groups, may modulate the pKa value where a range of 5-6 should be of interest for buffering capacity (Brown and Mora-Diez, 2006).

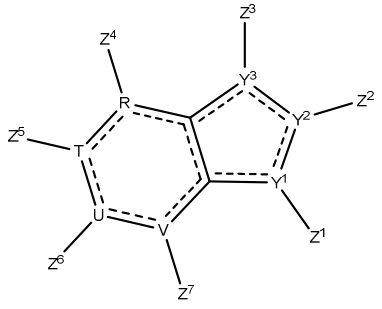
The inventors provide a way to improve transfection reagent by using benzo-fused heterocyclic compounds to fine-tune the affinity and binding to a nucleic acid molecule, *e.g.* DNA, optimize the buffering capacity in acidic conditions and/or increase the diffusion, binding and uptake in the nucleus.

Thus it is an object of the present disclosure to provide a more efficient transfection composition or a formulation for transfecting a nucleic acid molecule into a cell.

It is another object of the present disclosure to provide a method for transfecting a nucleic acid molecule using said composition or formulation comprising such composition for administration to cells.

The inventors carried out a structure-based screening of substituted heterocyclic compounds, in particular benzimidazole, benzopyrazole, benzotriazole, to improve the efficiency of transfection by cationic polymers. Such substituted heterocyclic compounds were grafted to cationic polymers, in particular polyethylenimine (PEI) polymers, of various molecular weight in order to fine-tune the conjugates. Many variations were proposed in order to define optimal structures facilitating transfection of a nucleic acid molecule, *e.g.* DNA. Heterocycles exhibiting hydrophobic properties were developed and may represent binding motifs to cytoplasmic proteins promoting potentially the nuclear import.

In an aspect, there is provided a composition comprising (i) at least one compound of general formula (II) or a tautomer, mesomer, racemate, enantiomer, diastereomer, or mixture thereof, or an acceptable salt thereof, and (ii) an acceptable excipient, buffering agent, cell culture medium, or transfection medium:



(II)

wherein:

- (i) $\mathbf{Y^1}$ and $\mathbf{Y^3}$ represent N, $\mathbf{Y^2}$ represents C; or (ii) $\mathbf{Y^1}$ and $\mathbf{Y^2}$ represent N, $\mathbf{Y^3}$ represents C; or (iii) $\mathbf{Y^2}$ and $\mathbf{Y^3}$ represent N, $\mathbf{Y^1}$ represents C; or (iv) $\mathbf{Y^1}$, $\mathbf{Y^2}$ and $\mathbf{Y^3}$ represent N and

with the proviso that at least one, but no more than two, of Y^1, Y^2 and Y^3 are substituted by Z^1, Z^2 and Z^3 respectively;

- **Z^1** represents H, X_1-R_3-X_2-P^+, X_1-R_3-P^+, X_1-X_2-P^+, R_3-X_2-P^+, X_1-P^+, R_3-P^+, or X_2-P^+; or **Z^1** is absent;
- **Z^2** represents H, SCH_3, CF_3, phenyl, CH_2-NH-CH_3, CH_2-O-CH_3, CH_2-F, a linear or branched, C_1-C_{18} alkyl, a linear or branched C_1-C_{18} alkenyl, a linear or branched C_1-C_{18} alkynyl, a linear or branched C_1-C_{18} alkenynyl, a C_1-C_{12} alkoxy, X_1-R_3-X_2-P^+, X_1-R_3-P^+, X_1-X_2-P^+, R_3-X_2-P^+, X_1-P^+, R_3-P^+, or X_2-P^+; or **Z^2** is absent;
- **Z^3** represents H, a linear or branched, C_1-C_{18} alkyl, a linear or branched C_1-C_6 alkenyl, a linear or branched C_1-C_6 alkynyl, or a linear or branched C_1-C_6 alkenynyl, a C_6-C_{18} aryl-linear or branched C_1-C_{18} alkyl, a C_6-C_{18} aryl-linear or branched C_1-C_{18} alkenyl, a C_6-C_{18} aryl-linear or branched C_1-C_{18} alkynyl, a C_6-C_{18} aryl-linear or branched C_1-C_{18} alkenynyl, fluorobenzyl, 4-hydroxyphenethyl, X_1-R_3-X_2-P^+, X_1-R_3-P^+, X_1-X_2-P^+, R_3-X_2-P^+, X_1-P^+, R_3-P^+, or X_2-P^+; or **Z^3** is absent;
- **X_1** and **X_2**, which may be identical or different, represent CO or CH_2;
- **R_3** represents $(CH_2)_m$, $(CH_2)_m$-$CHCH_3$-$(CH_2)_n$-, $(CH_2)_m$-$C(CH_3)_2$-$(CH_2)_n$-, $(CH_2)_m$-O-$(CH_2)_n$-, $(CH_2)_m$-S-$(CH_2)_n$-, $(CH_2)_m$-CH_2-O-, with m representing an integer between 1 and 3 and n representing an integer between 1 and 3;
- **P^+** represents a graft cationic polymer, which is a linear or branched polyethyleneimine (PEI);
- **R**, **T**, **U** and **V**, which are identical or different, represent C or N, with the proviso that the six-membered ring of (II) contains no more than 2 N atoms; and
- **Z^4**, **Z^5**, **Z^6** and **Z^7**, which are identical or different, represent H, a linear or branched, C_1-C_{18} alkyl, a linear or branched C_1-C_{18} alkenyl, a linear or branched C_1-C_{18} alkynyl, a linear or branched C_1-C_{18} alkenynyl, an amine, a linear or branched, C_1-C_{18} alkylamine, a linear or branched C_1-C_{18} alkenylamine, a linear or branched C_1-C_{18} alkynylamine, a linear or branched C_1-C_{18} alkenynylamine, carboxyphenyl, a C_1-C_{12} alkoxy, OH, halogen or halogen-substituted C_1-C_{12} alkyl; or (i) **Z^4** and **Z^5** or (ii) **Z^5** and **Z^6** or (iii) **Z^6** and **Z^7** together form a fused, 6- membered aryl or heteroaryl;

with the proviso that:

only one of **Z^1**, **Z^2** or **Z^3** represents X_1-R_3-X_2-P^+, X_1-R_3-P^+, X_1-X_2-P^+, R_3-X_2-P^+, X_1-P^+, R_3-P^+, or X_2-P^+.

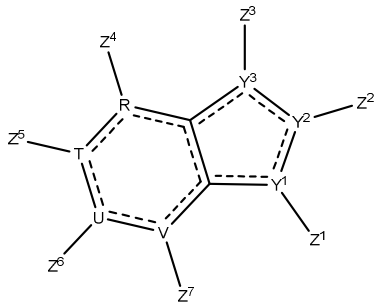
In another aspect, there is provided a method for *in vitro* or *ex vivo* transfection of live cells comprising introducing in the cells the composition as defined above.

