comprises: a housing (22) for receiving a drug container (24) or with the drug container (24) being arranged within the housing (22), the drug container (24) having a drug chamber (26), a drug outlet (28) of the drug chamber (26), and a drug being arranged within the drug chamber (26); an injection member for injecting the drug into an injection site; a pressure arrangement within the housing (22), the pressure arrangement being configured for providing a predetermined gas pressure; a pressure member, which is coupled or couplable to the drug container (24) and which is configured for pressing the drug through the drug outlet (28) out of the drug chamber (26) upon being moved by the predetermined gas pressure; a plunger (70), which is movable relative to the housing (22) from an initial position of the plunger (70) to an operating position of the plunger (70), the plunger preventing the predetermined gas pressure from being applied to the pressure member in its initial position and enabling the predetermined gas pressure to be applied to the pressure member in its operating position; and a fluid channel, which is coupled or couplable to the drug chamber (26) for receiving the drug from the drug outlet of the drug chamber (26), the fluid channel being provided to communicate with the injection member for guiding the drug to the injection member during a dispensing operation, wherein at least a section (58) of the fluid channel is coupled to the plunger (70) and is moved together with the plunger (70), when the plunger (70) is moved from its initial position to its operating position.

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Title

Drug delivery device

Background

The present disclosure relates to a drug delivery device, in particular a very compact and flat drug delivery device.

In drug delivery devices, drug is often delivered to a user via a needle which pierces the skin of the user (or patient). The drug may be accommodated within a drug container of the drug delivery device, e.g. within a syringe 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.

Such pen-type devices usually have a small bearing surface for being in contact with the user, e.g. on the skin in the vicinity of an injection site. In particular, in most cases, an axial end face of the pen-type device may be considered for being in contact with the user during injection of the corresponding dose. However, such an end face provides a very small basis for supporting the pen-type device. Further, the cylindrical form may be hard to handle, in particular if the user has some motoric impairment.

In many conventional drug delivery devices, the force needed for the dispensing operation is introduced mechanically. However, if 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 drives may be necessary to deliver larger amount of medication. Further, with mechanical solutions, the required installation space within the drug delivery devices is correspondingly larger. Furthermore, with increasing digitalization, there is a need for new forms of electrical 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, shape and operability, and/or to enable the injection of a relative high amount of drug automatically.

These objects are 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 receiving a drug container within the housing, the drug container having a drug chamber, a drug outlet of the drug chamber, and a drug within the drug chamber; an injection member for injecting the drug into an injection site; a pressure arrangement within the housing, the pressure arrangement being configured for providing a predetermined gas pressure; a pressure member, which is coupled or couplable to the drug container and which is configured for pressing the drug through the drug outlet out of the drug chamber upon being moved by the predetermined gas pressure; a plunger, which is movable relative to the housing from an initial position of the plunger to an operating position of the plunger, the plunger preventing the predetermined gas pressure from being applied to the pressure member in its initial position and enabling the predetermined gas pressure to be applied to the pressure member in its operating position; and a fluid channel, which is coupled or couplable to the drug chamber for receiving the drug from drug outlet of the drug chamber, the fluid channel being provide to communicate with the injection member for guiding the drug to the injection member during a dispensing operation, wherein, optionally, at least a section of the fluid channel is coupled to the plunger and is moved together with the plunger, when the plunger is moved from its initial position to its operating position.

For example, the fluid channel may comprise a first section, which is coupled or couplable to the drug chamber, and a second section, which is coupled to the first section, which sealingly communicates with the first section, and which is movable together with the plunger. The first section may be flexible in order to compensate for the movement of the second section. The drug delivery device operating with the predetermined gas pressure may be referred to as gas-powered autoinjector. The injection member may be a first needle or a nozzle. The drug container may be already arranged within the housing. Alternatively, the drug container may be arranged within the housing later.

The gas-powered drug delivery device provides a large degree of freedom with respect to the design, shape, and size of the housing. In particular, the housing may be formed very compact

and/or, easy and/or stable to handle. Further, because of the section of the fluid channel being movable together with the plunger, less space is needed as for a conventional drive. For example, the housing of the very compact drug delivery device may be (computer-)mouse-shaped. Such a mouse-shaped drug delivery device may be handled, e.g. gripped, easily and comfortably. In addition, a bearing surface of such a mouse-shaped drug delivery device may correspond to a bottom surface of the correspondingly mouse-shaped housing and may be much larger than a bearing surface of a conventional pen-type drug delivery device, with the bearing surface being configured to be in direct contact with a skin of the user during injection of the drug.

One advantage of this mouse-shape is the flat and compact design. The flat design enlarges the contact area on the skin, i.e. the bearing surface, for the injection, which makes the device more stable in place. The bearing surface may be a part of the housing and may be configured to be in contact with the injection site, in particular the skin of the user, during usage of the drug delivery device. In case of the mouse-shaped housing, the bearing surface may be a bottom surface of the housing. A height of the housing perpendicular the bearing surface may be smaller than a length of the housing parallel to the bearing surface. The bearing surface of the drug delivery device may be adjacent to a location where the drug may be injected into the skin for the drug delivery operation when the drug delivery device is used for the drug delivery operation. There may be a grip area opposite to the bearing surface, i.e. facing away from the skin of the user during usage. The mouse-design enables to provide a very large grip area compared to a pen-type drug delivery device. The large grip area also makes the drug delivery device easier to hold for patients with limited dexterity, as is the case with rheumatic patients, for example.

The injection member may be or may comprise a needle, in particular a first needle, for injecting the drug into an injection site, wherein the needle may be communicatively coupled or couplable to the drug container at the drug outlet of the drug container. The first needle may be configured for piercing the skin of the user. The needle may be in or may be brought into fluid communication with an interior of the drug container. For example, the first needle may be brought into fluid communication with the interior of the drug container by a second needle. The second needle may be provided for piercing a septum of the drug container or may be an integral part of the drug container. The medicament, e.g. a liquid medicament, may be expediently arranged in the interior of the drug container. The drug container may be a cartridge, which may have to be brought into fluid communication with the first needle and/or the second needle, e.g. by piercing the septum of the drug cartridge with the second needle. Alternatively, the medicament container may be a syringe, e.g. a syringe with a preinstalled needle, such as a staked needle, e.g. the second needle.

The drug delivery device may be a fully functional drug delivery device. The drug may be a medicament. The drug delivery device may be an autoinjector. 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 pressure reservoir, e.g. a gas reservoir, e.g. a gas cartridge, may be used as the energy storage member. In this case, the pressure reservoir may be pre-loaded and/or prefilled by gas under the predetermined gas pressure to provide the predetermined gas pressure for the drug delivery operation. Alternatively, a battery may be used as the energy storage member. In this case, the energy may be preloaded by loading the energy source or by providing the loaded energy source, wherein the batterie may be used for driving a pump for generating the predetermined gas pressure.

In one embodiment, the section of the fluid channel, which is movable together with the plunger, i.e. the second section, is configured for guiding the drug from the drug chamber to the injection member along an injection path and completely delimits the injection path circumferentially, and/or, in other words, completely encloses the drug perpendicular to the injection path. In further other words, if the drug flows through the fluid channel, the drug has a streaming direction and the second section of the fluid channel encloses the drug perpendicular to the streaming direction completely. In furthermore other words, the fluid path has a longitudinal extension, and the second section is a complete longitudinal section of the fluid path and/or completely surrounds the drug in radial direction, wherein the radial direction of the second section is always perpendicular to the longitudinal fluid path.

In one embodiment, the section of the fluid channel, in particular the second section, comprises or is arranged within a through-recess within the plunger. If the second section of the fluid channel comprises the through-recess, the second section may be formed by the through-recess of the plunger. Then, the through-recess may sealingly communicate with the fluid channel upstream the second section and the injection member downstream the second section. The first section may open out into the through-recess, and a fluid path within the injection member, e.g. a channel of the first needle, may open out into the through-recess of the plunger.

Alternatively, if the second section of the fluid channel is arranged within the through-recess of the plunger, the second section may be formed by a hose or tube, which sealingly communicate with the fluid channel upstream the second section and the injection member downstream the second section. For example, the first section may open out into the hose or, respectively, tube,

or the first section may be made of the same piece of hose or, respectively, tube. In other words, the first and second section of the fluid channel may be formed by the same continuous piece of hose or, respectively, tube. Alternatively or additionally, the fluid path within the injection member may open out into the hose or, respectively, tube.