In another aspect, there is provided an i*n vitro* or *ex vivo* use of the composition according to any one of claims 2 to 18 to transfect at least one nucleic acid molecule into a cell, cell line or cells, preferably a cell, cell line or cells selected from the group consisting of a mammalian cell, an insect cell, a primary cell, an adherent cell, a suspension cell, a dividing cell such as a stem cell, a non-dividing cell such as a neuronal cell, and a cancer cell, said cell, cell line or cells being optionally organized into spheroids, organoids, 2D or 3D cell culture, or provided as fibre or matrix culture, and/or within a bioreactor.

In another aspect, there is provided an *in vitro* or *ex vivo* use of the composition as defined above for genome engineering, for cell reprogramming, for differentiating cells, or for gene-editing.

In another aspect, there is provided an *in vitro* or *ex vivo* method comprising the *in vitro* or *ex vivo* use of the composition as defined above, wherein the method is for the production of (i) biologics, in particular biologics encoding a recombinant protein, peptide or antibody; or (ii) recombinant virus, such as adeno-associated virus (AAV), lentivirus (LV), adenovirus, oncolytic virus, or baculovirus, wherein said composition comprises multiple nucleic acid molecules for co-transfection; or (iii) viral or virus-like particles, wherein said composition comprises multiple nucleic acid molecules for co-transfection.

The present disclosure relates to a composition suitable for transfecting a nucleic acid molecule, preferably a deoxyribonucleic acid (DNA) into a cell, preferably a eukaryotic cell, comprising (i) at least one compound of general formula (II) or a tautomer, mesomer, racemate, enantiomer, diastereomer, or mixture thereof, or an acceptable salt thereof, and (ii) an acceptable excipient, buffering agent, cell culture medium, or transfection medium:

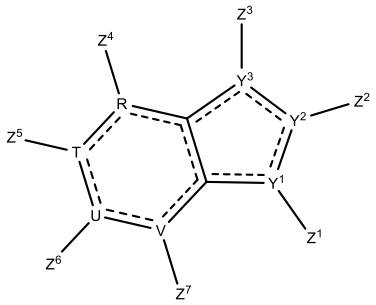


(II)

wherein:

CLAIMS

1. A composition comprising (i) at least one compound of general formula (II) or a tautomer, mesomer, racemate, enantiomer, diastereomer, or mixture thereof, or an acceptable salt thereof, and (ii) an acceptable excipient, buffering agent, cell culture medium, or transfection medium:



(II)

wherein:

- (i) **Y^1** and **Y^3** represent N, **Y^2** represents C; or (ii) **Y^1** and **Y^2** represent N, **Y^3** represents C; or (iii) **Y^2** and **Y^3** represent N, **Y^1** represents C; or (iv) **Y^1**, **Y^2** and **Y^3** represent N and with the proviso that at least one, but no more than two, of Y^1, Y^2 and Y^3 are substituted by Z^1, Z^2 and Z^3 respectively;
- **Z^1** represents H, X_1-R_3-X_2-P^+, X_1-R_3-P^+, X_1-X_2-P^+, R_3-X_2-P^+, X_1-P^+, R_3-P^+, or X_2-P^+; or **Z^1** is absent;
- **Z^2** represents H, SCH_3, CF_3, phenyl, CH_2-NH-CH_3, CH_2-O-CH_3, CH_2-F, a linear or branched, C_1-C_{18} alkyl, a linear or branched C_1-C_{18} alkenyl, a linear or branched C_1-C_{18} alkynyl, a linear or branched C_1-C_{18} alkenynyl, a C_1-C_{12} alkoxy, X_1-R_3-X_2-P^+, X_1-R_3-P^+, X_1-X_2-P^+, R_3-X_2-P^+, X_1-P^+, R_3-P^+, or X_2-P^+; or **Z^2** is absent;
- **Z^3** represents H, a linear or branched, C_1-C_{18} alkyl, a linear or branched C_1-C_6 alkenyl, a linear or branched C_1-C_6 alkynyl, or a linear or branched C_1-C_6 alkenynyl, a C_6-C_{18} aryl-linear or branched C_1-C_{18} alkyl, a C_6-C_{18} aryl-linear or branched C_1-C_{18} alkenyl, a C_6-C_{18} aryl-linear or branched C_1-C_{18} alkynyl, a C_6-C_{18} aryl-linear or branched C_1-C_{18} alkenynyl, fluorobenzyl, 4-hydroxyphenethyl, X_1-R_3-X_2-P^+, X_1-R_3-P^+, X_1-X_2-P^+, R_3-X_2-P^+, X_1-P^+, R_3-P^+, or X_2-P^+; or **Z^3** is absent;
- **X_1** and **X_2**, which may be identical or different, represent CO or CH_2;
- **R_3** represents $(CH_2)_m$, $(CH_2)_m$-$CHCH_3$-$(CH_2)_n$-, $(CH_2)_m$-$C(CH_3)_2$-$(CH_2)_n$-, $(CH_2)_m$-O-$(CH_2)_n$-, $(CH_2)_m$-S-$(CH_2)_n$-, $(CH_2)_m$-CH_2-O-, with m representing an integer between 1 and 3 and n representing an integer between 1 and 3;

- **P^+** represents a graft cationic polymer, which is a linear or branched polyethyleneimine (PEI);
- **R**, **T**, **U** and **V**, which are identical or different, represent C or N, with the proviso that the six-membered ring of (II) contains no more than 2 N atoms; and
- **Z^4**, **Z^5**, **Z^6** and **Z^7**, which are identical or different, represent H, a linear or branched, C_1-C_{18} alkyl, a linear or branched C_1-C_{18} alkenyl, a linear or branched C_1-C_{18} alkynyl, a linear or branched C_1-C_{18} alkenynyl, an amine, a linear or branched, C_1-C_{18} alkylamine, a linear or branched C_1-C_{18} alkenylamine, a linear or branched C_1-C_{18} alkynylamine, a linear or branched C_1-C_{18} alkenynylamine, carboxyphenyl, a C_1-C_{12} alkoxy, OH, halogen or halogen-substituted C_1-C_{12} alkyl; or (i) **Z^4** and **Z^5** or (ii) **Z^5** and **Z^6** or (iii) **Z^6** and **Z^7** together form a fused, 6- membered aryl or heteroaryl;

with the proviso that:

- only one of **Z^1**, **Z^2** or **Z^3** represents X_1-R_3-X_2-P^+, X_1-R_3-P^+, X_1-X_2-P^+, R_3-X_2-P^+, X_1-P^+, R_3-P^+, or X_2-P^+.