In one embodiment, the drug delivery device comprises a pressure chamber within the housing. The pressure chamber comprises a gas inlet communicating with the pressure arrangement in order to receive the gas pressure from the pressure arrangement, and a gas outlet configured for providing the gas pressure for moving the pressure member. The plunger may be arranged in the pressure chamber and may be movable within the pressure chamber from its initial position to its operating position by the gas pressure within the pressure chamber. The plunger may be configured for closing the gas outlet in its initial position and for opening the gas outlet in its operating position. The plunger may sealingly close the pressure chamber at a pressure side of the plunger. So, the pressure chamber may be sealingly enclosed by the injection housing and the plunger. The pressure arrangement may comprise the pressure chamber, a first conduit for guiding the gas to the gas inlet of the pressure chamber, and/or a second conduit for guiding the gas away from the gas outlet of the pressure chamber.

In one embodiment, the injection member is coupled to the plunger at an injection side of the plunger and is movable together with the plunger. For example, the injection member may comprise or may be made of the first needle for injecting the drug into the injection site. If the injection member is the first needle, the first needle may be moved together with the plunger, e.g. for piercing the skin of the user. The injection side of the plunger faces away from the pressure side of the plunger. The first needle may communicate with the fluid channel in order to receive the drug from the drug chamber through the fluid channel. Alternatively, the injection member may be a nozzle for injecting the drug into the skin under high pressure without piercing the skin by a needle, wherein the nozzle may communicate with the fluid channel in order to receive the drug from the drug chamber through the fluid channel.

In one embodiment, the pressure member comprises a stopper within the drug delivery device, wherein the stopper is arranged at a distance to the drug outlet in the initial state of the drug delivery device, and wherein the drug chamber is sealingly enclosed by the drug container, in particular inner side walls of the drug container, in particular the drug chamber, and the stopper. The pressure member may be formed by the stopper. The gas pressure for moving the plunger may be the same as the gas pressure for moving the stopper, e.g. the predetermined gas pressure. Alternatively, the gas pressure for moving the stopper may be different from the gas pressure for moving the stopper.

In one embodiment, the pressure arrangement comprises a pressure cavity within the drug container; the pressure cavity may be arranged at that side of the stopper facing away from the drug outlet; and the pressure cavity and the stopper may be formed and arranged such that the stopper is moved towards the drug outlet by a gas pressure within the pressure cavity, if the gas pressure within the pressure cavity corresponds to the predetermined gas pressure or more. If the stopper is moved towards the drug outlet, the stopper may be moved in a dispensing direction. The first needle may extend in a direction oblique to a dispensing direction. That the first needle may extend in a direction oblique to the dispensing direction comprises the case in which the first needle may extends perpendicular to the dispensing direction. If there is a second needle, e.g. for piercing a septum of the drug container, the second needle communicating with the first needle, the second needle may extend in a direction parallel or corresponding to the dispensing direction.

In one embodiment, the pressure arrangement comprises a pressure reservoir in which the predetermined gas pressure is present and/or in which the predetermined gas pressure can be build up. Alternatively or additionally, the pressure arrangement may comprise a pump for generating the gas pressure. The pressure reservoir may communicate with the pressure cavity and/or the pressure chamber. For example, the pressure reservoir may communicate with the gas inlet of the pressure chamber. Further, the pressure reservoir may be couplable with the pressure cavity in order to provide the pressure cavity with the gas pressure of the pressure reservoir. The pressure reservoir may be couplable with the pressure cavity via the pressure chamber and the gas outlet of the pressure chamber, if the plunger is in its operating position. The pump may be configured for building-up the gas pressure within the pressure reservoir, the pressure chamber, and/or the pressure cavity. Thus, the pump may communicate with the pressure reservoir, the pressure chamber, and/or the pressure cavity.

The use of the gas-powered autoinjector with the pump offers the additional advantage of a constant force curve over the entire injection time. As an alternative to the pump, the pressure reservoir may be prefilled and/or preloaded, e.g. by a manufacturer of the drug delivery device or of the drug.

In one embodiment, the drug delivery device comprises an injection sleeve for protecting the injection member, wherein the injection sleeve is configured such that the injection sleeve protects the injection member in a first position of the injection sleeve in the initial state of the drug delivery device and that the injection sleeve exposes the injection member in a second position of the injection sleeve for the dispensing operation, wherein the plunger and the injection sleeve are formed and arranged such that the plunger enables a movement of the injection sleeve from its first to its second position, if the plunger is in its initial position, and that

the movement of the injection sleeve from its first to its second position is prevented, if the plunger is in its operating position.

The injection sleeve may be translatory movable relative to the housing. For example, the injection sleeve may expose the injection member, if the injection sleeve is pushed into the housing. An injection housing enclosing the pressure chamber and accommodating the plunger may have at least one engaging recess, wherein at least a part of the engaging recess may be blocked by the plunger, when the plunger is in its initial position. The injection sleeve may surround the injection housing, may be movable relative to the injection housing, and may comprise one or more engaging features, wherein the engaging features may not be engaged with the blocked engaging recess, when the plunger is in its initial position, and wherein the engaging features may engage with the engaging recess, when the plunger is in its operating position and unblocks the engaging recess. In this way, the injection sleeve may be held in its third position after the dispensing operation. Optionally, the third position corresponds to the first position, wherein, in contrast to the first position, the engaging features are engaged with the corresponding engaging recesses in the third position.

The injection sleeve may be provided to cover the needle, in particular the first needle for piercing the skin. The injection sleeve may be provided to cover the needle before the needle pierces the skin and/or after the needle has been removed from the skin, e.g. after completion of the drug delivery operation. Before the drug delivery operation is commenced, the injection sleeve in its first position may protrude from the housing, e.g. to cover the tip of the needle (such as by axially extending beyond the tip of the first needle, e.g. at least with a contact surface of the injection sleeve). For the drug delivery operation, the injection sleeve may be displaced relative to the housing into its second position. After completion of the drug delivery operation, the injection sleeve may be moved relative to the housing, e.g. to cover the tip of needle and/or into the third position.

The drug delivery device may comprise a sleeve spring. The sleeve spring may be operatively couplable to or coupled to the injection sleeve in order to move the injection sleeve relative to the housing. The force of the sleeve spring may have to be overcome in order to move the injection sleeve into the housing. In the third position, e.g. after the drug delivery operation has been completed and the drug delivery device has been removed from the skin, the injection sleeve may be locked against a further movement with respect to the housing, such as by the above engaging features and corresponding engaging recesses. This may contribute to a safe handling of the drug delivery device after its usage by protecting the used needle.

In one embodiment, the drug delivery device comprises a trigger member configured for initiating the dispensing operation; and a release mechanism, wherein the release mechanism is mechanically coupled to the trigger member. The release mechanism may be configured for preventing the injection sleeve from being moved into its second position in the initial state of the drug delivery device and for releasing the injection sleeve such that it is movable into its second position, when the trigger member is activated. The trigger member may be a button, rod, knob, or a lever.

In one embodiment, the drug delivery device comprises a second needle, wherein the second needle is communicatively couplable or coupled to the first needle. The second needle may be mechanically coupled to the trigger member. The second needle and the trigger member may be configured such that an activation of the trigger member couples the second needle with the outlet of the drug container. The first needle may communicate with the second needle, e.g. by the fluid channel, for guiding the drug from the drug container through the second needle and the fluid channel towards the first needle. The second needle may extend perpendicular to the first needle. The second needle may extend in parallel to the dispensing direction.

If the second needle is not permanently coupled, but may be couplable to the drug container, the drug outlet may be sealed by a septum. In this case, the second needle may be permanently coupled to the trigger member. The septum may be pierced by the second needle for the dispensing operation. In other words, the drug outlet may be sealed by the septum in the initial state of the drug delivery device and the septum may be pierced by the corresponding needle for the dispensing operation. In contrast, if the second needle is permanently coupled to the drug container, the drug outlet may correspond to the second needle. In other words, the second needle may provide the drug outlet of the drug container. In this case, the septum for being pierced by the second needle may be provided for covering and protecting an entry of the fluid channel at the trigger member.

In one embodiment, the trigger member protrudes from the housing. The trigger member may be translatory movable relative to the housing. The second needle may be coupled to the trigger member such that the second needle is translatory movable together with the trigger member and that the second needle pierces the septum at the outlet of the drug container, when the trigger member is pushed towards the housing.

In one embodiment, the trigger member is electrically coupled to the pump, wherein an activation of the trigger member may activate the pump in order to build up the predetermined gas pressure. The gas pressure may be built up within the pressure reservoir, the pressure

chamber, the pressure cavity, and/or one, two or more conduits connecting the pump, the pressure reservoir, the pressure chamber, and/or the pressure cavity with each other.

In one embodiment, the trigger member provides a first activation mode and a second activation mode. The first activation mode may activate the pump and the second activation mode may couple the second needle with the drug outlet of the drug container. For example, the first activation mode may correspond to a rotation of the trigger member around its axis. So, with respect to the first activation mode, the trigger member may be rotated from a first angular position to a second angular position for activating the pump. In contrast, the second activation mode may correspond to the translatory movement of the trigger member towards the housing. So, with respect to the second activation mode, the trigger member may be pressed from a first axial position to a second axial position for coupling the second needle with the drug chamber of the drug container.