2. The composition according to claim 1, further comprising at least one nucleic acid molecule to be transfected in a cell, preferably a nucleic acid molecule selected from the group consisting of a deoxyribonucleic acid (DNA), a ribonucleic acid (RNA), a DNA/RNA hybrid, a short interfering RNA (siRNA), a microRNA (miRNA), a short hairpin RNA (shRNA), a messenger RNA (mRNA), a CRISPR guide RNA, more preferably a DNA, and an expression vector encoding said nucleic acid molecule, in particular a plasmid encoding said nucleic acid molecule or a plasmid expressing said nucleic acid molecule.

3. The composition according to claim 1 or 2, wherein:

(i) **Z^1** represents X_1-R_3-X_2-P^+, wherein **X_1** represents CH_2, **X_2** represents CO, **R_3** represents $(CH_2)_m$, with m representing an integer between 1 and 3, preferably m is equal to 2, and P^+ represents a linear or branched PEI; and

(ii) **Z^2** represents H, CH_3, CF_3 or OCH_3; and

(iii) **Z^3** represents fluorobenzyl or 4-hydroxyphenethyl.

4. The composition according to claim 1 or 2, wherein:

(i) **Z^2** represents X_1-R_3-X_2-P^+, wherein **X_1** represents CH_2, **X_2** represents CO, **R_3** represents $(CH_2)_m$, with m representing an integer between 1 and 3, preferably m is equal to 2, , and P^+ represents a linear or branched PEI; and

(ii) $\mathbf{Z^1}$ represents H; and
(iii) $\mathbf{Z^3}$ represents fluorobenzyl or 4-hydroxyphenethyl.

5. The composition according to claim 1 or 2, wherein:
(i) $\mathbf{Z^3}$ represents X_1-R_3-X_2-P^+, wherein $\mathbf{X_1}$ represents CH_2, $\mathbf{X_2}$ represents CO, $\mathbf{R_3}$ represents $(CH_2)_m$, with m representing an integer between 1 and 3, preferably m is equal to 2 , and P^+ represents a linear or branched PEI; and
(ii) $\mathbf{Z^1}$ represents H; and
(iii) $\mathbf{Z^2}$ represents H, CH_3, CF_3 or OCH_3.

6. The composition according to any one of claims 1 to 5, wherein the graft cationic polymer is a linear PEI.

7. The composition according to any one of claims 1 to 6, wherein
(i) the graft cationic polymer has a grafting ratio ranging from 1 to 50%, preferably from 5 to 30%, more preferably is 20%; and/or
(ii) the graft cationic polymer has an average molecular weight (Mw) ranging from 1 kDa to 500 kDa, preferably from 1 kDa to 50 kDa, more preferably from 5 kDa to 50 kDa or from 1 kDa to 15 kDa, even more preferably the graft cationic polymer has an average Mw of 6, 8, 10, 15, 22 or 30 kDa, preferably of 6, 8, 10, 15 or 30 kDa.

8. The composition according to any one of claims 1 to 7, wherein:
(i) **R**, **T**, **U** and **V** represent C; or
(ii) **R**, **T**, **U** and **V**, which are identical or different, represent C or N, with the proviso that the six-membered ring contains no more than 1 N atom; preferably, one of **R**, **T**, **U** or **V** represents N; or
(iii) **R** and **U** represent N, and **T** and **V** represent C; or
R and **T** represent N, and **U** and **V** represent C; or
R and **V** represent N, and **T** and **U** represent C; or
T and **U** represent N, and **R** and **V** represent C; or
T and **V** represent N, and **R** and **U** represent C;
preferably (i) **R**, **T**, **U** and **V** represent C.

9. The composition according to any one of claims 1 to 8, wherein

(i) $\mathbf{Z^1}$ represents X_1-R_3-X_2-P^+, wherein $\mathbf{X_1}$ represents CH_2, $\mathbf{X_2}$ represents CO, $\mathbf{R_3}$ represents $(CH_2)_m$, with m representing an integer between 1 and 3, preferably m is equal to 2 and $\mathbf{P^+}$ represents a linear PEI; or

(ii) $\mathbf{Z^2}$ represents a linear or branched, C_1-C_6 alkyl, a linear or branched C_1-C_6 alkenyl, a linear or branched C_1-C_6 alkynyl, or a linear or branched C_1-C_6 alkenynyl.

10. The composition according to any one of claims 1 to 9, wherein

(i) $\mathbf{Z^4}$, $\mathbf{Z^5}$, $\mathbf{Z^6}$ and $\mathbf{Z^7}$ represent H; or

(ii) one of $\mathbf{Z^4}$, $\mathbf{Z^5}$, $\mathbf{Z^6}$ or $\mathbf{Z^7}$ represents a linear or branched C_1-C_6 alkyl, a linear or branched C_1-C_6 alkenyl, a linear or branched C_1-C_6 alkynyl, or a linear or branched C_1-C_6 alkenynyl, preferably one of $\mathbf{Z^4}$, $\mathbf{Z^5}$, $\mathbf{Z^6}$ or $\mathbf{Z^7}$ represents CH_3; or

(iii) $\mathbf{Z^4}$ and $\mathbf{Z^6}$ represent a linear or branched C_1-C_6 alkyl, a linear or branched C_1-C_6 alkenyl, a linear or branched C_1-C_6 alkynyl, or a linear or branched C_1-C_6 alkenynyl preferably $\mathbf{Z^4}$ and $\mathbf{Z^6}$ represent CH_3; or

(iv) $\mathbf{Z^5}$ and $\mathbf{Z^6}$ represent a linear or branched, C_1-C_6 alkyl, a linear or branched C_1-C_6 alkenyl, a linear or branched C_1-C_6 alkynyl, or a linear or branched C_1-C_6 alkenynyl, preferably $\mathbf{Z^5}$ and $\mathbf{Z^6}$ represent CH_3.

11. The composition according to any one of claims 1 to 10, wherein:

- $\mathbf{Y^1}$ and $\mathbf{Y^3}$ represent N, $\mathbf{Y^2}$ represents C; and
- **R**, **T**, **U** and **V** represent C; and
- $\mathbf{Z^2}$, $\mathbf{Z^4}$ and $\mathbf{Z^6}$ represent a linear or branched, C_1-C_6 alkyl, a linear or branched C_1-C_6 alkenyl, a linear or branched C_1-C_6 alkynyl, or a linear or branched C_1-C_6 alkenynyl; preferably $\mathbf{Z^2}$, $\mathbf{Z^4}$ and $\mathbf{Z^6}$ represent CH_3.