In one embodiment, the drug delivery device comprises a pressure sensor and a notification member, wherein the pressure sensor and the notification member are configured such that the notification member signals that the drug delivery device is ready for use, if the pressure sensor senses the predetermined gas pressure. The pressure sensor and the notification member may be electrically coupled to a control unit of the drug delivery device. The pressure sensor may be coupled to the pressure reservoir, the pressure chamber, and/or the pressure cavity in order to sense the corresponding gas pressure.

In one embodiment, the drug container is a cartridge. Alternatively, the drug container may be a syringe or a flexible pouch. The drug container may comprise the needle, e.g. the 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.

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 perspective top view of an exemplary embodiment of a drug delivery device.

Figure 2 illustrates perspective bottom view of the drug delivery device of figure 1.

Figure 3 illustrates a perspective view of an interior of the drug delivery device of figure 1.

Figure 4 illustrates a cross-sectional side view of an interior of the drug delivery device of figure 1.

Figure 5 illustrates a cross-sectional bottom view of an interior of the drug delivery device of figure 1.

Figure 6 illustrates a cross-sectional front view of an interior of the drug delivery device of figure 1.

Figure 7 illustrates a cross-sectional bottom view of another exemplary embodiment of the drug delivery device of figure 1.

Figure 8 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 perspective top view of an exemplary embodiment of a drug delivery device 20. The drug delivery device 20 comprises a housing 22, a trigger member 21, a notification member 23, and an injection sleeve 25. A shape and/or size of the housing 22 may be flat and/or may correspond to the shape and, respectively, size of a conventional (computer-)mouse.

The trigger member 21 may be provided for initiating a drug delivery operation. The trigger member 21 may be a button, rod, knob, or a lever. The trigger member 21 may protrude from the housing 22. The trigger member 21 may be translatory movable and/or rotatable relative to the housing 22. The trigger member 21 may provide a first activation mode and a second activation mode. For example, the first activation mode may correspond to a rotation of the trigger member 21 around its axis and the second activation mode may correspond to a translatory movement of the trigger member 21 into the housing 22. The trigger member 21 may have an axis of rotation, wherein the trigger member 21 may be rotated around the axis of

rotation from a first angular position to a second angular position, in correspondence with the first activation mode, and wherein the trigger member 21 may be translatory moved from a first axial position to a second axial position, in correspondence with the second activation mode.

The notification member 23 may be provided for signaling a current state of the drug delivery device 20 to a user. For example, the notification member 23 may signal the user when the drug delivery operation is under preparation and afterwards when the drug delivery device is ready for use.

The injection sleeve 25 may be arranged for protecting an injection member (not shown in figure 1). The injection sleeve 25 may be translatory movable relative to the housing 22. The injection sleeve 25 may be configured such that the injection sleeve 25 protects the injection member in a first position of the injection sleeve 25 in an initial state of the drug delivery device 20 and that the injection sleeve 25 exposes the injection member in a second position of the injection sleeve 25 for a dispensing operation. For example, the injection sleeve 25 may expose the injection member, if the injection sleeve 25 is pushed into the housing 22. The injection sleeve 25 may be pushed into the housing 22 by arranging the drug delivery device 20 on the injection site, i.e. the skin of a user, and by pressing the drug delivery device 20 against the injection site.

The drug delivery device 20 may be an autoinjector. The energy for driving the drug delivery operation in an autoinjector may be provided by components integral to the drug delivery device 20 and does not have to be loaded into the drug delivery device 20 by the user during the operation as is the case in many spring-driven pen-type variable dose injectors, where, usually, the energy is loaded into a spring by the user during a dose setting procedure. 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.

Figure 2 illustrates a perspective bottom view of the drug delivery device 20 of figure 1. The housing 22 comprises a bearing surface 27 at its bottom. The bearing surface 27 may be configured to be in contact with the injection site, in particular the skin of the user, during usage of the drug delivery device 20. A height of the housing 22 perpendicular the bearing surface 27 may be smaller than a length of the housing 22 parallel to the bearing surface 27. The bearing surface 27 of the drug delivery device 20 may be adjacent to a location where a drug within the drug delivery device 20 may be injected under or into the skin of the user during a dispensing operation. There may be a grip area opposite to the bearing surface 27, i.e. on top of the housing 22 facing away from the skin of the user during usage. The drug may be injected by a needle, in particular a first needle 72 (see figure 6), for piercing the skin or by a nozzle (not

shown) for injecting the drug without piercing the skin. The injection member may be in or may be brought into fluid communication with an interior of the drug container 24.

Figure 3 illustrates a perspective view of an interior of the drug delivery device 20 of figure 1. The drug delivery device 20 comprises a drug container 24. The drug container 24 may be permanently arranged within the housing 22, e.g. already during mounting the drug container 24. Alternatively, the drug container 24 may be arranged after the drug container 24 is mounted and/or may be removably arranged within the housing 22. The drug container 24 may comprise a drug outlet 28. The drug outlet 28 may be sealed by a septum, wherein the septum may be held by a septum frame 29. The drug container 24 comprises a drug chamber 26. A drug, i.e. a medicament, e.g. liquid medicament, may be arranged within the chamber 26. The chamber 26 may be fluid-tight closed by a stopper 32. The stopper 32 may movably retained in the drug container 24 and may seal the drug container 24 remote from the drug outlet 28. The stopper 32 may be displaced towards the drug outlet 28 of the drug container 24 to dispense the drug retained within the chamber 26 through the drug outlet 28. The stopper 32 may be used as a pressure member for pressing the drug out of the drug chamber 26. In particular, the stopper 32 may be movable in a dispensing direction 40 towards the drug outlet 28, wherein the drug is dispensed through the drug outlet 28, if the stopper 32 is moved in the dispensing direction 40. Alternatively, a separate pressure member may be provided for moving the stopper 32.

The drug delivery device 20 comprises a pressure arrangement for providing a predetermined gas pressure. The pressure arrangement comprises the pressure member, which is coupled or couplable to the drug container 24 and which is configured for pressing the drug through the drug outlet 28 out of the drug chamber 26 upon being moved by the predetermined gas pressure. The pressure member may be the stopper 32. So, the predetermined gas pressure may be provided for moving the stopper 32 in the dispensing direction 40 during the dispensing operation. Alternatively, for example if the drug container 24 is a flexible pouch, the pressure member may be a piston for squeezing the pouch such that the drug is squeezed out of the drug chamber 26. The drug delivery device 20 operating with the predetermined gas pressure may be referred to as gas-powered autoinjector.

The pressure arrangement may comprise a pressure cavity 30. The pressure cavity 30 may be provided at a side of the stopper 32 facing away from the drug outlet 28. The pressure cavity 30 may be provided in a cavity housing 31 and/or within the drug container 24. For example, in the initial state of the drug delivery device 20, the pressure cavity 30 may be present in a small area within the cavity housing 31 and/or within a small region of the drug container 24. During the dispensing operation, when the stopper 32 moves in the dispensing direction 40, a volume of the pressure cavity 30 increases within the drug container 24 while a volume of the pressure

chamber 26 decreases, whereas a volume of the pressure cavity 30 within the cavity housing 31 remains the same. Alternatively, the pressure cavity 30 may be arranged within the drug container 24 only. The cavity housing 31 may provide a terminal for providing the predetermined gas pressure to the pressure cavity 30.

The pressure arrangement may further comprise a pump 34. The pump 34 may be an electrical pump and may be provided to generate the predetermined gas pressure. The pump 34 may be driven by an energy source, for example a battery (not shown). The trigger member may be electrically coupled to the pump 34. An activation of the trigger member 21 may activate the pump 34 in order to build up the predetermined gas pressure. The pump may be driven by a battery (not shown).

The pressure arrangement may further comprise a pressure reservoir 36. The pressure reservoir 36 may communicate with the pump 34. The pump 34 may generate the predetermined gas pressure within the pressure reservoir 36. Alternatively, the pressure reservoir 36 may be prefilled and/or preloaded by the predetermined gas pressure and the pump 34 may be omitted.

The pressure arrangement may further comprise a pressure chamber 80 (see figure 6), which may communicate with the pressure reservoir 36 and/or the pressure cavity 30. So, the predetermined gas pressure may be built up within the pressure reservoir 34, the pressure chamber 80, and/or the pressure cavity 30. The pressure chamber 80 may be arranged within an injection housing 38. The injection housing 38 may enclose the injection member for injecting the drug into the skin.