12. The composition according to claim 11, wherein $\mathbf{Z^1}$ represents X_1-R_3-X_2-P^+, wherein $\mathbf{X_1}$ represents CH_2, $\mathbf{X_2}$ represents CO, and $\mathbf{R_3}$ represents $(CH_2)_m$, with m representing an integer between 1 and 3, preferably m is equal to 2.

13. The composition according to any one of claims 1 to 12, wherein:

- $\mathbf{Y^1}$ and $\mathbf{Y^3}$ represent N, $\mathbf{Y^2}$ represents C; and

- **Z^1** or **Z^3** represents X_1-R_3-X_2-P^+, X_1-R_3-P^+, X_1-X_2-P^+, R_3-X_2-P^+, X_1-P^+, R_3-P^+, or X_2-P^+, wherein **X_1**, **X_2**, **R_3** and **P^+** are as defined in claim 1; and

wherein:

(i) **R**, **T**, **U** and **V** represent C, and/or **Z^2** represents H, CH_3, SCH_3, CF_3, phenyl, isopropyl, propyl, CH_2-NH-CH_3, CH_2-O-CH_3, or CH_2-F, and **Z^4** represents H, or CH_3, and **Z^5** represents H, F, OCH_3, carboxyphenyl, tert-butyl, Cl, OH, or CH_3, and **Z^6** represents H, CH_3, or F, and **Z^7** represents H; or

(ii) **T** and **V** represent N, and **R** and **U** represent C, and **Z^2** represents H, or CH_3, and **Z^4** represents H, NH_2, or $N(CH_3)_2$, and at least one of **Z^5**, **Z^6** or **Z^7** represents H; or

(iii) **R** and **U** represent N, and **T** and **V** represent C, and **Z^2** represents H, or CH_3, and **Z^4** represents H, NH_2, or $N(CH_3)_2$, and at least one of **Z^5**, **Z^6** or **Z^7** represents H; or

(iv) one of **R**, **T**, **U** or **V** represents N and at least one of **Z^2**, **Z^4**, **Z^5**, **Z^6** or **Z^7** represents H; or

(v) **R**, **T**, **U** and **V** represent C, **Z^5** and **Z^6** together form a naphtalene, and **Z^2** represents CH_3, and **Z^4** represents H, and **Z^7** represents H.

14. The composition according to any one of claims 1 to 13, wherein:

- **Y^1** and **Y^2** represent N, **Y^3** represents C; or **Y^2** and **Y^3** represent N, **Y^1** represents C; and
- **Z^1** or **Z^3** represents X_1-R_3-X_2-P^+, X_1-R_3-P^+, X_1-X_2-P^+, R_3-X_2-P^+, X_1-P^+, R_3-P^+, or X_2-P^+, wherein **X_1**, **X_2**, **R_3** and **P^+** are as defined in claim 1; and

wherein:

(i) **R**, **T**, **U** and **V** represent C, and at least one of **Z^4**, **Z^5**, **Z^6** or **Z^7** represents H; or

(ii) one of **R**, **U** or **V** represents N and at least one of **Z^4**, **Z^5**, **Z^6** or **Z^7** represents H.

15. The composition according to any one of claims 1 to 13, wherein:

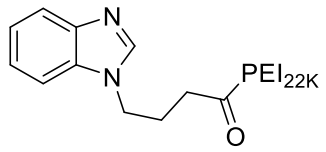
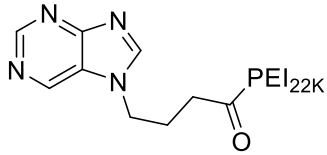
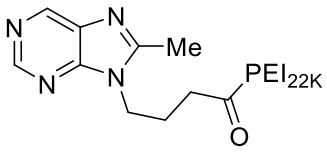
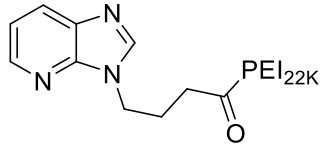
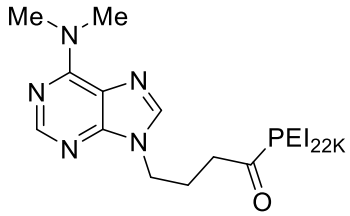
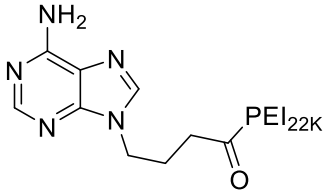
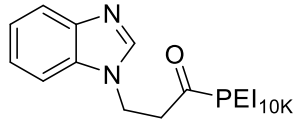
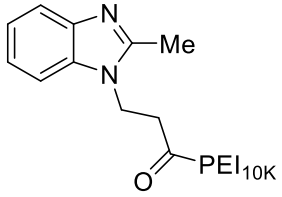
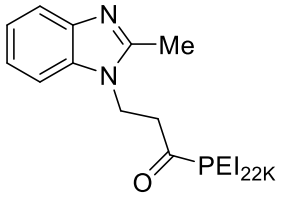
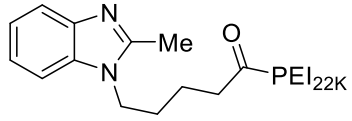
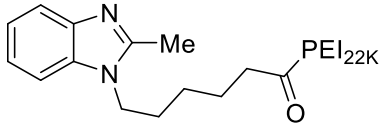
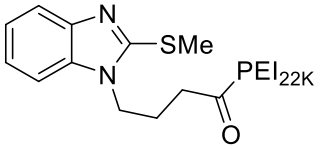
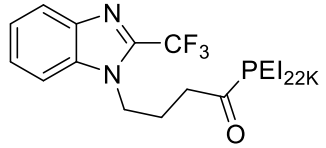
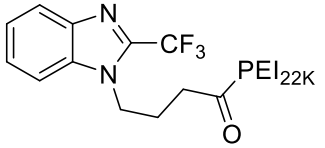
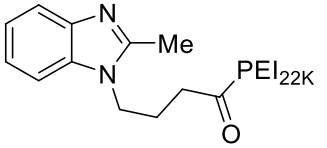
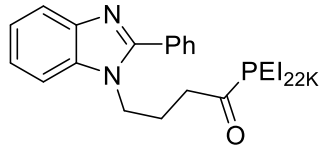
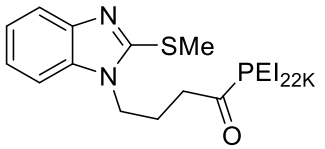
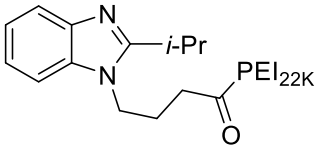
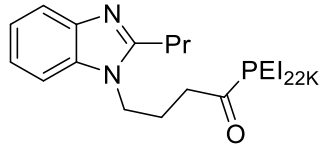
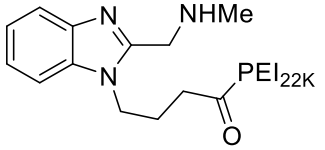
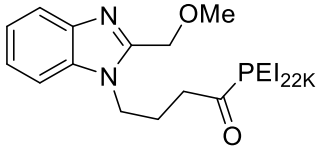
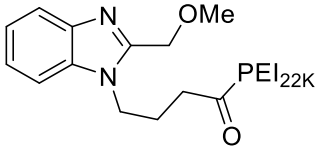
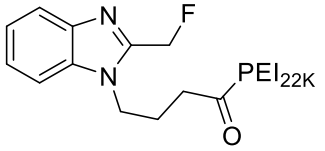
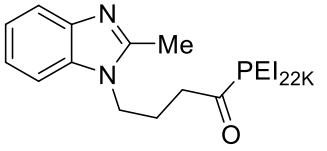
- **Y^1**, **Y^2** and **Y^3** represent N; and
- **Z^1** or **Z^2** represents X_1-R_3-X_2-P^+, X_1-R_3-P^+, X_1-X_2-P^+, R_3-X_2-P^+, X_1-P^+, R_3-P^+, or X_2-P^+, wherein **X_1**, **X_2**, **R_3** and **P^+** are as defined in claim 1; and