The notification member 23 may comprise a green light source 42, a red light source 44, and a valve 46. Further, a sensor for sensing the predetermined gas pressure may be arranged within or next to the notification member 23. The notification member 23, in particular the sensor, may communicate with the pressure arrangement, e.g. the pressure reservoir 36, in order to receive the gas pressure to be sensed. For example, when the drug delivery device 20 is activated such that the predetermined gas pressure may be built up within the pressure reservoir 36, the notification member 23 notifies the user about this preparatory measure by activating the red light source 44. If the sensor senses that the predetermined gas pressure is reached, the notification member 23 may notify the user about the drug delivery device 20 being ready for use by activating the green light source 42 and by shutting down the red light source 44. The pressure sensor and/or the notification member 23 may be electrically coupled to a control unit (not shown) of the drug delivery device 20.

A sleeve spring 50 may be arranged around the injection housing 38. The sleeve spring 50 may be configured for being loaded by the injection sleeve 25, when the drug delivery device 20, in particular the bearing surface 27, is arranged on and pressed against the injection site such that the injection sleeve 25 may be moved into the housing 22. The sleeve spring 50 may further be configured for being released and thereby pressing the injection sleeve 25 out of the housing 22, if the drug delivery device 20 is removed from the injection site.

In the embodiment shown in figure 3, the drug container 24 is a cartridge sealed by a septum. In this case, the septum has to be pierced in order to enable the dispensing operation. A second needle 52 may be arranged to pierce the septum of the drug container 24. The second needle 52 may extend in a direction parallel or corresponding to the dispensing direction 40. The second needle 52 may be coupled to the trigger member 21. In particular, the second needle 52 may be moved together with the trigger member 21 against the dispensing direction 40. For example, the first activation mode of the trigger member 21 may activate the pump 34, and the second activation mode of the trigger member 21 may couple the second needle 52 with the drug outlet 28 of the drug container 24. So, with respect to the first activation mode, the trigger member 21 may be rotated from its first angular position to its second angular position for activating the pump 34. With respect to the second activation mode, the trigger member 21 may be pressed from its first axial position to its second axial position for coupling the second needle 52 with the drug chamber 26 of the drug container 24. So, the first activation mode may be used for initiating a preparation of the drug delivery device 20, in particular for building-up the predetermined gas pressure, while red light source 44 of the notification member 23 may signal the preparation status, and the second activation mode may be used for initiating the dispensing operation, after the green light 42 of the notification member 23 may signal that the drug delivery device is ready to use.

A release member 54 may be coupled to the trigger member 21. The release member 54 may be configured for preventing a movement of the injection sleeve 25 in the initial state of the drug delivery device 20 and for enabling the movement of the injection sleeve 25 when the dispensing operation is triggered. For example, the release member 54 may comprise a rod, wherein a first end of the rod is coupled to the trigger member 21 and movable together with the trigger member 21 and wherein a second end of the rod is coupled to the injection sleeve 25. For example, the first end of the rod may be coupled to and guided by one or to guide bars for guiding the rod. For example, the rod may comprise two through-recesses which extend parallel to the dispensing direction 40 and in which the guide bars 56 are arranged. So, the release member 54 may be moved against the dispensing direction 40 while being guided by the guide bars 56. The second end of the bar may be arranged between the injection sleeve 25 and the sleeve spring 50 in the initial state of the drug delivery device, if the injection sleeve 25 is in its

first position. In this position, the rod blocks a movement of the injection sleeve 25 towards the sleeve spring 50. If the rod is moved together with the trigger member 28 against the dispensing direction 40, the second end of the rod may be removed from the space between the injection sleeve 25 and the sleeve spring 50, and thereby the movement of the injection sleeve 25 towards the sleeve spring 50 may be enabled.

The second needle 52 may communicate with a fluid channel. The fluid channel may be coupled or may be couplable to the drug chamber 26 for receiving the drug from the drug chamber 26. The fluid channel may communicate with the injection member for guiding the drug to the injection member during the dispensing operation. In particular, the fluid channel may couple the second needle 52 to the injection member. If the second needle 52 already pierced the septum, the fluid channel may couple the drug chamber 26 with the injection member. So, the fluid channel may communicate with the drug chamber 26 in order to provide the drug to the injection member.

The fluid channel may comprise a first section 58 and a second section. The first section 58 may extend through the injection housing 38. The first section 58 may comprise a slack loop 59 within the injection housing 38, in particular within the pressure chamber 80. The first section 58 of the fluid channel may be flexible. The first section 58 may be provided by a hose or a tube, e.g. an incompressible hose or tube, e.g. by a hose or tube made from Polytetrafluoroethylene (PTFE). The second section of the fluid channel may be arranged within the injection housing 38. The second section of the fluid channel may couple the first section 58 with the injection member. The first section 58 and the second section of the fluid channel may be made in one piece, e.g. by one continuous piece of hose or, respectively, tube. Alternatively, the second section of the fluid channel may be made separate from the first section 58 and may be coupled to the first section 58 of the fluid channel when mounting the drug delivery device 20.

The pressure reservoir 36 may be coupled to the injection housing 38 by a first conduit 60. The first conduit 60 may be arranged for providing the gas pressure from the pressure reservoir 36 to the pressure chamber 80 (see figure 6) within the injection housing 38. The injection housing 38 may be coupled to the pressure cavity 30, e.g. via the cavity housing 31, by a second conduit 62. The second conduit 62 may be arranged for providing the gas pressure from the pressure chamber 80 to the pressure cavity 30. The notification member 32, in particular the sensor, may be coupled to the pressure reservoir 36 by a third conduit 64. The third conduit 64 may be arranged for providing the gas pressure within the pressure reservoir 36 to the sensor such that the sensor is able to sense the gas pressure. The pump 34 may be coupled to the pressure reservoir 36 by a fourth conduit 66. The fourth conduit 66 may be arranged for providing the gas pressure generated by the pump 34 to the pressure reservoir 36.

An electric line 68 may be provided for coupling the trigger member 28 to the pump 34. A signal for activating the pump 34 for generating the predetermined gas pressure may be transferred from the trigger member 28 to the pump 34 by the electric line 68.

Figure 4 illustrates a cross-sectional side view of an interior of the drug delivery device 20 of figure 1.

Figure 5 illustrates a cross-sectional bottom view of an interior of the drug delivery device 20 of figure 1. In particular, figure 5 shows a cross-sectional view along the corresponding dashed line shown in figure 4. A plunger 70 may be arranged within the injection housing 38. The plunger 70 may be movably arranged within the housing 22 from an initial position of the plunger 70 to an operating position of the plunger 70. The plunger 70 may prevent the predetermined gas pressure from being applied to the pressure member in its initial position and may enable the predetermined gas pressure to be applied to the pressure member in its operating position.

The injection housing 38 may surround the plunger 70 and the injection sleeve 25 may surround the injection housing 38. The plunger 70 and the injection sleeve 25 may be formed and arranged such that the plunger 70 enables a movement of the injection sleeve 25 from its first to its second position, if the plunger 70 is in its initial position, and that the movement of the injection sleeve 25 from its first to its second position an/or to its third position is prevented, if the plunger 70 is in its operating position. Further, the second end of the rod of the release member 58 may partly overlap the injection sleeve 25 in the initial state of the drug delivery device 20. Furthermore it may be seen that the release member 58 is guided by the guide bars 56.

Figure 6 illustrates a cross-sectional front view of an interior of the drug delivery device 20 of figure 1. In particular, figure 5 shows a cross-sectional view along the corresponding dashed line shown in figure 4. The injection member, in particular the first needle 72, may be coupled to the plunger 70. In particular, the first needle 72 may be coupled to the plunger 70 at an injection side of the plunger 70. The first needle 72 may extend in a direction oblique to the dispensing direction 40. That the first needle 72 extends in a direction oblique to the dispensing direction 40 may comprise the case in which the first needle 72 extends perpendicular to the dispensing direction 40. The injection side of the plunger 70 faces the injection site during the drug delivery operation. The pressure chamber 80 may be delimited by a pressure side of the plunger 70. A sealing 78 together with the plunger 70 may sealingly close the pressure chamber 80. The pressure side of the plunger 70 may face away from the injection side of the plunger 70. A gas

inlet 74 may open out into the pressure chamber 80. The gas inlet 74 may be communicatively coupled to the pressure reservoir 36 by the first conduit 60.