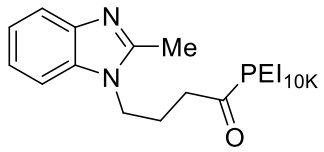
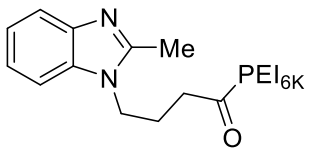
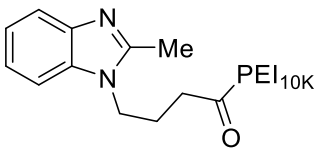
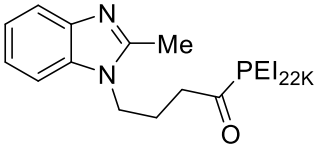
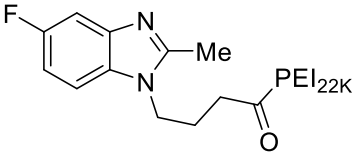
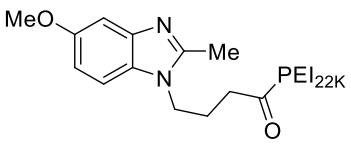
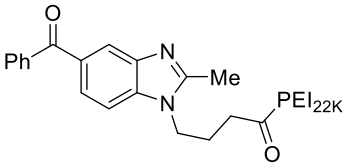
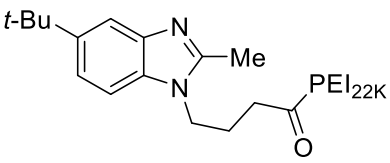
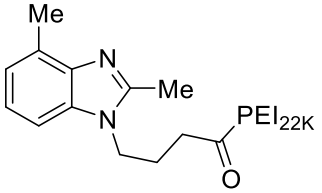
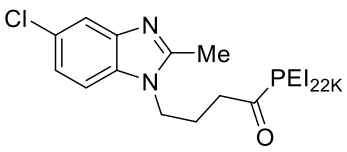
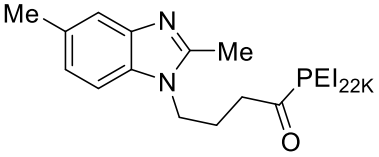
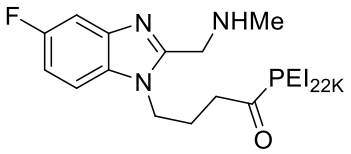
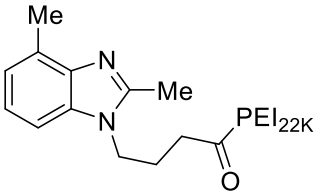
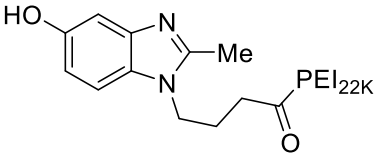
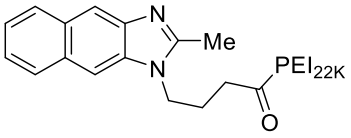
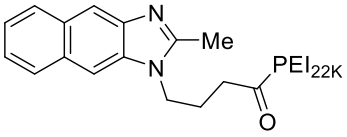
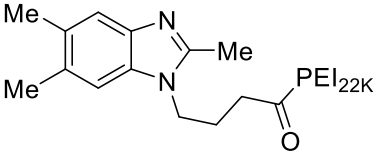
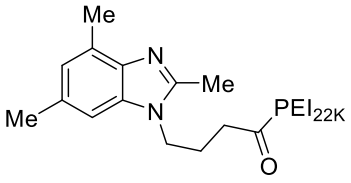
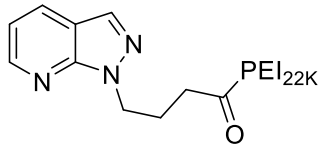
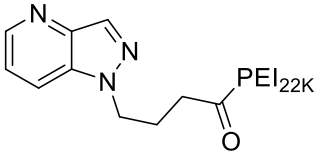
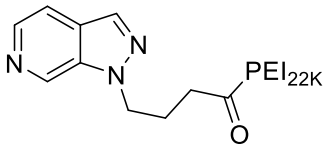
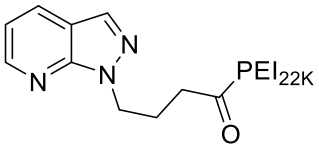
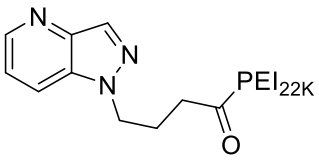
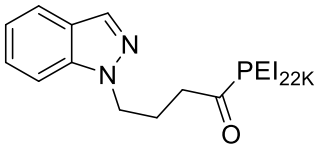
wherein:

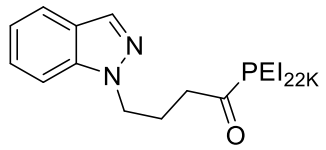
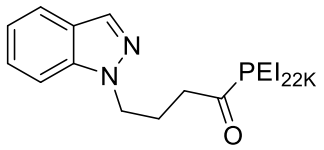
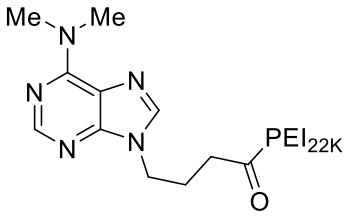
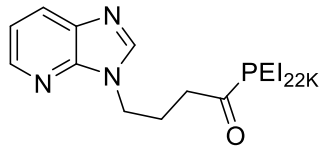
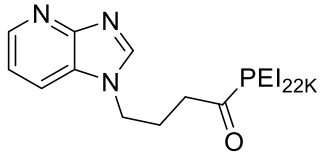
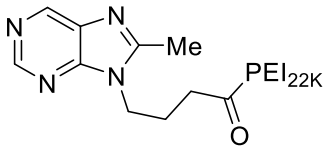
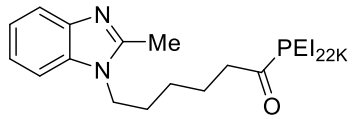
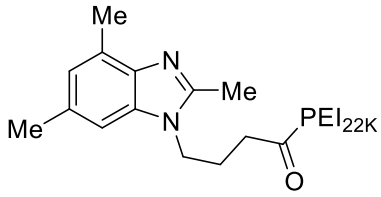
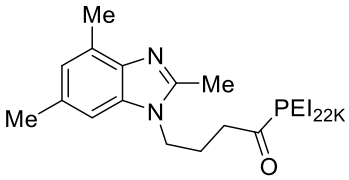
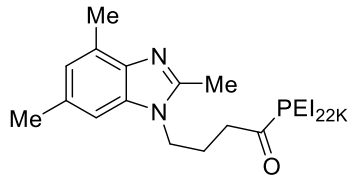
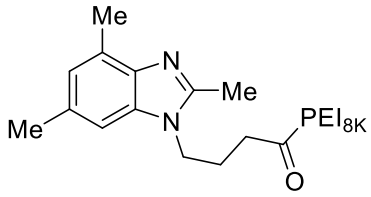
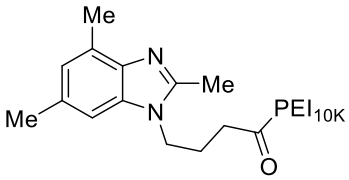
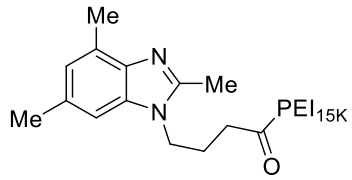
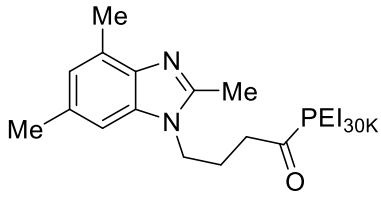
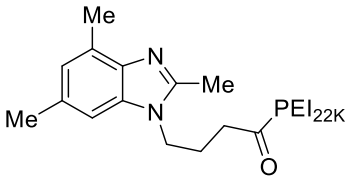
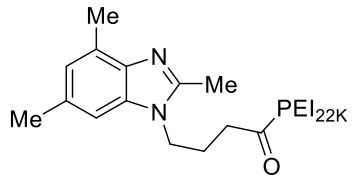
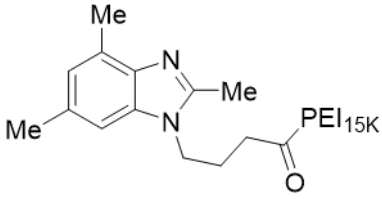
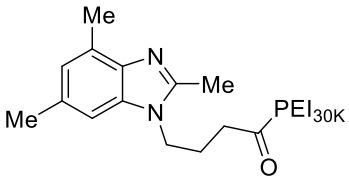
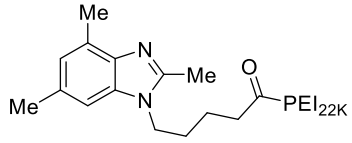
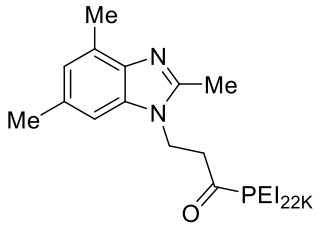
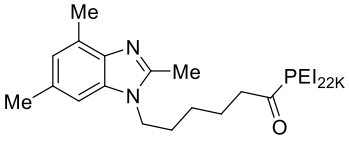
(i) **R**, **T**, **U** and **V** represent C, and **Z^4** represents H, and **Z^5** represents H, CH_3, or OCH_3, and **Z^6** represents H, or CH_3, and **Z^7** represents H; or

(ii) one of **R**, **T** or **U** represents N and at least one of **Z^4**, **Z^5**, **Z^6** or **Z^7** represents H.

16. The composition according to any one of claims 1 to 15, wherein the at least one compound of general formula (II) is selected from the group consisting of the following compounds:

 **1.01**	 **1.02**	 **1.03**
 **1.04**	 **1.05**	 **1.06**
 **1.07**	 **1.08**	 **1.09**
 **1.10**	 **1.11**	 **1.12**
 **1.13**	 **1.14**	 **1.15**
 **1.16**	 **1.17**	 **1.18**
 **1.19**	 **1.20**	 **1.21**
 **1.22**	 **1.23**	 **1.24**

 **1.25**	 **1.26**	 **1.27**
 **1.28**	 **1.29**	 **1.30**
 **1.31**	 **1.32**	 **1.33**
 **1.34**	 **1.35**	 **1.36**
 **1.37**	 **1.38**	 **1.39**
 **1.40**	 **1.41**	 **1.42**
 **1.43**	 **1.44**	 **1.45**
		

1.46	1.47	1.48
 **1.49**	 **1.50**	 **1.51**
 **1.52**	 **1.53**	 **1.54**
 **1.55**	 **1.56**	 **1.57**
 **1.58**	 **1.59**	 **1.60**
 **1.61**	 **1.62**	 **1.63**
 **1.64**	 **1.65**	 **1.66**
 **1.67**		 **1.69**

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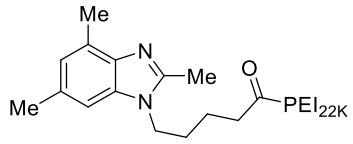
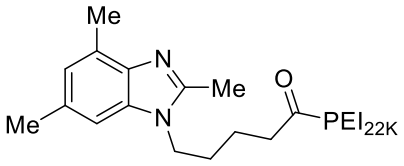
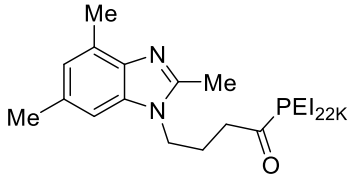
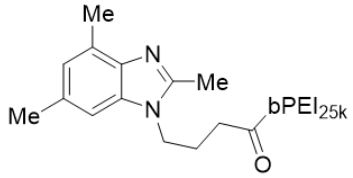
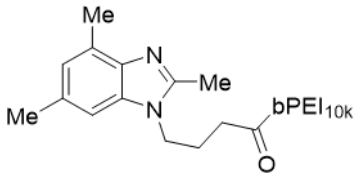
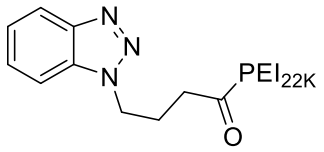
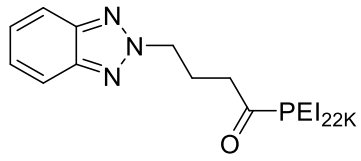
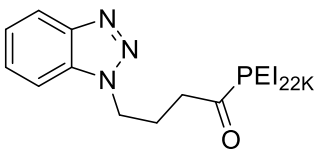
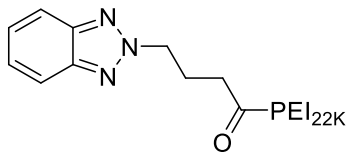
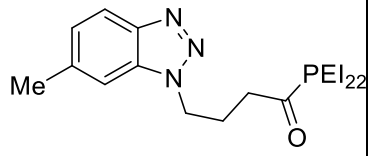
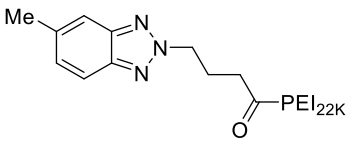
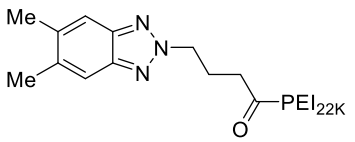
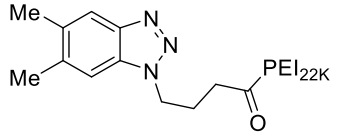
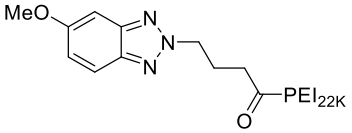
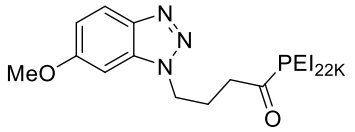
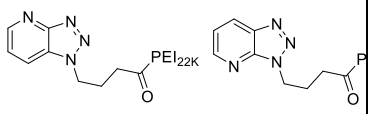
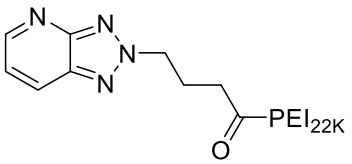
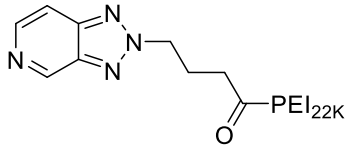
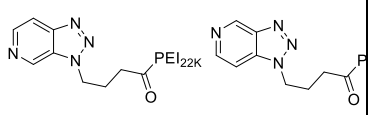
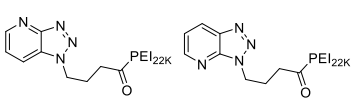
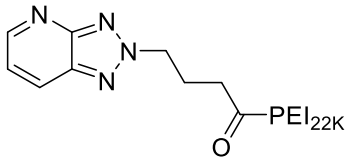
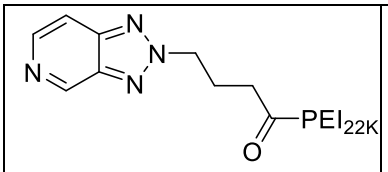
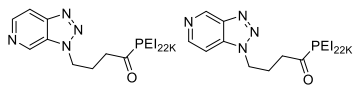
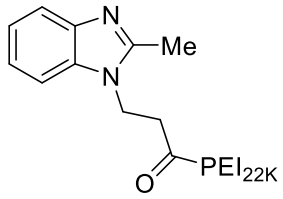
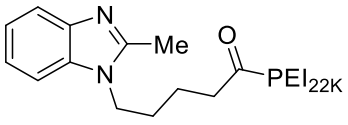
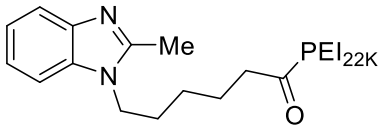
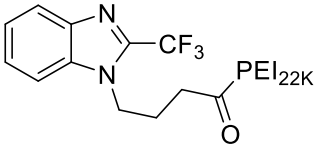
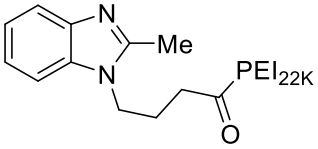
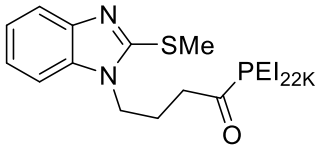
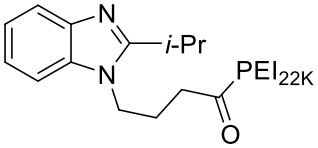
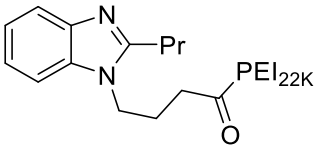
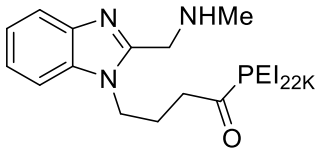
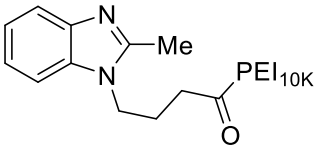
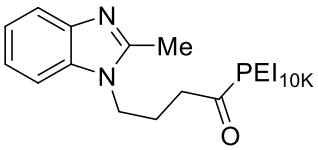
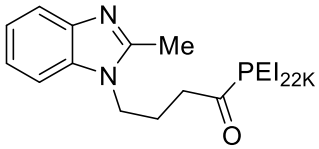
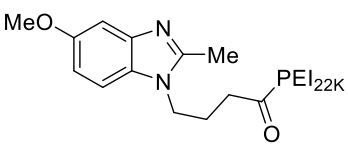
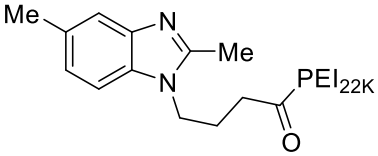
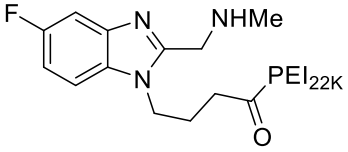
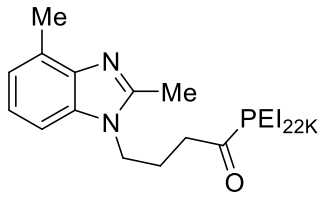
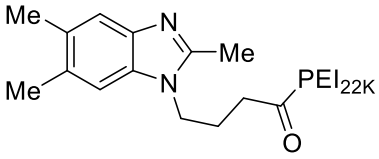
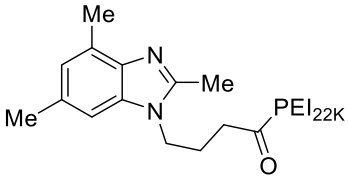
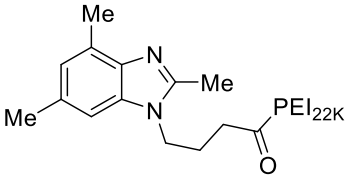
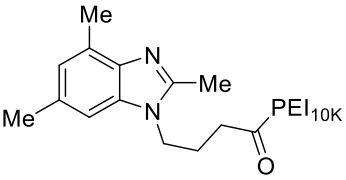
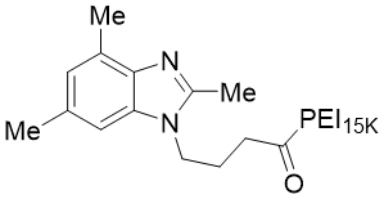
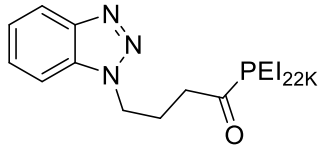
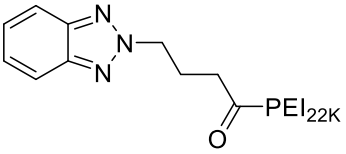
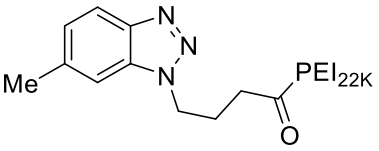
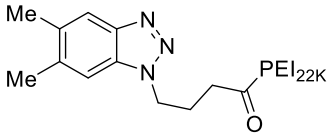
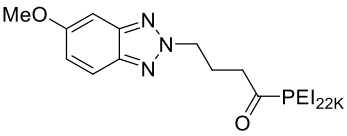
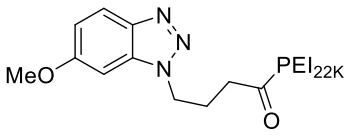
 **1.70**	 **1.71**	 **1.72**
 **1.74**	 **1.75**	
		 **2.01**
 **2.02**	 **2.03**	 **2.04**
 **2.05**	 **2.06**	 **2.07**
 **2.08**	 **2.09**	 **2.10**
 **2.11**	 **2.12**	 **2.13**
 **2.14**	 **2.15**	 **2.16**