Figure 6 shows the initial state of the drug delivery device 20. In the initial state of the drug delivery device 20, the plunger 70 may be in its initial position. So, figure 6 shows the plunger 70 in its initial position. If the plunger 70 is in its initial position, a gas outlet (not shown) is covered and thereby sealingly closed by the plunger 70. The gas outlet may communicate with the pressure cavity 30 via the second conduit 62. At least a section of the fluid channel, e.g. the second section, is coupled to the plunger 70 and is moved together with the plunger 70, if the plunger 70 is moved from its initial position to its operating position. For example, the first section 58 of the fluid channel may be coupled or couplable to the drug chamber 26, whereas the second section may be coupled to the first section 58. The second section may sealingly communicate with the first section 58. The first section 58 may be flexible in order to compensate for the movement of the second section. Further, the slack loop 59 may be provided in order to compensate for the movement of the second section.

The section of the fluid channel, which is movable together with the plunger 70, i.e. the second section, may be configured for guiding the drug from the drug chamber 26 to the injection member along an injection path. The second section may completely enclose the drug perpendicular to the injection path. Thus, if the drug flows through the fluid channel, the drug may have a streaming direction and the second section of the fluid channel encloses the drug perpendicular to the streaming direction completely. So, the fluid path may have a longitudinal extension, and the second section may be a complete longitudinal section of the fluid path and/or may completely surround the drug in radial direction, wherein the radial direction of the second section may always be perpendicular to the longitudinal fluid path.

The second section of the fluid channel may comprise a through-recess 79 within the plunger 70. Alternatively, the second section of the fluid channel may be arranged within the through-recess 79 within the plunger 70. If the second section of the fluid channel comprises the through-recess 79, the second section may be formed by the through-recess 79 of the plunger 70. Then, the through-recess 79 may sealingly communicate with the fluid channel upstream the second section and the injection member downstream the second section. The first section 58 may open out into the through-recess 79, and a fluid path within the injection member, e.g. a channel of the first needle 72, may open out into the through-recess 79 of the plunger 70. Alternatively, if the second section of the fluid channel is arranged within the through-recess 79 of the plunger 70, the second section may be formed by a hose or tube, which sealingly communicate with the fluid channel upstream the second section and the injection member downstream the second section.

The plunger 70 may comprise one or two protrusions 76 and the injection housing 38 may correspondingly comprise one or two engaging recesses 82. The protrusions 76 of the plunger 70 may be arranged within the corresponding engaging recesses 82 in the initial state of the drug delivery device 20. In particular, the protrusions 76 may be arranged within the corresponding engaging recesses 82, e.g. in an upper part of the corresponding engaging recesses 82, if the plunger 70 is in its initial position. So, in the initial position of the plunger 70 the engaging recesses 82 may be at least partly filled by the protrusions 76 of the plunger 70. The injection sleeve 25 may comprise one or two engaging features 84, for example flexible bars. The amount of the engaging features 84 may correspond to the amount of the protrusions 76. The position of the engaging features 84 in the initial position of the plunger 70 may correspond to the position of the protrusions 76. So, if the plunger 70 is in its initial position, the engaging features 84 may be biased and/or pre-flexed, and blocked by the protrusions 76 of the plunger 70 such that the engaging features 84 may not engage with the engaging recesses 82 of the injection housing 38 partly filled by the protrusions 76.

Before the drug delivery operation is commenced, the injection sleeve 25 may protrude from the housing 22, e.g. to cover the tip of the first needle 72 (such as by axially extending beyond the tip of the first needle 72, e.g. at least with a contact surface of the injection sleeve 25). If the trigger member 21 is pressed into the housing 22 by the user, the release member 54 may release the injection sleeve 25, e.g. by moving the second end of the rod of the release member 54 away from the injection sleeve 25, such that the injection sleeve 25 may be displaced relative to the housing 22 for the drug delivery operation.

If the trigger member 21 is pressed into the housing 22, the second needle 52 may pierce the septum of the drug container 24 and the injection sleeve 25 may be released. If the drug delivery device 20 is arranged on the skin of the user and if the drug delivery device 20 is pressed against the skin of the user, the injection sleeve 25 may be pressed into the housing 22. The gas from the pressure reservoir 36 may be guided into the pressure chamber 80 such that the pressure in the pressure chamber 80 may increase up to the predetermined gas pressure and may push the plunger 70 from its initial position to its operating position.

If the plunger 70 is moved from its initial position to its operating position, the gas outlet of the pressure chamber 26 may be opened and the gas from the pressure chamber 80 may be guided to the pressure cavity 30. The gas pressure in the pressure cavity 30 may press the stopper 32 in the dispensing direction 40 and thereby the drug through the second needle 52, the first section 58 of the fluid channel, and the second section of the fluid channel towards the first needle 72. Further, if the plunger 70 is moved from its initial position to its operating position

by the gas pressure in the pressure chamber 80 and if the first needle 72 is used as the injection member, the first needle 72 may pierce the skin of the user and the drug may be injected into the skin. The gas pressure for moving the plunger 70 may be the same as the gas pressure for moving the stopper 32, e.g. the predetermined gas pressure. Alternatively, the gas pressure for moving the plunger 70 may be different from the gas pressure for moving the stopper 32.

The engaging features 84 may not be engaged with the blocked engaging recess 82, if the plunger 70 is in its initial position. The engaging features 84 may engage with the engaging recess 82, if the plunger 70 is in its operating position and unblocks the engaging recess 82. In particular, if the plunger 70 is in its operating position, the upper areas of the engaging recesses 82 are exposed and free from the protrusion 76, and if the drug delivery device 20 is removed from the skin of the user after the drug delivery operation, the injection sleeve 25 may be pushed out of the housing 22 by the sleeve spring 50 into a final or third position, wherein the engaging features 84 may snap into the exposed parts of the engaging recesses 82 such that the injection sleeve 25 may not be pushed into the housing 22 again. In this way, the injection member may be permanently protected after the use of the drug delivery device 20.

Figure 7 illustrates a cross-sectional bottom view of another exemplary embodiment of the drug delivery device 20 of figure 1. The drug delivery device 20 may widely correspond to the above drug delivery device. Therefore, only those features are explained in the following in which the drug delivery device 20 shown in figure 7 differs from the above drug delivery device 20.

The drug container 24 may be a syringe, e.g. a syringe with a preinstalled second needle 52, such as a staked needle. In this case the septum may be arranged at an entry of the fluid channel, e.g. for preventing dirt from entering the fluid channel before the dispensing operation is commenced. The septum may be configured for being pierced by the second needle 52 of the syringe, if the trigger member 21 is pushed into the housing 22, wherein in this embodiment the second needle 52 is fixed and the septum is moved together with the trigger member 21.

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).

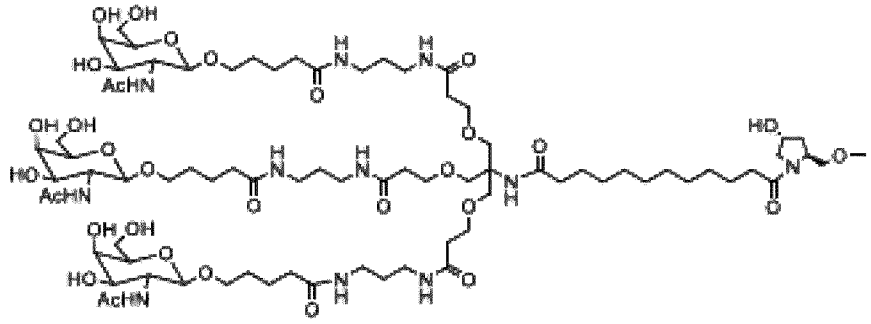
As further described in ISO 11608-1:2014(E), a single-dose container system may involve a needle-based injection device with a replaceable container. In one example for such a system, each container holds a single dose, whereby the entire deliverable volume is expelled (full evacuation). In a further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

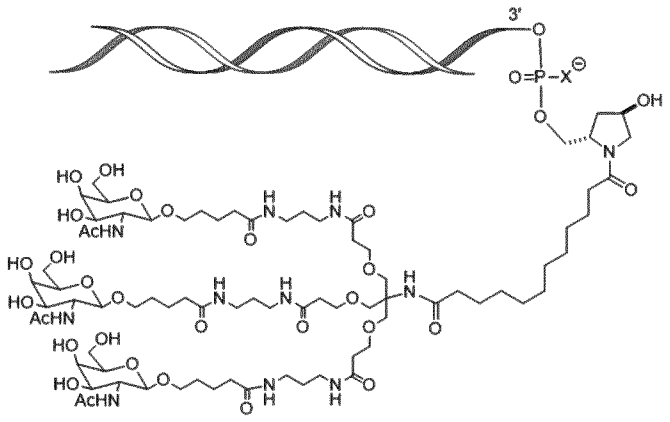
As used herein, the terms 2' -deoxy- 2'-fluorocytidine and 2'-fluorocytidine may be used interchangeably.

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 8.