 **2.17**	 **2.18**

17. The composition according to claim 16, wherein the at least one compound of general formula (II) is selected from the group consisting of the following compounds:

 **1.09**	 **1.10**	 **1.11**
 **1.14**	 **1.15**	 **1.17**
 **1.18**	 **1.19**	 **1.20**
 **1.25**	 **1.27**	 **1.28**
 **1.30**	 **1.35**	 **1.36**

 **1.37**	 **1.41**	 **1.42**
 **1.57**	 **1.60**	 **1.65**
 **2.03**	 **2.04**	 **2.05**
 **2.08**	 **2.09**	 **2.10**

18. The composition according to claim 17, wherein the at least one compound of general formula (II) is compound **1.42**, **1.57** or **1.65**.

19. A method for *in vitro* or *ex vivo* transfection of live cells comprising introducing in the cells the composition according to any one of claims 2 to 18.

20. *In vitro* or *ex vivo* use of the composition according to any one of claims 2 to 18 to transfect at least one nucleic acid molecule into a cell, cell line or cells, preferably a cell, cell line or cells selected from the group consisting of a mammalian cell, an insect cell, a primary cell, an adherent cell, a suspension cell, a dividing cell such as a stem cell, a non-dividing cell such as a neuronal cell, and a cancer cell, said cell, cell line or cells being optionally organized into spheroids, organoids, 2D or 3D cell culture, or provided as fibre or matrix culture, and/or within a bioreactor.

21. The *in vitro* or *ex vivo* use according to claim 20 to transfect at least one nucleic acid molecule, preferably at least one DNA, into a stem cell, said composition comprising (i) the compound **1.42**, and (ii) an acceptable excipient, buffering agent, cell culture medium, or transfection medium.

22. The *in vitro* or *ex vivo* use according to claim 20 to transfect at least one nucleic acid molecule, preferably at least one DNA, into a neuronal cell, said composition comprising (i) the compound **1.65** or the compound **1.60**, and (ii) an acceptable excipient, buffering agent, cell culture medium, or transfection medium.

23. *In vitro* or *ex vivo* use of the composition according to any one of claims 2 to 18 for genome engineering, for cell reprogramming, for differentiating cells, or for gene-editing.

24. An *in vitro* or *ex vivo* method comprising the *in vitro* or *ex vivo* use of the composition according to any one of claims 2 to 18, wherein the method is for the production of (i) biologics, in particular biologics encoding a recombinant protein, peptide or antibody; or (ii) recombinant virus, such as adeno-associated virus (AAV), lentivirus (LV), adenovirus, oncolytic virus, or baculovirus, wherein said composition comprises multiple nucleic acid molecules for co-transfection; or (iii) viral or virus-like particles, wherein said composition comprises multiple nucleic acid molecules for co-transfection.

25. The *in vitro* or *ex vivo* method according to claim 24,
(i) for the production of AAV or LV, said composition comprising (i) at least the compound **1.42**, and (ii) an acceptable excipient, buffering agent, cell culture medium, or transfection medium; or
(ii) for the production of LV, said composition comprising (i) at least the compound **1.57**, and (ii) an acceptable excipient, buffering agent, cell culture medium, or transfection medium; or
(iii) for the production of recombinant virus, said composition comprising a plurality of expression vectors such as plasmid vectors to transfect in an adherent or suspension cell, such as HEK293, HeLa, BHK-21, A549 or insect cells, wherein said vectors, in particular plasmids, are construct expressing viral structural sequences and transfer vector genome for virus or virus-like production and optionally expressing molecules of interest encoded by the transfer vector genome.

26. The *in vitro* or *ex vivo* method for the production of recombinant virus according to claim 25, wherein said recombinant virus is suitable for use in *in vivo* applications for cell therapy or for gene therapy.