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



Fitusiran is shown in Figure 8 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 (monohydrate)	<0.01	0.0885
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	trigger member
22	housing
23	notification member
24	drug container
25	injection sleeve
26	drug chamber
27	bearing surface
28	drug outlet
29	septum frame
30	pressure cavity
31	cavity housing
32	stopper
34	pump
36	pressure reservoir
38	injection housing
40	dispensing direction
42	green light source
44	red light source
46	valve
50	sleeve spring
52	second needle
54	release member
56	guide bar
58	first section
59	loop
60	first conduit
62	second conduit
64	third conduit
66	fourth conduit
68	electric line
70	plunger

72 first needle

74 gas inlet

76 protrusion

78 sealing

79 through-recess

80 pressure chamber

82 engaging recess

84 engaging features

Claims

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

a housing (22) for receiving a drug container (24) or with the drug container (24) being arranged within the housing (22), the drug container (24) having a drug chamber (26), a drug outlet (28) of the drug chamber (26), and a drug within the drug chamber (26);

an injection member for injecting the drug into an injection site;

a pressure arrangement within the housing (22), the pressure arrangement being configured for providing a predetermined gas pressure;

a pressure member, which is coupled or couplable to the drug container (24) and which is configured for pressing the drug through the drug outlet (28) out of the drug chamber (26) upon being moved by the predetermined gas pressure;

a plunger (70), which is movable relative to the housing (22) from an initial position of the plunger (70) to an operating position of the plunger (70), the plunger preventing the predetermined gas pressure from being applied to the pressure member in its initial position and enabling the predetermined gas pressure to be applied to the pressure member in its operating position; and

a fluid channel, which is coupled or couplable to the drug chamber (26) for receiving the drug from the drug outlet of the drug chamber (26), the fluid channel being provided to communicate with the injection member for guiding the drug to the injection member during a dispensing operation, wherein at least a section (58) of the fluid channel is coupled to the plunger (70) and is moved together with the plunger (70), when the plunger (70) is moved from its initial position to its operating position.

2. The drug delivery device (20) of claim 1, wherein the section (58) of the fluid channel, which is movable together with the plunger (70), is configured for guiding the drug from the drug chamber (26) to the injection member along an injection path and completely delimits the injection path circumferentially.

3. The drug delivery device (20) of any one of the preceding claims, wherein the section (58) of the fluid channel comprises or is arranged within a through-recess (79) within the plunger (70).

4. The drug delivery device (20) of any one of the preceding claims, comprising a pressure chamber (80) within the housing (20), the pressure chamber (80) comprising a gas inlet (74) communicating with the pressure arrangement in order to receive the gas pressure from the

pressure arrangement, and a gas outlet configured for providing the gas pressure for moving the pressure member, wherein

the plunger (70) is arranged in the pressure chamber (80) and is movable within the pressure chamber (80) from its initial position to its operating position by the gas pressure within the pressure chamber (80), and

the plunger (70) is configured for closing the gas outlet in its initial position and for opening the gas outlet in its operating position.

5. The drug delivery device (20) of any one of the preceding claims, wherein the injection member is coupled to the plunger (70) at an injection side of the plunger (70) and is movable together with the plunger (70).

6. The drug delivery device (20) of any one of the preceding claims, wherein the pressure member comprises a stopper (32) within the drug chamber (26), wherein the stopper (32) is arranged at a distance to the drug outlet (28) in the initial state of the drug delivery device (20), and wherein the drug chamber (26) is sealingly enclosed by the drug container (24) and the stopper (32).

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

the pressure arrangement comprises a pressure cavity (30) within the drug container (24);

the pressure cavity (30) is arranged at that side of the stopper (32) facing away from the drug outlet (28); and

the pressure cavity (30) and the stopper (32) are formed and arranged such that the stopper (32) is moved towards the drug outlet (28) by a gas pressure within the pressure cavity (30), when the gas pressure within the pressure cavity (30) corresponds to the predetermined gas pressure or more.

8. The drug delivery device (20) of any one of the preceding claims, wherein

the pressure arrangement comprises a pressure reservoir (36) in which the predetermined gas pressure is present and/or in which the predetermined gas pressure can be build up; and/or

the pressure arrangement comprises a pump (34) for generating the gas pressure.

9. The drug delivery device (20) of any of the preceding claims, comprising an injection sleeve (25) for protecting the injection member, wherein the injection sleeve (25) is configured such that the injection sleeve (25) protects the injection member in a first position of the injection sleeve (25) in the initial state of the drug delivery device (20) and that the injection sleeve (25)

exposes the injection member in a second position of the injection sleeve (25) for the dispensing operation, wherein the plunger (70) and the injection sleeve (25) are formed and arranged such that the plunger (70) enables a movement of the injection sleeve (25) from its first to its second position, when the plunger (70) is in its initial position, and that the movement of the injection sleeve (25) from its first to its second position is prevented, when the plunger (70) is in its operating position.

10. The drug delivery device (20) of any one of the preceding claims, comprising
a trigger member (21) configured for initiating the dispensing operation; and
a release mechanism, wherein the release mechanism is mechanically coupled to the trigger member (21) and is configured for preventing the injection sleeve (25) from being moved into its second position in the initial state of the drug delivery device (20) and for releasing the injection sleeve (25) such that it is movable into its second position, when the trigger member (21) is activated.

11. The drug delivery device (20) of claim 10, comprising a second needle (52), wherein
the second needle (52) is communicatively couplable or coupled to the first needle (72);
the second needle (52) is mechanically coupled to the trigger member (21); and
the second needle (52) and the trigger member (21) are configured such that an activation of the trigger member (21) couples the second needle (52) with the drug outlet (28) of the drug container (24).

12. The drug delivery device (20) of claim 11, wherein
the trigger member (21) protrudes from the housing (20);
the trigger member (21) is translatory movable relative to the housing (20);
the second needle (52) is coupled to the trigger member (21) such that the second needle (52) is translatory movable together with the trigger member (21) and that the second needle (52) pierces a septum at the drug outlet (28) of the drug container (24), when the trigger member (21) is pushed towards the housing (20).

13. The drug delivery device (20) of any one of claims 10 to 12, wherein the trigger member (21) is electrically coupled to the pump (34) and wherein an activation of the trigger member (21) activates the pump (34) in order to build up the gas pressure.

14. The drug delivery device (20) of claim 13, wherein
the trigger member (21) provides a first activation mode and a second activation mode;
the first activation mode activates the pump (34); and

the second activation mode couples the second needle (52) with the outlet of the drug container (24).

15. The drug delivery device (20) of any one of the preceding claims, comprising a pressure sensor and a notification member (23), wherein the pressure sensor and the notification member (23) are configured such that the notification member (23) signals that the drug delivery device (20) is ready for use, if the pressure sensor senses the predetermined gas pressure.

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

a housing (22) for receiving a drug container (24) or with the drug container (24) being arranged within the housing (22), the drug container (24) having a drug chamber (26), a drug outlet (28) of the drug chamber (26), and a drug within the drug chamber (26);

an injection member for injecting the drug into an injection site;

a pressure arrangement within the housing (22), the pressure arrangement being configured for providing a predetermined gas pressure;

a pressure member, which is coupled or couplable to the drug container (24) and which is configured for pressing the drug through the drug outlet (28) out of the drug chamber (26) upon being moved by the predetermined gas pressure;

a plunger (70), which is movable relative to the housing (22) from an initial position of the plunger (70) to an operating position of the plunger (70), the plunger preventing the predetermined gas pressure from being applied to the pressure member in its initial position and enabling the predetermined gas pressure to be applied to the pressure member in its operating position; and

a fluid channel, which is coupled or couplable to the drug chamber (26) for receiving the drug from the drug outlet of the drug chamber (26), the fluid channel being provided to communicate with the injection member for guiding the drug to the injection member during a dispensing operation, wherein at least a section (58) of the fluid channel is coupled to the plunger (70) and is moved together with the plunger (70), when the plunger (70) is moved from its initial position to its operating position,

the pressure arrangement comprises a pump (34) for generating the gas pressure.

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

a housing (22) for receiving a drug container (24) or with the drug container (24) being arranged within the housing (22), the drug container (24) having a drug chamber (26), a drug outlet (28) of the drug chamber (26), and a drug within the drug chamber (26);

an injection member for injecting the drug into an injection site;

a pressure arrangement within the housing (22), the pressure arrangement being configured for providing a predetermined gas pressure;

a pressure member, which is coupled or couplable to the drug container (24) and which is configured for pressing the drug through the drug outlet (28) out of the drug chamber (26) upon being moved by the predetermined gas pressure;

a plunger (70), which is movable relative to the housing (22) from an initial position of the plunger (70) to an operating position of the plunger (70), the plunger preventing the predetermined gas pressure from being applied to the pressure member in its initial position and enabling the predetermined gas pressure to be applied to the pressure member in its operating position; and

a fluid channel, which is coupled or couplable to the drug chamber (26) for receiving the drug from the drug outlet of the drug chamber (26), the fluid channel being provided to communicate with the injection member for guiding the drug to the injection member during a dispensing operation, wherein at least a section (58) of the fluid channel is coupled to the plunger (70) and is moved together with the plunger (70), when the plunger (70) is moved from its initial position to its operating position,

wherein the drug delivery device further comprises an injection sleeve (25) for protecting the injection member, wherein the injection sleeve (25) is configured such that the injection sleeve (25) protects the injection member in a first position of the injection sleeve (25) in the initial state of the drug delivery device (20) and that the injection sleeve (25) exposes the injection member in a second position of the injection sleeve (25) for the dispensing operation, wherein the plunger (70) and the injection sleeve (25) are formed and arranged such that the plunger (70) enables a movement of the injection sleeve (25) from its first to its second position, when the plunger (70) is in its initial position, and that the movement of the injection sleeve (25) from its first to its second position is prevented, when the plunger (70) is in its operating position.

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

a housing (22) for receiving a drug container (24) or with the drug container (24) being arranged within the housing (22), the drug container (24) having a drug chamber (26), a drug outlet (28) of the drug chamber (26), and a drug within the drug chamber (26);

an injection member for injecting the drug into an injection site;

a pressure arrangement within the housing (22), the pressure arrangement being configured for providing a predetermined gas pressure;

a pressure member, which is coupled or couplable to the drug container (24) and which is configured for pressing the drug through the drug outlet (28) out of the drug chamber (26) upon being moved by the predetermined gas pressure;

a plunger (70), which is movable relative to the housing (22) from an initial position of the plunger (70) to an operating position of the plunger (70), the plunger preventing the predetermined gas pressure from being applied to the pressure member in its initial position and

enabling the predetermined gas pressure to be applied to the pressure member in its operating position; and

a fluid channel, which is coupled or couplable to the drug chamber (26) for receiving the drug from the drug outlet of the drug chamber (26), the fluid channel being provided to communicate with the injection member for guiding the drug to the injection member during a dispensing operation, wherein at least a section (58) of the fluid channel is coupled to the plunger (70) and is moved together with the plunger (70), when the plunger (70) is moved from its initial position to its operating position,

the drug delivery device further comprising a pressure chamber (80) within the housing (20), the pressure chamber (80) comprising a gas inlet (74) communicating with the pressure arrangement in order to receive the gas pressure from the pressure arrangement, and a gas outlet configured for providing the gas pressure for moving the pressure member, wherein

the plunger (70) is arranged in the pressure chamber (80) and is movable within the pressure chamber (80) from its initial position to its operating position by the gas pressure within the pressure chamber (80), and

the plunger (70) is configured for closing the gas outlet in its initial position and for opening the gas outlet in its operating position.

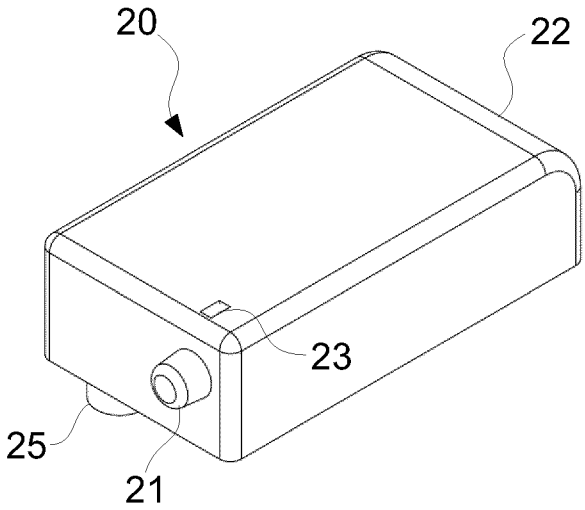


Fig. 1

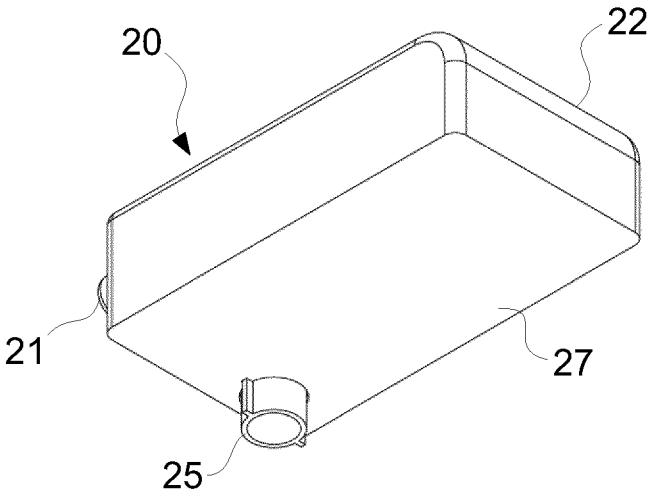


Fig. 2

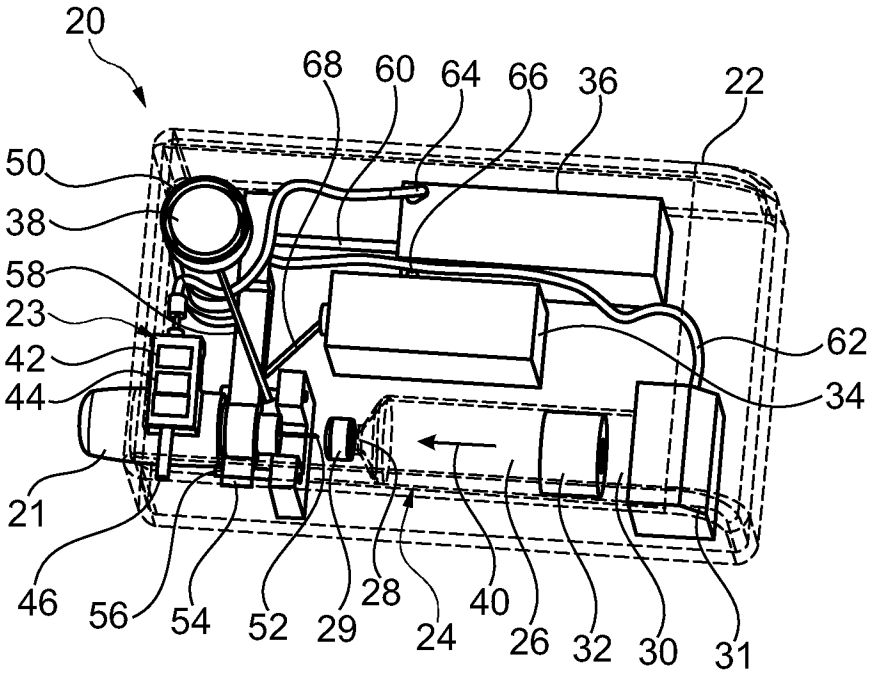

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Fig. 3

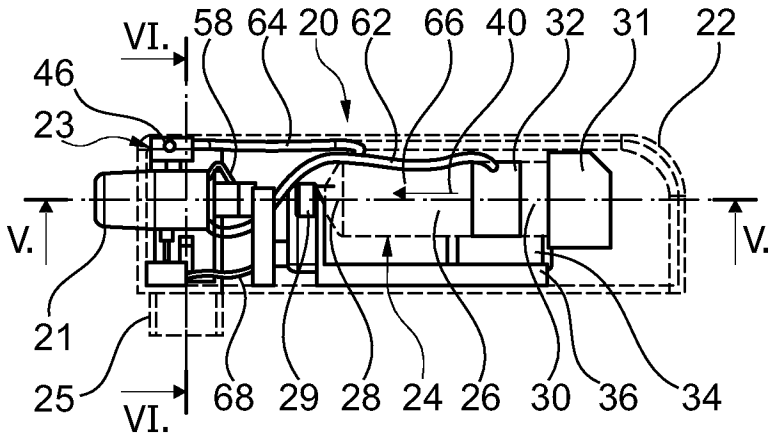
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Fig. 4

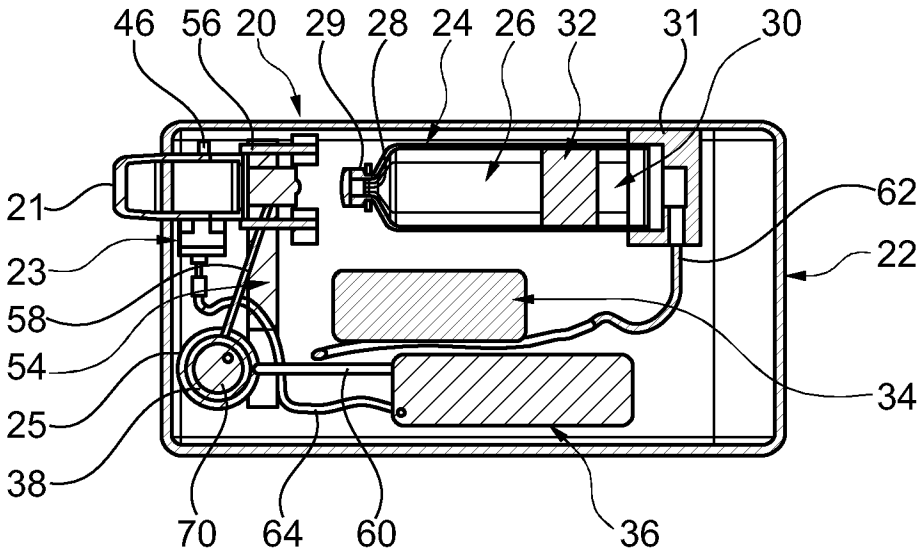
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Fig. 5

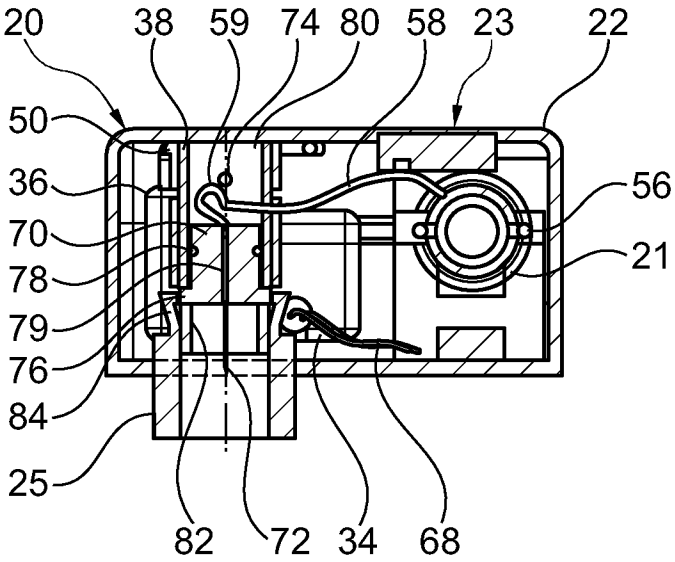
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Fig. 6

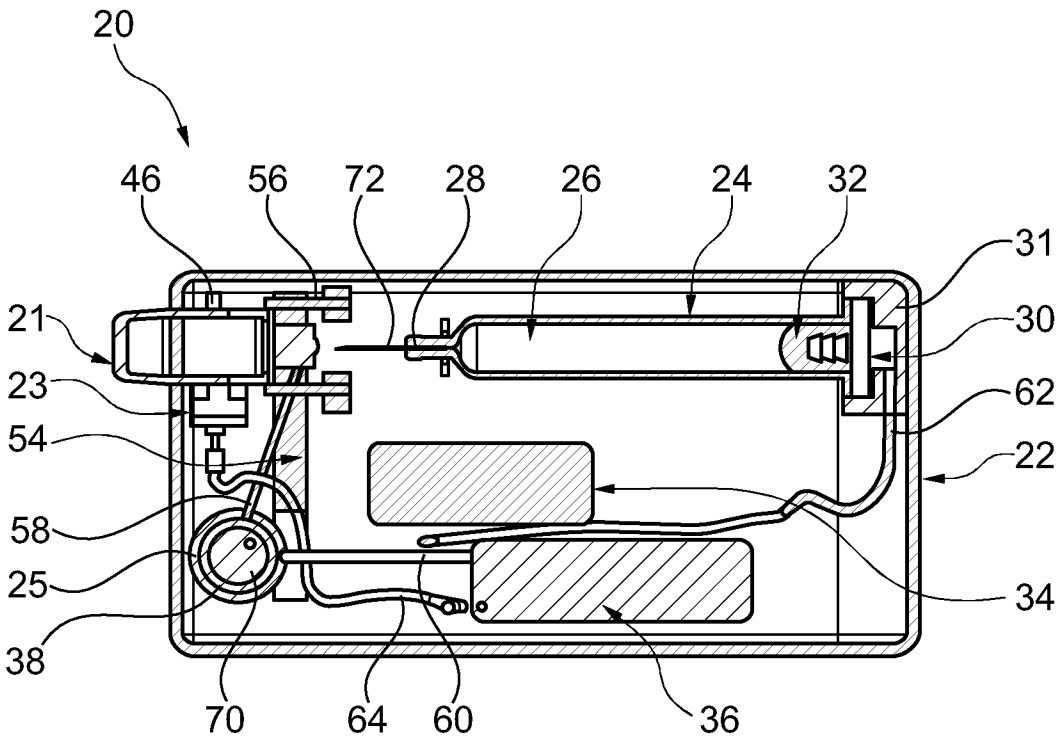
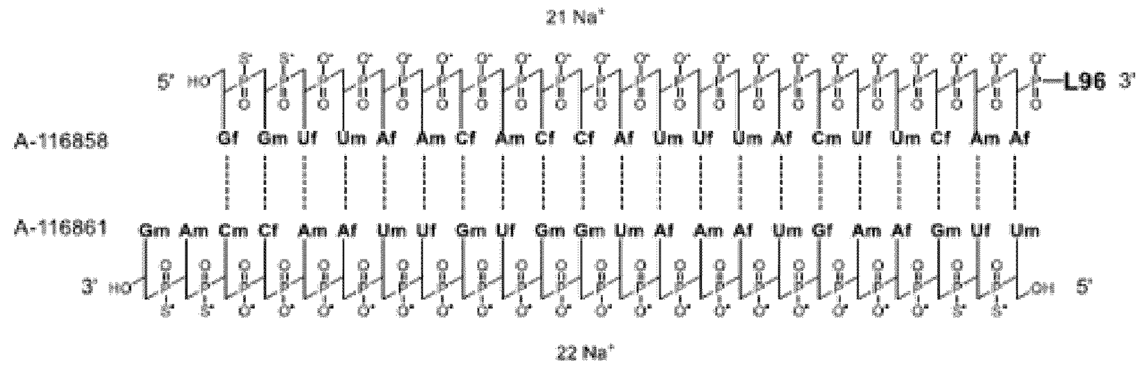
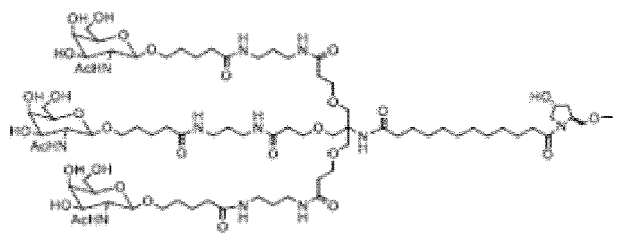


Fig. 7



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	$C_{520}H_{536}F_{21}N_{175}Na_{43}O_{309}P_{43}S_{6}$	$C_{285}H_{369}F_{12}N_{85}Na_{21}O_{164}P_{21}S_{2}$	$C_{235}H_{267}F_{9}N_{90}Na_{22}O_{145}P_{22}S_{4}$
Molecular formula free acid	$C_{520}H_{579}F_{21}N_{175}O_{309}P_{43}S_{6}$	$C_{285}H_{390}F_{12}N_{85}O_{164}P_{21}S_{2}$	$_{235}H_{289}F_{9}N_{90}O_{145}P_{22}S_{4}$
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. 8

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2024/065436

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61M5/20
ADD. A61M5/145 A61M5/32 A61M5/142

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, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2020/009324 A1 (BARROWS DANIEL [US] ET AL) 9 January 2020 (2020-01-09)	1-3,5-8, 10-16
A	the whole document	4,18

X	EP 2 099 434 B1 (KALEO INC [US]) 5 June 2019 (2019-06-05)	1-3,5,6, 8-14,16, 17
A	figures 18-45 paragraph [0061] - paragraph [0131]	4,18

X	US 2021/213201 A1 (MEYERS PAUL F [US] ET AL) 15 July 2021 (2021-07-15)	1-3, 5-14,16, 17
A	the whole document	4,18

☐ 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
9 September 2024	13/09/2024

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	Delmotte, Pierre

INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP2024/065436

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/EP2024/065436

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2020009324 A1	09-01-2020	US 2020009324 A1	09-01-2020
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		WO 2008064092 A2	29-05-2008
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		CA 3145580 A1	18-02-2021
		EP 4009936 A1	15-06-2022
		IL 290026 A	01-03-2022
		JP 2022543523 A	13-10-2022
		US 2021213201 A1	15-07-2021
		US 2022054753 A1	24-02-2022
		WO 2021030210 A1	18-02-2021